The Renal Drug Handbook

THIRD EDITION

Edited by
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UK Renal Pharmacy Group

Foreword by
Dr Aine Burns

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Foreword

This third edition of The Renal Drug Handbook is a fantastic publication. Nephrology is a complex speciality and, increasingly, specialist nurses and paramedics are involved in the care of patients. Each of us needs to be wary of prescribing for renal patients and this handbook provides a highly practical, user-friendly method of ensuring that appropriate prescriptions are given to patients, whether they have normal renal function, renal impairment, transplants or are receiving renal replacement therapy. In addition, the authors give very helpful information on pharmacokinetics and common indications for the use of each drug described. This information is not available in any other single textbook. It is an invaluable resource for all healthcare professionals but particularly for those involved in the care of renal patients. A copy of the second edition can be found chained to note trolleys in all of the wards where renal patients are cared for in my hospital. This third edition is even more comprehensive.

Aine Burns FRCP
Consultant Nephrologist
Centre for Nephrology
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September 2008
Preface

Welcome to the third edition of *The Renal Drug Handbook*. The information contained in this book has been compiled from a wide range of sources and from the clinical experience of the editorial board of the UK Renal Pharmacy Group, all of whom are involved in the pharmaceutical care of renally-impaired patients. As such, some of the information contained in the monographs may not be in accordance with the licensed indications or use of the drug.

The Handbook aims to:

- provide healthcare professionals with a single reference of easily retrievable, practical information relating to drug use, sourced from the practical experience of renal units throughout the UK. By referring to the monographs, the user is guided in how to prescribe, prepare and administer the drug with due regard to potentially serious drug interactions and to any renal replacement therapy the patient may be undergoing
- provide a practice-based review of drug utilisation in renal units across the UK indicating, where appropriate, any local methods of use, licensed or otherwise.

In recent years, the classification for chronic kidney disease (CKD) has changed, now being described as stages 1–5. Each stage is defined by the patient’s eGFR (or estimated GFR) which is calculated using the MDRD equation (modification of diet in renal disease). One point to note is that the eGFR is normalised to a standard body surface area of 1.73 m². There is relatively good correlation between the two equations for calculating renal function in patients of average weight, and either could be used for the majority of drugs. However, eGFR should not be used for calculating drug doses in patients at extremes of body weight nor for drugs with a narrow therapeutic window unless it is first corrected to the actual GFR for that patient. Actual GFR can be calculated from the following equation:

$$\text{Actual GFR} = \left(\frac{\text{eGFR} \times \text{BSA}}{1.73}\right)$$

At extremes of body weight neither the MDRD nor the Cockcroft-Gault equation is particularly accurate. If an accurate GFR is required, e.g. for some chemotherapy, then an isotope GFR determination should be performed.

The information on dosage adjustments in renal impairment given in this book is based on Cockcroft-Gault creatinine clearance and not eGFR, since the majority of published information available is based on creatinine clearance.

*The Handbook is not intended to offer definitive advice or guidance on how drugs should be used in patients with renal impairment, nor is it a comprehensive and complete list of all drugs licensed in the UK.*
The range of drugs covered will continue to grow with subsequent editions. The Handbook is not a guide to diagnosis nor to a drug's side-effect profile, except where adverse drug events are more pronounced in the presence of renal impairment. For more in-depth information, users are advised to refer to the Summary of Product Characteristics, the British National Formulary, package inserts or other product data.

The use of drugs in patients with impaired renal function can give rise to problems for several reasons:

- Altered pharmacokinetics of some drugs, i.e. changes in absorption, tissue distribution, extent of plasma protein binding, metabolism and excretion. In renal impairment these parameters are often variable and interrelated in a complex manner. This may be further complicated if the patient is undergoing renal replacement therapy.
- For many drugs, some or even all of the altered pharmacokinetic parameters and modified interrelationships are unknown. In such circumstances, the informed professional judgement of clinicians and pharmacists must be used to predict drug disposition. This must be based on knowledge of the drug, its class, chemistry and pharmacokinetics in patients with normal renal function.
- Sensitivity to some drugs is increased, even if elimination is unimpaired.
- Many side-effects are particularly poorly tolerated by renally impaired patients.
- Some drugs are ineffective when renal function is reduced.
- Renal function generally declines with age, and many elderly patients have a GFR less than 50 mL/min which, because of reduced muscle mass, may not be reflected by an elevated creatinine. Consequently, one can justifiably assume mild renal impairment when prescribing for the elderly.

Many of these problems can be avoided by careful choice and use of drugs. This Handbook seeks to assist healthcare professionals in this process.

Using the monographs
- **Drug name**: The approved (generic) name is usually stated.
- **Clinical use**: A brief account of the more common indications in renally impaired patients is given. Where an indication is unlicensed, this is usually stated.
- **Dose in normal renal function**: The doses quoted for patients with normal renal function are generally the licensed dosage recommendations stated in the Summary of Product Characteristics for each drug. Where a product is not licensed in the UK, dosage guidelines are provided by the relevant drug company.
- **Pharmacokinetics**: Basic pharmacokinetic data such as molecular weight, half-life, percentage protein-binding, volume of distribution and percentage excreted unchanged in the urine are quoted, to assist in predicting drug handling in both renal impairment and renal replacement therapy. ‘–’ denotes 'not known' or 'no data available'.
- **Dose in renal impairment**: The level of renal function below which the dose of a drug must be reduced depends largely on the extent of renal metabolism and elimination, and on the drug’s toxicity. Most drugs are relatively well tolerated, have a broad therapeutic index or are metabolised and excreted hepatically, so precise
dose modification is unnecessary. In such cases, the user is instructed to 'dose as in normal renal function.'

For renally excreted drugs with a narrow therapeutic index, the total daily maintenance dose may be reduced either by decreasing the dose or by increasing the dosing interval, or sometimes by a combination of both. Dosing guidelines for varying degrees of renal impairment are stated accordingly.

- **Dose in renal replacement therapy**: Details are given for dosing in continuous ambulatory peritoneal dialysis (CAPD), intermittent haemodialysis (HD), haemodiafiltration (HDF), continuous venovenous haemodialysis/haemodiafiltration (CVV HD/HDF), and continuous arteriovenous haemodialysis/haemodiafiltration (CAV HD/HDF), where known. Drugs are categorised into dialysable/not dialysable/dialysability unknown, to aid the practitioner in making an informed decision for dosing within a particular form of renal replacement therapy. Only a few specific guidelines are given for dosing in continuous arteriovenous/venovenous haemofiltration (CAV/VVH). In general, dosing schedules are the same as those quoted for CAV/VVHD, although it should be borne in mind that CAV/VVH may have a lower drug clearance capacity. Thus the clinician or pharmacist should use informed professional judgement, based on knowledge of the drug and its pharmacokinetics, when deciding whether to further modify dosing regimens.

It should be noted that HDF removes drugs more efficiently than HD, although there is limited information in this area.

The Intensive Care Group based at St Thomas’ Hospital, London, has an extensive database on drug removal by haemofiltration and haemodiafiltration, so any extra information can be obtained from them (Tel. 020 7188 7188, pager 1863 or 1830).

- **Important drug interactions**: The interactions listed are those identified by a black spot in Appendix 1 of the *British National Formulary*. They are defined as those interactions which are potentially serious, and where combined administration of the drugs involved should be avoided, or only undertaken with caution and appropriate monitoring. Users of the monographs are referred to Appendix 1 of the *British National Formulary* for a more comprehensive list of interactions deemed to be not so clinically significant.

- **Administration**: Information is given on reconstitution, route and rate of administration, and other relevant factors. Much of the information relates to local practice, including information on the minimum volume that drugs can be added to. Only the most commonly used and compatible reconstitution and dilution solutions are stated.

- **Other information**: Details given here are only relevant to the use of that particular drug in patients with impaired renal function or on renal replacement therapy. For more general information, please refer to the Summary of Product Characteristics for that drug.

Your contribution to future editions is vital. Any ideas, comments, corrections,
requests, additions, local practices, etc. on the drugs in the Handbook should be put in writing to the Editors-in-Chief: Caroline Ashley, Pharmacy Department, Royal Free Hospital, Hampstead, London NW3 2QG or Aileen Currie, Pharmacy Department, Crosshouse Hospital, Kilmarnock KA2 0BE.

Caroline Ashley
Aileen Currie
September 2008

The following texts have been used as reference sources for the compilation of the monographs in this book:

Electronic Medicines Compendium.
Cyclosporin Interaction File (Novartis Pharmaceuticals UK).
Drugdex Database. Micromedex Inc., USA.
Drug company information.
www.rxlist.com
medsafe.govt.nz
www.medicinescomplete.com
About the editors

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Royal Free Hospital, London

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Crosshouse Hospital, Kilmarnock
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABC</td>
<td>advanced breast cancer</td>
</tr>
<tr>
<td>ACE</td>
<td>angiotensin-converting enzyme</td>
</tr>
<tr>
<td>ADH</td>
<td>antidiuretic hormone</td>
</tr>
<tr>
<td>AIDS</td>
<td>acquired immunodeficiency syndrome</td>
</tr>
<tr>
<td>ALG</td>
<td>antilymphocyte immunoglobulin</td>
</tr>
<tr>
<td>ALT</td>
<td>alanine transaminase</td>
</tr>
<tr>
<td>APTT</td>
<td>activated partial thromboplastin time</td>
</tr>
<tr>
<td>ARF</td>
<td>acute renal failure</td>
</tr>
<tr>
<td>5-ASA</td>
<td>5-aminosalicylic acid</td>
</tr>
<tr>
<td>AST</td>
<td>aspartate transaminase</td>
</tr>
<tr>
<td>ATG</td>
<td>antithymocyte immunoglobulin</td>
</tr>
<tr>
<td>AT-II</td>
<td>angiotensin-II</td>
</tr>
<tr>
<td>ATN</td>
<td>acute tubular necrosis</td>
</tr>
<tr>
<td>AUC</td>
<td>area under the curve</td>
</tr>
<tr>
<td>AV</td>
<td>atrioventricular</td>
</tr>
<tr>
<td>BD</td>
<td>twice daily</td>
</tr>
<tr>
<td>BP</td>
<td>blood pressure</td>
</tr>
<tr>
<td>BSA</td>
<td>body surface area</td>
</tr>
<tr>
<td>BUN</td>
<td>blood urea nitrogen</td>
</tr>
<tr>
<td>BWt</td>
<td>body-weight</td>
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<tr>
<td>CAPD</td>
<td>continuous ambulatory peritoneal dialysis</td>
</tr>
<tr>
<td>CAVH</td>
<td>continuous arteriovenous haemofiltration</td>
</tr>
<tr>
<td>CAVHD</td>
<td>continuous arteriovenous haemodialysis</td>
</tr>
<tr>
<td>CIVAS</td>
<td>centralised intravenous additive service</td>
</tr>
<tr>
<td>CKD</td>
<td>chronic kidney disease</td>
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<tr>
<td>CLcr</td>
<td>creatinine clearance</td>
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<td>CLL</td>
<td>chronic lymphocytic leukaemia</td>
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<td>CMV</td>
<td>cytomegalovirus</td>
</tr>
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<td>CNS</td>
<td>central nervous system</td>
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<tr>
<td>COX-2</td>
<td>cyclo-oxygenase-2</td>
</tr>
<tr>
<td>CRF</td>
<td>chronic renal failure</td>
</tr>
<tr>
<td>CRIP</td>
<td>constant-rate infusion pump</td>
</tr>
<tr>
<td>CSF</td>
<td>cerebrospinal fluid</td>
</tr>
<tr>
<td>CSM</td>
<td>Committee on Safety of Medicines</td>
</tr>
<tr>
<td>CVVH</td>
<td>continuous venovenous haemofiltration</td>
</tr>
<tr>
<td>CVVHD</td>
<td>continuous venovenous haemodialysis</td>
</tr>
<tr>
<td>CVVHDF</td>
<td>continuous venovenous haemodiafiltration</td>
</tr>
<tr>
<td>CyA</td>
<td>ciclosporin</td>
</tr>
<tr>
<td>CYP</td>
<td>cytochrome pigment</td>
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<tr>
<td>DIC</td>
<td>disseminated intravascular coagulation</td>
</tr>
<tr>
<td>diC</td>
<td>disseminated intravascular coagulation</td>
</tr>
<tr>
<td>dVT</td>
<td>deep-vein thrombosis</td>
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<tr>
<td>E/C</td>
<td>enteric coated</td>
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<td>ECG</td>
<td>electrocardiogram</td>
</tr>
<tr>
<td>ECT</td>
<td>electroconvulsive therapy</td>
</tr>
<tr>
<td>ED</td>
<td>erectile dysfunction</td>
</tr>
<tr>
<td>EDTA</td>
<td>edetic acid</td>
</tr>
<tr>
<td>eGFR</td>
<td>estimated glomerular filtration rate</td>
</tr>
<tr>
<td>ERF</td>
<td>established renal failure</td>
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<tr>
<td>ESRD</td>
<td>end-stage renal disease</td>
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<tr>
<td>ESRF</td>
<td>end-stage renal failure</td>
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<tr>
<td>G-6-Pd</td>
<td>glucose-6-phosphate dehydrogenase</td>
</tr>
<tr>
<td>GFr</td>
<td>glomerular filtration rate</td>
</tr>
<tr>
<td>GI</td>
<td>gastrointestinal</td>
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<tr>
<td>GTN</td>
<td>glyceryl trinitrate</td>
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<tr>
<td>HCL</td>
<td>hairy-cell leukaemia</td>
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<tr>
<td>HD</td>
<td>intermittent haemodialysis</td>
</tr>
<tr>
<td>HDF</td>
<td>intermittent haemodiafiltration</td>
</tr>
<tr>
<td>HIT</td>
<td>heparin-induced thrombocytopenia</td>
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<td>HMG CoA</td>
<td>3-hydroxy-3-methyl-glutaryl coenzyme A</td>
</tr>
<tr>
<td>HUS</td>
<td>haemolytic uraemic syndrome</td>
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<tr>
<td>ICU</td>
<td>intensive care unit</td>
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<td>IM</td>
<td>intramuscular</td>
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<td>INR</td>
<td>international normalised ratio</td>
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<td>IP</td>
<td>intraperitoneal</td>
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<tr>
<td>IV</td>
<td>intravenous</td>
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<tr>
<td>LFT</td>
<td>liver function test</td>
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<tr>
<td>LHRH</td>
<td>luteinising hormone-releasing hormone</td>
</tr>
<tr>
<td>LMWH</td>
<td>low molecular weight heparin</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Definition</td>
</tr>
<tr>
<td>--------------</td>
<td>------------</td>
</tr>
<tr>
<td>LVF</td>
<td>left ventricular failure</td>
</tr>
<tr>
<td>MAO</td>
<td>monoamine oxidase</td>
</tr>
<tr>
<td>MAOI</td>
<td>monoamine oxidase inhibitor</td>
</tr>
<tr>
<td>MI</td>
<td>myocardial infarction</td>
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<tr>
<td>MMF</td>
<td>mycophenolate mofetil</td>
</tr>
<tr>
<td>MPA</td>
<td>mycophenolic acid</td>
</tr>
<tr>
<td>M/R</td>
<td>modified release</td>
</tr>
<tr>
<td>mw</td>
<td>molecular weight</td>
</tr>
<tr>
<td>NNRTI</td>
<td>non-nucleoside reverse transcriptase inhibitor</td>
</tr>
<tr>
<td>NSAID</td>
<td>non-steroidal anti-inflammatory drug</td>
</tr>
<tr>
<td>NSLC</td>
<td>non-small-cell lung cancer</td>
</tr>
<tr>
<td>NYHA</td>
<td>New York Heart Association</td>
</tr>
<tr>
<td>OA</td>
<td>osteoarthritis</td>
</tr>
<tr>
<td>OC</td>
<td>ovarian carcinoma</td>
</tr>
<tr>
<td>OD</td>
<td>daily</td>
</tr>
<tr>
<td>PAH</td>
<td>primary arterial pulmonary hypertension</td>
</tr>
<tr>
<td>PCA</td>
<td>patient-controlled analgesia</td>
</tr>
<tr>
<td>PCE</td>
<td>Pneumocystis jiroveci pneumonia</td>
</tr>
<tr>
<td>PCR</td>
<td>polymerase chain reaction</td>
</tr>
<tr>
<td>PD</td>
<td>peritoneal dialysis</td>
</tr>
<tr>
<td>PE</td>
<td>pulmonary embolism</td>
</tr>
<tr>
<td>PO</td>
<td>orally</td>
</tr>
<tr>
<td>PR</td>
<td>rectally</td>
</tr>
<tr>
<td>PRCA</td>
<td>pure red cell aplasia</td>
</tr>
</tbody>
</table>
Abacavir

**CLINICAL USE**
Nucleoside reverse transcriptase inhibitor:
- Used for HIV infection in combination with other antiretroviral drugs

**DOSE IN NORMAL RENAL FUNCTION**
600 mg daily in 1 or 2 divided doses

**PHARMACOKINETICS**
- Molecular weight: 286.3 (670.7 as sulphate)
- % Protein binding: 49%
- % Excreted unchanged in urine: 2%
- Volume of distribution: 0.8 L/kg

**DOSE IN RENAL IMPAIRMENT**
- 20–50 GFR (mL/MIN): Dose as in normal renal function
- 10–20 GFR (mL/MIN): Dose as in normal renal function
- <10 GFR (mL/MIN): Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux: Not dialysed. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs:
- Antivirals: concentration reduced by tipranavir

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
- Oral

**RATE OF ADMINISTRATION**
- COMMENTS
Abatacept

CLINICAL USE
Treatment of moderate to severe rheumatoid arthritis in people who have not responded adequately to other treatment

DOSE IN NORMAL RENAL FUNCTION
<60 kg: 500 mg, 60–100 kg: 750 mg, >100 kg: 1000 mg
every 4 weeks after loading

PHARMACOKINETICS
Molecular weight: 92,000
% Protein binding: No data
% Excreted: unchanged in urine
Volume of distribution: 0.07
Half-life – normal/ESRF (hrs): 13.1 days/

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function. Use with caution
<10 Dose as in normal renal function. Use with caution

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unlikely to be dialysed. Dose as in GFR<10mL/min
HD Unlikely to be dialysed. Dose as in GFR<10mL/min
HDF/High flux Unlikely to be dialysed. Dose as in GFR<10mL/min
CAV/VVHD Unlikely to be dialysed. Dose as in GFR=10–20mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
• Vaccines: avoid concomitant use with live vaccines

ADMINISTRATION
RECONSTITUTION
• With 10mL of water for injection per vial
ROUTE
• IV infusion
RATE OF ADMINISTRATION
• Over 30 minutes
COMMENTS
• DO NOT SHAKE when reconstituting
Add dose to 100mL of sodium chloride 0.9%

OTHER INFORMATION
• Stable for 24 hours at 2–8°C if made under aseptic conditions
• Administer with an infusion set with a low protein binding filter (pore size 0.2–1.2 μm)
• Manufacturer does not have any information on its use in renal impairment. Main side effects are infections and malignancies, to which renal patients may be at increased risk, therefore use with caution
Abciximab

**CLINICAL USE**

Antiplatelet agent:
- Prevention of ischaemic cardiac complications in patients undergoing percutaneous coronary intervention
- Short-term prevention of myocardial infarction in patients with unstable angina not responding to treatment or awaiting percutaneous coronary intervention

**DOSE IN NORMAL RENAL FUNCTION**

IV bolus: 250 mcg/kg then by infusion at 0.125 mcg/kg/minute for 12 hours after intervention (maximum 10 mcg/minute)

**PHARMACOKINETICS**

- Molecular weight (daltons): 47,455.4
- % Protein binding: Binds to platelets
- % Excreted unchanged in urine: Minimal (catabolised like other proteins)
- Volume of distribution (L/kg): 0.118
- Half-life – normal/ESRF (hrs): <10 minutes/unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function. Use with caution See ‘Other Information’</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Heparin, anticoagulants, antiplatelets and thrombolitics: increased risk of bleeding

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
- IV bolus, IV infusion

**RATE OF ADMINISTRATION**

- Bolus: 1 minute
- Infusion: 0.125 mcg/kg/minute (maximum 10 mcg/minute)

**COMMENTS**

- Dilute in sodium chloride 0.9% or glucose 5%
- Give via a non-pyrogenic low-protein-binding 0.2, 0.22 or 5 micron filter

**OTHER INFORMATION**

- Increased risk of bleeding in CKD 5, benefits of abciximab treatment may be reduced
- In the UK the licence says avoid in haemodialysis patients due to increased risk of bleeding (as on heparin for dialysis) but it is used in normal doses in the USA
- Antibodies to abciximab develop 2–4 weeks post dose in 5.8% of patients so monitor for hypersensitivity reactions if re-administered
- Abciximab remains in the body for at least 15 days, bound to platelets
- Once infusion is stopped, the concentration of abciximab falls rapidly for 6 hours then decreases at a slower rate

References:
Acamprosate calcium

**CLINICAL USE**
Maintenance of abstinence in alcohol dependence

**DOSE IN NORMAL RENAL FUNCTION**
- <60 kg: 666 mg 3 times a day
- >60 kg: 666 mg at breakfast, 333 mg at midday and 333 mg at night

**PHARMACOKINETICS**
- Molecular weight (daltons): 400.5
- % Protein binding: 0
- % Excreted unchanged in urine: Majority
- Volume of distribution (L/kg): Approximately 1
- Half-life – normal/ESRF (hrs): 33/85.8

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>333 mg 3 times daily</td>
</tr>
<tr>
<td>10–30</td>
<td>333 mg twice daily</td>
</tr>
<tr>
<td>&lt;10</td>
<td>333 mg once daily</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**: Dialysed. Dose as in GFR<10mL/min
- **HD**: Dialysed. Dose as in GFR<10mL/min
- **HDF/High flux**: Dialysed. Dose as in GFR<10mL/min
- **CAV/VVHD**: Dialysed. Dose as in GFR=10–30mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- Recommended treatment period is a year
- After a single dose of 666 mg in patients with severe renal impairment, the average maximum concentration was 4 times that in healthy individuals
- Bioavailability is reduced if administered with food

RETURN TO CONTENTS
Acarbose

**CLINICAL USE**
Antidiabetic agent

**DOSE IN NORMAL RENAL FUNCTION**
50–200 mg 3 times a day

**PHARMACOKINETICS**
- Molecular weight (daltons) 645.6
- % Protein binding 15
- % Excreted unchanged in urine 1.7 (35% including inactive metabolites)
- Volume of distribution (L/kg) 0.32
- Half-life – normal/ESRF (hrs) 3–9/Increased

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 25–50 Dose as in normal renal function
- 10–25 Avoid
- <10 Avoid

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Unknown dialysability. Avoid
- HD Unknown dialysability. Avoid. See ‘Other Information’
- HDF/High flux Unknown dialysability. Avoid. See ‘Other Information’
- CAV/VVHD Unknown dialysability. Avoid

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: hypoglycaemic effect possibly enhanced and increased gastrointestinal side effects with neomycin
- Lipid lowering agents: hypoglycaemic effect possibly enhanced by colestyramine

**ADMINISTRATION**

**RECONSTITUTION**
-

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
-

**COMMENTS**
-

**OTHER INFORMATION**
- Only 1–2% of active drug is absorbed
- In renal impairment, peak concentrations are 5 times higher than in the general population and the AUC is 6 times higher
Acebutolol

**CLINICAL USE**

Beta-adrenoceptor blocker:
- Hypertension
- Angina
- Arrhythmias

**DOSE IN NORMAL RENAL FUNCTION**

- Hypertension: 400 mg once a day or 200 mg twice a day, increased after 2 weeks to 400 mg twice daily if necessary
- Angina: 400 mg once a day, or 200 mg twice daily initially. Increase up to 300 mg 3 times daily; maximum 1200 mg
- Arrhythmias: 400–1200 mg/day (in 2–3 divided doses)

**PHARMACOKINETICS**

- Molecular weight (daltons): 336.4 (372.9 as hydrochloride)
- % Protein binding: 26
- % Excreted unchanged in urine: 55
- Volume of distribution (L/kg): 1.2
- Half-life – normal/ESRF (hrs): 3–4 (8–13 for active metabolite)/Increased (32 for active metabolite)

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function, but frequency should not exceed once daily in renal impairment</th>
<th>dose as in GFR&lt;10mL/min</th>
<th>50% of normal dose, but frequency should not exceed once daily in renal impairment</th>
<th>30–50% of normal dose, but frequency should not exceed once daily in renal impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>25–50</td>
<td>Dose as in normal renal function, but frequency should not exceed once daily in renal impairment</td>
<td>10–25</td>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Unknown dialysability. Dose as in GFR<10mL/min
- HD: Dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10mL/min
- CAV/VVHD: Dialysed. Dose as in GFR=10–25mL/min

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Anaesthetics: enhanced hypotensive effect
- Analgesics: NSAIDs antagonise hypotensive effect
- Anti-arrhythmics: increased risk of myocardial depression and bradycardia; increased risk of bradycardia, myocardial depression and AV block with amiodarone
- Antidepressants: enhanced hypotensive effect with MAOIs
- Antihypertensives: enhanced hypotensive effect; increased risk of withdrawal hypertension with clonidine; increased risk of first dose hypotensive effect with post-synaptic alpha-blockers such as prazosin
- Antimalarials: increased risk of bradycardia with mefloquine
- Antipsychotics enhanced hypotensive effect with phenothiazines
- Calcium-channel blockers: increased risk of bradycardia and AV block with diltiazem; hypotension and heart failure possible with nifedipine and nisoldipine; asystole, severe hypotension and heart failure with verapamil
- Diuretics: enhanced hypotensive effect
- Moxisylyte: possible severe postural hypotension
- Sympathomimetics: severe hypertension with adrenaline and noradrenaline and possibly with dobutamine
- Tropisetron: increased risk of ventricular arrhythmias – use with caution

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**: Oral
- **RATE OF ADMINISTRATION**: N/A
- **COMMENTS**: –

**OTHER INFORMATION**

- Administration of high doses in severe renal failure cautioned due to accumulation
- Dose frequency should not exceed once daily in renal impairment
- Has an active metabolite – diacetolol
Aceclofenac

**CLINICAL USE**
NSAID and analgesic

**DOSE IN NORMAL RENAL FUNCTION**
100 mg twice daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 354.2
- % Protein binding: >99
- % Excreted unchanged in urine: 66 (mainly as metabolites)
- Volume of distribution (L/kg): 25 litres

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function but use with caution
  - 10–20: Dose as in normal renal function but avoid if possible
  - <10: Dose as in normal renal function but only if on dialysis

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function. See ‘Other Information’
- HD: Not dialysed. Dose as in normal renal function. See ‘Other Information’
- HDF/High flux: Unknown dialysability. Dose as in normal renal function. See ‘Other Information’
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- ACE inhibitors and angiotensin-II antagonists: antagonism of hypotensive effect; increased risk of nephrotoxicity and hyperkalaemia
- Analgesics: avoid concomitant use of 2 or more NSAIDs, including aspirin (increased side effects); avoid with ketorolac (increased risk of side effects and haemorrhage)
- Antibacterials: possible increased risk of convulsions with quinolones
- Anticoagulants: effects of coumarins enhanced; possible increased risk of bleeding with heparins and coumarins
- Antidepressants: increased risk of bleeding with SSRIs and venlafaxine
- Antidiabetic agents: effects of sulphonylureas enhanced
- Anti-epileptics: possibly increased phenytoin concentration
- Antivirals: increased risk of haematological toxicity with zidovudine; concentration possibly increased by ritonavir
- Ciclosporin: may potentiate nephrotoxicity
- Cytotoxic agents: reduced excretion of methotrexate; increased risk of bleeding with erlotinib
- Diuretics: increased risk of nephrotoxicity; antagonism of diuretic effect, hyperkalaemia with potassium-sparing diuretics
- Lithium: excretion decreased
- Pentoxifylline: increased risk of bleeding
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- Use with caution in uraemic patients predisposed to gastrointestinal bleeding or uraemic coagulopathies
- Inhibition of renal prostaglandin synthesis by NSAIDs may interfere with renal function, especially in the presence of existing renal disease – avoid if possible; if not, check serum creatinine 48–72 hours after starting NSAID therapy – if raised, discontinue NSAID therapy
- Use normal doses in patients with ESRD on dialysis if they do not pass any urine
- Use with great caution in renal transplant recipients; it can reduce intrarenal autacoid synthesis
**Acenocoumarol (nicoumalone)**

### CLINICAL USE

Anticoagulant

### DOSE IN NORMAL RENAL FUNCTION

- **4–12 mg on 1st day; 4–8 mg on 2nd day**
- **Maintenance dose usually 1–8 mg daily according to INR**

### PHARMACOKINETICS

- **Molecular weight (daltons)**: 353.3
- **% Protein binding**: >98
- **% Excreted unchanged in urine**: <0.2
- **Volume of distribution (L/kg)**: 0.16–0.18 $R(\ast)$ enantiomer; 0.22–0.34 $S(\ast)$ enantiomer
- **Half-life – normal/ESRF (hrs)**: 8–11/Probably unchanged

### DOSE IN RENAL IMPAIRMENT

- **GFR (mL/MIN)**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

### DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

- **CAPD**: Unknown dialysability. Dose as in normal renal function
- **HD**: Unknown dialysability. Dose as in normal renal function
- **HDF/High flux**: Unknown dialysability. Dose as in normal renal function
- **CAV/VVHD**: Unknown dialysability. Dose as in normal renal function

### IMPORTANT DRUG INTERACTIONS

- **There Are Many Significant Interactions With Coumarins. Prescribe With Care With Regard To The Following**:
  - Anticoagulant effect enhanced by: alcohol, amiodarone, anabolic steroids, aspirin, azithromycin, aztreonam, bicalutamide, cephalosporins, chloramphenicol, cimetidine, ciprofloxacin, clarithromycin, fibrates, clopidogrel, cranberry juice, danazol, dextropropoxyphene, dipyriramole, disulfiram, erythromycin, esomeprazole, ezetimibe, fluconazole, flutamide, fluvastatin, grapefruit juice, itraconazole, ketoconazole, levamisole, levofloxacin, macrolides, methylphenidate, metronidazole, miconazole, nalidixic acid, neomycin, norfloxacin, NSAIDs, ofloxacin, omeprazole, pantoprazole, paracetamol, penicillins, propafenone, ritonavir, rosvuastatin, SSRIs, simvastatin, sitaxentan, sulfispyrazone, sulphonamides, tamoxifen, testosterone, tetracyclines, levothyroxine, tigecycline, toremifene, tramadol, trimethoprim, valproate, voriconazole
  - Anticoagulant effect decreased by: acitretin, azathioprine, barbiturates, carbamazepine, griseofulvin, mercaptopurine, mitotane, oral contraceptives, phenytoin, primidone, rifampicin, St John’s wort (avoid concomitant use), sucralfate, vitamin K
  - Anticoagulant effects enhanced/reduced by: amprenavir, anion exchange resins, corticosteroids, dietary changes, tricyclics
  - Analgesics: increased risk of bleeding with IV diclofenac and ketorolac – avoid concomitant use
  - Antidiabetic agents: enhanced hypoglycaemic effect with sulphonylureas
  - Ciclosporin: there have been a few reports of altered anticoagulant effect; decreased ciclosporin levels have been seen rarely
  - Cytotoxics: increased risk of bleeding with erlotinib and imatinib; enhanced effect with etoposide, fluorouracil, ifosfamide and sorafenib

### ADMINISTRATION

#### RECONSTITUTION

- **ROUTE**
  - Oral

#### RATE OF ADMINISTRATION

- **COMMENTS**

#### OTHER INFORMATION

- Acenocoumarol prolongs the thromboplastin time within approximately 36–72 hours
- Decreased protein binding in uraemia
● Titrate dose to INR
● Company advises to avoid in severe renal disease due to increased risk of haemorrhage
Acetazolamide

**CLINICAL USE**
Carbonic anhydrase inhibitor:
- Glaucoma
- Diuretic
- Epilepsy

**DOSE IN NORMAL RENAL FUNCTION**
Glaucoma/Epilepsy: 0.25–1 g daily in divided doses
Diuretic: 250–375 mg daily

**PHARMACOKINETICS**
- Molecular weight: 222.2 (daltons)
- % Protein binding: 70–90
- % Excreted unchanged in urine: 100
- Volume of distribution: 0.2 (L/kg)

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>250 mg up to 4 times a day</td>
</tr>
<tr>
<td>10–20</td>
<td>250 mg up to twice a day</td>
</tr>
<tr>
<td>&lt;10</td>
<td>250 mg daily</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>MODality</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely dialysability. Dose as in GFR&lt;10mL/min.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: high dose aspirin reduces excretion (risk of toxicity)
- Anti-arrhythmics: increased toxicity if hypokalaemia occurs
- Antibacterials: effects of methenamine antagonised
- Anti-epileptics: increased risk of osteomalacia with phenytoin, primidone and phenobarbital; concentration of carbamazepine increased and primidone reduced
- Antihypertensives: enhanced hypotensive effect
- Antipsychotics: increased risk of ventricular arrhythmias due to hypokalaemia
- Atomoxetine: increased risk of ventricular arrhythmias due to hypokalaemia
- Beta-blockers: increased risk of ventricular arrhythmias due to hypokalaemia with sotalol
- Cardiac glycosides: increased toxicity if hypokalaemia occurs
- Lithium: lithium excretion increased

**ADMINISTRATION**

RECONSTITUTION
- Add at least 5 mL of water for injection

ROUTE
- Oral, IM, IV

RATE OF ADMINISTRATION
- Give slow IV

COMMENTS
- Avoid IM due to alkaline pH
- Monitor for signs of extravasation and skin necrosis during administration

**OTHER INFORMATION**

- Use cautioned in severe renal failure
- Acetazolamide sodium (Diamox) parenteral contains 2.36 millimoles of sodium per vial
- Severe metabolic acidosis may occur in the elderly and in patients with reduced renal function
Acetylcysteine

CLINICAL USE

- Treatment of paracetamol overdose
- Renal protection during radiological scans involving contrast media (unlicensed)

DOSE IN NORMAL RENAL FUNCTION

- IV infusion: Initially 150 mg/kg in 200 mL glucose 5% over 15 minutes, followed by 50 mg/kg in 500 mL glucose 5% over 4 hours, then 100 mg/kg in 1000 mL over 16 hours
- Renal protection – see ‘Other Information’

PHARMACOKINETICS

- Molecular weight (daltons): 163.2
- % Protein binding: 50
- % Excreted unchanged in urine: 20–30
- Volume of distribution (L/kg): 0.33–0.47
- Half-life – normal/ESRF (hrs): 2–6/–

DOSE IN RENAL IMPAIRMENT

GFR (mL/MIN)

- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function. See ‘Other Information’

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

- CAPD: Likely to be Dialysed. Dose as in normal renal function
- HD: Dialysed. Dose as in normal renal function
- HDF/High flux: Dialysed. Dose as in normal renal function
- CAV/VVHD: Likely to be Dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs

- None known

ADMINISTRATION

RECONSTITUTION

- Glucose 5%

ROUTE

- IV, PO (PO route unlicensed in the UK)

RATE OF ADMINISTRATION

- See under Dose

COMMENTS

- Children should be treated with the same doses and regimen as adults; however, the quantity of IV fluid should be modified to account for age and weight
- Acetylcysteine has been administered neat or in a 1 to 1 dilution using an infusion pump. These are unlicensed methods of administration
- Minimum dilutions can range from 100–250 mL. It is advised to give strong solutions centrally. (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006)

OTHER INFORMATION

- Bennett recommends administering 75% of dose for patients with severe renal impairment; however, Evans Medical does not recommend a dose reduction and, from its records, neither does the National Poisons Centre
- There is some evidence that acetylcysteine may have a renoprotective effect during scans involving the use of contrast media, in patients with already impaired renal function
- Dose = 600 mg PO BD the day before the scan, repeated the day of the scan, together with IV or PO fluids. Injection may be taken orally, or tablets are available from IDIS
- Alternatively, give 1 g acetylcysteine IV in 500 mL sodium chloride 0.9% or dextrose 5%, the day before the scan, repeated the day of the scan
Aciclovir IV

CLINICAL USE

Antiviral agent:
- Herpes simplex and herpes zoster infection

DOSE IN NORMAL RENAL FUNCTION

- Herpes simplex treatment: normal or immunocompromised 5 mg/kg every 8 hours
- Recurrent varicella zoster infection: normal immune status 5 mg/kg every 8 hours
- Primary and recurrent varicella zoster infection: immunocompromised 10 mg/kg every 8 hours
- Herpes simplex encephalitis: normal or immunocompromised 10 mg/kg every 8 hours

PHARMACOKINETICS

Molecular weight (daltons) 225.2
% Protein binding 9–33
% Excreted unchanged in urine 40–70
Volume of distribution (L/kg) 0.7
Half-life – normal/ESRF (hrs) 2.9/19.5 (dialysis: 5.7)

DOSE IN RENAL IMPAIRMENT

GFR (mL/min)

25–50 5–10 mg/kg every 12 hours
10–25 5–10 mg/kg every 24 hours (some units use 3.5–7 mg/kg every 24 hours)
<10 2.5–5 mg/kg every 24 hours

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

CAPD Not dialysed. Dose as in GFR<10mL/min
HD Dialysed. Dose as in GFR<10mL/min
HDF/High flux Dialysed. Dose as in GFR<10mL/min
CAV/ VVHD Dialysed. Dose as in GFR=10–25mL/min

IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs
- Ciclosporin: reports of increased and decreased ciclosporin levels. Some editors report no experience of interaction locally; possibly increased risk of nephrotoxicity
- Higher plasma levels of aciclovir and mycophenolate mofetil with concomitant administration
- Tacrolimus: possibly increased risk of nephrotoxicity

ADMINISTRATION

RECONSTITUTION

- Sodium chloride 0.9% or water for injection; 10 mL to each 250 mg vial; 20 mL to 500 mg vial (Resulting solution contains 25 mg/mL)

ROUTE

- IV

RATE OF ADMINISTRATION

- 1 hour; can worsen renal impairment if injected too rapidly!

COMMENTS

- Reconstituted solution may be further diluted to concentrations not greater than 5 mg/mL
- Use 100 mL infusion bags for doses of 250–500 mg; use 2 × 100 mL bags for 500–1000 mg
- Compatible with sodium chloride 0.9% and glucose 5%
- DO NOT REFRIGERATE
- Do not use turbid or crystal-containing solutions
- Reconstituted solution very alkaline (pH 11)

OTHER INFORMATION

- Aciclovir clearance in CAVHD is approximately equivalent to urea clearance, i.e. lower clearance than in intermittent haemodialysis
- Monitor aciclovir levels in critically ill patients. Reports of neurological toxicity at maximum recommended doses
- Renal impairment developing during treatment with aciclovir usually responds rapidly to rehydration of the patient, and/or dosage reduction or withdrawal of the drug. Adequate hydration of the patient should be maintained
Plasma aciclovir concentration is reduced by 60% during haemodialysis.

References:
1. Dose from CVVH Initial Drug Dosing Guidelines on www.thedrugmonitor.com
Aciclovir oral

CLINICAL USE
Antiviral agent:
- Herpes simplex and herpes zoster infection

DOSE IN NORMAL RENAL FUNCTION
- Simplex treatment: 200–400 mg 5 times daily
- Prophylaxis (immunocompromised): 200–400 mg every 6 hours
- Suppression: 200 mg every 6 hours, or 400 mg every 12 hours
- Zoster: 800 mg 5 times a day for 7 days

PHARMACOKINETICS
- Molecular weight (daltons) 225.2
- % Protein binding 9–33
- % Excreted unchanged in urine 40–70
- Volume of distribution (L/kg) 0.7
- Half-life – normal/ESRF (hrs) 2.9/19.5 (dialysis: 5.7)

DOSE IN RENAL IMPAIRMENT
- GFR (mL/min)
  - 25–50: Dose as in normal renal function
  - 10–25: Simplex: 200 mg 3–4 times daily. Zoster: 800 mg every 8–12 hours
  - <10: Simplex: 200 mg every 12 hours. Zoster: 400–800 mg every 12 hours

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD: Not dialysed. Dose as in GFR<10mL/min
- HD: Dialysed. Dose as in GFR<10mL/min. Give dose after dialysis
- HDF/High flux: Dialysed. Dose as in GFR<10mL/min. Give dose after dialysis
- CAV/VVHD: Dialysed. Dose as in GFR=10–20mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Ciclosporin: reports of increase and decrease in ciclosporin levels; some editors report no experience of interaction locally; possibly increased risk of nephrotoxicity.
- Higher plasma levels of aciclovir and mycophenolate mofetil with concomitant administration
- Tacrolimus: possibly increased risk of nephrotoxicity

ADMINISTRATION
RECONSTITUTION
- ROUTE
  - Oral

RATE OF ADMINISTRATION
- COMMENTS
  - Dispersible tablets may be dispersed in a minimum of 50 mL of water or swallowed whole with a little water

OTHER INFORMATION
- Consider IV therapy for herpes zoster infection if patient severely immunocompromised
- Plasma aciclovir concentration is reduced by 60% during haemodialysis
Acipimox

**CLINICAL USE**
Hyperlipidaemia

**DOSE IN NORMAL RENAL FUNCTION**
250 mg 2 or 3 times daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 154.1
- % Protein binding: 0
- % Excreted unchanged in urine: 86–90
- Volume of distribution (L/kg): 0.3–0.4
- Half-life – normal/ESRF (hrs): 2/Increased

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min):
  - 40–80: 250 mg daily
  - 20–40: 250 mg alternate days. See ‘Other Information’
  - <20: See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Likely dialysability. Dose as in GFR<20 mL/min
- HD: Dialysed. Dose as in GFR<20 mL/min
- HDF/High flux: Dialysed. Dose as in GFR<20 mL/min
- CAV/ VVHD: Dialysed. Dose as in GFR=20–40 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  - Take with or after meals

**OTHER INFORMATION**
- Females are twice as likely as males to suffer from side effects, e.g. flushing, pruritus and skin rashes
- Doses up to 1200 mg have been given safely for long periods
- After a 5 hour dialysis 70% of the drug had been removed
- Dollery advises the doses given in the table, down to 20 mL/minute, but nothing after that.
- Micromedex gives the following recommendations:
  - GFR: 30–60 mL/min 150 mg twice daily
  - GFR: 10–30 mL/min 150 mg once daily
  - GFR: <10 mL/min 150 mg alternate days
Acitretin

**CLINICAL USE**
- Severe extensive psoriasis, palmoplantar pustular psoriasis
- Severe congenital ichthyosis
- Severe Darier’s disease

**DOSE IN NORMAL RENAL FUNCTION**
- Initially: 25–30 mg daily (Darier’s disease 10 mg daily) for 2–4 weeks, adjusted according to response
- Ongoing: usually 25–50 mg/day (maximum 75 mg) for further 6–8 weeks. (In Darier’s disease and ichthyosis not more than 50 mg daily for up to 6 months)

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight</td>
<td>326.4 daltons</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>&gt;99 (&lt; 0.1% present as unbound drug in pooled human plasma)</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>Excreted as metabolites</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>9</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>50/–</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>No data available. Assume dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>No data available. Assume dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>No data available. Assume dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibiotics: possibly increased risk of benign intracranial hypertension with tetracyclines – avoid concomitant use
- Anticoagulants: possible antagonism of the anticoagulant effect of coumarins
- Cytotoxics: increased concentration of methotrexate (also increased risk of hepatotoxicity) – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**
  - Take once daily with meals or with milk

**OTHER INFORMATION**
- Manufacturer’s literature contraindicates the use of acitretin in renal failure
Acrivastine

**CLINICAL USE**

Antihistamine:
- Symptomatic relief of allergy such as hayfever, urticaria

**DOSE IN NORMAL RENAL FUNCTION**

8 mg 3 times a day

**PHARMACOKINETICS**

- Molecular weight: 348.4 daltons
- % Protein binding: 50
- % Excreted unchanged in urine: 60
- Volume of distribution: 0.6–0.7 L/kg
- Half-life – normal/ESRF (hrs): 1.5–

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>8 mg twice a day</td>
</tr>
<tr>
<td>10–20</td>
<td>8 mg 1–2 times a day</td>
</tr>
<tr>
<td>&lt;10</td>
<td>8 mg 1–2 times a day</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**: Unknown dialysability. Dose as in GFR<10 mL/min
- **HD**: Unknown dialysability. Dose as in GFR<10 mL/min
- **HDF/High flux**: Unknown dialysability. Dose as in GFR<10 mL/min
- **CAV/VVHD**: Unknown dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Antidepressants: MAOIs and tricyclics increase the antimuscarinic and sedative effects

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**

- **COMMENTS**

**OTHER INFORMATION**

- Manufacturers do not recommend use in patients with significant renal impairment
Adefovir dipivoxil

**CLINICAL USE**
Treatment of chronic hepatitis B infection

**DOSE IN NORMAL RENAL FUNCTION**
10 mg once daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>501.5</td>
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<tr>
<td>% Protein binding</td>
<td>&lt;4</td>
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<tr>
<td>% Excreted unchanged in urine</td>
<td>45</td>
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<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.4</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>7/15</td>
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**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>10 mg every 48 hours</td>
</tr>
<tr>
<td>10–20</td>
<td>10 mg every 72 hours</td>
</tr>
<tr>
<td>&lt;10</td>
<td>10 mg every 72 hours</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. 10 mg weekly or after a cumulative total of 12 hours dialysis. See 'Other Information'</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Use with caution in combination with other nephrotoxins

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**

**OTHER INFORMATION**
- Nephrotoxic in higher IV doses, but risk is lower with oral doses; although cases of raised creatinine and ARF have been reported
- Discontinue treatment if any of the following occur: lactic acidosis, rapid increase in aminotransferase, progressive hepatomegaly or steatosis
- 35% of dose is removed with a 4 hour dialysis session
- Administered as a prodrug converted to adefovir
- There is a case report of it being used at a dose of 10 mg 3 times a week post dialysis. (Tillmann HL, Bock CT, Bleck JS, *et al.* Successful treatment of fibrosing cholestatic hepatitis using adefovir dipivoxil in a patient with cirrhosis and renal insufficiency. *Liver Transpl.* 2003 Feb; 9(2): 191–6)
Adenosine

**CLINICAL USE**

- Rapid reversion to sinus rhythm of paroxysmal supraventricular tachycardias
- Diagnosis of broad or narrow complex supraventricular tachycardias

**DOSE IN NORMAL RENAL FUNCTION**

Initially: 3 mg over 2 seconds with cardiac monitoring followed, if necessary, by 6 mg after 1–2 minutes and then by 12 mg after a further 1–2 minutes

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Molecular weight (daltons)</th>
<th>267.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Protein binding</td>
<td>0</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>No data</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>&lt;10 seconds/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

- **GFR (mL/Min)**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs

- Anti-arrhythmics: increased risk of myocardial depression
- Antipsychotics: increased risk of ventricular arrhythmias with antipsychotics that prolong the QT interval
- Beta-blockers: increased risk of myocardial depression
- Effect is enhanced and extended by dipyridamole; therefore if use of adenosine is essential, dosage should be reduced by a factor of 4 (i.e. initial dosage of 0.5–1 mg)
- Theophylline and other xanthines are potent inhibitors of adenosine

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - IV

**RATE OF ADMINISTRATION**

- Rapid IV bolus (see dose)

**COMMENTS**

- Do not refrigerate
- Administer into central vein, large peripheral vein, or into an IV line. If IV line used, follow dose by rapid sodium chloride 0.9% flush

**OTHER INFORMATION**

- Neither the kidney nor the liver is involved in the degradation of exogenous adenosine, so dose adjustments are not required in hepatic or renal insufficiency
- Unlike verapamil, adenosine may be used in conjunction with a beta-blocker
- Common side effects: facial flushing, chest pain, dyspnoea, bronchospasm, nausea and lightheadedness; the side effects are short-lived
## Adrenaline (epinephrine)

### Clinical Use
Sympathomimetic and inotropic agent

### Dose in Normal Renal Function
1–20 micrograms/minute

### Pharmacokinetics
- Molecular weight (daltons): 183.2
- % Protein binding: 50
- % Excreted unchanged in urine: 1
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs):
  - Phase 1: 3 minutes
  - Phase 2: 10 minutes

### Dose in Renal Impairment

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

### Dose in Patients Undergoing Renal Replacement Therapies
- **CAPD**: Not dialysed. Dose as in normal renal function
- **HD**: Not dialysed. Dose as in normal renal function
- **HDF/High flux**: Unknown dialysability. Dose as in normal renal function
- **CAV/VVHD**: Not dialysed. Dose as in normal renal function

### Important Drug Interactions
Potentially hazardous interactions with other drugs
- Alpha-blockers: avoid with tolazoline
- Anaesthetics: increased risk of arrhythmias if given with volatile anaesthetics
- Antidepressants: increased risk of arrhythmias and hypertension if given with tricyclics; MAOIs and moclobemide may cause hypertensive crisis.
- Beta-blockers: increased risk of severe hypertension
- Clonidine: possible increased risk of hypertension
- Dopaminergics: effects possibly increased by entacapone; avoid concomitant use with rasagiline
- Sympathomimetics: effects possibly enhanced by dopexamine

### Administration
- **Reconstitution**: 1 mg in 100 mL glucose 5%
- **Rate of Administration**: 6 mL/hour = 1 microgram/minute – according to local protocol
- **Route**: IV, IM, SC
- **Rate of Administration**: Monitor blood pressure and adjust dose according to response
- **Comments**: 

### Other Information
- Catecholamines have a high non-renal systemic clearance; therefore the effect of any renal replacement therapy is unlikely to be relevant

---

RETURN TO CONTENTS
Albendazole (unlicensed product)

**CLINICAL USE**
- Treatment of *Echinococcus granulosus* (hydatid disease), in combination with surgery
- Treatment of nematode infections

**DOSE IN NORMAL RENAL FUNCTION**

*Echinococcus granulosus:*
- >60 kg: 400 mg twice daily for 28 days
- <60 kg: 15 mg/kg in 2 divided doses to a maximum of 800 mg daily

Treatment of nematode infections: 400 mg as a single dose

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>265.3</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>70</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>No data</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>8–12 (metabolite)/Probably unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Dexamethasone: increased concentrations of metabolite of albendazole

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**

- **COMMENTS**
  -

**OTHER INFORMATION**

- Available on a named patient basis from IDIS (Zentel®)
- Undergoes first pass metabolism

---

RETURN TO CONTENTS
Alemtuzumab (MabCampath)

CLINICAL USE
- Treatment of chronic lymphocytic leukaemia not totally responsive to other treatment
- Induction therapy in renal transplantation (unlicensed)

DOSE IN NORMAL RENAL FUNCTION
3 mg increasing to 30 mg
Maximum dose: 30 mg 3 times a week

PHARMACOKINETICS
- Molecular weight (daltons): 150 000
- % Protein binding: No data
- % Excreted unchanged in urine: No data
- Volume of distribution (L/kg): 0.15
- Half-life – normal/ESRF (hrs): 2–32 hours (single dose), 1–14 days (repeated dosing)

DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Use with extreme caution. See ‘Other Information’</td>
</tr>
<tr>
<td>10–20</td>
<td>Use with extreme caution. See ‘Other Information’</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Use with extreme caution. See ‘Other Information’</td>
</tr>
</tbody>
</table>

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Unlikely to be dialysed. Dose as in GFR=10–20 mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Other chemotherapy: do not give within 3 weeks of each other
- Live vaccines: avoid for at least 12 months after treatment

ADMINISTRATION
RECONSTITUTION
- ROUTE
  - IV infusion
  - RATE OF ADMINISTRATION
    - 2 hours
  - COMMENTS
    - Add to 100 mL sodium chloride 0.9% or glucose 5%
    - Once diluted protect from light and use within 8 hours
    - Add dose through a low protein binding 5 micron filter

OTHER INFORMATION
- Patients should have a premedication of an antihistamine and paracetamol 30 minutes before treatment
- Patients should also receive anti-herpes and anti-infective prophylaxis against PCP during, and up to 2 months after stopping, treatment.
- More than 80% of patients will experience side effects, usually during the first week of therapy
- There have been no studies using alemtuzumab for CLL in patients with renal failure and there is no information on excretion, therefore if it must be used it should be with great care at the consultant’s discretion
- Doses of 20–30 mg given on the day of transplantation (and on day 1 according to local protocol) have been used for induction therapy in renal and combined kidney/pancreas transplantation
Alendronic acid

**CLINICAL USE**
Treatment and prophylaxis of osteoporosis

**DOSE IN NORMAL RENAL FUNCTION**
5–10 mg daily or 70 mg once weekly

**PHARMACOKINETICS**
- Molecular weight (daltons): 249.1 (325.1 as sodium salt)
- % Protein binding: 78
- % Excreted unchanged in urine: Approx 50
- Volume of distribution (L/kg): 28 litres
- Half-life – normal/ESRF (hrs): >10 years/Increased

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min):
  - 35–50: Dose as in normal renal function
  - <35: Avoid. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in GFR<35 mL/min
- HD: Not dialysed. Dose as in GFR<35 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<35 mL/min
- CAV/VVHD: Unlikely to be dialysed. Dose as in GFR<35 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Calcium salts: reduced absorption of alendronate

**ADMINISTRATION**

**RECONSTITUTION**

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**

**COMMENTS**

**OTHER INFORMATION**
- Swallow whole with a glass of water on an empty stomach, at least 30 minutes before breakfast and any other oral medication
- Patient should stand or sit upright for at least 30 minutes after taking tablets
- Combination therapy with alendronate and intravenous calcitriol, for the treatment of secondary hyperparathyroidism in haemodialysis patients, has been used at a dose of 10 mg alendronate plus IV calcitriol 2 mcg post dialysis to reduce PTH levels. (McCarthy JT, Kao PC, Demick DS, et al. Combination therapy with alendronate and intravenous calcitriol for the treatment of secondary hyperparathyroidism in hemodialysis patients. *J Am Soc Nephrol.* 1999; 10 Program, 81A–82A.)
- Manufacturers do not recommend use of alendronate in severe renal impairment due to lack of data
- One paper reviewed all the information available and concluded that 50% of the recommended dose may be possible in ESRD, but more trials are required and osteomalacia and adynamic bone disease must first be excluded. (Miller PD. Treatment of osteoporosis in chronic kidney disease and end-stage renal disease. *Curr Osteoporos Rep.* 2005; 3: 5–12.)
- Anecdotally, several renal units use either 70 mg weekly or standard doses of all preparations in patients with CKD 3, 4 and 5 to good effect

RETURN TO CONTENTS
Alfacalcidol

CLINICAL USE
Vitamin D analogue:
- Increase serum calcium levels
- Inhibition of parathyroid hormone release
- Suppression of PTH production

DOSE IN NORMAL RENAL FUNCTION
0.25–1 microgram daily according to response Alternatively, up to 4 micrograms 3 times a week

PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>400.6</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>Extensive plasma protein binding</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>13</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>No data</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>&lt;3/–</td>
</tr>
</tbody>
</table>

DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
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</tr>
<tr>
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DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in normal renal function</td>
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<tr>
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<td>Not dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Carbamazepine, phenytoin, phenobarbital and primidone may increase metabolism of alfacalcidol, necessitating larger doses than normal to produce the desired effect

ADMINISTRATION

RECONSTITUTION

ROUTE
- O, IV
RATE OF ADMINISTRATION
- Over 30 seconds
COMMENTS
-

OTHER INFORMATION

- Adjust dose according to response
- Serum calcium ref range 2.1–2.6 mmol/L (total)
- An IV preparation (2 micrograms/mL) and an oral solution (2 micrograms/mL) are also available
- Doses of 1 microgram daily for 5 days may need to be given immediately prior to parathyroidectomy. Alternatively, give 5 micrograms immediately prior to parathyroidectomy
- Capsules of One-Alfa (Leo) contain sesame oil
Alfentanil

**CLINICAL USE**
Opioid analgesic:
- Short surgical procedures
- Intensive care sedation

**DOSE IN NORMAL RENAL FUNCTION**
- IV injection:
  - Spontaneous respiration: up to 500 micrograms over 30 seconds; supplemental dose: 250 micrograms
  - Assisted ventilation: 30–50 micrograms/kg; supplemental dose: 15 micrograms/kg
- By IV infusion with assisted ventilation:
  - Loading dose 50–100 micrograms/kg as bolus or fast infusion over 10 minutes, followed by 0.5–1 micrograms/kg/minute. Discontinue infusion 30 minutes before anticipated end of surgery
- For analgesia and suppression of respiratory activity during intensive care with assisted ventilation: 2 mg/hour, adjusted according to response (usual range 0.5–10 mg/hour)
- For more rapid initial control give 5 mg IV in divided portions over 10 minutes (slower if hypotension or bradycardia develops); additional doses of 0.5–1 mg may be given by IV injection during short painful procedures

**PHARMACOKINETICS**
- Molecular weight: 453 (as hydrochloride) daltons
- % Protein binding: 92
- % Excreted unchanged in urine: 0.4
- Volume of distribution (L/kg): 0.4–1
- Half-life – normal/ESRF (hrs): 1–2 (average 90 minutes)/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High-flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
- Antidepressants: possible CNS excitation or depression (hypertension or hypotension) in patients also receiving MAOIs (including moclobemide) – avoid concomitant use; possibly increased sedative effects with tricyclics
- Antifungals: metabolism inhibited by fluconazole and ketoconazole (risk of prolonged or delayed respiratory depression); metabolism possibly inhibited by itraconazole
- Antivirals: concentration possibly increased by ritonavir
- Sodium oxybate: enhanced effect of sodium oxybate – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - IV bolus, IV infusion
- **RATE OF ADMINISTRATION**
  - See dose
- **COMMENTS**
  - Alfentanil can be mixed with sodium chloride 0.9%, glucose 5%, or compound sodium lactate injection (Hartmann’s solution) at a concentration of 0.5 mg/mL, but can be used at 2 mg/mL or even undiluted at 5 mg/mL. (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006)
OTHER INFORMATION

- Free fraction of drug is increased in renal failure, hence dose requirements may be reduced.
- IV administration: 500 micrograms alfentanil has peak effect in 90 seconds, and provides analgesia for 5–10 minutes (in unpremedicated adults).
- Transient fall in BP and bradycardia may occur on administration.
- Analgesic potency = ¼ that of fentanyl.
- Duration of action = ⅓ that of an equi-analgesic dose of fentanyl.
- Onset of action = 4 times more rapid than an equi-analgesic dose of fentanyl.
Alimemazine tartrate (trimeprazine)

**CLINICAL USE**
- Urticaria and pruritus
- Pre-med in children

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  -

**OTHER INFORMATION**
- Significant amounts of alimemazine are excreted in urine. It is therefore contraindicated by the manufacturer in renal failure; reduced clearance and elevated serum levels will occur in patients with impaired renal function
- However, it can be used at a dose of 10 mg at night to treat uraemic pruritus

**DOSE IN NORMAL RENAL FUNCTION**
- 10 mg every 8–12 hours, maximum 100 mg/day
- Elderly: 10 mg once or twice daily

**PHARMACOKINETICS**
- Molecular weight: 747 daltons
- % Protein binding: >90
- % Excreted unchanged in urine: >70
- Volume of distribution (L/kg): Large
- Half-life – normal/ESRF (hrs): 4.8/-

**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**
- 20–50: Dose as in normal renal function
- 10–20: Reduce frequency to every 12–24 hours
- <10: Reduce frequency to every 12–24 hours

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Unlikely to be dialysed. Dose as in GFR=10–20 mL/min

**RETURN TO CONTENTS**
Aliskiren fumarate

**CLINICAL USE**
Renin inhibitor, used for hypertension and diabetic nephropathy

**DOSE IN NORMAL RENAL FUNCTION**
150–300 mg once daily

**PHARMACOKINETICS**
- Molecular weight (daltons) 1219.6
- % Protein binding 47–51
- % Excreted unchanged in urine 0.6
- Volume of distribution (L/kg) 135 litres
- Half-life – normal/ESRF (hrs) 34–41/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50 Dose as in normal renal function
  - 10–20 Dose as in normal renal function
  - <10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD
  - Unlikely to be dialysed. Dose as in normal renal function
- HD
  - Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux
  - Unlikely to be dialysed. Dose as in normal renal function
- CAV/VVHD
  - Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Other antihypertensive agents: enhanced antihypertensive effect; concentration possibly reduced by irbesartan
- Antifungals: plasma concentration of aliskiren increased by ketoconazole
- Diuretics: may reduce concentration of furosemide; hyperkalaemia with potassium-sparing diuretics
- Heparins: increased risk of hyperkalaemia
- Potassium salts: increased risk of hyperkalaemia

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - COMMENTS
  -

**OTHER INFORMATION**
- Potassium should be monitored in patients with renal impairment, diabetes or heart failure
- Oral bioavailability is only 2–3%

RETURN TO CONTENTS
Allopurinol

**CLINICAL USE**
- Gout prophylaxis
- Hyperuricaemia

**DOSE IN NORMAL RENAL FUNCTION**
100–900 mg/day (usually 300 mg/day)
Doses above 300 mg should be given in divided doses

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>136.1</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>&lt;5</td>
</tr>
<tr>
<td>% Excreted in urine unchanged</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1.6</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1–2/Increased</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in mg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>200–300 daily</td>
</tr>
<tr>
<td>10–20</td>
<td>100–200 daily</td>
</tr>
<tr>
<td>&lt;10</td>
<td>100 mg daily or 100 mg on alternate days</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- ACE inhibitors: increased risk of toxicity with captopril
- Ciclosporin: isolated reports of raised ciclosporin levels (risk of nephrotoxicity)
- Cytotoxics: effects of azathioprine and mercaptopurine enhanced with increased toxicity; avoid concomitant use with capecitabine

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**
    - In all grades of renal impairment commence with 100 mg/day and increase if serum and/or urinary urate response is unsatisfactory. Doses less than 100 mg/day may be required in some patients
    - Take as a single daily dose, preferably after food

**OTHER INFORMATION**
- A parenteral preparation is available from Glaxo Wellcome on a named patient basis
- HD patients may be given 300 mg post dialysis, i.e. on alternate days
- Increased incidence of skin rash in patients with renal impairment
- Efficient dialysis usually controls serum uric acid levels
- If a patient is prescribed azathioprine or 6-mercaptopurine concomitantly, reduce azathioprine or 6-mercaptopurine dose by 66–75%
- Main active metabolite: oxipurinol – renally excreted; plasma protein binding 17%; half-life: Normal/ESRF = 13–30/>125 hours – 1 week
Almotriptan

**CLINICAL USE**
Acute relief of migraine

**DOSE IN NORMAL RENAL FUNCTION**
12.5 mg repeated after 2 hours if migraine recurs (do not take 2nd dose for the same attack)
Maximum 25 mg in 24 hours

**PHARMACOKINETICS**
- Molecular weight: 469.6 (as malate)
- % Protein binding: 35
- % Excreted unchanged in urine: 40–50
- Volume of distribution (L/kg): 195 litres
- Half-life – normal/ESRF (hrs): 3.5/7

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>12.5 mg. Use with caution</td>
</tr>
<tr>
<td>10–30</td>
<td>6.25 mg; maximum daily dose</td>
</tr>
<tr>
<td>&lt;10</td>
<td>6.25 mg; maximum daily dose</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR<10 mL/min
- HD: Likely dialysability. Dose as in GFR<10 mL/min
- HDF/High flux: Likely dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–30 mL/min

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Antidepressants: possibly increased serotonergic effects with duloxetine; increased serotonergic effects with St John’s wort – avoid concomitant use
  - Antifungals: concentration increased by ketoconazole (increased risk of toxicity)
  - Ergot alkaloids: increased risk of vasospasm

**ADMINISTRATION**

**RECONSTITUTION**
- Route
  - Oral

**RATE OF ADMINISTRATION**
- Comments
Alteplase (rt-PA) (recombinant human tissue-type plasminogen activator)

**CLINICAL USE**
Fibrinolytic drug:
- Acute myocardial infarction
- Pulmonary embolism
- Acute ischaemic stroke
- To unblock dialysis lines (unlicensed indication)

**DOSE IN NORMAL RENAL FUNCTION**
- Myocardial infarction: accelerated regimen (initiated within 6 hours) 15 mg IV bolus, 50 mg over 30 minutes, then 35 mg over 1 hour (total dose 100 mg); or (if initiated within 6–12 hours) 10 mg over 1–2 minutes followed by IV infusion of 50 mg over 1 hour, then 4 infusions each of 10 mg over 30 minutes (total dose – 100 mg over 3 hours)
- Pulmonary embolism: 10 mg by IV injection over 1–2 minutes, followed by an infusion of 90 mg over 2 hours. Total dose should not exceed 1.5 mg/kg in patients who weigh <65 kg
- Acute ischaemic stroke: 0.9 mg/kg over 60 minutes, 10% of dose as initial bolus; maximum 90 mg. Start within 3 hours of symptoms

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Risk of haemorrhage can be increased by the use of coumarin derivatives, platelet aggregation inhibitors, heparin, and other agents influencing coagulation

**ADMINISTRATION**

**RECONSTITUTION**
- 50 mg vial: dissolve in 50 mL water for injection
- 20 mg vial: dissolve in 20 mL water for injection.
- The reconstituted solutions can be further diluted (minimum concentration 0.2 mg/mL) with sterile sodium chloride 0.9%

**ROUTE**
- IV

**RATE OF ADMINISTRATION**
- See under dose

**COMMENTS**
- Water or glucose solution must NOT be used for dilution
- 50 mg vial = 29 mega units/vial
- 20 mg vial = 11.6 mega units/vial

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>65,000 (non-glycosylated protein)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>No data</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>Minimal</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.1</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>α: 4–5 minutes; β: 40 minutes</td>
</tr>
</tbody>
</table>
OTHER INFORMATION

- Patients weighing less than 65 kg should receive a total dose of 1.5 mg/kg according to dose schedule
- Allergic reactions are less likely with alteplase than streptokinase and repeated administration is possible
- 1.7 g arginine in the 50 mg vial, 0.7 g arginine in 20 mg vial – may lead to hyperkalaemia in renal failure

- Pay attention to potential bleeding sites during treatment
- To unblock dialysis lines, use 2 mg in 2 mL down each lumen and leave in situ for at least 60 minutes or until the next dialysis session
- Alternative regimens for unblocking dialysis lines: an infusion of 20 mg over 20 hours, or 50 mg over 12 hours
Aluminium hydroxide

**CLINICAL USE**
- Phosphate binding agent
- Antacid

**DOSE IN NORMAL RENAL FUNCTION**
- Phosphate binder: 4–20 capsules daily in divided doses
- Antacid: 1 capsule 4 times daily and at bedtime

**PHARMACOKINETICS**
- Molecular weight (daltons): 78
- % Protein binding: 70–90
- % Excreted unchanged in urine: No data
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): No data

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Unknown dialysability. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - None known

**ADMINISTRATION**
- RECONSTITUTION
  - ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - COMMENTS

**OTHER INFORMATION**
- K/DOQI guidelines caution that CKD 5 patients on chronic therapy may develop aluminium toxicity; therefore best avoided in all but short-term therapy (calcium carbonate, calcium acetate, lanthanum or sevelamer are used in chronic therapy)
- Take/administer with or immediately before meals
- In patients undergoing chronic therapy with aluminium hydroxide, serum aluminium levels should be monitored using the Desferrioxamine Test (5 mg/kg); see local protocol
Amantadine hydrochloride

CLINICAL USE
- Parkinson’s disease (but not drug induced extrapyramidal symptoms)
- Post-herpetic neuralgia
- Prophylaxis and treatment of influenza A

DOSE IN NORMAL RENAL FUNCTION
- Parkinson’s disease: 100 mg once a day, increased after one week to 100–200 mg twice a day
- Post-herpetic neuralgia: 100 mg twice a day for 14 days
- Influenza A: treatment – 100 mg twice a day for 4–5 days; prophylaxis – 100 mg once a day

PHARMACOKINETICS
Molecular weight (daltons) 187.7
% Protein binding 67
% Excreted unchanged in urine 90
Volume of distribution (L/kg) 5–10
Half-life – normal/ESRF (hrs) 15/500

DOSE IN RENAL IMPAIRMENT
GFR (mL/MIN)
35–50 100 mg every 24 hours
15–35 100 mg every 48–72 hours
<15 100 mg every 7 days

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Not dialysed. Dose as in GFR<10mL/min
HD Not dialysed. Dose as in GFR<10mL/min
HDF/High flux Unknown dialysability. Dose as in GFR<15mL/min
CAV/VVHD Unknown dialysability. Dose as in GFR=15–35mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Memantine: increased risk of CNS toxicity – avoid concomitant use; effects of amantadine possibly enhanced

ADMINISTRATION
RECONSTITUTION
- ROUTE
- Oral
RATE OF ADMINISTRATION
- COMMENTS

OTHER INFORMATION
- Peripheral oedema may occur in some patients; should be considered when the drug is prescribed for those with congestive heart failure
- Side effects are often mild and transient; usually appear within 2–4 days of treatment and disappear 24–48 hours after discontinuation of the drug
- Due to extensive tissue binding, <5% of a dose is removed by a 4 hour haemodialysis session
- A reduction in creatinine clearance to 40mL/min may result in a 5-fold increase in elimination half-life
Amikacin

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
15 mg/kg/day in 2 divided doses (maximum dose: 1.5 g/day; maximum cumulative dose: 15 g)

**PHARMACOKINETICS**
- Molecular weight (daltons) 585.6
- % Protein binding <20
- % Excreted unchanged in urine 94–98
- Volume of distribution (L/kg) 0.22–0.29
- Half-life – normal/ESRF (hrs) 2–3/17–150

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>5–6 mg/kg every 12 hours</td>
</tr>
<tr>
<td>10–20</td>
<td>3–4 mg/kg every 24 hours</td>
</tr>
<tr>
<td>&lt;10</td>
<td>2 mg/kg every 24–48 hours</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD** Dialysed. Dose as in GFR<10 mL/min
- **HD** Dialysed. Give 5 mg/kg after dialysis.
- **HDF/High flux** Dialysed. Give 5 mg/kg after dialysis.
- **CAV/VVHD** Dialysed. 7.5 mg/kg every 24 hours and monitor levels

**IMPORTANT DRUG INTERACTIONS**

- Botulinum toxin: neuromuscular block enhanced – risk of toxicity
- Ciclosporin: increased risk of nephrotoxicity
- Cytotoxics: increased risk with platinum compounds of nephrotoxicity and possibly of ototoxicity
- Diuretics: increased risk of ototoxicity with loop diuretics
- Muscle relaxants: enhanced effects of non-depolarising muscle relaxants and suxamethonium
- Parasympathomimetics: antagonism of effect of neostigmine and pyridostigmine
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - 1M/IV
- **RATE OF ADMINISTRATION**
  - IV bolus – slow over 2–3 minutes
  - Infusion – at concentration 2.5 mg/mL over 30 minutes
  - (Diluents: sodium chloride 0.9%, glucose 5% and others)

**COMMENTS**

- May be used intraperitoneally
- Can be given in 50 mL. (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006.)
- Do not mix physically with any other antibacterial agents

**OTHER INFORMATION**

- Nephrotoxic and ototoxic; toxicity no worse when hyperbilirubinaemic
- Serum levels must be measured for efficacy and toxicity
- Peritoneal absorption increases in the presence of inflammation
- Volume of distribution increases with oedema, obesity and ascites
- Peak serum concentration should not exceed 30 mg/L
- Trough serum concentration should be less than 5 mg/L
- Amikacin affects auditory function to a greater extent than gentamicin

**References:**
1. Dose from CVVH Initial Drug Dosing Guidelines on [www.thedrugmonitor.com](http://www.thedrugmonitor.com)
Amiloride hydrochloride

**CLINICAL USE**
- Oedema
- Potassium conservation with thiazide and loop diuretics

**DOSE IN NORMAL RENAL FUNCTION**
5–10 mg daily; maximum 20 mg daily

**PHARMACOKINETICS**
- Molecular weight: 302.1 daltons
- % Protein binding: 30–40
- % Excreted unchanged in urine: 50
- Volume of distribution: 5 L/kg
- Half-life – normal/ESRF (hrs): 6–20/100

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Use 50% of dose
  - 10–20: Use 50% of dose
  - <10: Avoid

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not applicable. Avoid
- HD: Not applicable. Avoid
- HDF/High flux: Not applicable. Avoid
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - ACE inhibitor and angiotensin-II antagonists: increased risk of hyperkalaemia and hypotension
  - Antibacterials: avoid concomitant use with lymecycline
  - Antidepressants: increased risk of postural hypotension with tricyclics; enhanced hypotensive effect with MAOIs
  - Antihypertensives: enhanced hypotensive effect
  - Ciclosporin: increased risk of hyperkalaemia and nephrotoxicity
  - Lithium excretion reduced
  - NSAIDS: increased risk of hyperkalaemia; increased risk of nephrotoxicity; antagonism of diuretic effect
  - Potassium salts: increased risk of hyperkalaemia
  - Tacrolimus: increased risk of hyperkalaemia

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**
- Monitor for hyperkalaemia
- Greatly increased risk of hyperkalaemia in patients with a GFR<30 mL/min, especially in diabetics
- Increased risk of hyperchloraemic metabolic acidosis in patients with reduced GFR
- Bioavailability is 50% and can be reduced by administering with food
- Reduced natriuretic effect once the GFR<50 mL/min
- Diuretic effect starts 2 hours after administration, peaks after 6–10 hours and can last up to 24 hours

RETURN TO CONTENTS
Aminophylline

CLINICAL USE
- Reversible airways obstruction
- Acute severe asthma

DOSE IN NORMAL RENAL FUNCTION
Modified release: 225–450 mg twice daily
IV loading dose: 5 mg/kg (250–500 mg)
Maintenance dose: 0.5 mg/kg/hour adjusted according to levels

PHARMACOKINETICS
- Molecular weight: 420.4 daltons
- % Protein binding: 40–60 (theophylline)
- % Excreted unchanged in urine: <10
- Volume of distribution: 0.4–0.7 (theophylline)

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD: Not dialysed. Dose as in GFR<10 mL/min. Monitor blood levels. See ‘Other Information’
- HD: Not dialysed. Dose as in GFR<10 mL/min. Monitor blood levels. See ‘Other Information’
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min. Monitor blood levels. See ‘Other Information’
- CAV/VVHD: Not dialysed. Dose as in GFR=10–20 mL/min. Monitor blood levels. See ‘Other Information’

DOSE IN DIALYSIS PATIENTS
- CAPD: Not dialysed. Dose as in GFR<10 mL/min. Monitor blood levels. See ‘Other Information’
- HD: Not dialysed. Dose as in GFR<10 mL/min. Monitor blood levels. See ‘Other Information’
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min. Monitor blood levels. See ‘Other Information’
- CAV/VVHD: Not dialysed. Dose as in GFR=10–20 mL/min. Monitor blood levels. See ‘Other Information’

DOSE IN RENAL IMPAIRMENT

GFR (mL/min)
- 20–50: Oral: Dose as in normal renal function and adjust in accordance with blood levels
- IV: Dose as in normal renal function and adjust in accordance with blood levels
- 10–20: Oral: Dose as in normal renal function and adjust in accordance with blood levels
- IV: Dose as in normal renal function and adjust in accordance with blood levels
- <10: Oral: Dose as in normal renal function and adjust in accordance with blood levels
- IV: Dose as in normal renal function and adjust in accordance with blood levels

IMPORTANT DRUG INTERACTIONS
- Potentially hazardous interactions with other drugs:
  - Antibacterials: increased concentration with azithromycin, clarithromycin, erythromycin, ciprofloxacin, norfloxacin and isoniazid; decreased erythromycin levels if erythromycin is given orally; increased risk of convulsions if given with quinolones; rifampicin accelerates metabolism of theophylline
  - Antidepressants: concentration increased by fluvoxamine – avoid concomitant use or halve theophylline dose and monitor levels; concentration reduced by St John’s wort – avoid concomitant use
  - Anti-epileptics: metabolism increased by carbamazepine and primidone; concentration of both drugs increased with phenytoin
  - Antifungals: concentration increased by fluconazole and ketoconazole
  - Antivirals: metabolism of theophylline increased by ritonavir
  - Calcium-channel blockers: concentration increased by diltiazem and verapamil and possibly other calcium-channel blockers
  - Tacrolimus: may increase tacrolimus levels
  - Ulcer-healing drugs: metabolism inhibited by cimetidine; absorption possibly reduced by sucralfate
### Administration

**Reconstitution**
- IV, oral

**Rate of Administration**
- Loading dose over 20 minutes by slow IV injection

**Comments**
- Can be added to glucose 5%, sodium chloride 0.9% and compound sodium lactate
- Minimum volumes range from 2–25 mg/mL, give concentrated solution via central line. (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006)

### Other Information

- Aminophylline: 80% theophylline + 20% ethylenediamine
- In bodily fluids, aminophylline rapidly dissociates from ethylenediamine and releases free theophylline in the body. It is therefore not present in the body long enough to be dialysed, whereas theophylline is dialysed, see theophylline monograph
- Optimum response obtained at plasma theophylline levels of 10–20 mg/L (55–110 micromol/L)
- Increased incidence of GI and neurological side effects in renal impairment at plasma levels above optimum range
Amiodarone hydrochloride

**CLINICAL USE**
Cardiac arrhythmias

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: 200 mg 3 times a day for 1 week, then twice a day for 1 week, then 200 mg daily maintenance dose or minimum required to control arrhythmia
- IV: via central catheter – 5 mg/kg (maximum 1.2 g in 24 hours)
- Ventricular arrhythmias or pulseless ventricular tachycardias: 300 mg over at least 3 minutes

**PHARMACOKINETICS**
- Molecular weight: 681.8 daltons
- % Protein binding: 96
- % Excreted unchanged in urine: <5
- Volume of distribution (L/kg): 70–140
- Half-life – normal/ESRF (hrs): 20–100 days/Unchanged

**DOSE IN RENAL IMPAIRMENT GFR (mL/min)**
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anti-arrhythmics: additive effect and increased risk of myocardial depression; increased risk of ventricular arrhythmias with disopyramide – avoid; increased flecainide dose; increased procainamide concentration – avoid
- Antibacterials: increased risk of ventricular arrhythmias with parenteral erythromycin, co-trimoxazole and moxifloxacin – avoid concomitant use
- Anticoagulants: metabolism inhibited (increased anticoagulant effect)
- Antidepressants: increased risk of ventricular arrhythmias with tricyclic antidepressants – avoid concomitant use
- Anti-epileptics: phenytoin metabolism inhibited (increased plasma concentration)
- Antihistamines: increased risk of ventricular arrhythmias with mizolastine – avoid
- Antimalarials: increased risk of ventricular arrhythmias with chloroquine, hydroxychloroquine, mefloquine and quinine – avoid concomitant use; avoid concomitant use with arteether/lumefantrine
- Antipsychotics: increased risk of ventricular arrhythmias with antipsychotics that prolong the QT interval; increased risk of ventricular arrhythmias with amisulpiride, haloperidol, phenothiazines, pimozide or sertindole – avoid
- Antivirals: increased risk of ventricular arrhythmias with amprenavir, nelfinavir and ritonavir – avoid concomitant use; concentration possibly increased by atazanavir; avoid with indinavir
- Atomoxetine: increased risk of ventricular arrhythmias
- Beta-blockers, diltiazem, verapamil: increased risk of bradycardia, AV block and myocardial depression; increased risk of ventricular arrhythmias with sotalol – avoid
- Ciclosporin: increased levels of ciclosporin possible
- Digoxin: increased plasma concentration (halve digoxin maintenance dose)
- 5HT3 antagonists: increased risk of ventricular arrhythmias with dolasetron – avoid concomitant use; caution with tropisetron
- Ivabradine: increased risk of ventricular arrhythmias – avoid concomitant use
- Lipid-lowering drugs: increased risk of myopathy with simvastatin – do not exceed 20 mg of simvastatin.¹
- Lithium: increased risk of ventricular arrhythmias – avoid concomitant use
- Pentamidine: increased risk of ventricular arrhythmias – avoid concomitant use
- Grapefruit juice: may increase concentration of amiodarone – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral, IV via central catheter or peripherally in veins with good blood flow

- **RATE OF ADMINISTRATION**
  - 20–120 minutes (max 1.2 g in up to 500 mL glucose 5% in 24 hours)

- **COMMENTS**
  - Add dose to 250 mL glucose 5%
  - Solutions containing less than 300 mg in 500 mL glucose 5% should not be used, as unstable

- Minimum volumes for central use only are up to 900 mg in 48–50 mL. (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006.)
- Volumetric pump should be used as amiodarone can reduce drop size

**OTHER INFORMATION**

- Amiodarone and desethylamiodarone levels can be monitored to assess compliance
- In extreme clinical emergency, may be given by slow IV bolus using 150–300 mg in 10–20 mL glucose 5% over a minimum of 3 minutes with close monitoring. This should not be repeated for at least 15 minutes
- Incompatible with sodium chloride 0.9%
- Rapid IV administration has been associated with anaphylactic shock, hot flushes, sweating, and nausea

References:
Amisulpride

**CLINICAL USE**
Treatment of acute and chronic schizophrenia

**DOSE IN NORMAL RENAL FUNCTION**
50–1200 mg daily (in divided doses if >300 mg); varies according to indication

**PHARMACOKINETICS**
- Molecular weight: 369.5 daltons
- % Protein binding: 16
- % Excreted unchanged in urine: 50
- Volume of distribution: 5.8 L/kg
- Half-life – normal/ESRF (hrs): 12/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 30–60: Reduce dose by 50%
  - 10–30: Use a third of the dose. See ‘Other Information’
  - <10: Use with caution. Start with minimum dose and increase according to patient’s response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Poorly dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Poorly dialysed. Dose as in GFR=10–30 mL/min

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Alcohol: may enhance CNS effects of alcohol
  - Anaesthetics: enhanced hypotensive effect
  - Analgesics: increased risk of convulsions with tramadol; enhanced hypotensive and sedative effects with opioids
  - Anti-arrhythmics: increased risk of ventricular arrhythmias with anti-arrhythmics that prolong the QT interval; avoid concomitant use with amiodarone, disopyramide and procainamide (risk of ventricular arrhythmias)
  - Antibacterials: avoid concomitant use with parenteral erythromycin (increased risk of ventricular arrhythmias)
  - Antidepressants: increased level of tricyclics
  - Anti-epileptics: antagonises anticonvulsant effect
  - Antihypertensives: increased risk of hypotension
  - Antimalarials: avoid concomitant use with artemether/lumefantrine
  - Antipsychotics: increased risk of ventricular arrhythmias with sertindole – avoid concomitant use
  - Antivirals: concentration possibly increased by ritonavir
  - Anxiolytics & hypnotics: increased sedative effects
  - Atomoxetine: increased risk of ventricular arrhythmias
  - Beta-blockers: increased risk of ventricular arrhythmias with sotalol
  - Diuretics: increased risk of ventricular arrhythmias due to hypokalaemia
  - Pentamidine: increased risk of ventricular arrhythmias – avoid
  - Sibutramine: increased risk of CNS toxicity – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**
- Elimination half-life is unchanged in patients with renal insufficiency, while systemic clearance is reduced by a factor of 2.5–3. The area under the curve of amisulpride in mild renal failure is increased 2-fold, and almost 10-fold in moderate renal failure. Experience is limited and there is no data with doses >50 mg

RETURN TO CONTENTS
Amitriptyline hydrochloride

**Clinical Use**

Tricyclic antidepressant:
- Depression, used especially where sedation is required
- Neuropathic pain

**Dose in Normal Renal Function**

10–200 mg daily depending on indication

**Pharmacokinetics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>313.9</td>
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<tr>
<td>% Protein binding</td>
<td>96</td>
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<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;2</td>
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<tr>
<td>Volume of distribution (L/kg)</td>
<td>6–36</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>9–25/Unchanged</td>
</tr>
</tbody>
</table>

**Dose in Renal Impairment GFR (mL/min)**

- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function

**Dose in Patients Undergoing Renal Replacement Therapies**

- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**Important Drug Interactions**

Potentially hazardous interactions with other drugs:
- Alcohol: increased sedative effect
- Analgesics: increased risk of CNS toxicity with tramadol; possibly increased risk of side effects with nefopam; possibly increased sedative effects with opioids
- Anti-arrhythmics: increased risk of ventricular arrhythmias with amiodarone
- Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin
- Anticoagulants: may alter anticoagulant effect of coumarins
- Antidepressants: possibly increased serotonergic effects with duloxetine; enhanced CNS excitation and hypertension with MAOIs and moclobemide; concentration possibly increased with SSRIs; concentration reduced by St John’s wort
- Anti-epileptics: convulsive threshold lowered; concentration reduced by carbamazepine, primidone, barbiturates and possibly phenytoin
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: increased risk of ventricular arrhythmias especially with pimozide; increased antimuscarinic effects with clozapine and phenothiazines; concentration increased by antipsychotics
- Antivirals: increased tricyclic side effects with amprenavir; concentration possibly increased with ritonavir
- Atomoxetine: increased risk of ventricular arrhythmias with propafenone
- Clonidine: tricyclics antagonise hypotensive effect; increased risk of hypertension on clonidine withdrawal
- Dopaminergics: avoid use with entacapone; CNS toxicity reported with selegiline and rasagiline
- Pentamidine: increased risk of ventricular arrhythmias
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use.
- Sympathomimetics: increased risk of hypertension and arrhythmias with adrenaline and noradrenaline; metabolism possibly inhibited by methylphenidate
ADMINISTRATION

RECONSTITUTION

ROUTE

- Oral

RATE OF ADMINISTRATION

- COMMENTS

OTHER INFORMATION

- Introduce treatment gradually in renal impairment due to dizziness and postural hypotension
- Withdraw treatment gradually
- Anticholinergic side effects: causes urinary retention, drowsiness, dry mouth, blurred vision and constipation
Amlodipine

**CLINICAL USE**
Calcium-channel blocker:
- Hypertension
- Angina prophylaxis

**DOSE IN NORMAL RENAL FUNCTION**
5–10 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 567.1 (as besilate)
- % Protein binding: >95
- % Excreted unchanged in urine: <10
- Volume of distribution (L/kg): 20
- Half-life – normal/ESRF (hrs): 35–50/50

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unlikely to be dialysed. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs:
- Anaesthetics: enhanced hypotensive effect
- Antihypertensives: enhanced hypotensive effect; increased risk of first dose hypotensive effect of post-synaptic alpha-blockers
- Antivirals: concentration possibly increased by ritonavir
- Theophylline: possibly increased theophylline concentration

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**
- Amlodipine is extensively metabolised to inactive metabolites

RETURN TO CONTENTS
Amoxicillin

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
250 mg – 1 g every 8 hours (maximum 6 g per day, up to 12 g in endocarditis)

**PHARMACOKINETICS**
- Molecular weight (daltons): 365.4
- % Protein binding: 20
- % Excreted unchanged in urine: 60
- Volume of distribution (L/kg): 0.3
- Half-life – normal/ESRF (hrs): 1–1.5/7–20

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>250 mg – 1 g every 8 hours (Maximum 6 g per day in endocarditis)</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**: Not dialysed. Dose as in GFR<10mL/min
- **HD**: Dialysed. Dose as in GFR<10mL/min
- **HDF/High flux**: Dialysed. Dose as in GFR<10mL/min
- **CAV/VVHD**: Dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Amoxicillin can reduce the excretion of methotrexate (increased risk of toxicity)

**ADMINISTRATION**

**RECONSTITUTION**
- IV: Dissolve each 250 mg in 5 mL water for injection
- IV Infusion: Dilute in 100 mL glucose 5% or sodium chloride 0.9%
- IM: Dissolve 250 mg in 1.5 mL water for injection; 500 mg in 2.5 mL water for injection; 1 g in 2.5 mL water for injection or 1% sterile lidocaine hydrochloride

**ROUTE**
- Oral, IV, IM

**RATE OF ADMINISTRATION**
- Slow bolus IV over 3–4 minutes
- Infusion over 30–60 minutes

**COMMENTS**
- Stability in infusion depends upon diluent

**OTHER INFORMATION**
- Sodium – 3.3 mmol/g vial of Amoxil
- Do not mix with aminoglycosides
Amphotericin IV – Abelcet (lipid complex)

**CLINICAL USE**

Antifungal agent:
- Systemic fungal infections (yeasts and yeast-like fungi including *Candida albicans*).

**DOSE IN NORMAL RENAL FUNCTION**

5 mg/kg/day for at least 14 days (see individual product data sheet).

**PHARMACOKINETICS**

- Molecular weight (daltons): 924.1
- % Protein binding: 90
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): 2286
- Half-life – normal/ESRF (hrs): 173.4/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Ciclosporin: increased nephrotoxicity
- Tacrolimus: increased nephrotoxicity
- Increased risk of nephrotoxicity with aminoglycosides and other nephrotoxic agents and cytotoxics
- Cardiac glycosides: increased toxicity if hypokalaemia occurs
- Corticosteroids: increased risk of hypokalaemia (avoid concomitant use unless corticosteroids are required to control reactions)
- Flucytosine: enhanced toxicity in combination with amphotericin

**ADMINISTRATION**

**RECONSTITUTION**

- See individual data sheet. Prepare intermittent infusion in glucose 5% (incompatible with sodium chloride 0.9%, electrolytes or other drugs).
- Dilute to a concentration of 1–2 mg/mL.

**ROUTE**

- IV infusion

**RATE OF ADMINISTRATION**

- 2.5 mg/kg/hour

**COMMENTS**

- Paracetamol and parenteral pethidine may alleviate rigors associated with amphotericin administration. Can also use antihistamines to control reactions.
- Flush existing IV line with glucose 5% before and after infusion administration.
- For patients on CAV/VVHD, amphotericin should be given into the venous return of the dialysis circuit.
- Should be given post dialysis.

**OTHER INFORMATION**

*** AMPHOTERICIN IS HIGHLY NEPHROTOXIC ***

- Can cause distal tubular acidosis
- May cause polyuric, hypovolaemia, hypokalaemia and acidosis.
- Amphotericin and flucytosine act synergistically when co-administered enabling lower doses to be used effectively.
- A test dose of amphotericin is recommended at the beginning of a new course (1 mg over 15 minutes).
- Monitor renal function, full blood count, potassium, magnesium and calcium levels.
- Liposomal amphotericin is considerably less nephrotoxic compared with conventional amphotericin B, but is considerably more expensive.

RETURN TO CONTENTS
Amphotericin IV – Ambisome (liposomal)

CLINICAL USE
Antifungal agent:
- Systemic fungal infections (yeasts and yeast-like fungi including Candida albicans)
- Treatment of visceral leishmaniasis

DOSE IN NORMAL RENAL FUNCTION
1–3 mg/kg/day, maximum 5 mg/kg (unlicensed dose)
Visceral leishmaniasis: total dose of 21–30 mg/kg given over 10–21 days

PHARMACOKINETICS
Molecular weight (daltons) 924.1
% Protein binding 90
% Excreted unchanged in urine 2–5
Volume of distribution (L/kg) 0.1–0.44
Half-life – normal/ESRF (hrs) 6.3–10.7/Unchanged

DOSE IN RENAL IMPAIRMENT
GFR (mL/Min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Not dialysed. Dose as in normal renal function
HD Not dialysed. Dose as in normal renal function
HDF/High flux Unknown dialysability. Dose as in normal renal function
CAV/VVHD Not dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Ciclosporin: increased nephrotoxicity
- Tacrolimus: increased nephrotoxicity
- Increased risk of nephrotoxicity with aminoglycosides and other nephrotoxic agents and cytotoxics
- Cardiac glycosides: increased toxicity if hypokalaemia occurs
- Corticosteroids: increased risk of hypokalaemia (avoid concomitant use unless corticosteroids are required to control reactions)
- Fluocytosine: enhanced toxicity in combination with amphotericin

ADMINISTRATION
RECONSTITUTION
- See SPC. Prepare intermittent infusion in glucose 5% (incompatible with sodium chloride 0.9%, electrolytes or other drugs).
- Reconstitute vial contents with water for injection
- Dilute to a concentration of 0.2–2 mg/mL

ROUTE
- IV infusion

RATE OF ADMINISTRATION
- 30–60 minutes

COMMENTS
- Paracetamol and parenteral pethidine may alleviate rigors associated with amphotericin administration. Antihistamines can also be administered to control reactions
- Flush existing IV line with glucose 5% before and after infusion administration
- For patients on CAV/VVHD, amphotericin should be given into the venous return of the dialysis circuit
- Should be given post dialysis
OTHER INFORMATION

*** AMPHOTERICIN IS HIGHLY NEPHROTOXIC ***
- Can cause distal tubular acidosis
- May cause polyurea, hypovolaemia, hypokalaemia and acidosis.
- Amphotericin and flucytosine act synergistically when co-administered enabling lower doses to be used effectively
- A test dose of amphotericin is recommended at the beginning of a new course (1 mg over 10 minutes then stop and observe for next 30 minutes)
- Monitor renal function, full blood count, potassium, magnesium and calcium levels
- Liposomal amphotericin is considerably less nephrotoxic compared with amphotericin, but is considerably more expensive
Amphotericin IV – Amphocil (complex with sodium cholesteryl sulphate)

CLINICAL USE
Antifungal agent:
- Systemic fungal infections (yeasts and yeast-like fungi including Candida albicans)

DOSE IN NORMAL RENAL FUNCTION
1–6 mg/kg/day

PHARMACOKINETICS
- Molecular weight (daltons) 924.1
- % Protein binding 90–97
- % Excreted unchanged in urine 2–5
- Volume of distribution (L/kg) 2.25–3.61
- Half-life – normal/ESRF (hrs) 22.1–27.2/Unchanged

DOSE IN RENAL IMPAIRMENT
- GFR (mL/MIN)
  - 20–50 Dose as in normal renal function
  - 10–20 Dose as in normal renal function
  - <10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD Not dialysed. Dose as in normal renal function
- HD Not dialysed. Dose as in normal renal function
- HDF/High flux Not dialysed. Dose as in normal renal function
- CAV/VVHD Not dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
- Cardiac glycosides: increased toxicity if hypokalaemia occurs
- Corticosteroids: increased risk of hypokalaemia – avoid concomitant use unless corticosteroids are required to control reactions
- Flucytosine: enhanced toxicity in combination with amphotericin

ADMINISTRATION
RECONSTITUTION
- See SPC. Prepare intermittent infusion in glucose 5% (incompatible with sodium chloride 0.9%, electrolytes or other drugs).
- Reconstitute vial contents with water for injection

ROUTE
- IV infusion

RATE OF ADMINISTRATION
- 1–2 mg/kg/hour

COMMENTS
- Paracetamol and parenteral pethidine may alleviate rigors associated with amphotericin administration. Antihistamines can also be administered to control reactions
- Flush existing IV line with glucose 5% before and after infusion administration
- For patients on CAV/VVHD, amphotericin should be given into the venous return of the dialysis circuit
- Should be given post dialysis

OTHER INFORMATION
*** AMPHOTERICIN IS HIGHLY NEPHROTOXIC ***
- Can cause distal tubular acidosis
- May cause polyuria, hypovolaemia, hypokalaemia and acidosis.
- Amphotericin and flucytosine act synergistically when co-administered enabling lower doses to be used effectively
- A test dose of amphotericin is recommended at the beginning of a new course (2 mg over 10 minutes)
- Monitor renal function, full blood count, potassium, magnesium and calcium levels
- Less nephrotoxic than conventional amphotericin B
Amphotericin IV – Fungizone

CLINICAL USE
Antifungal agent:
- Systemic fungal infections (yeasts and yeast-like fungi including Candida albicans)

DOSE IN NORMAL RENAL FUNCTION
250 micrograms – 1.5 mg/kg/day
Can be given on alternate days if using a higher dose

PHARMACOKINETICS
Molecular weight (daltons) 924.1
% Protein binding >90
% Excreted unchanged in urine 2–5
Volume of distribution (L/kg) 4
Half-life – normal/ESRF (hrs) 24–48 (up to 15 days with long-term use)/Unchanged

DOSE IN RENAL IMPAIRMENT
GFR (mL/MIN)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Not dialysed. Dose as in GFR<10mL/min
HD Not dialysed. Dose as in GFR<10mL/min
HDF/High flux Not dialysed. Dose as in GFR<10mL/min
CAV/ VVHD Not dialysed. Dose as in GFR=10–20mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Ciclosporin: increased nephrotoxicity
- Tacrolimus: increased nephrotoxicity
- Increased risk of nephrotoxicity with aminoglycosides and other nephrotoxic agents and cytotoxics
- Cardiac glycosides: increased toxicity if hypokalaemia occurs
- Corticosteroids: increased risk of hypokalaemia – avoid concomitant use unless corticosteroids are required to control reactions
- Flucytosine: enhanced toxicity in combination with amphotericin

ADMINISTRATION
RECONSTITUTION
- See SPC. Prepare intermittent infusion in glucose 5% (incompatible with sodium chloride 0.9%, electrolytes or other drugs). Reconstitute vial contents with water for injection. pH should be adjusted to >4.2
- Dilute to a concentration of 10mg in 100mL

ROUTE
- IV infusion
RATE OF ADMINISTRATION
- 2–6 hours
- If given over 12–24 hours there is a reduced incidence of side effects

COMMENTS
- Minimum volume peripherally 0.2mg/mL, centrally 0.5mg/mL. (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006)
- Higher rates of infusion are associated with greater risk of adverse reactions. Administration over less than 1 hour, particularly in renal failure, has been associated with hyperkalaemia and arrhythmias
- Paracetamol and parenteral pethidine may alleviate rigors associated with amphotericin administration. Can also give antihistamines and corticosteroids to control reactions
- Flush existing IV line with glucose 5% before and after infusion administration
- For patients on CAV/VVHD, amphotericin should be given into the venous return of the dialysis circuit
OTHER INFORMATION

*** AMPHOTERICIN IS HIGHLY NEPHROTOXIC ***

- Permanent renal impairment may occur, particularly in patients receiving conventional amphotericin B at doses >1 mg/kg/day, or with pre-existing renal impairment, prolonged therapy, sodium depletion or concurrent nephrotoxic drugs.
- Nephrotoxicity may be reduced by giving an IV infusion of sodium chloride 0.9% 250–500 mL over 30–45 minutes immediately before administering amphotericin B.
- Can cause distal tubular acidosis.
- May cause polyurea, hypovolaemia, hypokalaemia and acidosis.

- Amphotericin and flucytosine act synergistically when co-administered enabling lower doses to be used effectively.
- A test dose of amphotericin is recommended at the beginning of a new course (1 mg over 20–30 minutes then stop and observe for 30 minutes).
- Monitor renal function, full blood count, potassium, magnesium and calcium levels.
- Liposomal amphotericin is considerably less nephrotoxic compared with conventional amphotericin B, but is considerably more expensive.
- There are reports of the use of amphotericin in 20% lipid solution being as well tolerated as liposomal amphotericin.
Ampicillin

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
Oral: 250 mg – 1 g every 6 hours
IM/IV: 500 mg – 2 g every 4–6 hours

**PHARMACOKINETICS**
Molecular weight (daltons) 349.4
% Protein binding 20
% Excreted unchanged in urine Oral: 20–60; Parenteral: 60–80
Volume of distribution (L/kg) 0.17–0.31
Half-life – normal/ESRF (hrs) 1–1.5/7–20

**DOSE IN RENAL IMPAIRMENT**
GFR (mL/min)
20–50  Dose as in normal renal function
10–20  250 mg – 2 g every 6 hours
<10  250 mg – 1 g every 6 hours

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
CAPD  Not dialysed. Dose as in GFR<10mL/min
HD  Dialysed. Dose as in GFR<10mL/min
HDF/High flux  Dialysed. Dose as in GFR<10mL/min
CAV/ VVHD  Dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Ciclosporin: may increase ciclosporin levels
- Reduces excretion of methotrexate (increased risk of toxicity)

**ADMINISTRATION**
**RECONSTITUTION**
- Use water for injection: 5 mL for each 250 mg (1.5 mL for 250 mg or 500 mg for IM administration)

**ROUTE**
- Oral, IV, IM

**RATE OF ADMINISTRATION**
- Slow IV bolus over 3–4 minutes. Doses greater than 500 mg should be given by infusion

**COMMENTS**
- Can be diluted in glucose 5% or sodium chloride 0.9%

**OTHER INFORMATION**
- Rashes more common in patients with renal impairment
- Can cause nephrotoxicity if dose not reduced in renal impairment
- Sodium content of injection 1.47 mmol/500 mg vial
- Ampicillin may be used in peritoneal dialysis fluids for treatment of peritonitis
- Do not mix with aminoglycosides

RETURN TO CONTENTS
Amprenavir

**CLINICAL USE**
Protease inhibitor:
- HIV infection, in combination with other antiretroviral drugs

**DOSE IN NORMAL RENAL FUNCTION**
Capsules:
- >50 kg: 1.2 g, twice a day
- <50 kg: 20 mg/kg, twice a day; maximum 2.4 g daily
With ritonavir 100 mg, twice a day:
- >50 kg: 600 mg, twice a day
Oral solution: 17 mg/kg every 8 hours; maximum 2.8 g daily

**PHARMACOKINETICS**
- Molecular weight (daltons) 505.6
- % Protein binding 90
- % Excreted unchanged in urine <3
- Volume of distribution (L/kg) 6
- Half-life – normal/ESRF (hrs) 7.1–10.6/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unlikely to be dialysed. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anti-arrhythmics: possibly increase concentration of amiodarone, flecainide, lidocaine and propafenone (increased risk of ventricular arrhythmias) – avoid concomitant use
- Antibacterials: concentration of both drugs increased with erythromycin; increased concentration of rifabutin – reduce rifabutin dose; concentration significantly reduced by rifampicin – avoid concomitant use; possibly increased dapsone concentration; avoid concomitant use with telithromycin in severe renal and hepatic impairment
- Antidepressants: concentration reduced by St John’s wort – avoid concomitant use; possibly increased side effects of tricyclics; possibly reduced paroxetine concentration
- Antimalarials: avoid concomitant administration with artemether/lumefantrine
- Antipsychotics: possibly inhibit aripiprazole metabolism – reduce aripiprazole dose; possibly increased clozapine concentration; increased pimoze and sertindole concentration (increased risk of ventricular arrhythmias) – avoid concomitant use
- Antivirals: concentration reduced by efavirenz, lopinavir and tipranavir; concentration possibly reduced by nevirapine; concentration increased by ritonavir
- Anxiolytics and hypnotics: increased risk of prolonged sedation and respiratory depression with alprazolam, clonazepam, diazepam, flurazepam and midazolam
- Cilostazol: possibly increased cilostazol concentration – avoid concomitant use
- Ergot alkaloids: increased risk of ergotism – avoid concomitant use.
- Immunosuppressants: monitor ciclosporin, tacrolimus and sirolimus levels
- Statins: possibly increased risk of myopathy with atorvastatin; possibly increased myopathy with simvastatin – avoid concomitant use
### ADMINISTRATION

<table>
<thead>
<tr>
<th>RECONSTITUTION</th>
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<table>
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<tbody>
<tr>
<td>Oral</td>
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<table>
<thead>
<tr>
<th>RATE OF ADMINISTRATION</th>
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<table>
<thead>
<tr>
<th>COMMENTS</th>
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</table>

### OTHER INFORMATION

- Oral solution contains vitamin E 46 units/mL, potassium 26 micromol/mL and sodium 174 micromol/mL
- Avoid oral solution in renal impairment due to possible accumulation of propylene glycol
- Bioavailability of oral solution is 14–19% less than the capsules
## Amsacrine

### CLINICAL USE
Antineoplastic agent:
- Acute leukaemias

### DOSE IN NORMAL RENAL FUNCTION
- Induction of remission: 90–120 mg/m² daily for 5–8 days, repeated at 2–4 week intervals according to response
- Maintenance: 150 mg/m² as a single dose or divided over 3 consecutive days every 3–4 weeks
- Or according to local policy

### PHARMACOKINETICS
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tbody>
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<td>Molecular weight (daltons)</td>
<td>393.5</td>
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<tr>
<td>% Protein binding</td>
<td>96–98</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>2–10</td>
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<tr>
<td>Volume of distribution (L/kg)</td>
<td>1.67</td>
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<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>5–8/Unchanged</td>
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### DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose (mg/m² daily)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>60–75</td>
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<tr>
<td>10–20</td>
<td>60–75</td>
</tr>
<tr>
<td>&lt;10</td>
<td>60–75</td>
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</table>

### DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose (mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

### IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- None known

### ADMINISTRATION

#### RECONSTITUTION
- ROUTE
  - IV
- RATE OF ADMINISTRATION
  - 60–90 minutes
- COMMENTS
  - Dilute in 500 mL of glucose 5%
  - Use glass syringes
  - Incompatible with sodium chloride

### OTHER INFORMATION
- Increased risk of side effects in renal impairment
- Amsacrine is extensively metabolised in the liver. The principal metabolites, via microsomal oxidation, are much more cytotoxic than the parent drug. Excretion is via the bile; >50% excreted in faeces within 2 hours; 35% in urine.
**Anagrelide**

**CLINICAL USE**
Platelet-reducing agent

**DOSE IN NORMAL RENAL FUNCTION**
1–10 mg daily in divided doses; maximum single dose 2.5 mg; normal range 1–3 mg daily

**PHARMACOKINETICS**
- Molecular weight: 292.5 (as hydrochloride)
- % Protein binding: No data
- % Excreted unchanged in urine: <1
- Volume of distribution: 12 (L/kg)
- Half-life – normal/ESRF (hrs): 1.3

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–30</td>
<td>Dose as in normal renal function, but use with caution and keep to lowest dose possible</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function, but use with caution and keep to lowest dose possible</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>GFR=10–30mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Cilostazol: avoid concomitant use
- Phosphodiesterase inhibitors: avoid concomitant use with milrinone and enoximone
- Aspirin: potential risks and benefits must first be assessed, additive antiplatelet effect
- Grapefruit juice: may reduce clearance of anagrelide

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
  -

**OTHER INFORMATION**
- May cause fluid retention, tachycardia and various cardiac complications
- Rarely can increase creatinine levels
- High doses can cause a drop in blood pressure

RETURN TO CONTENTS
Anastrozole

**CLINICAL USE**
Treatment of breast cancer in post-menopausal women

**DOSE IN NORMAL RENAL FUNCTION**
1 mg daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>293.4</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>40</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>No data</td>
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<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>40–50/Probably unchanged</td>
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**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Dialysed. Dose as in normal renal function
- HD: Dialysed. Dose as in normal renal function
- HDF/High flux: Dialysed. Dose as in normal renal function
- CAV/VVHD: Dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Oestrogen-containing therapies: avoid concomitant administration as would negate pharmacological action
- Tamoxifen: avoid concomitant administration

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - COMMENTS

**OTHER INFORMATION**

- Anastrozole is extensively metabolised in the liver; only 10% of unchanged drug and 60% of metabolites (largely inactive) are excreted in the urine
- Although renal clearance of anastrozole decreases proportionally with creatinine clearance, the reduction in renal clearance does not affect total body clearance of anastrozole. According to the American SPC a dose reduction is not required in renal impairment
- In the UK, the SPC recommends avoiding the use of anastrozole in patients with GFR<20mL/min
Anidulafungin

**CLINICAL USE**
Antifungal agent:
- Invasive candidiasis

**DOSE IN NORMAL RENAL FUNCTION**
200 mg loading dose then 100 mg daily
Oesophageal candidiasis: 100 mg loading
dose then 50 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons) 1140.2
- % Protein binding >99
- % Excreted unchanged in urine <1
- Volume of distribution (L/kg) 30–50 litres
- Half-life – normal/ESRF (hrs) 40–50/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unlikely to be dialysed. Dose as in normal renal function
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**
- RECONSTITUTION
  - With diluent provided
- ROUTE
  - IV infusion
- RATE OF ADMINISTRATION
  - 1.1 mg/minute (3 mL/minute)
- COMMENTS
  - Can be further diluted in sodium chloride 0.9% or glucose 5%
  - Add 100 mg to 250 mL or 200 mg to 500 mL of fluid
Apomorphine hydrochloride

**CLINICAL USE**
Treatment of refractory motor fluctuations in Parkinson's disease

**DOSE IN NORMAL RENAL FUNCTION**
3–30 mg daily in divided doses (maximum single dose 10 mg); infusion: 1–4 mg/hour during waking hours
Maximum dose 100 mg daily

**PHARMACOKINETICS**
Molecular weight 312.8 (daltons)
% Protein binding 90
% Excreted unchanged in urine <2
Volume of distribution (L/kg) 2–19
Half-life – normal/ESRF (hrs) 29.1–36.9 minutes

**DOSE IN RENAL IMPAIRMENT**
GFR (mL/min)
20–50 Dose as in normal renal function. Start with 1 mg
10–20 Dose as in normal renal function. Start with 1 mg
<10 Dose as in normal renal function. Start with 1 mg

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
CAPD Unlikely to be dialysed. Dose as in GFR<10 mL/min
HD Unlikely to be dialysed. Dose as in GFR<10 mL/min
HDF/High flux Unlikely to be dialysed. Dose as in GFR<10 mL/min
CAV/VVHD Unlikely to be dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Nitrates: enhanced hypotensive effect
- Antihypertensives: enhanced hypotensive effect

**ADMINISTRATION**
RECONSTITUTION
- ROUTE
  - SC
RATE OF ADMINISTRATION
  - 1–4 mg/hour
COMMENTS
  - Change site every 4 hours for SC administration

**OTHER INFORMATION**
- Pre-treatment with domperidone is required for at least 2 days before and at least 3 days after treatment
- Bioavailability by subcutaneous administration is 17–18%
- Most of dose is excreted in the urine as active metabolites
Aprepitant

**CLINICAL USE**
Prevention of acute and delayed nausea and vomiting associated with moderate and highly emetogenic cancer chemotherapy

**DOSE IN NORMAL RENAL FUNCTION**
125 mg once daily on day 1 followed by 80 mg once daily on days 2 and 3

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>534.4</td>
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<tr>
<td>% Protein binding</td>
<td>&gt;95</td>
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<tr>
<td>% Excreted unchanged in urine</td>
<td>0</td>
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<tr>
<td>Volume of distribution (L/kg)</td>
<td>66 litres</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>9–13/Unchanged</td>
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</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
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<td>Dose as in normal renal function</td>
</tr>
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<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**
  - Not dialysed. Dose as in normal renal function
- **HD**
  - Not dialysed. Dose as in normal renal function
- **HDF/High flux**
  - Unlikely to be dialysed. Dose as in normal renal function
- **CAV/VVHD**
  - Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Avoid concurrent administration with pimozide or St John’s wort
- Oestrogens and progestogens: may cause contraceptive failure

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
  -

**OTHER INFORMATION**
- Less than 0.2% of a dose is recovered in dialysate after haemodialysis
Argatroban

CLINICAL USE
Anticoagulant:
- Prophylaxis or treatment of thrombosis in patients with heparin-induced thrombocytopenia (HIT)
- Adjunct in patients at risk of HIT undergoing percutaneous coronary intervention

DOSE IN NORMAL RENAL FUNCTION
- Anticoagulant for prophylaxis or treatment of thrombosis: infusion of 2 mcg/kg/min; adjust according to response (APTT); maximum 10 mcg/kg/min
- Anticoagulant for patients undergoing percutaneous coronary intervention: initially a bolus of 350 mcg/kg administered via a large bore IV line over 3–5 minutes, followed by an infusion of 25 mcg/kg/min. Additional IV bolus doses of 150 mcg/kg may be given if required and the infusion rate changed to 15–40 mcg/kg/min

PHARMACOKINETICS
Molecular weight (daltons) 508.6
% Protein binding 54
% Excreted unchanged in urine 16
Volume of distribution (L/kg) 0.17
Half-life – normal/ESRF (hrs) 39–51 minutes/Unchanged

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD Unlikely to be dialysed. Dose as in normal renal function
- HD Not dialysed. Dose as in normal renal function
- HDF/High flux Not dialysed. Dose as in normal renal function
- CAV/VVHD Unlikely to be dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Heparin: avoid concomitant administration
- Urokinase: may increase the risk of bleeding
- Thrombolytics: may increase risk of bleeding complications; enhance effect of argatroban
- Antiplatelets and anticoagulants: increased risk of bleeding complications

ADMINISTRATION
RECONSTITUTION
- ROUTE
- IV
RATE OF ADMINISTRATION
- Bolus: over 3–5 minutes
- Infusion: 2–25 mcg/kg/min
COMMENTS
- Physically and chemically stable for up to 96 hours if refrigerated or at controlled room temperature and protected from light
- Dilute to 1 mg/mL with sodium chloride 0.9%, glucose 5% or Lactated Ringer's solution, i.e. 250 mg (2.5 mL) into 250 mL of diluent. The solution must be mixed by inversion for 1 minute

OTHER INFORMATION
- Can also be used for haemodialysis anticoagulation: 0.1 mg/kg bolus, followed by a continuous infusion of 0.1-0.2 mcg/kg/hour, dosing being adjusted to maintain an APTT 1.5–3 times normal.
- For CVVHD a dose of 0.5–1 mcg/kg/min was suggested, dosing being adjusted to maintain an APTT 1.5–2 times normal. (O Shea SI, Ortel TL, Kovalik EC. Alternative methods of anticoagulation for dialysis-dependent patients with heparin-induced thrombocytopenia. Seminars in Dialysis. 2003. 16(1): 61–67)
- 20% of argatroban is removed during a 4 hour dialysis session
- There is no specific antidote
- Contraindicated in patients with overt major bleeding
Aripiprazole

**CLINICAL USE**
Atypical antipsychotic for the treatment of schizophrenia

**DOSE IN NORMAL RENAL FUNCTION**
10–30 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 448.4
- % Protein binding: >99
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): 4.9
- Half-life – normal/ESRF (hrs): 75 (146 in poor metabolisers)/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unlikely to be dialysed. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Analgesics: increased risk of convulsions with tramadol; enhanced hypotensive and sedative effects with opioids
- Antiarrhythmics: increased risk of ventricular arrhythmias with antiarrhythmics that prolong the QT interval
- Antibacterials: concentration possibly reduced by rifabutin and rifampicin – increase dose of aripiprazole
- Antidepressants: fluoxetine and paroxetine possibly inhibit metabolism – reduce dose of aripiprazole; concentration possibly reduced by St John’s wort – increase aripiprazole dose; increased concentration of tricyclics
- Anti-epileptics: antagonises anticonvulsant effect; concentration reduced by carbamazepine and possibly reduced by phenytoin, phenobarbital and primidone – increase dose of aripiprazole
- Antifungals: metabolism inhibited by ketoconazole and possibly by itraconazole – reduce dose of aripiprazole
- Antivirals: metabolism possibly inhibited by amprenavir, atazanavir, indinavir, lopinavir, nelfinavir, ritonavir and saquinavir – reduce dose of aripiprazole; concentration possibly reduced by efavirenz and nevirapine – increase dose of aripiprazole
- Anxiolytics and hypnotics: increased sedative effects
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**

**COMMENTS**

**OTHER INFORMATION**
- Hepatic metabolism and elimination
- Can cause QT prolongation
## Arsenic trioxide

### CLINICAL USE

Antineoplastic agent:
- Acute promyelocytic leukaemia (APL)

### DOSE IN NORMAL RENAL FUNCTION

- **150 mcg/kg daily until remission occurs**
- **Consolidation:** 150 mcg/kg daily for 5 days per week for 25 doses spread over up to 5 weeks (to start 3–4 weeks after completion of induction)

### PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>197.8</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>96% bound to haemoglobin</td>
</tr>
<tr>
<td>% Excreted in urine</td>
<td>1–8</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>4 litres</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>92/Increased</td>
</tr>
</tbody>
</table>

### DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Reduce dose, use with caution</td>
</tr>
<tr>
<td>10–20</td>
<td>Reduce dose, use with caution</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Reduce dose, use with caution</td>
</tr>
</tbody>
</table>

### DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

- **CAPD**
  - Unknown dialysability. Dose as in GFR<10 mL/min
- **HD**
  - Dialysed. Dose as in GFR<10 mL/min
- **HDF/High flux**
  - Dialysed. Dose as in GFR<10 mL/min
- **CAV/VVHD**
  - Unknown dialysability. Dose as in GFR=10–20 mL/min

### IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs
- Use with care in combination with other drugs known to cause QT interval prolongation

### ADMINISTRATION

- **RECONSTITUTION**
  - **ROUTE**
  - IV
  - **RATE OF ADMINISTRATION**
  - Over 1–4 hours
  - **COMMENTS**
  - Dilute with 100–250 mL glucose 5% or sodium chloride 0.9%

### OTHER INFORMATION

- Can cause QT interval prolongation and hypokalaemia
- Arsenic trioxide is under investigation for other conditions, e.g. multiple myeloma, acute myeloid leukaemias and myelodysplastic syndromes
- Intensive monitoring is required
- Renal excretion is the main route of elimination; can accumulate in renal impairment
- Arsenic is stored mainly in liver, kidney, heart, lung, hair and nails. Trivalent forms of arsenic are methylated in humans and mostly excreted in urine. In APL patients, daily administration of 0.15 mg/kg/day of arsenic trioxide resulted in an approximate 4-fold increase in the urinary excretion of arsenic after 2 to 4 weeks of continuous dosing, when compared to baseline values.
Artemether with lumefantrine

**CLINICAL USE**
Treatment of malaria

**DOSE IN NORMAL RENAL FUNCTION**

>35 kg: 6 doses of 4 tablets, i.e. 24 tablets given over 60 hours
Give 4 tablets at 0, 8, 24, 36, 48 and 60 hours

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>Artemether: 298.4; lumefantrine: 528.9</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>Artemether: 95.4; lumefantrine: 99.9</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>No data</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>Artemether: 5.4–8.6; lumefantrine: 3.8</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>Artemether 0.8–7; lumefantrine: 48–72 (4–6 days in people with falciparum malaria)</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Dose as in normal renal function</th>
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<tbody>
<tr>
<td>20–50</td>
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<td>10–20</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt;10</td>
<td></td>
<td></td>
<td>Use with caution</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Anti-arrhythmics: avoid concomitant use with amiodarone, disopyramide, flecanide and procainamide – risk of ventricular arrhythmias
- Antibacterials: avoid concomitant use with macrolides and quinolones.
- Antidepressants: avoid concomitant use
- Antifungals: avoid concomitant use with imidazoles and triazoles.
- Antimalarials: increased risk of ventricular arrhythmias with quinine – avoid concomitant use.
- Antipsychotics: avoid concomitant use
- Antivirals: avoid concomitant use with amprenavir, atazanavir, indinavir, lopinavir, nelfinavir, ritonavir and saquinavir; possibly increased risk of ventricular arrhythmias with tipranavir – avoid concomitant use
- Beta-blockers: avoid concomitant use with metoprolol and sotalol
- Grapefruit juice: may increase bioavailability and inhibit metabolism – avoid concomitant use
- Ulcer-healing drugs: avoid concomitant use with cimetidine

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
  - Take with food to increase absorption
  - If patient vomits within 1 hour of taking the tablet the dose should be repeated

**OTHER INFORMATION**
- In renal impairment monitor ECG and potassium levels
- Undergoes extensive metabolism by the liver
Ascorbic acid

**CLINICAL USE**
- Acidification of urine
- Vitamin C deficiency

**DOSE IN NORMAL RENAL FUNCTION**
- Up to 4 g daily in divided doses
- Prophylaxis: 25–75 mg daily
- Therapeutic: 250 mg daily in divided doses
- IV: 0.5–1 g daily
- Preventative therapy: 200–500 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons) 176.1
- % Protein binding 25
- % Excreted unchanged in urine Minimal\(^1\)
- Volume of distribution (L/kg) No data
- Half-life – normal/ESRF (hrs) 3–4/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50 Dose as in normal renal function
  - 10–20 Dose as in normal renal function
  - <10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Dialysed. Dose as in normal renal function
- HD Dialysed. Dose as in normal renal function
- HDF/High flux Dialysed. Dose as in normal renal function
- CAV/VVHD Dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral, IV

**RATE OF ADMINISTRATION**
- COMMENTS
  -

**OTHER INFORMATION**
- No scientific evidence from clinical trial of efficacy in reducing UTI via acidification of urine
- In CKD 5 on dialysis, requirements are usually about 75–90 mg per day. (Kalanter-Zadeh K, Kopple JD. Trace elements and vitamins in maintenance dialysis patients. *Adv Ren Replace Ther*. 2003; 10(3): 170–82.)
- Try to use lower doses in CKD 5 patients due to risk of oxalate formation

References:
Aspirin

CLINICAL USE

NSAID:
- Analgesic and antipyretic
- Prophylaxis of cerebrovascular disease or myocardial infarction

DOSE IN NORMAL RENAL FUNCTION

- Analgesia: 300 mg – 1 g every 4 hours. Maximum 8 g daily in acute conditions
- Prophylaxis of cerebrovascular disease or myocardial infarction: 75–300 mg daily

PHARMACOKINETICS

- Molecular weight (daltons): 180.2
- % Protein binding: 80–90
- % Excreted unchanged in urine:
  - 2 (acidic urine); 30 (alkaline urine)
- Volume of distribution (L/kg): 0.1–0.2

DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)

- 20–50: Dose as in normal renal function. See 'Other Information'
- 10–20: Dose as in normal renal function. See 'Other Information'
- <10: Dose as in normal renal function. See 'Other Information'

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

- CAPD: Dialysed. Dose as in normal renal function
- HD: Dialysed. Dose as in normal renal function
- HDF/High flux: Dialysed. Dose as in normal renal function
- CAV/ VVHD: Dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs:
- ACE inhibitors and angiotensin-II antagonists: antagonism of hypotensive effect, increased risk of nephrotoxicity and hyperkalaemia
- Analgesics: avoid concomitant use of 2 or more NSAIDs, including aspirin – increased side effects; avoid with ketorolac – increased risk of side effects and haemorrhage
- Antibacterials: possibly increased risk of convulsions with quinolones
- Anticoagulants: effects of coumarins enhanced; possibly increased risk of bleeding with heparins and coumarins
- Antidepressants: increased risk of bleeding with SSRIs and venlafaxine
- Antidiabetic agents: effects of sulphonylureas enhanced
- Anti-epileptics: possibly increased phenytoin concentration
- Antivirals: increased risk of haematological toxicity with zidovudine; concentration possibly increased by ritonavir
- Ciclosporin: may potentiate nephrotoxicity
- Cytotoxic agents: reduced excretion of methotrexate; increased risk of bleeding with erlotinib
- Diuretics: increased risk of nephrotoxicity; antagonism of diuretic effect, hyperkalaemia with potassium-sparing diuretics
- Lithium: excretion decreased
- Pentoxifylline: increased risk of bleeding
- Tacrolimus: increased risk of nephrotoxicity

ADMINISTRATION

RECONSTITUTION
- ROUTE
- Oral
- RATE OF ADMINISTRATION
- COMMENTS
- OTHER INFORMATION

- Aspirin at analgesic/antipyretic dose is best avoided in patients with renal impairment, especially if severe
- Antiplatelet effect may add to uraemic gastrointestinal and haematologic symptoms
- Degree of protein binding reduced in ESRD

RETURN TO CONTENTS
Atazanavir

**CLINICAL USE**
Protease inhibitor:
- HIV infection, in combination with other antiretroviral drugs

**DOSE IN NORMAL RENAL FUNCTION**
300 mg once daily with ritonavir 100 mg once daily

**PHARMACOKINETICS**
- Molecular weight: 802.9 (as sulphate) (daltons)
- % Protein binding: 86
- % Excreted unchanged in urine: 7
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 7/no data

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
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<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
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</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapies</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs:
- Anti-arrhythmics: possibly increased plasma levels of amiodarone and lidocaine
- Antibacterials: concentration of both drugs increased when given with clarithromycin; rifabutin concentration increased – reduce dose of rifabutin; rifampicin reduces atazanavir concentration – avoid concomitant use; avoid concomitant use with telithromycin in severe renal and hepatic impairment
- Antidepressants: concentration reduced by St John's wort – avoid concomitant use
- Antimalarials: avoid concomitant administration with artemether/lumefantrine
- Antipsychotics: possibly inhibits metabolism of aripiprazole – reduce dose of aripiprazole; possibly increased concentration of pimozide – avoid concomitant use
- Antivirals: concentration reduced by efavirenz – increase dose of atazanavir; concentration possibly reduced by nevirapine – avoid concomitant use; saquinavir concentration increased; concentration reduced by tenofovir and tenofovir concentration possibly increased; avoid concomitant use with indinavir
- Calcium-channel blockers: concentration of diltiazem increased – reduce dose of diltiazem; possibly increased verapamil concentration
- Ciclosporin: possibly increased concentration of ciclosporin
- Cytotoxics: possibly inhibits metabolism of irinotecan – increased risk of toxicity
- Ergot alkaloids: possibly increased concentration of ergot alkaloids – avoid concomitant use
- Oestrogens: increased concentration of ethinylestradiol – avoid concomitant use
- Sildenafil: possibly increased side effects of sildenafil
- Sirolimus: possibly increased concentration of sirolimus
- Statins: avoid concomitant use with simvastatin – increased risk of myopathy; possibly increased risk of myopathy with atorvastatin
Tacrolimus: possibly increased concentration of tacrolimus
Ulcer-healing drugs: concentration significantly reduced by omeprazole and esomeprazole and possibly other proton pump inhibitors – avoid concomitant use; concentration possibly reduced by histamine H₂ antagonists

ADMINISTRATION

RECONSTITUTION

- ROUTE
  - Oral

RATE OF ADMINISTRATION
  - Take with food

COMMENTS
  - Take didanosine 2 hours after atazanavir if used in combination
Atenolol

**CLINICAL USE**

Beta-adrenoceptor blocker:
- Hypertension, angina, arrhythmias

**DOSE IN NORMAL RENAL FUNCTION**

**Oral:**
- Hypertension: 25–50 mg daily
- Angina: 100 mg daily in 1 or 2 divided doses
- Arrhythmias: 50–100 mg daily

**IV:**
- Arrhythmias: 2.5 mg at a rate of 1 mg/min repeated at 5 minute intervals to a maximum of 10 mg

**Infusion:**
- 150 mcg/kg, repeated every 12 hours if required

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>266.3</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>3</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&gt;90</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1.1</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>6–7/15–35</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Anaesthetics: enhanced hypotensive effect
- Analgesics: NSAIDs antagonise hypotensive effect
- Anti-arrhythmics: increased risk of myocardial depression and bradycardia; increased risk of bradycardia, myocardial depression and AV block with amiodarone
- Antidepressants: enhanced hypotensive effect with MAOIs
- Antihypertensives: enhanced hypotensive effect; increased risk of withdrawal hypertension with clonidine; increased risk of first dose hypotensive effect with post-synaptic alpha-blockers such as prazosin
- Antimalarials: increased risk of bradycardia with mefloquine
- Antipsychotics enhanced hypotensive effect with phenothiazines
- Calcium-channel blockers: increased risk of bradycardia and AV block with diltiazem; hypotension and heart failure possible with nifedipine and nisoldipine; asystole, severe hypotension and heart failure with verapamil
- Diuretics: enhanced hypotensive effect
- Moxisylyte: possible severe postural hypotension
- Sympathomimetics: severe hypertension with adrenaline and noradrenaline and possibly with dobutamine
- Tropisetron: increased risk of ventricular arrhythmias – use with caution

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral, IV

**RATE OF ADMINISTRATION**

- Infusion: 20 minutes
- IV injection: 1 mg/minute

**COMMENTS**

- Dilute with glucose 5% or sodium chloride 0.9%

**OTHER INFORMATION**

- CSM advise that beta-blockers are contraindicated in patients with asthma or history of obstructive airway disease

RETURN TO CONTENTS
ATG (Rabbit) (Thymoglobuline)

**CLINICAL USE**
Prophylaxis and treatment of acute or steroid resistant transplant rejection

**DOSE IN NORMAL RENAL FUNCTION**
Prophylaxis:
- Kidney 1–1.5 mg/kg/day
- Heart 1–2.5 mg/kg/day for 3–9 days
Treatment: 1.5 mg/kg/day for 7–14 days

**PHARMACOKINETICS**
- Molecular weight (daltons): No data
- % Protein binding: No data
- % Excreted unchanged in urine: No data
- Volume of distribution (L/kg): 0.12

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/MIN)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Risk of over-immunosuppression with concomitant prescribing of standard maintenance immunosuppressive regimens

- Safety of immunisation with attenuated live vaccines following Thymoglobuline therapy has not been studied; therefore, immunisation with attenuated live vaccines is not recommended for patients who have recently received ATG

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - IV via central line or via peripheral vein with good blood flow rates

**RATE OF ADMINISTRATION**
- 4–16 hours

**COMMENTS**
- Dilute dose in 250 mL sodium chloride 0.9%, maximum concentration 5 mg/mL for peripheral administration
- To minimise risk of adverse effects, chlorphenamine (10 mg IV) and hydrocortisone (100 mg IV) may be given 15–60 minutes before administration of full dose ATG
- Chlorphenamine, hydrocortisone and adrenaline should be immediately available in case of severe anaphylaxis

**OTHER INFORMATION**
- Aim to keep total lymphocyte count below 3% of total white cell count or 50 cells/µL. Alternatively, keep absolute T cell count below 50 cells/µL, and only dose when above this
- The manufacturers advise that overdosage of Thymoglobuline may result in leucopenia (including lymphopenia and neutropenia) and/or thrombocytopenia.
- The dose of ATG should be reduced by one-half if the WBC count is between 2000 and 3000 cells/mm³ or if the platelet count is between 50 000 and 75 000 cells/mm³.
- Stopping ATG treatment should be considered if the WBC count falls below 2000 cells/mm³ or platelets below 50 000 cells/mm³
- Avoid simultaneous transfusions of blood or blood derivatives and infusions of other solutions, particularly lipids
The recommended route of administration for ATG is IV infusion using a high-flow vein; however, it may be administered through a peripheral vein. In this instance, concomitant use of heparin and hydrocortisone in an infusion solution of 0.9% sodium chloride may minimise the potential for superficial thrombophlebitis and deep vein thrombosis.

The combination of ATG, heparin and hydrocortisone in a dextrose infusion solution has been noted to precipitate and is not recommended.

ATG should not be administered in presence of: fluid overload, allergy to rabbit protein, pregnancy or acute viral illness.

Total rabbit IgG remains detectable in 81% of patients at 60 days. Active ATG (i.e. IgG that is available to bind to human lymphocytes and cause desired immunological effects) disappears from the circulation faster, with only 12% of patients having detectable active ATG levels at day 90.
Atorvastatin

**CLINICAL USE**
Hyperlipidaemia and hypercholesterolaemia

**DOSE IN NORMAL RENAL FUNCTION**
10–80 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 558.6 (1209.4 as calcium salt)
- % Protein binding: >98
- % Excreted unchanged in urine: Negligible
- Volume of distribution (L/kg): 381 litres
- Half-life – normal/ESRF (hrs): 14 (active metabolite)/20–30/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: erythromycin, clarithromycin or fusidic acid possibly increased risk of myopathy; concentration increased by clarithromycin – do not exceed 20 mg of atorvastatin; avoid concomitant use with telithromycin; increased risk of myopathy with daptomycin.
- Anticoagulants: may transiently reduce anticoagulant effect of warfarin
- Antifungals: increased risk of myopathy with itraconazole – do not exceed 40 mg of atorvastatin; posaconazole and possibly other imidazoles and triazoles – avoid concomitant use
- Antivirals: increased risk of myopathy with amprenavir, atazanavir, indinavir, lopinavir, nelfinavir, ritonavir or saquinavir; concentration reduced by efavirenz
- Ciclosporin: increased risk of myopathy – do not exceed 10 mg of atorvastatin.
- Lipid lowering agents: increased risk of myopathy with fibrates, gemfibrozil (avoid) and nicotinic acid

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**
  -

**OTHER INFORMATION**
- Rhabdomyolysis with renal dysfunction secondary to myoglobinemia has been reported with other statins

**References:**
1. MHRA. *Drug Safety Update*. 2008; Jan; 1(6): 2–4
Atovaquone

**CLINICAL USE**
Treatment of PCP if intolerant to co-trimoxazole

**DOSE IN NORMAL RENAL FUNCTION**
750 mg twice daily for 21 days

**PHARMACOKINETICS**
- Molecular weight: 366.8 daltons
- % Protein binding: 99.9
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): 0.62 ± 0.19
- Half-life – normal/ESRF (hrs): 2–3 days/no data

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function. Use with caution

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: rifampicin, rifabutin and tetracyclines reduce levels by 50%
- Metoclopramide: significant reduction in plasma atovaquone levels

**RECONSTITUTION**
- ROUTE: Oral
- RATE OF ADMINISTRATION:
- COMMENTS

**OTHER INFORMATION**
- Administer with food. The presence of food, particularly high fat food, increases bioavailability 2 or 3-fold.
- The most commonly reported abnormalities in laboratory parameters are increased liver function tests and amylase levels, and hyponatraemia
# Atracurium besilate

## CLINICAL USE
Non-depolarising muscle relaxant of short to medium duration

## DOSE IN NORMAL RENAL FUNCTION

<table>
<thead>
<tr>
<th>Duration</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initially:</td>
<td>300–600 mcg/kg, depending on duration of full block required</td>
</tr>
<tr>
<td>Maintenance:</td>
<td>100–200 mcg/kg as required or IV infusion: 300–600 mcg/kg/hour</td>
</tr>
<tr>
<td>Intensive care: Initially,</td>
<td>300–600 mcg/kg then by infusion: 4.5–29.5 mcg/kg/minute (usual dose: 11–13 mcg/kg/minute)</td>
</tr>
</tbody>
</table>

## PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>1243.5</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>82</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>0</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.16</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>Approx 20 minutes/unchanged</td>
</tr>
</tbody>
</table>

## DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
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</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

## IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs

- Anaesthetics: enhanced effect with volatile liquid general anaesthetics
- Anti-arrhythmics: procainamide enhances muscle relaxant effect
- Antibacterials: aminoglycosides, clindamycin, polymyxin, piperacillin enhance effect of atracurium
- Atracurium enhances the neuromuscular block produced by botulinum toxin (risk of toxicity)

## ADMINISTRATION

### RECONSTITUTION

- **ROUTE**
  - IV bolus, IV infusion
- **RATE OF ADMINISTRATION**
  - IV infusion: Initial bolus dose of 0.3–0.6 mg/kg over 60 seconds, then administer as a continuous infusion at rates of 0.3–0.6 mg/kg/hour
- **COMMENTS**
  - Stable in sodium chloride 0.9% for 24 hours, and glucose 5% for 8 hours when diluted to concentrations of 0.5 mg/mL or above

### DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>
Auranofin

**CLINICAL USE**
Active progressive rheumatoid arthritis in adults when NSAIDs inadequate alone

**DOSE IN NORMAL RENAL FUNCTION**
6 mg daily (maximum 9 mg in 3 divided doses)

**PHARMACOKINETICS**
- Molecular weight (daltons) 678.5
- % Protein binding 60
- % Excreted unchanged in urine 9–17 (approx 60% of absorbed gold)
- Volume of distribution No data
- Half-life – normal/ESRF (hrs) 26 days/

**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**
- 20–50 3–6 mg daily
- 10–20 3 mg daily
- <10 Avoid

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Unknown dialysability. Dose as in GFR<10 mL/min
- HD Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD Not dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  - Take with or after food
  - Start initially with morning and evening dose; if well tolerated, can take dose once a day

**OTHER INFORMATION**
- Warn patients to tell the doctor immediately if any of the following develop: sore throat, mouth ulcers, bruising, fever, malaise, rash, diarrhoea or non-specific illness
- Blood tests should be carried out monthly, and treatment should be withdrawn if the platelets fall below 100 000/mm³, or if signs and symptoms suggestive of thrombocytopenia appear
- Gold can produce nephrotic syndrome or less severe glomerular disease with proteinuria and haematuria, which are usually mild and transient. If persistent or clinically significant proteinuria develops, treatment with gold should be discontinued. Minor transient changes in renal function may also occur
- Urine tests should be carried out monthly to test for proteinuria and haematuria
Azathioprine

CLINICAL USE
Immunosuppressive:
- Prophylaxis of transplant rejection
- Treatment of various auto-immune conditions

DOSE IN NORMAL RENAL FUNCTION
1–5 mg/kg/day

PHARMACOKINETICS
Molecular weight (daltons) 277.3
% Protein binding <30
% Excreted unchanged in urine <2
Volume of distribution (L/kg) 0.55–0.8
Half-life – normal/ESRF (hrs) 3–5/Increased

DOSE IN RENAL IMPAIRMENT
GFR (mL/MIN)
20–50 Dose as in normal renal function
10–20 75–100%
<10 50–100%

DOSE IN PATIENTS UNDERGOING
RENAL REPLACEMENT THERAPIES
CAPD Dialysed. Dose as in normal renal function
HD Dialysed. Dose as in normal renal function
HDF/High flux Dialysed. Dose as in normal renal function
CAV/VVHD Dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Allopurinol: enhances effect with increased toxicity. Reduce azathioprine dose by 50–75% if administered concomitantly
- Antibacterials: increased risk of haematological toxicity with co-trimoxazole
- Anticoagulants: possibly reduced anticoagulant effect of coumarins
- Antipsychotics: avoid concomitant use with clozapine
- Ciclosporin: decreased ciclosporin absorption and bioavailability
- Cytotoxic agents may be additive or synergistic in producing toxicity, particularly on the bone marrow

ADMINISTRATION
RECONSTITUTION
- Add 5 mL water for injection to each vial (50 mg)
ROUTE
- Oral, IV
RATE OF ADMINISTRATION
- Over not less than 1 minute
COMMENTS
- Some units dilute to 100 mL sodium chloride or glucose 5% and infuse over 1 hour. (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006)
- IV bolus peripherally, preferably in the side arm of a fast-running infusion
- Very irritant to veins. Flush with 50 mL sodium chloride 0.9% after administration
- Take tablets with or after food

OTHER INFORMATION
- Extensively metabolised to mercaptopurine
- 1 mg by IV injection is equivalent to 1 mg by oral route
- 6-mercaptopurine levels can be monitored in patients with low urate clearance
- Monitor white cell and platelet counts
- Cytotoxic Drug – Do Not Handle
- Can be given as an intermittent infusion (up to 250 mg in 100 mL)
- About 40–60% is removed by haemodialysis
Azithromycin

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
- Genital chlamydial infections: 1 g as single dose
- All other indications: 500 mg daily for 3 days
- Typhoid (unlicensed): 500 mg daily for 7 days

**PHARMACOKINETICS**
- Molecular weight (daltons): 785
- % Protein binding: 12–52
- % Excreted unchanged in urine: 6–12
- Volume of distribution (L/kg): 31.1

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/MIN)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Unknown dialysability. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: possibly increased rifabutin concentration (increased risk of uveitis) – reduce dose of rifabutin
- Anticoagulants: effect of coumarins may be enhanced
- Antidepressants: the manufacturer of reboxetine advises to avoid concomitant use
- Antihistamines: may inhibit the metabolism of mizolastine (risk of hazardous arrhythmias) – avoid concomitant use
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: possibly increased quetiapine concentration – reduce quetiapine dose; possibly increased risk of ventricular arrhythmias with sertindole – avoid concomitant use
- Antivirals: concentration possibly increased by ritonavir
- Cyclosporin: may inhibit the metabolism of cyclosporin (increased plasma cyclosporin levels)
- Ergot alkaloids: increased risk of ergotism – avoid concomitant use
- Theophylline: possibly increased theophylline concentration

**ADMINISTRATION**

**RECONSTITUTION**
- Powder for oral suspension to be reconstituted with water (200 mg/5 mL strength)

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  - Administer as a once daily dose 1 hour before food or 2 hours after food

RETURN TO CONTENTS
Aztreonam

CLINICAL USE
Antibacterial agent

DOSE IN NORMAL RENAL FUNCTION
- 1 g every 8 hours or 2 g every 12 hours
- Severe infections: 2 g every 6–8 hours
- UTI: 0.5–1 g every 8–12 hours

PHARMACOKINETICS
Molecular weight: 435.4 daltons
% Protein binding: 60%
% Excreted unchanged in urine: 60–70%
Volume of distribution: 0.5–1 L/kg
Half-life – normal/ESRF (hrs): 1.7/6–8

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
- 30–50: Dose as in normal renal function
- 10–30: 1–2 g loading dose, then maintenance of 50% of appropriate normal dose
- <10: 1–2 g loading dose, then maintenance of 25% of appropriate normal dose

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD: Not dialysed. Dose as in GFR<10mL/min
HD: Dialysed. Dose as in GFR<10mL/min
HDF/High flux: Dialysed. Dose as in GFR<10mL/min
CAV/VVH: Dialysed. Loading dose of 2 g then 1–2 g every 12 hours
CVVH/HDF: Dialysed. 2 g every 12 hours

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Possibly enhanced anticoagulant effect of coumarins

ADMINISTRATION
RECONSTITUTION
- 3 mL of water for injection per 1 g vial

ROUTE
- IM, IV bolus, IV infusion

RATE OF ADMINISTRATION
- IM injection: Give by deep injection into a large muscle mass
- IV: Slowly inject directly into the vein over a period of 3–5 minutes
- IV infusion: Give over 20–60 minutes

COMMENTS
- Suitable infusion solutions: glucose 5%, sodium chloride 0.9%, compound sodium lactate
- Dilute to a concentration of not less than 20 mg/mL
- Once reconstituted aztreonam can be stored in a refrigerator for 24 hours
- IV route recommended for single doses >1 g

OTHER INFORMATION
- Manufacturers recommend that patients with renal impairment be given the usual initial dose followed by a maintenance dose adjusted according to creatinine clearance. The normal dose interval should not be altered

References:
1. Dose from CVVH Initial Drug Dosing Guidelines on www.thedrugmonitor.com

RETURN TO CONTENTS
Baclofen

CLINICAL USE
Chronic severe spasticity of voluntary muscles

DOSE IN NORMAL RENAL FUNCTION
5 mg, 3 times a day; increase dose gradually up to 100 mg/day

PHARMACOKINETICS
Molecular weight 213.7 (daltons)
% Protein binding 30
% Excreted unchanged in urine 70
Volume of distribution 0.7 (L/kg)
Half-life – normal/ESRF (hrs) 3–4/

DOSE IN RENAL IMPAIRMENT
GFR (mL/Min)
20–50 5 mg, 3 times a day and titrate according to response
10–20 5 mg, twice a day and titrate according to response
<10 5 mg, once a day and titrate according to response

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unknown dialysability. Dose as in GFR<10 mL/min
HD Dialysed. Dose as in GFR<10 mL/min
HDF/High flux Dialysed. Dose as in GFR<10 mL/min
CAV/ VVHD Unknown dialysability. Dose as in GFR=10–20 mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● Anti-arrhythmics: enhanced muscle relaxant effect with procainamide
● Antidepressants: enhanced muscle relaxant effect with tricyclics
● Antihypertensives: enhanced hypotensive effect

ADMINISTRATION
RECONSTITUTION
–
ROUTE
● Oral, intrathecal injection
RATE OF ADMINISTRATION
–
COMMENTS
● Take with or after food
● Baclofen can be given intrathecally (at doses greatly reduced compared with oral dose), by bolus injection, or continuous infusion. Individual titration of dosage is essential due to variability in response. Test doses must be given. Maintenance dose: 10–2000 micrograms/day

OTHER INFORMATION
● Withdraw treatment gradually over 1–2 weeks to avoid anxiety and confusional state, etc
● Drowsiness and nausea frequent at the start of therapy
● Use with caution as a case report of encephalopathy has been reported in a haemodialysis patient.

References:
Balsalazide sodium

**CLINICAL USE**
Treatment, and maintenance of remission, in mild to moderate ulcerative colitis

**DOSE IN NORMAL RENAL FUNCTION**
Acute treatment: 2.25 g, 3 times a day
Maintenance: 1.5 g twice daily, maximum 6 g/day

**PHARMACOKINETICS**
- Molecular weight: 437.3 daltons
- % Protein binding: 40 (similar to mesalazine), (NASA – 80%)
- % Excreted unchanged in urine: 25 (as metabolites)
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): No data (T½ NASA = 6–9)

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Use with caution and only if necessary
  - <10: Start with low doses and monitor closely

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in GFR<10mL/min
- HD: Unlikely to be dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Unlikely to be dialysed. Dose as in GFR<10mL/min
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**
- RECONSTITUTION
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
- COMMENTS

**OTHER INFORMATION**
- Balsalazide is a prodrug of mesalazine (5-amino-salicylic acid)
- Mesalazine is best avoided in patients with established renal impairment, but if necessary should be used with caution and the patient carefully monitored
- Serious blood dyscrasias have been reported with mesalazine – monitor full blood count closely
- NASA: N-acetylated metabolite
Basiliximab

**CLINICAL USE**
Chimeric murine/human monoclonal anti CD25 antibody:
- Prophylaxis of acute allograft rejection in combination with maintenance immunosuppression

**DOSE IN NORMAL RENAL FUNCTION**
20 mg 2 hours before transplant and 20 mg 4 days after transplant

**PHARMACOKINETICS**
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>Approx 144000</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>See ‘Other Information’</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>No data</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>4.5–12.7 litres</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>4–10.4 days/Unchanged</td>
</tr>
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</table>

**DOSE IN RENAL IMPAIRMENT**
<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
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</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
<table>
<thead>
<tr>
<th>Modality</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Ciclosporin: may alter ciclosporin requirements
- Tacrolimus: may alter tacrolimus requirements

**ADMINISTRATION**

**RECONSTITUTION**
- Reconstitute each vial with 5 mL water for injection then dilute to 50 mL or greater with sodium chloride 0.9% or glucose 5%

**RATE OF ADMINISTRATION**
- 20–30 minutes

**OTHER INFORMATION**
- *In vitro* studies indicate that basiliximab binds only to activated lymphocytes
- Basiliximab is detectable in serum for up to 3 months after 15–25 mg doses
- Use with caution in patients who have previously had basiliximab due to increased risk of developing hypersensitivity reactions
Bemiparin sodium (LMWH)

**CLINICAL USE**
- Prophylaxis of thromboembolic disorders of venous origin
- Treatment of deep vein thrombosis and pulmonary embolism
- Anticoagulation of the extracorporeal circulation during haemodialysis

**DOSE IN NORMAL RENAL FUNCTION**
- Prophylaxis DVT:
  - Moderate risk surgery, 2500 units once daily for 7–10 days
  - High risk surgery, 3500 units once daily for 7–10 days
- Treatment DVT and PE: 115 units/kg every 24 hours for 5–9 days
- Anticoagulation of extracorporeal circuits – see ‘Other Information’

**PHARMACOKINETICS**
- Molecular weight (daltons) 3600 (3000–4200)
- % Protein binding –
- % Excreted unchanged in urine –
- Volume of distribution (L/kg) –
- Half-life – normal/ESRF (hrs) 5–6

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50  Dose as in normal renal function
- 10–20  Dose as in normal renal function for prophylaxis only. See ‘Other Information’
- <10   Dose as in normal renal function for prophylaxis only. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD  Not dialysed. Dose as in GFR<10mL/min
- HD    Not dialysed. Dose as in GFR<10mL/min
- HDF/High flux  Dialysed. Dose as in GFR<10mL/min
- CAV/ VVHD  Not dialysed. Dose as in GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: increased risk of bleeding with NSAIDs – avoid concomitant use with IV diclofenac; increased risk of haemorrhage with ketorolac – avoid concomitant use
- Drotrecogin alfa: manufacturer advises to avoid use of high doses of heparin with drotrecogin alfa
- Nitrate: GTN infusions increase the excretion of bemiparin; anticoagulant effect reduced
- Use with care in patients receiving oral anticoagulants, platelet aggregation inhibitors, aspirin or dextran

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - SC
- RATE OF ADMINISTRATION
  - COMMENTS
  -

**OTHER INFORMATION**
- In extracorporeal circulation during a 4-hour or less haemodialysis session, for patients <60 kg, 2500 units bemiparin is administered into the arterial line of the circuit at the beginning of the session; for patients >60 kg, 3500 units bemiparin is used
- Additional doses may be required if using LMWHs for anticoagulation in HDF
- 1.4 mg of protamine should neutralise the effect of 100 units of bemiparin
- Low molecular weight heparins are renally excreted and hence accumulate in severe renal impairment. While the doses recommended for prophylaxis against DVT and prevention of thrombus formation in extracorporeal circuits are well tolerated in patients with ESRF, the doses recommended for treatment of DVT and PE have been associated with severe, sometimes fatal, bleeding episodes in such patients. Hence the use of unfractionated heparin would be preferable in these instances
Bendroflumethiazide

**CLINICAL USE**

Thiazide diuretic:
- Hypertension
- Oedema

**DOSE IN NORMAL RENAL FUNCTION**

Oedema: 5–10 mg in the morning or alternate days
Maintenance: 5–10 mg, 1–3 times weekly
Hypertension: 2.5 mg daily

**PHARMACOKINETICS**

- Molecular weight (daltons): 421.4
- % Protein binding: 94
- % Excreted unchanged in urine: 30
- Volume of distribution (L/kg): 1.2–1.5

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in normal renal function</th>
<th>Dose as in normal renal function</th>
<th>Unlikely to work</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Unlikely to be dialysed. Unlikely to work.
- HD: Not dialysed. Unlikely to work
- HDF/High flux: Unknown dialysability. Unlikely to work
- CAV/VVHD: Probably not dialysed. Unlikely to work

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Analgesics: increased risk of nephrotoxicity with NSAIDs; antagonism of diuretic effect
- Anti-arrhythmics: hypokalaemia leads to increased cardiac toxicity; effects of lidocaine and mexiletine antagonised
- Antibacterials: avoid administration with lymecycline
- Antidepressants: increased risk of hypokalaemia with reboxetine; enhanced hypotensive effect with MAOIs; increased risk of postural hypotension with tricycles
- Anti-epileptics: increased risk of hyponatraemia with carbamazepine
- Antifungals: increased risk of hypokalaemia with amphotericin
- Antihypertensives: enhanced hypotensive effect; increased risk of first dose hypotension with post-synaptic alpha-blockers like prazosin; hypokalaemia increases risk of ventricular arrhythmias with sotalol
- Antipsychotics: hypokalaemia increases risk of ventricular arrhythmias with amisulpride or sertindole; enhanced hypotensive effect with phenothiazines; hypokalaemia increases risk of ventricular arrhythmias with pimozide – avoid concomitant use
- Atomoxetine: hypokalaemia increases risk of ventricular arrhythmias
- Cardiac glycosides: increased toxicity if hypokalaemia occurs
- Ciclosporin: increased risk of nephrotoxicity and hypomagnesaemia
- Lithium excretion reduced, increased toxicity

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

- **RATE OF ADMINISTRATION**

- **COMMENTS**

**OTHER INFORMATION**

- Monitor for hypokalaemia
- Thiazide diuretics are unlikely to be of use once GFR<30mL/min

RETURN TO CONTENTS
Benzatropine mesilate (benztropine)

**Clinical Use**
- Parkinson’s disease
- Drug-induced extrapyramidal side effects

**DOSE IN NORMAL RENAL FUNCTION**
IV/IM (emergency use): 1–2 mg

**Pharmacokinetics**
- Molecular weight (daltons): 403.5
- % Protein binding: 95
- % Excreted unchanged in urine: Majority (as unchanged drug and metabolites)
- Volume of distribution (L/kg): See ‘Other Information’
- Half-life – normal/ESRF (hrs): See ‘Other Information’

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Start with low doses and adjust according to response</td>
</tr>
<tr>
<td>10–20</td>
<td>Start with low doses and adjust according to response</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Start with low doses and adjust according to response</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR<10mL/min
- HD: Unknown dialysability. Dose as in GFR<10mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10mL/min
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–20mL/min

**Important Drug Interactions**
Potentially hazardous interactions with other drugs:
- Phenothiazines and tricyclic antidepressants: may cause paralytic ileus which can be fatal

**Administration**

**Reconstitution**
- –

**Route**
- IV, IM

**Rate of Administration**
- –

**Comments**
- –

**Other Information**
- Benzatropine pharmacokinetics are not well studied, but the drug apparently is hepatically metabolised to conjugates and may undergo entero-hepatic recycling
- Benzatropine has a cumulative effect and a prolonged duration of action; therefore, treatment should commence with the lowest possible dosage and be titrated according to response
Benzbromarone (unlicensed product)

**CLINICAL USE**
Treatment of hyperuricaemia, chronic gout and tophaceous gout

**DOSE IN NORMAL RENAL FUNCTION**
50–200 mg daily
(Usual dose 50–100 mg daily)

**PHARMACOKINETICS**
- Molecular weight (daltons): 424.1
- % Protein binding: >99%
- % Excreted: 6–18 (as metabolites)
- Volume of distribution (L/kg): 19 litres
- Half-life – normal/ESRF (hrs): 2–4

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
</table>
| 40–60        | 50–200 mg daily
| 20–40        | 50–100 mg daily
| <20          | Avoid. Ineffective

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Avoid. Ineffective</td>
</tr>
<tr>
<td>HD</td>
<td>Avoid. Ineffective</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Avoid. Ineffective</td>
</tr>
<tr>
<td>CAV/</td>
<td>Use with caution. Dose as in GFR=20–40 mL/min</td>
</tr>
<tr>
<td>VVHD</td>
<td>GFR=20–40 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Aspirin and salicylates: antagonise uricosuric effects of benzbromarone
- Anticoagulants: may enhance effect of warfarin
- Pyrazinamide: antagonise uricosuric effects of benzbromarone
- Hepatotoxic agents: enhanced hepatotoxicity

**ADMINISTRATION**
- **RECONSTITUTION**
  - **ROUTE**
    - Oral
  - **RATE OF ADMINISTRATION**
  - **COMMENTS**

**OTHER INFORMATION**
- Monitor LFTs while on benzbromarone as can cause fulminant liver failure
- As with other uricosurics, treatment with benzbromarone should not be started during an acute attack of gout
- Maintain an adequate fluid intake to reduce the risk of uric acid renal calculi
- Biological effect of 100 mg benzbromarone is equivalent to 1.5 g probenecid or greater than 300 mg of allopurinol. (Masbernard A. Ten years’ experience with benzbromarone in the management of gout and hyperuricaemia. SA Medical Journal. 1981, May 9: 701–6.)
- Benzobromarone is considered unsafe in patients with acute porphyria

References:

RETURN TO CONTENTS
Benzylpenicillin

CLINICAL USE
Antibacterial agent

DOSE IN NORMAL RENAL FUNCTION
2.4–14.4 g daily in 4–6 divided doses

PHARMACOKINETICS
Molecular weight (daltons) 334.4
% Protein binding 60
% Excreted unchanged in urine 60–90
Volume of distribution (L/kg) 0.3–0.42
Half-life – normal/ESRF (hrs) 0.5/10

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
20–50 Dose as in normal renal function
10–20 600 mg – 2.4 g every 6 hours depending on severity of infection
<10 600 mg – 1.2 g every 6 hours depending on severity of infection

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Dialysed. Dose as in GFR<10mL/min
HD Dialysed. Dose as in GFR<10mL/min
HDF/High flux Dialysed. Dose as in GFR<10mL/min
CAV/VVHD Dialysed. Dose as in GFR=10–20mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Reduced excretion of methotrexate

ADMINISTRATION
RECONSTITUTION
- IV Bolus: 600 mg in 5 mL water for injection
- IV Infusion: 600 mg in at least 10 mL sodium chloride 0.9%
- IM: 600 mg in 1.6 mL water for injection 600 mg displaces 0.4 mL
ROUTE
- IV Bolus, IV Infusion, IM
RATE OF ADMINISTRATION
- IV bolus: over 3–4 minutes
- IV infusion: over 30–60 minutes
COMMENTS
- IV doses in excess of 1.2 g must be given slowly at minimum rate of 300 mg/minute

OTHER INFORMATION
- Dose in normal renal function: meningitis up to 14.4 g daily; bacterial endocarditis 4.8 g daily
- Maximum dose in severe renal impairment: 4.8 g per day
- 600 mg of benzylpenicillin sodium (1 mega unit) contains 1.68 mmol of sodium
- 600 mg of benzylpenicillin potassium contains 1.7 mmol potassium
- Increased incidence of neurotoxicity in renal impairment (seizures)
- False positive urinary protein reactions may be caused by benzylpenicillin therapy
### Betahistine dihydrochloride

**CLINICAL USE**
Treatment of vertigo, tinnitus and hearing loss associated with Ménière's syndrome

**DOSE IN NORMAL RENAL FUNCTION**
8–16 mg, 3 times a day

**PHARMACOKINETICS**
- Molecular weight: 209.1 (daltons)
- % Protein binding: 0–5
- % Excreted unchanged in urine: 85–90
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 3.4/–

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>8–16 mg, 2–3 times a day</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Type</th>
<th>Dialysability</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Likely dialysability</td>
<td>Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Likely dialysability</td>
<td>Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Likely dialysability</td>
<td>Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Likely dialysability</td>
<td>Dose as in GFR=10–20 mL/min</td>
</tr>
<tr>
<td>VVHD</td>
<td>Likely dialysability</td>
<td>Dose as in GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

### IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- None known

### ADMINISTRATION

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

### OTHER INFORMATION
- Betahistine is rapidly and completely absorbed after oral administration
- It is excreted almost exclusively in the urine as 2-pyridylacetic acid within 24 hours of administration
Betamethasone

**CLINICAL USE**
Corticosteroid:
- Suppression of inflammatory and allergic disorders
- Congenital adrenal hyperplasia

**DOSE IN NORMAL RENAL FUNCTION**
Oral: 0.5–5 mg daily
Injection: 4–20 mg repeated up to 4 times in 24 hours

**PHARMACOKINETICS**
- Molecular weight: 392.5 (daltons)
- % Protein binding: 65
- % Excreted unchanged in urine: 5
- Volume of distribution: 1.4 (L/kg)
- Half-life – normal/ESRF (hrs): 5.5/

**DOSE IN RENAL IMPAIRMENT**
<table>
<thead>
<tr>
<th>GFR (mL/ MIN)</th>
<th>DOSE</th>
</tr>
</thead>
<tbody>
<tr>
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<td>&lt;10</td>
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</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Unknown dialysability. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs

- Antibacterials: metabolism accelerated by rifampicin; metabolism possibly inhibited by erythromycin
- Anticoagulants: efficacy of coumarins may be altered
- Anti-epileptics: metabolism accelerated by carbamazepine, barbiturates, phenytoin and primidone
- Antifungals: increased risk of hypokalaemia with amphotericin – avoid concomitant use; metabolism possibly inhibited by itraconazole and ketoconazole
- Antivirals: concentration possibly increased by ritonavir
- Ciclosporin: rare reports of convulsions in patients on ciclosporin and high-dose corticosteroids
- Cytotoxics: increased risk of haematological toxicity with methotrexate
- Diuretics: enhanced hypokalaemic effects of acetazolamide, loop diuretics and thiazide diuretics
- Vaccines: high-dose corticosteroids can impair immune response to vaccines; avoid concomitant use with live vaccines

**ADMINISTRATION**

**RECONSTITUTION**
- –

**ROUTE**
- Orally, IV, IM, topically

**RATE OF ADMINISTRATION**
- IV bolus: over half to one minute

**COMMENTS**
- Can be added to glucose 5% or sodium chloride 0.9%

**OTHER INFORMATION**
- 750 micrograms betamethasone = 5 mg prednisolone
- Even when applied topically, sufficient corticosteroid may be absorbed to give a systemic effect
- Effects of betamethasone on sodium and water retention are less than those of prednisolone and approximately equal to those of dexamethasone
Betaxolol hydrochloride

**CLINICAL USE**
Beta-adrenoceptor blocker:
- Topical use in glaucoma

**DOSE IN NORMAL RENAL FUNCTION**
Apply twice daily

**PHARMACOKINETICS**
- Molecular weight 343.9 (daltons)
- % Protein binding 50
- % Excreted unchanged in urine 15
- Volume of distribution (L/kg) 5–10

**DOSE IN RENAL IMPAIRMENT**

<table>
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<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
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<tr>
<td>20–50</td>
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<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD** Not dialysed. Dose as in normal renal function
- **HD** Not dialysed. Dose as in normal renal function
- **HDF/High flux** Unknown dialysability. Dose as in normal renal function
- **CAV/VVHD** Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Analgesics: NSAIDs antagonise hypotensive effect
- Anti-arrhythmics: increased risk of myocardial depression and bradycardia; increased risk of bradycardia, myocardial depression and AV block with amiodarone
- Antidepressants: enhanced hypotensive effect with MAOIs
- Antihypertensives: enhanced hypotensive effect; increased risk of withdrawal hypertension with clonidine; increased risk of first dose hypotensive effect with post-synaptic alpha-blockers such as prazosin
- Antimalarials: increased risk of bradycardia with mefloquine
- Antipsychotics: enhanced hypotensive effect with phenothiazines
- Calcium-channel blockers: increased risk of bradycardia and AV block with diltiazem; hypotension and heart failure possible with nifedipine and nisoldipine; astystole, severe hypotension and heart failure with verapamil
- Diuretics: enhanced hypotensive effect
- Moxisylyte: possible severe postural hypotension
- Sympathomimetics: severe hypertension with adrenaline and noradrenaline, and possibly with dobutamine

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Topically

**RATE OF ADMINISTRATION**
- **COMMENTS**
  -

**OTHER INFORMATION**
- Use with caution in patients with asthma, or a history of obstructive airways disease or diabetes
- Systemic absorption may follow topical administration to the eye
Bevacizumab

**CLINICAL USE**
Treatment of metastatic carcinoma of the colon or rectum

**DOSE IN NORMAL RENAL FUNCTION**
5 mg/kg every 14 days

**PHARMACOKINETICS**
- Molecular weight (daltons) 149,000
- % Protein binding: No data
- % Excreted unchanged in urine: No data
- Volume of distribution (L/kg): 0.046
- Half-life – normal/ESRF (hrs): 11–50 days (average 20 days)

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Use with caution See ‘Other Information’</td>
</tr>
<tr>
<td>10–20</td>
<td>Use with caution See ‘Other Information’</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Use with caution See ‘Other Information’</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Use with caution. See ‘Other Information’
- HD: Not dialysed. Use with caution. See ‘Other Information’
- HDF/High flux: Not dialysed. Use with caution. See ‘Other Information’
- CAV/VVHD: Not dialysed. Use with caution. See ‘Other Information’

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - IV infusion
- **RATE OF ADMINISTRATION**
  - 30–90 minutes depending on how the patient tolerates it

**COMMENTS**
- Dilute in 100 mL of sodium chloride 0.9%
- DO NOT mix with glucose solutions

**OTHER INFORMATION**
- Increased incidence of hypertension has been seen with treatment
- People with a history of hypertension may be at an increased risk of proteinuria. Discontinue therapy in patients with Grade 4 proteinuria (nephrotic syndrome)
- Can delay wound healing
- Bevacizumab has been used in a haemodialysis patient at a dose of 5 mg/kg every 14 days. (Garnier-Viogeat N, Rixe O, Paintaud G, et al. Pharmacokinetics of bevacizumab in haemodialysis. *Nephrol Dial Transplant*. 2007; 22: 975)
Bezafibrate

CLINICAL USE
Hyperlipidaemia

DOSE IN NORMAL RENAL FUNCTION
200 mg, 3 times a day
Modified release: 400 mg daily

PHARMACOKINETICS
Molecular weight (daltons) 361.8
% Protein binding 95
% Excreted unchanged in urine 50
Volume of distribution (L/kg) 0.24–0.35
Half-life – normal/ESRF (hrs) 1–2 (XL: 3.4)/7.8–20

DOSE IN RENAL IMPAIRMENT
GFR (mL/Min)
40–60 400 mg daily
15–40 200 mg every 24–48 hours
<15 Avoid

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Not dialysed. 200 mg every 72 hours
HD Not dialysed. 200 mg every 72 hours
HDF/High flux Unknown dialysability. 200 mg every 72 hours
CAV/ VVHD Unknown dialysability. Dose as in

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Antibacterials: increased risk of myopathy with daptomycin – try to avoid concomitant use
- Anticoagulants: enhances effect of coumarins and phenindione; dose of anticoagulant should be reduced by up to 50% and adjusted by monitoring INR
- Antidiabetics: may improve glucose tolerance and have an additive effect with insulin or sulphonylureas
- Ciclosporin: may increase nephrotoxicity and reduce ciclosporin levels
- Lipid-regulating drugs: increased risk of myopathy in combination with statins and ezetimibe – avoid with ezetimibe; do not exceed 10 mg of simvastatin

ADMINISTRATION
RECONSTITUTION
- ROUTE
- Oral
RATE OF ADMINISTRATION
- COMMENTS
- OTHER INFORMATION
- Take dose with or after food
- Contraindicated in nephrotic syndrome
- There should be an interval of 2 hours between intake of ion exchange resin and bezafibrate
- Modified-release preparation is not appropriate in renal impairment

References:
1. MHRA. Drug Safety Update. 2008, Jan; 1(6): 2–4
Bicalutamide

**CLINICAL USE**
Treatment of prostate cancer

**DOSE IN NORMAL RENAL FUNCTION**
50–150 mg daily
(with orchidectomy or gonadorelin therapy)

**PHARMACOKINETICS**
- Molecular weight (daltons): 430.4
- % Protein binding: 96
- % Excreted unchanged in urine: approx 50
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 6–7 days/Unchanged

**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Cisapride: avoid concomitant use
- See ‘Other Information’

**ADMINISTRATION**
- RECONSTITUTION
  - ROUTE
    - Oral
  - RATE OF ADMINISTRATION
    - COMMENTS
    -

**OTHER INFORMATION**
- In vitro studies have shown that bicalutamide is an inhibitor of CYP450 3A4. For drugs eliminated by this route, e.g. ciclosporin, tacrolimus, sirolimus, it is recommended that plasma concentrations and clinical condition be monitored following initiation or cessation of bicalutamide therapy.
Bisacodyl

CLINICAL USE
Laxative

DOSE IN NORMAL RENAL FUNCTION
Oral: 5–10 mg at night
Rectal: 10 mg in the morning
Bowel evacuation: 10–20 mg orally at night followed by 10 mg as suppositories the next morning

PHARMACOKINETICS
Molecular weight: 361.4 daltons
% Protein binding: Negligible
% Excreted unchanged in urine: 30
Volume of distribution (L/kg): See ‘Other Information’
Half-life – normal/ESRF (hrs): See ‘Other Information’

DOSE IN RENAL IMPAIRMENT
GFR (mL/Min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unknown dialysability. Dose as in normal renal function
HD Unknown dialysability. Dose as in normal renal function
HDF/High flux Unknown dialysability. Dose as in normal renal function
CAV/HD Unknown dialysability. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● None known

ADMINISTRATION
RECONSTITUTION
–
ROUTE
● Oral, rectal
RATE OF ADMINISTRATION
–
COMMENTS
–

OTHER INFORMATION
● Absorption is <5% orally or rectally
● Rapidly converted in the gut (by intestinal and bacterial enzymes) to its active, but non-absorbed, desacetyl metabolite
Bisoprolol fumarate

**CLINICAL USE**
Beta-1 adrenocceptor blocker:
- Hypertension, angina
- Adjunctive treatment for heart failure

**DOSE IN NORMAL RENAL FUNCTION**
5–20 mg daily
Heart failure: 1.25 mg daily increasing to 10 mg daily

**PHARMACOKINETICS**
Molecular weight (daltons) 767
% Protein binding 30
% Excreted unchanged in urine 50
Volume of distribution (L/kg) 3.5
Half-life – normal/ESRF (hrs) 9–12/18–24

**DOSE IN RENAL IMPAIRMENT**
GFR (mL/Min)

- 20–50  Dose as in normal renal function
- 10–20  Dose as in normal renal function
- <10   Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
CAPD  Not dialysed. Dose as in normal renal function
HD   Not dialysed. Dose as in normal renal function
HDF/High flux  Unknown dialysability. Dose as in normal renal function
CAV/VVHD  Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Analgesics: NSAIDs antagonise hypotensive effect
- Anti-arrhythmics: increased risk of myocardial depression and bradycardia; increased risk of bradycardia, myocardial depression and AV block with amiodarone
- Antibacterials: concentration reduced by rifampicin
- Antidepressants: enhanced hypotensive effect with MAOIs
- Antihypertensives: enhanced hypotensive effect; increased risk of withdrawal hypertension with clonidine; increased risk of first dose hypotensive effect with post-synaptic alpha-blockers such as prazosin
- Antimalarials: increased risk of bradycardia with mefloquine
- Antipsychotics: enhanced hypotensive effect with phenothiazines
- Calcium-channel blockers: increased risk of bradycardia and AV block with diltiazem; hypotension and heart failure possible with nifedipine and nisoldipine; asystole, severe hypotension and heart failure with verapamil
- Diuretics: enhanced hypotensive effect
- Moxisylyte: possible severe postural hypotension
- Sympathomimetics: severe hypertension with adrenaline and noradrenaline, and possibly with dobutamine

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- Use with caution in patients with chronic obstructive airways disease, asthma or diabetes

RETURN TO CONTENTS
Bivalirudin

CLINICAL USE
Anticoagulant:
- Percutaneous coronary intervention

DOSE IN NORMAL RENAL FUNCTION
Initially bolus of 750 mcg/kg then an infusion of 1.75 mg/kg/hour

PHARMACOKINETICS
- Molecular weight (daltons): 2180.3
- % Protein binding: 0
- % Excreted unchanged in urine: 20
- Volume of distribution (L/kg): 0.1
- Half-life – normal/ESRF (hrs): 13–37 minutes/57 minutes (310 minutes in dialysis patients on non-HD days)

DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Dose as for GFR&lt;10 mL/min</th>
<th>Dose as for GFR&lt;10 mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>Dose as in normal renal function</td>
<td>Dose as for GFR&lt;10 mL/min</td>
<td>Dose as for GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>10–30</td>
<td>Normal bolus dose. Reduce infusion dose by 20% (1.4 mg/kg/hour). See ‘Other Information’</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Normal bolus dose. Reduce infusion dose by 80% and monitor ACT. See ‘Other Information’</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>CAPD</th>
<th>Unknown dialysability. Dose as for GFR&lt;10 mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD</td>
<td>Dialysed. Dose as for GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as for GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as for GFR=10–29 mL/min</td>
</tr>
</tbody>
</table>

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Antiplatelets and anticoagulants: increased risk of bleeding
- Thrombolytics: may increase risk of bleeding complications; enhance effect of bivalirudin

ADMINISTRATION
RECONSTITUTION
- Reconstitute each 250 mg vial with 5 mL water for injection

ROUTE
- IV

RATE OF ADMINISTRATION
- 1.75 mg/kg/hour

COMMENTS
- Further dilute with 50 mL sodium chloride 0.9% or glucose 5% if for infusion
- Stable for 24 hours at room temperature

OTHER INFORMATION
- Monitor ACT in renal impairment
- Can start bivalirudin 30 minutes after stopping unfractionated heparin and 8 hours after stopping LMWH
- No known antidote
- Dose recommendations vary from country to country; doses above are from New Zealand
- UK doses:
  - GFR=30–59 mL/min: reduce dose by 20%
  - GFR<30 mL/min: contraindicated
- USA doses:
  - Normal dose: 1 mg/kg bolus then 2.5 mg/kg infusion
  - GFR=30–59 mL/min: reduce dose by 20%
  - GFR=10–29 mL/min: reduce dose by 60%
  - Dialysis dependent: reduce dose by 90%
- Lobo BL. Use of newer anticoagulants in patients with chronic kidney disease.
  *Am J Health-Syst Pharm.* 2007, Oct 1; 64: 2017–26:
  - GFR=30–50 mL/min: 1.75 mg/kg/hour
  - GFR<30 mL/min: 1 mg/kg/hour
  - On haemodialysis: 0.25 mg/kg/hour
Bleomycin

**CLINICAL USE**

Antineoplastic agent

**DOSE IN NORMAL RENAL FUNCTION**

Squamous cell carcinoma and testicular teratoma:
- range 45–60 × 10^3 IU per week IM/IV (total cumulative dose up to 500 × 10^3 IU)
- OR, continuous IV infusion 15 × 10^3 IU/24 hours for up to 10 days
- OR, 30 × 10^3 IU/24 hours for up to 5 days

Malignant lymphomas:
- 15–30 × 10^3 IU/week IM to total dose of 225 × 10^3 IU Lower doses required in combination chemotherapy

Malignant effusions:
- 60 × 10^3 IU in 100 mL sodium chloride 0.9% intrapleurally (total cumulative dose of 500 × 10^3 IU)

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>Approximately 1500</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>&lt;1</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>60–70</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.3</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>4 (bolus), 9 (continuous infusion)/20</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>75% of normal dose (100% for malignant effusions)</td>
</tr>
<tr>
<td>10–20</td>
<td>50% of normal dose (100% for malignant effusions)</td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Antipsychotics: avoid concomitant use with clozapine, increased risk of agranulocytosis
- Cytotoxics: increased pulmonary toxicity with cisplatin; in combination with vinca alkaloids can lead to Raynaud’s syndrome and peripheral ischaemia

**ADMINISTRATION**

**RECONSTITUTION**
- IM: dissolve required dose in up to 5 mL sodium chloride 0.9% (or 1% solution of lidocaine if pain on injection)
- IV: dissolve dose in 5–200 mL sodium chloride 0.9%
- Intracavitary: 60 × 10^3 IU in 100 mL sodium chloride 0.9%
- Locally: dissolve in sodium chloride 0.9% to make a 1–3 ×10^3 IU/mL solution

**ROUTE**
- IM, IV, also intra-arterially, intrapleurally, intraperitoneally, locally into tumour

**RATE OF ADMINISTRATION**
- Give by slow IV injection, or add to reservoir of a running IV infusion

**OTHER INFORMATION**
- Lesions of skin and oral mucosa common after full course of bleomycin
- Pulmonary toxicity: interstitial pneumonia and fibrosis – most serious delayed effect
- In patients with moderately severe renal impairment less than 20% of the dose is excreted in the urine
- Rapid distribution to body tissues (highest concentration is in skin, lungs, peritoneum and lymph)
- Inactivation takes place primarily in the liver. Approximately 60–70% of drug is excreted unchanged in the urine, probably by glomerular filtration

RETURN TO CONTENTS
Bortezomib

**CLINICAL USE**
Treatment of multiple myeloma for people who have already tried at least 2 prior therapies and have disease progression

**DOSE IN NORMAL RENAL FUNCTION**
1.3 mg/m² twice weekly for 2 weeks (days 1, 4, 8 and 11) followed by a 10-day rest period

**PHARMACOKINETICS**
- Molecular weight (daltons) 384.2
- % Protein binding 82.9
- % Excreted unchanged in urine Small amount
- Volume of distribution (L/kg) >500 litres
- Half-life – normal/ESRF (hrs) 5–15/unknown

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 30–50 Dose as in normal renal function
  - 10–30 Dose as in normal renal function. Monitor carefully. See 'Other Information'
  - <10 A reduced dose may be required. Monitor carefully

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Unlikely to be dialysed. Dose as in GFR<10mL/min
- HD Unlikely to be dialysed. Dose as in GFR<10mL/min
- HDF/High flux Unknown dialysability. Dose as in GFR<10mL/min
- CAV/ VVHD Unlikely to be dialysed. Dose as in GFR=10–30mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- 3.5 mL sodium chloride 0.9%

**ROUTE**
- IV bolus

**RATE OF ADMINISTRATION**
- 3 to 5 seconds

**COMMENTS**
- Administer within 8 hours of reconstitution

**OTHER INFORMATION**
- Consecutive doses should be at least 72 hours apart
- Normal doses have been used in patients with a GFR of 10–30mL/min but there is an increased risk of adverse effects. (Jagannath S, Barlogie B, Berenson JR, et al. Bortezomib in recurrent and/or refractory multiple myeloma. *Cancer.* 2005; 103(6): 1195–1200)
- Some trials have used doses of 1 mg/m² in patients with a GFR of 10–30mL/min, with similar efficacy and incidence of side effects
- Both hypo- and hyperkalaemia have been reported with bortezomib as has hypophosphataemia and hypomagnesaemia
- There have been incidences of renal impairment, renal colic, proteinuria, dysuria, urinary frequency, urinary hesitation and haematuria
- Anecdotally, has been used at normal doses in a few haemodialysis patients; in some of the patients platelet infusions have been required
- In patients with peripheral neuropathy then bortezomib has a high probability of exacerbating it
Bosentan

**CLINICAL USE**

Treatment of primary arterial pulmonary hypertension (PAH), and PAH secondary to scleroderma without significant interstitial pulmonary disease

**DOSE IN NORMAL RENAL FUNCTION**

62.5–250 mg twice daily

**PHARMACOKINETICS**

- Molecular weight (daltons): 551.6
- % Protein binding: >98
- % Excreted unchanged in urine: <3
- Volume of distribution (L/kg): 18 litres
- Half-life – normal/ESRF (hrs): 5–8/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Not dialysed. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs

- Antibacterials: concentration reduced by rifampicin – avoid concomitant use
- Antidiabetics: increased risk of hepatotoxicity with glibenclamide – avoid concomitant use
- Antifungals: fluconazole, ketoconazole and itraconazole cause large increases in plasma concentrations of bosentan – avoid concomitant use
- Antivirals: ritonavir causes greatly increased bosentan levels – avoid concomitant use
- Ciclosporin: co-administration of ciclosporin and bosentan is contraindicated. When ciclosporin and bosentan are co-administered, initial trough concentrations of bosentan are 30 times higher than normal. At steady state, trough levels are 3–4 times higher than normal. Blood concentrations of ciclosporin decreased by 50%
- Lipid lowering agents: concentration of simvastatin reduced by 45% – monitor cholesterol levels and adjust dose of statin
- Oestrogens and progestogens: may be failure of contraception – use alternative method

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  -
- **COMMENTS**
  -

**OTHER INFORMATION**

- Bosentan should only be used if the systemic systolic blood pressure is >85 mm/Hg
- Treatment with bosentan is associated with a dose-related, modest decrease in haemoglobin concentration
- Bosentan is an inducer of CYP 3A4 and CYP 2C9
- Bosentan has been associated with dose-related elevations in liver aminotransferases
- Side effects include leg oedema and hypotension
Bromocriptine

CLINICAL USE
- Parkinsonism (but not drug-induced extrapyramidal symptoms)
- Endocrine disorders

DOSE IN NORMAL RENAL FUNCTION
- Parkinson’s disease:
  - Week 1: 1–1.25 mg at night
  - Week 2: 2–2.5 mg at night
  - Week 3: 2.5 mg twice daily
  - Week 4: 2.5 mg, 3 times daily
  - then increasing by 2.5 mg every 3–14 days according to response – usual range 10–40 mg daily
- Hypogonadism/galactorrhoea, infertility: 1–1.25 mg at night, increased gradually; usual dose 7.5 mg daily in divided doses (maximum 30 mg daily); infertility without hyperprolactinaemia: 2.5 mg twice daily
- Cyclical benign breast disease and cyclical menstrual disorders: 1–1.25 mg at night increased gradually; usual dose 2.5 mg twice daily
- Acromegaly: 1–1.25 mg at night increased gradually to 5 mg every 6 hours
- Prolactinoma: 1–1.25 mg at night increased gradually to 5 mg every 6 hours (maximum 30 mg daily)

PHARMACOKINETICS
- Molecular weight: 750.7 (as mesilate)
- % Protein binding: 90–96
- % Excreted unchanged in urine: 2.5–5.5
- Volume of distribution (L/kg): 1–3
- Half-life – normal/ESRF (hrs): 8–20

DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>As normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>As normal renal function</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>As normal renal function</td>
<td></td>
</tr>
</tbody>
</table>

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Increased risk of toxicity with bromocriptine and isometheptene or phenylpropanolamine

ADMINISTRATION
- RECONSTITUTION
  - ROUTE: Oral
  - RATE OF ADMINISTRATION
  - COMMENTS
  - Take with food

OTHER INFORMATION
- Hypotensive reactions may occur during the first few days of treatment. Tolerance may be reduced by alcohol
- Digital vasospasm can occur
- Concomitant administration of macrolide antibiotics may elevate bromocriptine levels
Budesonide

CLINICAL USE
- Asthma
- Allergic and vasomotor rhinitis
- Inflammatory skin disorders

DOSE IN NORMAL RENAL FUNCTION
- Inhaler/Turbohaler: 200–1600 micrograms daily in divided doses
- Respules: 1–2 mg twice daily; half doses for maintenance
- Nasal spray: 100 micrograms each nostril twice daily or 200 micrograms each nostril once daily; reduce to 100 micrograms each nostril once daily when symptoms controlled
- Topical preparations: apply 1–2 times daily
- Capsules: 3 mg, 3 times a day, CR: 9 mg once daily
- Enema: 2 mg/100 mL at bedtime

PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>430.5</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>85–90</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>0</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>3</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1.8–2.2 (inhaled), 3–4 (oral)/–</td>
</tr>
</tbody>
</table>

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux: Unlikely to be dialysed. Dose as in normal renal function
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Antifungals: concentration of inhaled budesonide increased by itraconazole and ketoconazole
- Antivirals: concentration of inhaled and intranasal budesonide increased by ritonavir

ADMINISTRATION
- Respules: may be diluted up to 50% with sterile sodium chloride 0.9%
- Inhalation, topical, oral

OTHER INFORMATION
- Special care is needed in patients with quiescent lung tuberculosis, fungal and viral infections in the airways
# Bumetanide

## CLINICAL USE
Loop diuretic

## DOSE IN NORMAL RENAL FUNCTION
- **Oral:** 1–10 mg daily, may be given in 2 divided doses
- **Injection:** IV 1–2 mg repeated after 20 minutes; IM if necessary, 1 mg then adjust according to response
- **IV infusion:** 2–5 mg over 30–60 minutes

## PHARMACOKINETICS
- **Molecular weight (daltons):** 364.4
- **% Protein binding:** 95
- **% Excreted unchanged in urine:** 50
- **Volume of distribution (L/kg):** 0.2–0.5
- **Half-life – normal/ESR (hrs):** 0.75–2.6/1.5

## DOSE IN RENAL IMPAIRMENT GFR (mL/Min)
<table>
<thead>
<tr>
<th>GFR</th>
<th>Dose</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
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</tbody>
</table>

## DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
<td></td>
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<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in normal renal function</td>
<td></td>
</tr>
</tbody>
</table>

## IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Analgesics: increased risk of nephrotoxicity with NSAIDs; antagonism of diuretic effect with NSAIDs
- Anti-arrhythmics: risk of cardiac toxicity with anti-arrhythmics if hypokalaemia occurs; effects of lidocaine and mexiletine antagonised
- Antibacterials: increased risk of ototoxicity with aminoglycosides, polymyxins and vancomycin; avoid concomitant use with lymecycline
- Antidepressants: increased risk of hypokalaemia with reboxetine; enhanced hypotensive effect with MAOIs; increased risk of postural hypotension with tricyclics
- Anti-epileptics: increased risk of hyponatraemia with carbamazepine
- Antifungals: increased risk of hypokalaemia with amphotericin
- Antihypertensives: enhanced hypotensive effect; increased risk of first dose hypotensive effect with alpha-blockers; increased risk of ventricular arrhythmias with sotalol if hypokalaemia occurs
- Antipsychotics: increased risk of ventricular arrhythmias with amisulpride, serontide or pimozide if hypokalaemia occurs – avoid with pimozide; enhanced hypotensive effect with phenothiazines
- Atomoxetine: increased risk of ventricular arrhythmias if hypokalaemia occurs
- Cardiac glycosides: increased toxicity if hypokalaemia occurs
- Lithium: risk of toxicity

## ADMINISTRATION

### RECONSTITUTION
- **Route:** Oral, IV, IM
- **RATE OF ADMINISTRATION**
  - **IV infusion:** 2–5 mg in 500 mL of infusion fluid over 30–60 minutes
  - **IV bolus:** 1–2 mg over 3–4 minutes

### COMMENTS
- Compatible with glucose 5% or sodium chloride 0.9%

## OTHER INFORMATION
- 1 mg bumetanide = 40 mg furosemide at low doses, but avoid direct substitution at high doses
- In patients with severe chronic renal failure given high doses of bumetanide there are reports of musculoskeletal pain and muscle spasm
- Oral: diuresis begins within 30 minutes, peaks after 1–2 hours, lasts 3 hours
- IV: diuresis begins within few minutes and ceases in about 2 hours
- Use with caution in patients receiving nephrotoxic or otoxic drugs
- Smaller doses may be sufficient in the elderly and cirrhotics (500 micrograms)
- Use twice daily for higher doses
Buprenorphine

**CLINICAL USE**

Opioid analgesic

**DOSE IN NORMAL RENAL FUNCTION**

Sublingual: 200–400 mcg every 6–8 hours
IM, Slow IV: 300–600 mcg every 6–8 hours
Transdermal:
Transtec: 35–140 mcg/hour every 96 hours
Butrans: 5–40 mcg/hour, change patch every 7 days

**PHARMACOKINETICS**

| Molecular weight (daltons) | 467.6 |
| % Protein binding | 96 |
| % Excreted unchanged in urine | Minimal |
| Volume of distribution (L/kg) | 2.5 |
| Half-life – normal/ESRF (hrs) | 20–25 (Transdermal 30 hours)/Unchanged |

**DOSE IN RENAL IMPAIRMENT**

| GFR (mL/min) | Dose as in normal renal function |
| 20–50 | |
| 10–20 | |
| <10 | Reduce dose by 25–50% initially and increase as tolerated; avoid very large single doses |

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

| CAPD | Dialysed. Dose as in GFR<10mL/min |
| HD | Dialysed. Dose as in GFR<10mL/min |
| HDF/High flux | Dialysed. Dose as in GFR<10mL/min |
| CAV/VVHD | Not dialysed. Dose as in GFR=10–20mL/min |

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- **Antidepressants:** possible CNS excitation or depression (hypotension or hypertension) if administered with MAOIs or moclobemide – avoid concomitant use; sedative effects possibly increased when given with tricyclics
- **Antifungals:** metabolism inhibited by ketoconazole – reduce buprenorphine dose
- **Sodium oxybate:** avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Sublingual, IM, IV, transdermal

**RATE OF ADMINISTRATION**

- **COMMENTS**

**OTHER INFORMATION**

- It may take up to 30 hours for plasma buprenorphine concentration to decrease by 50% after the Transtec or Butrans patch has been removed
- Do not give another opiate for 24 hours after the Transtec or Butrans patch has been removed
- Naloxone 5–12 mg may reverse the effects of Transtec or Butrans but the effect may be delayed by 30 minutes
- Patches are not suitable for acute pain
Bupropion hydrochloride (amfebutamone HCl)

**CLINICAL USE**
Adjunct to smoking cessation

**DOSE IN NORMAL RENAL FUNCTION**
150 mg once daily for 6 days, then twice daily

**PHARMACOKINETICS**
- Molecular weight (daltons) 276.2
- % Protein binding 84
- % Excreted unchanged in urine 0.5
- Volume of distribution (L/kg) 2000 litres
- Half-life – normal/ESRF (hrs) 14–20

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50 150 mg daily
  - 10–20 150 mg daily
  - <10 150 mg daily

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Not dialysed. Dose as in GFR<10 mL/min
- HD Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux Not dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD Unlikely to be dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antidepressants: avoid MAOIs and linezolid with and for 2 weeks before starting treatment; avoid concomitant treatment with moclobemide; possibly increased citalopram concentration
- Antivirals: concentration increased by ritonavir, risk of toxicity – avoid concomitant use
- Ciclosporin: may reduce ciclosporin levels

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**
- Bupropion and metabolites may accumulate in renal failure

RETURN TO CONTENTS
Buspirone hydrochloride

**CLINICAL USE**

Anxiolytic

**DOSE IN NORMAL RENAL FUNCTION**

Initially 5 mg 2–3 times daily. Usual range 15–30 mg daily in divided doses (maximum 45 mg daily)

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>422</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>95</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>0</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>2.69–7.91</td>
</tr>
</tbody>
</table>
| Half-life – normal/ESRF (hrs)   | 2–11/Increased by 2 hours

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Reduce by 25–50% if patient is anuric</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
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<tr>
<td>10–20</td>
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<tr>
<td>&lt;10</td>
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</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
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<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

- Antifungals: concentration increased by itraconazole – reduce dose
- Antipsychotics: enhanced sedative effects; haloperidol concentration increased
- Antivirals: concentration increased by ritonavir, increased risk of toxicity
- Calcium-channel blockers: concentration increased by diltiazem and verapamil – reduce dose
- Grapefruit juice: concentration increased by grapefruit juice – reduce dose

**ADMINISTRATION**

**RECONSTITUTION**

- –

**ROUTE**

- Oral

**RATE OF ADMINISTRATION**

- –

**COMMENTS**

- –

**OTHER INFORMATION**

- Peak plasma levels occur 60–90 minutes after dosing
- Steady state plasma concentrations achieved within 2 days, although response to treatment may take 2 weeks
- Non-sedative
- Do not use in patients with severe hepatic disease
- Use in severe renal impairment not recommended; risk of accumulation of active metabolites

References:


RETURN TO CONTENTS
Busulfan

CLINICAL USE
- Chronic myeloid leukaemia
- Remission of polycythaemia vera
- Essential thrombocythaemia and myelofibrosis
- Conditioning before bone marrow transplantation

DOSE IN NORMAL RENAL FUNCTION
Oral:
- Chronic myeloid leukaemia: 60 mcg/kg daily (maximum 4 mg daily); maintenance: 0.5–2 mg daily
- Polycythaemia vera: 4–6 mg daily; maintenance: 2–3 mg daily
- Myelofibrosis: 2–4 mg daily
- IV infusion:
- Conditioning before bone marrow transplantation: 0.8 mg/kg every 6 hours over 4 days for 16 doses

PHARMACOKINETICS
Molecular weight (daltons) 246.3
% Protein binding 7–32
% Excreted unchanged in urine 1–2
Volume of distribution (L/kg) 0.62–0.85
Half-life – normal/ESRF (hrs) 3/–

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unknown dialysability. Dose as in normal renal function
HD Dialysed. Dose as in normal renal function
HDF/High flux Dialysed. Dose as in normal renal function
CAV/VVHD Unknown dialysability. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Antibacterials: concentration increased by metronidazole
- Antipsychotics: avoid concomitant use with clozapine, increased risk of agranulocytosis
- Antifungals: metabolism inhibited by itraconazole, monitor for signs of busulfan toxicity

ADMINISTRATION
RECONSTITUTION
–
ROUTE
- Oral, IV infusion
RATE OF ADMINISTRATION
- Over 2 hours
COMMENTS
- Dilute the solution to 500 mcg/mL with sodium chloride or glucose 5%
- Give via a central venous catheter

OTHER INFORMATION
- Can cause haemorrhagic cystitis
- Can cause an increase in creatinine and haematuria
Cabergoline

**CLINICAL USE**
- Endocrine disorders
- Adjunct to levodopa (with a decarboxylase inhibitor) in Parkinson's disease
- Inhibition/suppression of lactation

**DOSE IN NORMAL RENAL FUNCTION**
- Parkinson's disease: 2–6 mg daily
- Hyperprolactinaemic disorders: 0.25–2 mg weekly
- Inhibition of lactation: single 1 mg dose during first day post partum
- Suppression of lactation: 0.25 mg twice a day for 2 days

**PHARMACOKINETICS**
- Molecular weight (daltons) 451.6
- % Protein binding 41–42
- % Excreted unchanged in urine 2–3
- Volume of distribution (L/kg) No data
- Half-life – normal/ESRF (hrs) 63–68 (healthy individuals), 79–115 (hyperprolactinaemic individuals)/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50 Dose as in normal renal function
  - 10–20 Dose as in normal renal function
  - <10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Dialysed. Dose as in normal renal function
- HD Dialysed. Dose as in normal renal function
- HDF/High flux Dialysed. Dose as in normal renal function
- CAV/VVHD Dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - None known

**ADMINISTRATION**
- RECONSTITUTION
  - ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - COMMENTS
  -

**OTHER INFORMATION**
- 18% of radiolabelled dose is excreted as inactive metabolites in urine
- 72% of dose is excreted in faeces
Calcitonin (salmon)/salcatonin

**CLINICAL USE**
- Hypercalcaemia of malignancy
- Paget's disease of bone
- Post-menopausal osteoporosis
- Prevention of acute bone loss due to sudden immobility

**DOSE IN NORMAL RENAL FUNCTION**
- Hypercalcaemia of malignancy: 100–400 units every 6–8 hours (SC/IM); in severe or emergency situation, up to 10 units/kg by IV infusion
- Paget's disease of bone: 50 units 3 times a week to 100 units daily (SC/IM)
- Post-menopausal osteoporosis: 200 units (1 spray) into 1 nostril daily with calcium and vitamin D supplements
- Prevention of acute bone loss due to sudden immobility: 100 units daily in 1–2 divided doses for 2–4 weeks then reduce to 50 units daily until fully mobile (SC/IM)

**PHARMACOKINETICS**
- Molecular weight (daltons): 3431.9
- % Protein binding: 30–40
- % Excreted unchanged in urine: Minimal
- Volume of distribution (L/kg): 9.9 litres
- Half-life – normal/ESRF (hrs): 50–90 minutes (parenteral); 16–43 minutes (intranasal)/Increased

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAP: Unlikely to be dialysed. Dose as in normal renal function
- HD: Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux: Unlikely to be dialysed. Dose as in normal renal function
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**
- RECONSTITUTION
  - ROUTE: Intranasal, IM, IV, SC
  - RATE OF ADMINISTRATION: Over at least 6 hours
  - COMMENTS: Dilute in 500 ml sodium chloride 0.9% and administer immediately; dilution may result in a loss of potency

**OTHER INFORMATION**
- Peak plasma concentration occurs 30–40 minutes after intranasal administration, and 15–25 minutes after parenteral administration
- Mainly GI side effects
Calcitriol

**CLINICAL USE**
Vitamin D analogue:
- Promotes intestinal calcium absorption
- Suppresses PTH production and release

**DOSE IN NORMAL RENAL FUNCTION**
- Orally: 250 nanograms daily or on alternate days, increased if necessary in steps of 250 nanograms at intervals of 2–4 weeks. Usual dose 0.5–1 micrograms daily
- IV: treatment of hyperparathyroidism in haemodialysis patients: initially 500 nanograms (10 nanograms/kg) 3 times a week, increased if necessary in steps of 250–500 nanograms at intervals of 2–4 weeks. Usual dose 0.5–3 micrograms 3 times a week after dialysis

**PHARMACOKINETICS**
- Molecular weight (daltons) 416.6
- % Protein binding 99.9
- % Excreted unchanged in urine 7–10
- Volume of distribution (L/kg) No data
- Half-life – normal/ESRF (hrs) 9–10/18–20

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function. Titrate to response</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
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<tr>
<td>10–20</td>
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<tr>
<td>&lt;10</td>
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</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Not dialysed. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- The effects of vitamin D may be reduced in patients taking barbiturates or anticonvulsants
- Increased risk of hypercalcaemia if thiazides given with vitamin D

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
- Oral, IV

**RATE OF ADMINISTRATION**
- Bolus

**COMMENTS**
- Other Information
  - Check plasma calcium concentrations at regular intervals (initially weekly)
  - Dose of phosphate-binding agent may need to be modified as phosphate transport in the gut and bone may be affected
  - Hypercalcaemia and hypercalciuria are the major side effects, and indicate excessive dosage
Calcium acetate

**CLINICAL USE**
Phosphate binding agent

**DOSE IN NORMAL RENAL FUNCTION**
1–4 tablets, 3 times daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
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<th>Value</th>
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<tbody>
<tr>
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<td>% Protein binding</td>
<td>–</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>–</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>–</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
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</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose as in normal renal function.</th>
<th>Titrate to response</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
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<tr>
<td>10–20</td>
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<tr>
<td>&lt;10</td>
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</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability.</td>
</tr>
<tr>
<td>HD</td>
<td>Unknown dialysability.</td>
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<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability.</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unknown dialysability.</td>
</tr>
<tr>
<td>VVHD</td>
<td>Unknown dialysability.</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Can impair absorption of some drugs, e.g. iron, ciprofloxacin

**ADMINISTRATION**

**RECONSTITUTION**
- 
**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 
**COMMENTS**
- Take tablets with meals

**OTHER INFORMATION**

- Calcium acetate (anhydrous): calcium content per gram = 250 mg (6.2 mmol)

RETURN TO CONTENTS
Calcium carbonate

**CLINICAL USE**
- Phosphate binding agent
- Calcium supplement

**DOSE IN NORMAL RENAL FUNCTION**
Dose adjusted according to serum phosphate and calcium levels

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
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<td>% Protein binding</td>
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<tr>
<td>% Excreted unchanged in urine</td>
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<tr>
<td>Volume of distribution (L/kg)</td>
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</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
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</table>

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function. Titrating to response</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function. Titrating to response</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function. Titrating to response</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Renal Replacement Therapy</th>
<th>Dose Recommendation</th>
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<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
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</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Can impair absorption of some drugs, e.g. iron, ciprofloxacin

**ADMINISTRATION**

**RECONSTITUTION**
- Oral

**RATE OF ADMINISTRATION**
-

**COMMENTS**
- Take with or immediately before meals

**OTHER INFORMATION**
- Monitor for hypercalcaemia particularly if patient is also taking alfacalcidol
- Calcichew contains 1250 mg calcium carbonate (500 mg elemental calcium)
- Calcium 500 contains 1250 mg calcium carbonate (500 mg elemental calcium)
- Cacit contains 1250 mg calcium carbonate (500 mg elemental calcium)
Calcium gluconate

CLINICAL USE
Hypocalcaemia

DOSE IN NORMAL RENAL FUNCTION
Depending on indication
Acute hypocalcaemia: 10–20mL calcium gluconate 10% (2.25–4.5 mmol calcium) slow IV injection over 3–10 minutes
Oral: Dose varies depending on requirements

PHARMACOKINETICS
Molecular weight 448.4 (daltons)
% Protein binding –
% Excreted – unchanged in urine
Volume of distribution –
(L/kg)
Half-life – normal/ESRF (hrs) –

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
20–50 Dose as in normal renal function. Titrate to response
10–20 Dose as in normal renal function. Titrate to response
<10 Dose as in normal renal function. Titrate to response

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Dialysed. Dose as in normal renal function
HD Dialysed. Dose as in normal renal function
HDF/High flux Dialysed. Dose as in normal renal function
CAV/VVHD Dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● Can impair absorption of some drugs, e.g. iron, ciprofloxacin

ADMINISTRATION
RECONSTITUTION
● –
ROUTE
● Oral, IV, IM
RATE OF ADMINISTRATION
● IV: slow 3–4 minutes for each 10mL (2.25mmol calcium); not greater than 20mmol/hour for continuous infusions

COMMENTS
● IV: Can be used undiluted for continuous and intermittent infusions (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006)

OTHER INFORMATION
● Check patient’s magnesium levels
● Monitor calcium and PO₄ serum levels
● Calcium-Sandoz 400: 10mmol calcium per tablet
● Calcium-Sandoz 1000: 25 mmol calcium per tablet
● Calcium levels cannot be corrected until magnesium levels are normal
### Calcium Resonium

#### CLINICAL USE
Hyperkalaemia (not for emergency treatment)

#### DOSE IN NORMAL RENAL FUNCTION
Oral: 15 g 3–4 times daily in water
PR: 30 g in methylcellulose solution retained for 9 hours

#### PHARMACOKINETICS

| Molecular weight (daltons) | – |
| % Protein binding | – |
| % Excreted unchanged in urine | 0 |
| Volume of distribution (L/kg) | – |
| Half-life – normal/ESRF (hrs) | – |

#### DOSE IN RENAL IMPAIRMENT GFR (mL/Min)

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function. Titrate to response</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
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<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

#### IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- None known

#### ADMINISTRATION

##### RECONSTITUTION
- PR: Mix with methylcellulose solution 2%
- Oral: Mix with a little water, sweetened if preferred

##### ROUTE
- Oral or PR

##### RATE OF ADMINISTRATION
- –

##### COMMENTS
- –

#### OTHER INFORMATION
- Ensure a regular laxative is prescribed – can mix Calcium Resonium powder with lactulose to be taken orally
- Some units mix dose with a little water and give PR 4 times/day. Not retained for so long, but still effective
- Calcium Resonium is not absorbed
Candesartan cilexetil

**CLINICAL USE**

Angiotensin-II antagonist:
- Hypertension
- Heart failure

**DOSE IN NORMAL RENAL FUNCTION**

2–32 mg daily

**PHARMACOKINETICS**

- Molecular weight (daltons) 610.7
- % Protein binding >99
- % Excreted unchanged in urine 26
- Volume of distribution (L/kg) 0.1
- Half-life – normal/ESRF (hrs) 9/18

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
<th>Initial dose 2 mg and increase according to response</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td>Initial dose 2 mg and increase according to response</td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
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</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD** Unlikely to be dialysed. Dose as for GFR<10 mL/min
- **HD** Not dialysed. Dose as for GFR<10 mL/min
- **HDF/High flux** Not dialysed. Dose as for GFR<10 mL/min
- **CAV/VVHD** Unlikely to be dialysed. Dose as for GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**

- Analgesics: antagonism of hypotensive effect and increased risk of renal impairment with NSAIDs; hyperkalaemia with ketorolac and other NSAIDs
- Ciclosporin: increased risk of hyperkalaemia and nephrotoxicity
- Diuretics: enhanced hypotensive effect; hyperkalaemia with potassium-sparing diuretics
- Epoetin: increased risk of hyperkalaemia; antagonism of hypotensive effect
- Lithium: reduced excretion, possibility of enhanced lithium toxicity
- Potassium salts: increased risk of hyperkalaemia.
- Tacrolimus: increased risk of hyperkalaemia and nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
- **RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**

- In patients with mild–moderate renal impairment $C_{\text{max}}$ and AUC are increased by 50% and 70% respectively. Corresponding changes in patients with severe renal impairment are 50% and 110% respectively
- Adverse reactions, especially hyperkalaemia, are more common in patients with renal impairment
- Renal failure has been reported in association with angiotensin-II antagonists in patients with renal artery stenosis, post renal transplant, and in those with congestive heart failure
- Close monitoring of renal function during therapy is necessary in those with renal insufficiency

*It is not licensed for use by anyone else.*
Capecitabine

**CLINICAL USE**
Antineoplastic agent (antimetabolite):  
- Colorectal, colon and breast cancer

**DOSE IN NORMAL RENAL FUNCTION**
1.25g/m² twice daily for 14 days, repeated after 7 days

**PHARMACOKINETICS**
- Molecular weight: 359.4 daltons  
- % Protein binding: 54  
- % Excreted unchanged in urine: 3  
- Volume of distribution (L/kg): No data  
- Half-life – normal/ESRF (hrs): 0.85/Increased

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 30–50: 75% of dose (950mg/m² twice daily) use with care  
  - 10–30: Avoid  
  - <10: Avoid

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR<10mL/min  
- HD: Unlikely to be dialysed. Dose as in GFR<10mL/min  
- HDF/High flux: Unknown dialysability. Dose as in GFR<10mL/min  
- CAV/ VVHD: GFR=10–30mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs:
- Allopurinol: avoid concomitant use  
- Anticoagulants: possibly enhances effect of coumarins  
- Anti-epileptics: reported toxicity with phenytoin, due to increased phenytoin levels  
- Antipsychotics: avoid concomitant use with clozapine – increased risk of agranulocytosis

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**  
  - Oral
  - Rate of Administration
    - Give after food

**OTHER INFORMATION**
- Capecitabine is a prodrug that is metabolised to fluorouracil  
- Contraindicated in severe renal impairment due to increased incidence of grade 3 or 4 adverse reactions in patients with GFR of 30–50mL/min  
- Extensive absorption (~70%) after food intake. First metabolised in the liver and then in the tumour. Up to 96% dose is recovered in the urine. Terminal T½ = 0.85 hours
Capreomycin

CLINICAL USE
Antibacterial agent in combination with other drugs:
- Tuberculosis that is resistant to first-line drugs

DOSE IN NORMAL RenAL FUNCTION
Deep IM injection: 1 g daily (not more than 20 mg/kg) for 2–4 months, then 1 g 2–3 times each week

PHARMACOKINETICS
- Molecular weight: 668.7 daltons
- % Protein binding: No data
- % Excreted unchanged in urine: 50
- Volume of distribution (L/kg): 0.37–0.42
- Half-life – normal/ESRF (hrs): 2/55.5

DOSE IN RenAL IMPAIRMENT
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: 1 g every 48 hours

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD: Not dialysed. Dose as in GFR<10mL/min
- HD: Dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10mL/min
- CAV/VVHD: Not dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs:
- Increased risk of nephrotoxicity and ototoxicity with aminoglycosides and vancomycin

ADMINISTRATION
RECONSTITUTION
- Dissolve in 2 mL of sodium chloride 0.9% or water for injection. 2–3 minutes should be allowed for complete dissolution

ROUTE
- Deep IM injection

RATE OF ADMINISTRATION

COMMENTS

OTHER INFORMATION
- Nephrotoxic
- Check potassium levels as hypokalaemia may occur
- Desired steady state serum capreomycin level is 10 micrograms/mL
- Dose should not exceed 1 g/day in renal failure
- Capreomycin sulphate 1 000 000 Units approximately equivalent to capreomycin base 1 g

RETURN TO CONTENTS
**Captopril**

**CLINICAL USE**
Angiotensin-converting enzyme inhibitor:
- Hypertension
- Heart failure
- Post myocardial infarction
- Diabetic nephropathy

**DOSE IN NORMAL RENAL FUNCTION**
6.25–50 mg 2–3 times daily
Diabetic nephropathy: 75–100 mg daily in divided doses

**PHARMACOKINETICS**
- Molecular weight (daltons) 217.3
- % Protein binding 25–30
- % Excreted unchanged in urine 40–50
- Volume of distribution (L/kg) 2
- Half-life – normal/ESRF (hrs) 2–3/21–32

**DOSE IN RENAL IMPAIRMENT**


<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Start low – adjust according to response</td>
</tr>
<tr>
<td>10–20</td>
<td>Start low – adjust according to response</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Start low – adjust according to response</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**


<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs:
- Anaesthetics: enhanced hypotensive effect
- Analgesics: antagonism of hypotensive effect and increased risk of renal impairment with NSAIDs; hyperkalaemia with ketorolac and other NSAIDs
- Ciclosporin: increased risk of hyperkalaemia and nephrotoxicity
- Diuretics: enhanced hypotensive effect; hyperkalaemia with potassium-sparing diuretics
- Epoetin: increased risk of hyperkalaemia; antagonism of hypotensive effect
- Lithium: reduced risk of hyperkalaemia; possibility of enhanced lithium toxicity
- Potassium salts: increased risk of hyperkalaemia.
- Tacrolimus: increased risk of hyperkalaemia and nephrotoxicity

**ADMINISTRATION**


<table>
<thead>
<tr>
<th>RECONSTITUTION</th>
<th>–</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROUTE</td>
<td>Oral</td>
</tr>
<tr>
<td>RATE OF ADMINISTRATION</td>
<td>–</td>
</tr>
<tr>
<td>COMMENTS</td>
<td>Tablets may be dispersed in water</td>
</tr>
</tbody>
</table>

**OTHER INFORMATION**


| Adverse reactions, especially hyperkalaemia, are more common in patients with renal impairment |
| Effective sub-lingually in emergencies |
| As renal function declines a hepatic elimination route for captopril becomes increasingly more significant |
| Renal failure has been reported in association with ACE inhibitors in patients with renal artery stenosis, post renal transplant, or in those with congestive heart failure |
| A high incidence of anaphylactoid reactions has been reported in patients dialysed with high-flux polyacrylonitrile membranes and treated concomitantly with an ACE inhibitor – this combination should therefore be avoided |
| Close monitoring of renal function during therapy is necessary in those with renal insufficiency |

RETURN TO CONTENTS
**Carbamazepine**

**CLINICAL USE**
- All forms of epilepsy except absence seizures
- Trigeminal neuralgia
- Prophylaxis in manic depressive illness

**DOSE IN NORMAL RENAL FUNCTION**
- Epilepsy: initially 100–200 mg 1–2 times daily, increased to maintenance of 0.4–1.2 g daily in divided doses; maximum 1.6–2 g daily
- Rectal: maximum 1 g daily in 4 divided doses for up to 7 days use
- Trigeminal neuralgia: initially 100 mg 1–2 times daily; usual dose 200 mg 3–4 times daily; maximum 1.6 g/day; reduce dose gradually as pain goes into remission
- Prophylaxis in manic-depressive illness: 400–600 mg daily in divided doses, maximum 1.6 g/day

**PHARMACOKINETICS**
- Molecular weight (daltons): 236.3
- % Protein binding: 70–80
- % Excreted unchanged in urine: 2
- Volume of distribution (L/kg): 0.8–1.9
- Half-life – normal/ESRF (hrs): 5–26/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/Min)**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**: Not dialysed. Dose as in normal renal function
- **HD**: Not dialysed. Dose as in normal renal function
- **HDF/High flux**: Unknown dialysability. Dose as in normal renal function
- **CAV/VVHD**: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: effect enhanced by dextropropoxyphene; decreased effect of tramadol and methadone
- Antibacterials: reduced effect of doxycycline; concentration increased by clarithromycin, erythromycin and isoniazid; increased risk of isoniazid hepatotoxicity; concentration reduced by rifabutin; concentration of telithromycin reduced – avoid concomitant use
- Anticoagulants: metabolism of coumarins accelerated (reduced anticoagulant effect)
- Antidepressants: antagonism of anticonvulsant effect; concentration increased by fluoxetine and fluvoxamine; concentration of mianserin, mirtazepine, paroxetine and tricyclics reduced; avoid concomitant use with MAOIs; concentration reduced by St John’s wort – avoid concomitant use
- Antifungals: concentration possibly increased by fluconazole, ketoconazole and miconazole; concentration of itraconazole, caspofungin, posaconazole and voriconazole possibly reduced, avoid with voriconazole, consider increasing caspofungin dose
- Antimalarials: chloroquine, hydroxychloroquine and mefloquine antagonise anticonvulsant effect
- Antipsychotics: antagonism of anticonvulsant effect; reduced concentration of aripiprazole (increase aripiprazole dose), haloperidol, clozapine, olanzapine, quetiapine, risperidone and sertindole; avoid concomitant use with other drugs that can cause agranulocytosis
- Antivirals: reduced concentration of amprenavir, darunavir, indinavir, lopinavir, nelfinavir and saquinavir; concentration possibly increased by ritonavir; concentration of both drugs reduced in combination with efavirenz
- Calcium-channel blockers: effects enhanced by diltiazem and verapamil; reduced effect of felodipine, isradipine and probably dihydropyridines, nicardipine and nifedipine
- Ciclosporin: metabolism accelerated (reduced ciclosporin concentration)
Corticosteroids: reduced effect of corticosteroids
Diuretics: increased risk of hyponatraemia; concentration increased by acetazolamide; reduced eplerenone concentration – avoid concomitant use
Hormone antagonists: metabolism inhibited by danazol; accelerated metabolism of gestrinone and possibly toremifene
Oestrogens and progestogens: reduced contraceptive effect
Ulcer-healing drugs: concentration increased by cimetidine

RATE OF ADMINISTRATION

COMMENTS

When switching a patient from tablets to liquid the same total dose may be used, but given in smaller more frequent doses
125 mg suppository is equivalent to 100 mg of tablets

OTHER INFORMATION

Important to initiate carbamazepine therapy at a low dose and build this up over 1–2 weeks, as it autoinduces its metabolism
May cause inappropriate antidiuretic hormone secretion
Therapeutic plasma concentration range: 4–12 micrograms/mL (20–50 micromol/L at steady state)
Carbimazole

**CLINICAL USE**
Treatment of hyperthyroidism

**DOSE IN NORMAL RENAL FUNCTION**
5–40 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 186.2
- % Protein binding: Unbound (methimazole is 5%)
- % Excreted unchanged in urine: <12 (methimazole)
- Volume of distribution (L/kg): 0.5 (methimazole)
- Half-life – normal/ESRF (hrs): 3–6.4 (methimazole)/Increased

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**
**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**
  -

**OTHER INFORMATION**
- Carbimazole is a prodrug which is rapidly and completely metabolised to methimazole the active moiety
- There have been reports of glomerulonephritis associated with the development of antineutrophil cytoplasmic antibodies in patients receiving thiourea anti-thyroid drugs
Carboplatin

**CLINICAL USE**

Antineoplastic agent:
- Ovarian carcinoma of epithelial origin
- Small cell carcinoma of the lung

**DOSE IN NORMAL RENAL FUNCTION**

Dose = Target AUC × [GFR (mL/min) + 25] where AUC is commonly 5 or 6 depending on protocol used (Calvert equation)

**PHARMACOKINETICS**

- Molecular weight: 371.2 daltons
- % Protein binding: 29–89
- % Excreted unchanged in urine: 32–70
- Volume of distribution (L/kg): 0.23–0.28
- Half-life – normal/ESRF (hrs): 1.5–6/ Increased

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function. See ‘Other Information’</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function. See ‘Other Information’</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function. See ‘Other Information’</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**
  - Unknown dialysability. Dose as in GFR<10mL/min
- **HD**
  - Dialysed. Dose as in GFR<10mL/min
- **HDF/High flux**
  - Dialysed. Dose as in GFR<10mL/min
- **CAV/VVHD**
  - Unknown dialysability. Dose as in GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Aminoglycosides: increased risk of nephrotoxicity and possibly ototoxicity with aminoglycosides, capreomycin, polymyxins or vancomycin
- Antipsychotics: avoid concomitant use with clozapine, increased risk of agranulocytosis

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - IV
- **RATE OF ADMINISTRATION**
  - IV infusion over 15–60 minutes

**COMMENTS**

- Therapy should not be repeated until 4 weeks after the previous carboplatin course
- May be diluted with glucose 5%, or sodium chloride 0.9% to concentrations as low as 0.5 mg/mL

**OTHER INFORMATION**

- Patients with abnormal kidney function or receiving concomitant therapy with nephrotoxic drugs are likely to experience more severe and prolonged myelotoxicity
- Blood counts and renal function should be monitored closely
- Some units still use a dose in normal renal function of 400 mg/m². In this instance, the dose should be reduced to 50% of normal for a GFR of 10–20 mL/min, and to 25% of normal for a GFR<10 mL/min
- There is little, if any, true metabolism of carboplatin. Excretion is primarily by glomerular filtration in the urine, with most of the drug excreted in the first 6 hours. Approximately 32% of the dose is excreted unchanged.
- Platinum from carboplatin slowly becomes protein bound, and is subsequently excreted with a terminal half-life of 5 days or more
Carmustine

**CLINICAL USE**
Alkylating agent:
- Myeloma, lymphoma and brain tumours

**DOSE IN NORMAL RENAL FUNCTION**
- 150–200 mg/m² as a single dose or 75–100 mg/m² on 2 consecutive days every 6 weeks
- Implants: 7.7mg, maximum 8 implants

**PHARMACOKINETICS**
- Molecular weight: 214.1 daltons
- % Protein binding: 77%
- % Excreted unchanged in urine: 60–70%
- Volume of distribution: 3.25 L/kg
- Half-life – normal/ESRF (hrs): 22 minutes/

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min): 20–50 Dose as in normal renal function
- 10–20 Dose as in normal renal function
- <10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- 3 mL of the supplied diluent (absolute ethanol) then add 27 mL of sterile water for injection
- This solution may be further diluted with sodium chloride 0.9% or glucose 5% for injection

**ROUTE**
- IV

**RATE OF ADMINISTRATION**
- Administer by IV drip over a period of 1–2 hours

**COMMENTS**
- Therapy should not be repeated before 6 weeks
- Can further dilute the reconstituted solution with 500 mL of sodium chloride 0.9% or glucose 5%

**OTHER INFORMATION**
- Renal abnormalities, e.g. a decrease in kidney size: progressive azotaemia and renal failure have been reported in patients receiving large cumulative doses after prolonged therapy
- Partially metabolised to active species by liver microsomal enzymes, which have a long T½. It is thought that the antineoplastic activity may be due to metabolites. Approximately 30% of a dose is excreted in the urine after 24 hours, and 60–70% of the total dose after 96 hours. About 10% is excreted as respiratory CO₂. Terminal half-life of the metabolites are about 1 hour
Carvedilol

**CLINICAL USE**

Beta-adrenoceptor blocker with alpha1-blocking action:
- Hypertension, angina and heart failure

**DOSE IN NORMAL RENAL FUNCTION**
- Hypertension: 12.5–50 mg daily in single or divided doses
- Angina: 12.5–25 mg twice daily
- Heart failure: 3.125–25 mg twice daily (50 mg twice daily if wt>85 kg)

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>406.5</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>&gt;98</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;2</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>2</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>6–10/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

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<tr>
<th>GFR (mL/Min)</th>
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<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapeutic Modality</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely dialysability. Dose as in normal renal function. Start with low doses and titrate according to response</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function. Start with low doses and titrate according to response</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function. Start with low doses and titrate according to response</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely dialysability. Dose as in normal renal function. Start with low doses and titrate according to response</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Analgesics: NSAIDs antagonise hypotensive effect
- Anti-arrhythmics: increased risk of myocardial depression and bradycardia; increased risk of bradycardia, myocardial depression and AV block with amiodarone
- Antibacterials: concentration reduced by rifampicin
- Antidepressants: enhanced hypotensive effect with MAOIs
- Antihypertensives: enhanced hypotensive effect; increased risk of withdrawal hypertension with clonidine; increased risk of first dose hypotensive effect with post-synaptic alpha-blockers such as prazosin
- Antimalarials: increased risk of bradycardia with mefloquine
- Antipsychotics enhanced hypotensive effect with phenothiazines
- Calcium-channel blockers: increased risk of bradycardia and AV block with diltiazem; hypotension and heart failure possible with nifedipine and nisoldipine; asystole, severe hypotension and heart failure with verapamil
- Ciclosporin: increased trough concentration, reduce dose by 20% in affected patients
- Diuretics: enhanced hypotensive effect
- Moxisylyte: possible severe postural hypotension
- Sympathomimetics: severe hypertension with adrenaline and noradrenaline and possibly with dobutamine
- Tropisetron: increased risk of ventricular arrhythmias – use with caution

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- First pass elimination of 60–75% following oral administration
Caspofungin

**CLINICAL USE**
- Invasive aspergillosis in adult patients who are refractory to or intolerant of amphotericin B and/or itraconazole
- Invasive candidiasis
- Empirical treatment of systemic fungal infections in patients with neutropenia

**DOSE IN NORMAL RENAL FUNCTION**
- 70 mg loading dose on day 1 followed by 50 mg daily, thereafter
- If patient weighs >80 kg use 70 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 1213.4 (as acetate)
- % Protein binding: 97
- % Excreted unchanged in urine: 1.4
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 12–15 days/Increased but not significantly. See ‘Other Information’

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unlikely to be dialysed. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Ciclosporin: monitor liver enzymes as transient increases in ALT and AST have been reported with concomitant administration. Avoid co-administration if possible. Increases AUC of caspofungin by 35%
  - Tacrolimus: reduces tacrolimus trough concentration by 26%

**ADMINISTRATION**
- RECONSTITUTION:
  - 10.5 mL water for injection
- ROUTE:
  - IV infusion
- RATE OF ADMINISTRATION:
  - Approximately 1 hour
- COMMENTS:
  - Caspofungin is unstable in fluids containing glucose; add to 250 mL sodium chloride 0.9% or lactated Ringer’s solution
  - If patient is fluid restricted, doses of 35 or 50 mg may be added to 100 mL infusion fluid

**OTHER INFORMATION**
- In established renal failure the AUC is increased by 30–49% but a change in dosage schedule is not required
- Plasma concentrations of caspofungin decline in a polyphasic manner. A short α-phase occurs immediately post infusion, followed by a β-phase with a half-life of 9–11 hours. An additional γ-phase also occurs with a half-life of 40–50 hours. Distribution rather than excretion or biotransformation is the dominant mechanism influencing plasma clearance
- Caspofungin has been used at a dose of 50 mg daily in combination with IV amphotericin B to successfully treat fungal peritonitis in 1 case study; the catheter was removed. (Fourtounas C, Marangos M, Kalliakmani P, et al. Treatment of peritoneal dialysis related fungal peritonitis with caspofungin plus amphotericin B combination therapy. *Nephrol Dial Transplant*. 2006; 21: 236)
Cefaclor

CLINICAL USE
Antibacterial agent

DOSE IN NORMAL RENAL FUNCTION
250 mg every 8 hours (dose may be doubled for more severe infections – maximum 4 g daily)

PHARMACOKINETICS
Molecular weight (daltons) 385.8
% Protein binding 25
% Excreted unchanged in urine 60–85
Volume of distribution (L/kg) 0.24–0.35
Half-life – normal/ESRF (hrs) 0.5–0.9/2.3–2.8

DOSE IN RENAL IMPAIRMENT
GFR (mL/MIN)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 250 mg every 8 hours

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Dialysed. 250 mg every 8–12 hours
HD Dialysed. 250–500 mg every 8 hours
HDF/High flux Dialysed. 250–500 mg every 8 hours
CAV/VVHD Dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● Anticoagulants: effects of coumarins may be enhanced

ADMINISTRATION
RECONSTITUTION
–
ROUTE
● Oral
RATE OF ADMINISTRATION
–
COMMENTS
–

OTHER INFORMATION
● Cefaclor associated with protracted skin reactions
Cefadroxil

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
500 mg – 1 g every 12–24 hours

**PHARMACOKINETICS**
- Molecular weight (daltons): 381.4
- % Protein binding: 20
- % Excreted unchanged in urine: >90
- Volume of distribution (L/kg): 0.31

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: 500 mg – 1 g every 24 hours

### DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: effects of coumarins may be enhanced

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
-
Cefalexin

CLINICAL USE
Antibacterial agent

DOSE IN NORMAL RENAL FUNCTION
250 mg every 6 hours or 500 mg every 8–12 hours; maximum 6 g daily
Recurrent UTI prophylaxis: 125 mg at night

PHARMACOKINETICS
Molecular weight 365.4 (daltons)
% Protein binding 15
% Excreted unchanged in urine 80–90
Volume of distribution 0.35 (L/kg)
Half-life – normal/ESRF (hrs) 1/16

DOSE IN RENAL IMPAIRMENT
GFR (mL/Min)
20–50 Dose as in normal renal function
10–20 500 mg every 8–12 hours
<10 250–500 mg every 8–12 hours

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD dialysed. Dose as in GFR<10 mL/min
HD Dialysed. Dose as in GFR<10 mL/min
HDF/High flux Dialysed. Dose as in GFR<10 mL/min
CAV/VVHD Dialysed. Dose as in GFR=10–20 mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● Anticoagulants: effects of coumarins may be enhanced

ADMINISTRATION
RECONSTITUTION
–
ROUTE
● Oral
RATE OF ADMINISTRATION
–
COMMENTS
–

OTHER INFORMATION
● Use dose for normal renal function to treat urinary tract infection in ERF
● High doses, together with the use of nephrotoxic drugs such as aminoglycosides or potent diuretics, may adversely affect renal function
Cefixime

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
200–400 mg/day (given as a single dose or in 2 divided doses)

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>507.5</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>65</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>20 (50% of absorbed dose)</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.11–0.6</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>3–4/11.5</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: 200 mg/day

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Dialysis Method</th>
<th>Dose Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Dialysed. Dose as in GFR=10–</td>
</tr>
<tr>
<td>VVHD</td>
<td>20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: effects of coumarins may be enhanced

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  -

**OTHER INFORMATION**
- Manufacturer recommends that patients having regular APD or HD should not have a dose greater than 200 mg/day
**Cefotaxime**

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
- Mild infection: 1 g every 12 hours
- Moderate infection: 1 g every 8 hours
- Severe infection: 2 g every 6 hours
- Life-threatening infection: up to 12 g daily in 3–4 divided doses

**PHARMACOKINETICS**
- Molecular weight: 477.4 (as sodium salt)
- % Protein binding: 40
- % Excreted unchanged in urine: 40–60
- Volume of distribution: 0.15–0.55 (L/kg)
- Half-life – normal/ESRF (hrs): 0.9–1.14/2.5 (10 hours for the metabolite)

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: 1 g every 8–12 hours

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**: Not dialysed. Dose as in GFR<10mL/min
- **HD**: Dialysed. Dose as in GFR<10mL/min
- **HDF/High flux**: Dialysed. Dose as in GFR<10mL/min
- **CAV/VVHD**: Dialysed. 1–2 g every 12 hours
- **CVVHD/HDF**: Dialysed. 2 g every 12 hours

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Anticoagulants: effects of coumarins may be enhanced

**ADMINISTRATION**

**RECONSTITUTION**
- IV Bolus/IM: 4 mL water for injection to 1 g
- IV Infusion: 1 g in 50 mL sodium chloride 0.9%

**ROUTE**
- IV, IM

**RATE OF ADMINISTRATION**
- Bolus over 3–4 minutes; infusion over 20–60 minutes

**OTHER INFORMATION**
- 1 g contains 2.09 mmol sodium
- Reduce dose further if concurrent hepatic and renal failure

References:
Cefpodoxime

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
100–200 mg every 12 hours

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>557.6 (as proxetil)</td>
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<tr>
<td>% Protein binding</td>
<td>20–40</td>
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<tr>
<td>% Excreted unchanged in urine</td>
<td>80</td>
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<td>Volume of distribution (L/kg)</td>
<td>0.6–1.2</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>2.4/26</td>
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**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>100–200 mg every 24 hours</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs

- Anticoagulants: effects of coumarins may be enhanced

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
- Take with food
- Antacids and H₂-blockers should be taken 2–3 hours after administration of cefpodoxime
Cefradine

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
Oral: 250–500 mg every 6 hours (or 500 mg – 1 g every 12 hours)
Severe infections: 1 g every 6 hours
Injection: 0.5–2 g every 6 hours
Surgical prophylaxis: 1–2 g at induction

**PHARMACOKINETICS**
- Molecular weight: 349.4 daltons
- % Protein binding: 8–12
- % Excreted unchanged in urine: >90
- Volume of distribution: 0.25–0.46 L/kg
- Half-life – normal/ESRF (hrs): 1/6–15

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: 250–500 mg every 6 hours

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: dialysed. Dose as in GFR<10 mL/min
- HD: Dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: effects of coumarins may be enhanced

**ADMINISTRATION**

**RECONSTITUTION**
- IM: 2 mL of water for injection or sodium chloride 0.9% to each 500 mg
- IV bolus: 5 mL of water for injection, sodium chloride 0.9% or glucose 5% to each 500 mg
- IV infusions: 10 mL of suitable diluent to 1 g vial then add to infusion solution

**ROUTE**
- Oral, IM, IV

**RATE OF ADMINISTRATION**
- IV bolus: over 3–5 minutes

**COMMENTS**
-
Ceftazidime

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
- 0.5–2 g every 8–12 hours
- Severe infections: 3 g every 12 hours
- Pseudomonal lung infections in cystic fibrosis: 100–150 mg/kg in 3 divided doses
- Surgical prophylaxis: 1 g at induction

**PHARMACOKINETICS**
- Molecular weight: 637.7 daltons
- % Protein binding: <10
- % Excreted unchanged in urine: 80–90
- Volume of distribution: 0.28–0.4 L/kg

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>31–50</td>
<td>1−2 g every 12 hours</td>
</tr>
<tr>
<td>16–30</td>
<td>1−2 g every 24 hours</td>
</tr>
<tr>
<td>6–15</td>
<td>500 mg – 1 g every 24 hours</td>
</tr>
<tr>
<td>&lt;5</td>
<td>500 mg – 1 g every 48 hours</td>
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**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose</th>
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<tbody>
<tr>
<td>CAPD</td>
<td>Dialysed. 500 mg – 1 g every 24 hours</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. 500 mg – 1 g every 24–48 hours</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. 500 mg – 1 g every 24–48 hours</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. 2 g every 8 hours or 1–2 g every 12 hours</td>
</tr>
<tr>
<td>CVVHD/HDF</td>
<td>Dialysed. 2 g every 12 hours</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: effects of coumarins may be enhanced
- Ciclosporin: may cause increased ciclosporin levels

**ADMINISTRATION**

**RECONSTITUTION**
- Amount of water for injection to be added to vials:
  - 1.5 mL to 500 mg vial for IM administration
  - 5 mL to 500 mg vial for IV injection
  - 3 mL to 1 g vial for IM administration
  - 10 mL to 1 g vial for IV injection

**ROUTE**
- IV/IM rarely

**RATE OF ADMINISTRATION**
- Bolus: 3–4 minutes
- Infusion: over 30 minutes

**COMMENTS**
- May be given IP in CAPD fluid 50–125 mg/L fluid
- Reconstituted solutions vary in colour, but this is quite normal
- Compatible with most IV fluids, e.g. sodium chloride 0.9%, glucose-saline, glucose 5%

**OTHER INFORMATION**
- Volume of distribution increases with infection
- In exceptional circumstances, patients on haemodialysis may be given a dose of 2 g, 3 times a week post HD

References:
2. Dose from CVVH Initial Drug Dosing Guidelines on www.thedrugmonitor.com

RETURN TO CONTENTS
Ceftriaxone

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
1 g daily (severe infections: 2–4 g daily)
Gonorrhoea: single dose 250 mg IM

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>661.6 (as sodium salt)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>85–95</td>
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<tr>
<td>% Excreted unchanged in urine</td>
<td>40–60</td>
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<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.12–0.18</td>
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<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>6–9/14.7</td>
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**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
<td>Maximum 2 g daily</td>
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**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Type</th>
<th>Dose</th>
<th>Remarks</th>
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<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
<td></td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
<td></td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. 2 g every 12–24 hours</td>
<td></td>
</tr>
<tr>
<td>CVVHD/HDF</td>
<td>Likely dialysability. 2 g every 12–24 hours</td>
<td></td>
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</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: effects of coumarins may be enhanced
- Ciclosporin: may cause increased ciclosporin levels

**ADMINISTRATION**

**RECONSTITUTION**
- Bolus 250 mg: IV – 5 mL water for injection, IM – 1 mL 1% lidocaine hydrochloride
- Bolus 1 g: IV – 10 mL water for injection, IM – 3.5 mL 1% lidocaine hydrochloride
- Infusion: 2 g in 40 mL of calcium-free solution, e.g. sodium chloride 0.9%, glucose 5%
- Incompatible with calcium containing solutions, e.g. Hartmann’s, Ringer’s

**ROUTE**
- IV, IM, SC

**RATE OF ADMINISTRATION**
- Bolus: over 2–4 minutes
- Infusion: over at least 30 minutes

**COMMENTS**
- Doses of 50 mg/kg or over should be given by slow IV infusion
- For IM injection: doses greater than 1 g should be divided and injected at more than one site

**OTHER INFORMATION**
- Calcium ceftriaxone has appeared as a precipitate in urine, or been mistaken as gallstones in patients receiving higher than recommended doses
- Contains 3.6 mmol sodium per gram of ceftriaxone
- Information from the company shows that the bioavailability of SC administration is equivalent to IV. The maximum amount able to be given in a single SC injection is 500 mg dissolved in 2 mL lidocaine 1%. Administration was said to be tolerable

References:
# Cefuroxime (oral)

## CLINICAL USE
Antibacterial agent

## DOSE IN NORMAL RENAL FUNCTION
125–500 mg every 12 hours
Gonorrhoea: single dose of 1 g

## PHARMACOKINETICS
- **Molecular weight (daltons)**: 510.5 (as axetil)
- **% Protein binding**: 50
- **% Excreted unchanged in urine**: 85–90
- **Volume of distribution (L/kg)**: 0.13–1.8
- **Half-life – normal/ESRF (hrs)**: 1.2/17

## DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
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</table>

## IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Anticoagulants: effects of coumarins may be enhanced

## ADMINISTRATION
- **RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**
  - Take with or after food

## DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- **CAPD**
  - Dialysed. Dose as in normal renal function
- **HD**
  - Dialysed. Dose as in normal renal function
- **HDF/High flux**
  - Dialysed. Dose as in normal renal function
- **CAV/VVHD**
  - Dialysed. Dose as in normal renal function
Cefuroxime (parenteral)

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
750 mg – 1.5 g every 6–8 hours

Meningitis: 3 g every 8 hours

**PHARMACOKINETICS**
Molecular weight 446.4 (as sodium salt) (daltons)
% Protein binding 50
% Excreted unchanged in urine 85–90
Volume of distribution 0.13–1.8 (L/kg)
Half-life – normal/ESRF (hrs) 1.2/17

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>750 mg – 1.5 g every 8 hours</td>
</tr>
<tr>
<td>10–20</td>
<td>750 mg – 1.5 g every 8–12 hours</td>
</tr>
<tr>
<td>&lt;10</td>
<td>750 mg – 1.5 g every 12–24 hours</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**: dialysed. Dose as in GFR<10 mL/min
- **HD**: Dialysed. Dose as in GFR<10 mL/min
- **HDF/High flux**: Dialysed. Dose as in GFR<10 mL/min
- **CAV/VVHD**: Dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: effects of coumarins may be enhanced

**ADMINISTRATION**

**RECONSTITUTION**
- **IM**: 1 mL of water for injection to each 250 mg
- **IV bolus**: 2 mL of water for injection to each 250 mg, but 15 mL of water for injection to 1.5 g
- **IV infusion**: 1.5 g in 50 mL of water for injection

**ROUTE**
- IM, IV

**RATE OF ADMINISTRATION**
- **IV bolus**: over 3–5 minutes
- **IV infusion**: over 30 minutes

**COMMENTS**
- Do not mix in syringe with aminoglycoside antibiotics
- Injection may also be reconstituted with: sodium chloride 0.9%, glucose 5%, glucose saline, Hartmann’s solution
- Cefuroxime and metronidazole can be mixed (see manufacturer’s guidelines)

**OTHER INFORMATION**
- At high doses, take care in patients receiving concurrent treatment with potent diuretics such as furosemide, or aminoglycosides, as combination can adversely affect renal function
- Each 750 mg vial ≈ 1.8 mmol sodium
Celecoxib

CLINICAL USE
Cox 2 inhibitor and analgesic

DOSE IN NORMAL RENAL FUNCTION
200 mg once or twice daily

PHARMACOKINETICS
Molecular weight (daltons) 381.4
% Protein binding 97
% Excreted unchanged in urine <3
Volume of distribution (L/kg) 400 litres
Half-life – normal/ESRF (hrs) 8–12/Unchanged

DOSE IN RENAL IMPAIRMENT
GFR (mL/MIN)
30–50 Dose as in normal renal function.
10–30 Dose as in normal renal function, but avoid if possible
<10 Dose as in normal renal function, but only use if on dialysis

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unlikely to be dialysed. Dose as in normal renal function See 'Other Information'
HD Unlikely to be dialysed. Dose as in normal renal function See 'Other Information'
HDF/High flux Unknown dialysability. Dose as in normal renal function See 'Other Information'
CAV/ VVHD GFR=10–20mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
• ACE inhibitors and angiotensin-II antagonists: antagonism of hypotensive effect; increased risk of nephrotoxicity and hyperkalaemia
• Analgesics: avoid concomitant use of 2 or more NSAIDs, including aspirin (increased side effects); avoid with ketorolac (increased risk of side effects and haemorrhage)
• Antibacterials: possibly increased risk of convulsions with quinolones
• Anticoagulants: effects of coumarins enhanced; possibly increased risk of bleeding with heparins and coumarins
• Antidepressants: increased risk of bleeding with SSRIs and venlafaxine
• Antidiabetic agents: effects of sulphonylureas enhanced
• Anti-epileptics: possibly increased phenytoin concentration
• Antifungals: if used with fluconazole, halve the dose of celecoxib.
• Antivirals: increased risk of haematological toxicity with zidovudine; concentration possibly increased by ritonavir
• Ciclosporin: may potentiate nephrotoxicity
• Cytotoxic agents: reduced excretion of methotrexate; increased risk of bleeding with erlotinib
• Diuretics: increased risk of nephrotoxicity; antagonism of diuretic effect; hyperkalaemia with potassium-sparing diuretics
• Lithium: excretion decreased
• Pentoxifylline: possibly increased risk of bleeding
• Tacrolimus: increased risk of nephrotoxicity

ADMINISTRATION

RECONSTITUTION
–

ROUTE
• Oral

RATE OF ADMINISTRATION
–

COMMENTS
–

OTHER INFORMATION
• Clinical trials have shown renal effects similar to those observed with comparative NSAIDs. Monitor patient for deterioration in renal function and fluid retention
• Inhibition of renal prostaglandin synthesis by NSAIDs may interfere with renal function, especially in the presence of existing renal disease. Avoid if possible; if not, check serum creatinine 48–72 hours after starting NSAID. If raised, discontinue NSAID therapy
Use normal doses in patients with ERF on dialysis if they do not pass any urine.

Use with caution in renal transplant recipients – can reduce intrarenal autocoid synthesis.

Celecoxib should be used with caution in uraemic patients predisposed to gastrointestinal bleeding or uraemic coagulopathies.

Contraindicated in patients with ischaemic heart disease or cerebrovascular disease and class II–IV NYHA congestive heart failure.
Celiprolol hydrochloride

**CLINICAL USE**
Beta-adrenoceptor blocker:
- Mild to moderate hypertension

**DOSE IN NORMAL RENAL FUNCTION**
200–400 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 416
- % Protein binding: 25
- % Excreted unchanged in urine: 12–18
- Volume of distribution (L/kg): 4.5
- Half-life – normal/ESRF (hrs): 5–6/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Start low – adjust according to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR<10 mL/min
- HD: Unknown dialysability. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs:
- Analgesics: NSAIDs antagonise hypotensive effect
- Anti-arrhythmics: increased risk of myocardial depression and bradycardia; increased risk of bradycardia, myocardial depression and AV block with amiodarone
- Antidepressants: enhanced hypotensive effect with MAOIs
- Antihypertensives: enhanced hypotensive effect; increased risk of withdrawal hypertension with clonidine; increased risk of first dose hypotensive effect with post-synaptic alpha-blockers such as prazosin
- Antimalarials: increased risk of bradycardia with mefloquine
- Antipsychotics enhanced hypotensive effect with phenothiazines
- Calcium-channel blockers: increased risk of bradycardia and AV block with diltiazem; hypotension and heart failure possible with nifedipine and nisoldipine; asystole, severe hypotension and heart failure with verapamil
- Diuretics: enhanced hypotensive effect
- Moxisylyte: possible severe postural hypotension
- Sympathomimetics: severe hypertension with adrenaline and noradrenaline and possibly with dobutamine
- Tropisetron: increased risk of ventricular arrhythmias – use with caution

**ADMINISTRATION**

**RECONSTITUTION**
- Oral

**RATE OF ADMINISTRATION**
- Oral

**COMMENTS**
- Take half to one hour before food
Cetirizine hydrochloride

**CLINICAL USE**
Antihistamine:
- Symptomatic relief of allergy such as hay fever, urticaria

**DOSE IN NORMAL RENAL FUNCTION**
10 mg daily or 5 mg twice daily

**PHARMACOKINETICS**
- Molecular weight: 461.8 daltons
- % Protein binding: 93
- % Excreted unchanged in urine: 50–60
- Volume of distribution (L/kg): 0.45
- Half-life – normal/ESRF (hrs): 8–10/20

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>5–10 mg daily</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**
  - Unlikely dialysability. Dose as in GFR<10mL/min
- **HD**
  - Not dialysed. Dose as in GFR<10mL/min
- **HDF/High flux**
  - Not dialysed. Dose as in GFR<10mL/min
- **CAV/VVHD**
  - Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
- **COMMENTS**
  - Available as tablets and solution

**OTHER INFORMATION**
- Manufacturers recommend halving dose in renal impairment
- Dose may be titrated up but may result in increased sedation
- Less than 10% of a dose is removed by haemodialysis

RETURN TO CONTENTS
Cetuximab

**CLINICAL USE**
Monoclonal antibody:
- Treatment of EGFR-expressing metastatic colorectal cancer in combination with irinotecan after failure of irinotecan-including cytotoxic therapy

**DOSE IN NORMAL RENAL FUNCTION**
Initial dose 400 mg/m² then 250 mg/m² weekly

**PHARMACOKINETICS**
- Molecular weight: 152,000 daltons
- % Protein binding: No data
- % Excreted: minimal
- Volume of distribution (L/kg): 1.5–6.2 L/m²
- Half-life – normal/ESRF (hrs): 70–100/unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function.</th>
<th>Use with caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
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<tr>
<td>&lt;10</td>
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</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose as in normal renal function.</th>
<th>Use with caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
<td></td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
<td></td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in GFR=10–20 mL/min</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
- IV infusion

**RATE OF ADMINISTRATION**
- 1st dose: 120 minutes
- Further doses: 60 minutes
- Maximum infusion rate must not exceed 5 mL/min

**COMMENTS**
- Administer via a 0.2 micrometer in-line filter
- The filter may clog and need to be replaced during the infusion

**OTHER INFORMATION**
- Delayed hypersensitivity reactions may occur and patients should be warned to contact their doctor if this occurs
- Premedication with an antihistamine is recommended
- 2% of patients receiving cetuximab developed renal failure
- Give irinotecan at least 1 hour after the end of cetuximab infusion
Chloral hydrate

**CLINICAL USE**
Insomnia (short-term use)

**DOSE IN NORMAL RENAL FUNCTION**
- Mixture: 5–20 mL at night
- Welldorm (707 mg): 1–2 tablets at night; maximum 2 g (5 tablets/day)
- Syrup: 15–45 mL at night

**PHARMACOKINETICS**
- Molecular weight (daltons): 165.4
- % Protein binding: 70–80
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): 0.6
- Half-life – normal/ESRF (hrs): 7–11/–

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min):
  - 20–50: Dose as in normal renal function
  - 10–20: 1 tablet at night
  - <10: Avoid

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Avoid
- HD: Dialysed. Avoid
- HDF/High flux: Dialysed. Avoid
- CAV/VVHD: Dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: may transiently enhance effect of coumarins
- Antipsychotics: enhanced sedative effects
- Antivirals: concentration possibly increased by ritonavir

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- Take with water (or milk) 15–30 minutes before bedtime

**OTHER INFORMATION**
- Avoid in patients with marked hepatic or renal impairment, severe cardiac disease, marked gastritis and those susceptible to acute attacks of porphyria
- Chloral hydrate followed by intravenous furosemide may result in sweating, hot flushes, and variable blood pressure including hypertension
Chlorambucil

**Clinical Use**

Alkylating agent:
- Hodgkin's disease
- Non-Hodgkin's lymphoma (NHL)
- Chronic lymphocytic leukaemia (CLL)
- Waldenström's macroglobulinaemia (WM)
- Ovarian carcinoma (OC)
- Advanced breast cancer (ABC)

**Dose in Normal Renal Function**

- Hodgkin's disease: 200 mcg/kg/day (4–8 wks)
- NHL: 100–200 mcg/kg/day (4–8 wks) then reduce dose or give intermittently
- CLL: initially 150 mcg/kg/day, then 4 weeks after 1st course ended 100 mcg/kg/day
- WM: initially 6–12 mg daily, then reduce to 2–8 mg daily
- OC = 200 mcg/kg/day
- ABC = 200 mcg/kg/day for 6 wks (or 14–20 mg/day)

**Pharmacokinetics**

- Molecular weight: 304.2 daltons
- % Protein binding: 99
- % Excreted unchanged in urine: <1
- Volume of distribution: 0.86 L/kg
- Half-life – normal/ESRF: 1.5/–

**Dose in Renal Impairment**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in normal renal function. See 'Other Information'</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
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</tbody>
</table>

**Dose in Patients Undergoing Renal Replacement Therapies**

<table>
<thead>
<tr>
<th>Dialysis Type</th>
<th>Dose Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**Important Drug Interactions**

Potentially hazardous interactions with other drugs:
- Ciclosporin: ciclosporin concentration possibly reduced
- Patients who receive phenylbutazone may require reduced doses of chlorambucil

**Administration**

**Contraindications**

- Ciclosporin: ciclosporin concentration possibly reduced
- Patients who receive phenylbutazone may require reduced doses of chlorambucil

**Route**
- Oral

**Rate of Administration**

- Comments

**Other Information**

- Chlorambucil is extensively metabolised in the liver via the hepatic microsomal enzyme oxidation system, principally to phenylacetic acid mustard, which is pharmacologically active
- Chlorambucil is excreted in the urine, almost exclusively as metabolites
- Monitor patients with renal impairment closely as they are at increased risk of myelosuppression associated with azotaemia
- Oral absorption slowed and decreased by 10–20% if ingested with food
Chloramphenicol

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
Oral/IV: 50 mg/kg/day in divided doses every 6 hours (maximum 100 mg/kg/day)

**PHARMACOKINETICS**
- Molecular weight (daltons): 323.1
- % Protein binding: 60
- % Excreted unchanged in urine: 5–10
- Volume of distribution (L/kg): 0.5–1.0
- Half-life – normal/ESRF (hrs): 1.5–4/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/MIN):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Dialysed. Dose as in normal renal function
- HDF/High flux: Dialysed. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: effect of coumarins enhanced
- Antidiabetics: effect of sulphonylureas enhanced
- Anti-epileptics: metabolism accelerated by barbiturates and primidone (reduced plasma concentration of chloramphenicol); increased plasma concentration of phenytoin (risk of toxicity)
- Antipsychotics: avoid concomitant use with clozapine (increased risk of agranulocytosis)
- Ciclosporin: possibly increases ciclosporin concentration
- Tacrolimus: possibly increases tacrolimus concentration

**ADMINISTRATION**

**RECONSTITUTION**
- Kemicetine: 1 g vial – reconstitute with water for injection, sodium chloride 0.9% or glucose 5%.
  - 1.7 mL = 400 mg/mL solution
  - 3.2 mL = 250 mg/mL solution
  - 4.2 mL = 200 mg/mL solution

**ROUTE**
- Oral, IV, IM (Kemicetine only)

**RATE OF ADMINISTRATION**
- Over at least 1 minute

**OTHER INFORMATION**
- Manufacturers recommend monitoring serum levels in patients with renal impairment – Micromedex therapeutic range 10–25 micrograms/mL
- Levels should be taken 1 hour after IV administration, aim for 15–25 mg/L, trough <15 mg/L
- Kemicetine 1 g vial = 3.14 mmol sodium
Chlordiazepoxide hydrochloride

**CLINICAL USE**
- Anxiety (short-term use)
- Alcohol withdrawal

**DOSE IN NORMAL RENAL FUNCTION**
- Anxiety: 30–100 mg daily in divided doses
- Alcohol withdrawal: 10–50 mg 4 times a day, reducing gradually

**PHARMACOKINETICS**
- Molecular weight (daltons) 336.2
- % Protein binding 96
- % Excreted unchanged in urine 1–2
- Volume of distribution (L/kg) 0.3–0.5
- Half-life – normal/ESRF (hrs) 6–30/Unchanged

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: 50% of normal dose

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- **HD**: Not dialysed. Dose as in GFR<10 mL/min
- **HDF/High flux**: Unknown dialysability. Dose as in GFR<10 mL/min
- **CAV/VVHD**: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Antibacterials: metabolism possibly increased by rifampicin
  - Antipsychotics: enhanced sedative effects
  - Antivirals: concentration possibly increased by ritonavir
  - Sodium oxybate: enhanced effects of sodium oxybate – avoid
  - Ulcer-healing drugs: metabolism inhibited by cimetidine

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- Active metabolite (desmethyldiazepam) has a half-life of a few days
Chloroquine

**CLINICAL USE**
- Treatment and prophylaxis of malaria
- Discoid and systemic lupus erythematosus
- Rheumatoid arthritis

**DOSE IN NORMAL RENAL FUNCTION**
- Orally (as base)
  - Malaria treatment: 600 mg, followed by 300 mg 6–8 hours later, then 300 mg/day for 2 days
  - Malaria prophylaxis: 300 mg once a week on the same day each week (start 1 week before exposure to risk and continue until 4 weeks after leaving the malarial area
- SLE: 150 mg daily
- Rheumatoid arthritis: 150 mg daily; maximum 2.5 mg/kg

**PHARMACOKINETICS**
- Molecular weight (daltons) 319.9 (515.9 as phosphate), (436 as sulphate)
- % Protein binding 50–70
- % Excreted unchanged in urine 42–47
- Volume of distribution (L/kg) >100
- Half-life – normal/ESRF (hrs) 10–60 days/5–50 days

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50  Dose as in normal renal function
  - 10–20  Dose as in normal renal function
  - <10  50% of normal dose

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD  Not dialysed. Dose as in GFR<10mL/min
- HD  Not dialysed. Dose as in GFR<10mL/min
- HDF/High flux  Unknown dialysability. Dose as in GFR<10mL/min
- CAV/ VVHD  Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anti-arrhythmics: increased risk of ventricular arrhythmias with amiodarone – avoid concomitant use
- Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin – avoid concomitant use
- Anti-epileptics: antagonism of anticonvulsant effect
- Antimalarials: increased risk of convulsions with mefloquine; avoid concomitant use with artemether/lumefantrine
- Ciclosporin: increases ciclosporin concentration – increased risk of toxicity
- Digoxin: possibly increased concentration of digoxin
- Lanthanum: absorption possibly reduced by lanthanum, give at least 2 hours apart

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral, IV, IM/SC in rare cases

**RATE OF ADMINISTRATION**
- IV infusion: Administer dose 10 mg/kg of chloroquine base in sodium chloride 0.9% by slow IV infusion over 8 hours followed by 3 further 8 hour infusions containing 5 mg base/kg (total dose 25 mg base/kg over 32 hours)

**COMMENTS**
- Oral: Do not take indigestion remedies at the same time of day as this medicine
- Chloroquine sulphate inj. is available: 5.45% w/v (equivalent to 40 mg chloroquine base per mL)

**OTHER INFORMATION**
- Excretion is increased in alkaline urine
- Caution in patients with renal or hepatic disease
- Bone marrow suppression may occur with extended treatment
- 150 mg chloroquine base is equivalent to 200 mg of sulphate and 250 mg of phosphate
Chlorphenamine maleate (chlorpheniramine)

**CLINICAL USE**

Antihistamine:
- Relief of allergy, pruritus
- Treatment/prophylaxis of anaphylaxis

**DOSE IN NORMAL RENAL FUNCTION**

- Oral: 4 mg 4–6 times a day (maximum 24 mg/day)
- IV/IM/SC: 10–20 mg (maximum 40 mg/day)

**PHARMACOKINETICS**

- Molecular weight (daltons): 390.9
- % Protein binding: Approx 70%
- % Excreted unchanged in urine: Approx 22%
- Volume of distribution (L/kg): 3
- Half-life – normal/ESRF (hrs): 12–43/–

**DOSE IN RENAL IMPAIRMENT**

- GFR (mL/min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function. See 'Other Information'

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Not dialysed. Dose as in normal renal function
- HD: Dialysed. Dose as in normal renal function
- HDF/High flux: Dialysed. Dose as in normal renal function
- CAH/Dialysed. Dose as in normal renal function
- VVHD: Dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Inhibits phenytoin metabolism and can lead to phenytoin toxicity

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral, IV
- **RATE OF ADMINISTRATION**
  - Bolus over 1 minute
- **COMMENTS**
  - Injection reported to cause stinging or burning sensation at site of injection

**OTHER INFORMATION**

- Increased cerebral sensitivity in patients with renal impairment
Chlorpromazine hydrochloride

**CLINICAL USE**
- Anti-emetic
- Anxiolytic
- Antipsychotic
- Hiccups

**DOSE IN NORMAL RENAL FUNCTION**
- Anti-emetic:
  - Oral: 10–25 mg every 4–6 hours
  - IM: 25–50 mg every 3–4 hours
- Antipsychotic, anxiolytic:
  - Oral: 25 mg every 8 hours (or 75 mg at night) initially; increase as necessary; usual maintenance dose 75–300 mg daily (up to 1 g daily)
  - IM: 25–50 mg every 6–8 hours
- Induction of hypothermia: 25–50 mg every 6–8 hours
- Hiccups: Oral: 25–50 mg every 6–8 hours
- PR (unlicensed): 100 mg every 6–8 hours

**PHARMACOKINETICS**
- Molecular weight (daltons) 355.3
- % Protein binding 95–98
- % Excreted unchanged in urine <1
- Volume of distribution (L/kg) 7–20
- Half-life – normal/ESRF (hrs) 23–37/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/min)**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Start with small dose and increase according to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10mL/min
- HD: Not dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10mL/min
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Anaesthetics: enhanced hypotensive effect
  - Analgesics: increased risk of convulsions with tramadol; enhanced hypotensive and sedative effects with opioids
  - Anti-arrhythmics: increased risk of ventricular arrhythmias with anti-arrhythmics that prolong the QT interval; avoid concomitant use with amiodarone
  - Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin – avoid concomitant use
  - Antidepressants: increased level of tricyclics, possibly increased risk of ventricular arrhythmias and antimuscarinic side effects
  - Anticonvulsant: antagonises anticonvulsant effect
  - Antimalarials: avoid concomitant use with artemether/lumefantrine
  - Antipsychotics: increased risk of ventricular arrhythmias with pimozide – avoid concomitant use
  - Antivirals: concentration possibly increased with ritonavir
  - Anxiolytics and hypnotics: increased sedative effects
  - Atomoxetine: increased risk of ventricular arrhythmias
  - Beta-blockers: enhanced hypotensive effect; increased risk of ventricular arrhythmias with sotalol
  - Diuretics: enhanced hypotensive effect
  - Lithium: increased risk of extrapyramidal side effects and possibly neurotoxicity
  - Pentamidine: increased risk of ventricular arrhythmias
  - Sibutramine: increased risk of CNS toxicity – avoid concomitant use
  - Ulcer-healing drugs: effects enhanced by cimetidine

**ADMINISTRATION**

**RECONSTITUTION**

**ROUTE**
- Oral, deep IM, PR (unlicensed)

**RATE OF ADMINISTRATION**

**COMMENTS**

OTHER INFORMATION

- Start with small doses in severe renal impairment due to increased cerebral sensitivity

References:
Chlorpropamide

**CLINICAL USE**
- Diabetes mellitus
- Diabetes insipidus

**DOSE IN NORMAL RENAL FUNCTION**
- Diabetes mellitus: initially 250 mg daily (elderly 100–125 mg, but avoid). Maximum 500 mg daily
- Diabetes insipidus: 100–350 mg daily

**PHARMACOKINETICS**
- Molecular weight: 276.7 daltons
- % Protein binding: 88–96%
- % Excreted unchanged in urine: 47%
- Volume of distribution (L/kg): 0.09–0.27 L/kg

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: 50% of normal dose
  - 10–20: Avoid. See ‘Other Information’
  - <10: Avoid. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Avoid
- HD: Not dialysed. Avoid
- HDF/High flux: Unknown dialysability. Avoid
- CAV/VVHD: Unknown dialysability. Avoid

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Analgesics: effects enhanced by NSAIDs
  - Antibacterials: effects enhanced by chloramphenicol, sulphonamides, and trimethoprim; effect reduced by rifamycins
  - Anticoagulants: effect possibly enhanced by coumarins; also possibly changes to INR
  - Antifungals: concentration increased by fluconazole and miconazole and possibly voriconazole
  - Sulfinpyrazone: enhanced effect of sulphonylureas

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- Take with breakfast

**OTHER INFORMATION**
- Chlorpropamide can enhance antidiuretic hormone and very rarely cause hyponatraemia
- Contraindicated in patients with serious impairment of hepatic, renal or thyroid function – severe risk of metabolic acidosis
- Prolonged hypoglycaemia can occur in azotaemic patients
Chlortalidone (chlorthalidone)

**CLINICAL USE**
Thiazide-like diuretic:
- Hypertension
- Ascites
- Oedema
- Diabetes insipidus
- Mild to moderate heart failure

**DOSE IN NORMAL RENAL FUNCTION**
- Hypertension: 25–50 mg daily
- Oedema: 50 mg daily initially
- Diabetes insipidus: 100 mg every 12 hours initially, reducing to 50 mg daily where possible
- Heart failure: 25–50 mg daily increasing to 100–200 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 338.8
- % Protein binding: 76
- % Excreted unchanged in urine: 50
- Volume of distribution (L/kg): 3.9
- Half-life – normal/ESRF (hrs): 40–60/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min):
  - 30–50: Dose as in normal renal function
  - <30: Avoid. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Avoid
- HD: Not dialysed. Avoid
- HDF/High flux: Unknown dialysability. Avoid
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs:
  - Analgesics: increased risk of nephrotoxicity with NSAIDs; antagonism of diuretic effect
  - Anti-arrhythmics: hypokalaemia leads to increased cardiac toxicity; effects of lidocaine and mexiletine antagonised
  - Antibacterials: avoid administration with lymecycline
  - Antidepressants: increased risk of hypokalaemia with reboxetine; enhanced hypotensive effect with MAOIs; increased risk of postural hypotension with tricyclics
  - Anti-epileptics: increased risk of hyponatraemia with carbamazepine
  - Antifungals: increased risk of hypokalaemia with amphotericin
  - Antihypertensives: enhanced hypotensive effect; increased risk of first dose hypotension with post-synaptic alpha-blockers like prazosin; hypokalaemia increases risk of ventricular arrhythmias with sotalol
  - Antipsychotics: hypokalaemia increases risk of ventricular arrhythmias with amisulpiride or sertindole; enhanced hypotensive effect with phenothiazines; hypokalaemia increases risk of ventricular arrhythmias with pimozide – avoid concomitant use.
  - Atomoxetine: hypokalaemia increases risk of ventricular arrhythmias
  - Cardiac glycosides: increased toxicity if hypokalaemia occurs
  - Ciclosporin: increased risk of nephrotoxicity and hypomagnesaemia
  - Lithium: excretion reduced, increased toxicity

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - COMMENTS
  - A single dose at breakfast time is preferable

**OTHER INFORMATION**
- Can precipitate diabetes mellitus and gout, and cause severe electrolyte disturbances and an increase in serum lipids
- Thiazide diuretics are unlikely to be of use once GFR<30 mL/min
Ciclosporin

**CLINICAL USE**
Immunosuppressant:
- Prophylaxis of solid organ transplant rejection
- Nephrotic syndrome
- Atopic dermatitis
- Psoriasis
- Rheumatoid arthritis

**DOSE IN NORMAL RENAL FUNCTION**
- Organ transplantation:
  - Oral: 2–15 mg/kg/day based on levels.
    (See local protocol.)
  - IV: One-third to one-half of oral dose.
    (See local protocol.)
- Bone marrow transplantation:
  - Oral: 12.5–15 mg/kg daily
  - IV: 3–5 mg/kg daily
- Nephrotic syndrome: 5 mg/kg orally in 2 divided doses
- Atopic dermatitis/psoriasis: 2.5–5 mg/kg orally in 2 divided doses
- Rheumatoid arthritis: Oral: 2.5–4 mg/kg in 2 divided doses

**PHARMACOKINETICS**
- Molecular weight (daltons): 1202.6
- % Protein binding: Approx 90%
- % Excreted unchanged in urine: 0.1
- Volume of distribution (L/kg): 3–5
- Half-life – normal/ESRF (hrs): 5–20/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function; adjust according to levels
- HD: Not dialysed. Dose as in normal renal function; adjust according to levels
- HDF/High flux: Unknown dialysability. Dose as in normal renal function; adjust according to levels
- CAV/VHVD: Not dialysed. Dose as in normal renal function; adjust according to levels

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Increased risk of hyperkalaemia with ACE inhibitors, angiotensin-II antagonists, potassium-sparing diuretics, potassium salts
- Increased risk of nephrotoxicity with aciclovir, aminoglycosides, amphotericin, colchicine, co-trimoxazole, disopyramide, foscarnet, melphalan, NSAIDs, polymyxins, quinolones, sulphonamides, thiazide diuretics, trimethoprim and vancomycin
- Increased plasma ciclosporin levels with aciclovir, amiodarone, atazanavir, carvedilol, chloramphenicol, chloroquine, cimetidine, clarithromycin, colchicine, danazol, diltiazem, doxycycline, erythromycin, famotidine, fluconazole, fluoxetine, fluvoxamine, glibenclamide, glipizide, grapefruit juice, hydroxychloroquine, itraconazole, ketoconazole, lercanidipine (concentration of both drugs increased – avoid), miconazole, high-dose methylprednisolone, metoclopramide, metronidazole, muromonab-CD3, nelfinavir, nicardipine, nifedipine, posaconazole, progestogens, propafenone,
quinupristin/dalfopristin, ritonavir, saquinavir (concentration of both drugs increased), tacrolimus, telithromycin, verapamil and voriconazole

- Decreased plasma ciclosporin levels with barbiturates, bupropion, carbamazepine, griseofulvin, lanreotide, modafinil, octreotide, phenytoin, primidone, quinine, red wine, rifampicin, St John’s wort, sulfadiazone, IV sulfadimidine, sulfasalazine, sulfipyrazone, ticlopidine and IV trimethoprim

- Antibacterials: increased risk of myopathy with daptomycin – try to avoid concomitant use

- Basiliximab: may alter ciclosporin levels

- Bosentan: co-administration of ciclosporin and bosentan is contraindicated. When ciclosporin and bosentan are co-administered, initial trough concentrations of bosentan are 30 times higher than normal. At steady state, trough levels are 3–4 times higher than normal. Blood concentrations of ciclosporin decreased by 50%

- Calcium-channel blockers: increased nifedipine concentration and toxicity

- Cardiac glycosides: increased digoxin concentration and toxicity

- Caspofungin: caspofungin concentration increased – avoid concomitant use

- Colchicine: risk of myopathy or rhabdomyolysis; also increased blood-ciclosporin concentrations and nephrotoxicity

- Cytoxics: increased risk of neurotoxicity with doxorubicin; increased toxicity with methotrexate; seizures have been reported in bone marrow transplants taking busulfan and cyclophosphamide; concentration of etoposide possibly increased (increased risk of toxicity); possible interaction with docetaxol

- Lipid-lowering agents: increased risk of myopathy with statins (max dose of simvastatin and atorvastatin should be 10 mg); avoid with rosuvastatin; increased risk of nephrotoxicity with fenofibrate; bezafibrate may increase creatinine and reduce ciclosporin levels; concentration of both drugs may be increased with ezetimibe

- Mycophenolate mofetil: some studies show that ciclosporin decreases plasma MPA AUC levels – no dose change required

- NSAIDs: diclofenac concentration increased – reduce diclofenac dose.

- Omeprazole: may alter ciclosporin concentration

- Orlstat: absorption of ciclosporin possibly reduced

- Oxcarbazepine: may reduce ciclosporin concentration

- Prednisolone: increased prednisolone concentration

- Sirolimus: increased absorption of sirolimus – give sirolimus 4 hours after ciclosporin; sirolimus concentration increased; long-term concomitant administration may be associated with deterioration in renal function

- Sitaxentan: concentration of sitaxentan increased – avoid concomitant use

- Tacrolimus: increased tacrolimus concentration and toxicity – avoid concomitant use

- Ursodeoxycholic acid: unpredictably increased absorption and raised ciclosporin levels in some patients

**ADMINISTRATION**

**RECONSTITUTION**

- Dilute 50 mg in 20–100mL with sodium chloride 0.9% or glucose 5%

**ROUTE**

- Oral, IV peripherally or centrally

**RATE OF ADMINISTRATION**

- Over 2–6 hours peripherally or 1 hour centrally

**COMMENTS**

- To convert from IV to oral multiply by 2–3 (usually 2.5).

- Dose and monitor blood levels in accordance with local protocol

**REFERENCES**

Cidofovir

**CLINICAL USE**
- Treatment of CMV retinitis in patients with AIDS, if other agents are unsuitable
- Treatment of BK polyoma virus in transplant patients (unlicensed)

**DOSE IN NORMAL RENAL FUNCTION**
5 mg/kg weekly for 2 weeks then once every 2 weeks
(See further information for BK polyoma virus treatment)

**PHARMACOKINETICS**
- Molecular weight: 279.2 daltons
- % Protein binding: <6
- % Excreted unchanged in urine: 80–100
- Volume of distribution (L/kg): 0.3–0.8
- Half-life – normal/ESRF (hrs): 1.7–2.7/16–25

**DOSE IN RENAL IMPAIRMENT GFR (mL/min)**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;55</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;55</td>
<td>Avoid. See 'Other Information'</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose (mg/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. 0.5 mg/kg/dose</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. 0.5 mg/kg/dose</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. 0.5 mg/kg/dose</td>
</tr>
<tr>
<td>CAV/ VVHD</td>
<td>Unknown dialysability. 0.5 mg/kg/dose</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - None known

**ADMINISTRATION**

**RECONSTITUTION**

---

**ROUTE**
- IV infusion

**RATE OF ADMINISTRATION**
- Over 60 minutes

**COMMENTS**
- Dilute in 100 mL sodium chloride 0.9%

**OTHER INFORMATION**
- Always administer with oral probenecid and intravenous sodium chloride 0.9%
- Administer 2 hours before dialysis session to benefit from peak concentration without having delayed clearance
- 52–75% of dose dialysed out with high-flux haemodialysis
- Information for the treatment of BK polyoma virus in transplant patients is from Pittsburgh. Starting dose was 0.25 mg/kg (if GFR<30 mL/min) in 100 mL sodium chloride 0.9% administered over 1 hour, given every 10–14 days. Hydration pre- and post-dose with 1 litre of sodium chloride 0.9% if tolerated. If no change within 10–14 days increase to 0.3–0.5 mg/kg; dose can be increased up to 1 mg/kg depending on response and side effects. Most patients would need a cumulative dose of 1–1.5 mg/kg. Initially use without probenecid. Monitor blood and urine samples for PCR measurement of viral load.
- The manufacturer advises to avoid in renal failure but theoretical doses, based on a 70 kg person, are suggested in the following paper:

References:
## Cilazapril

### CLINICAL USE

Angiotensin-converting enzyme inhibitor: Hypertension, heart failure

### DOSE IN NORMAL RENAL FUNCTION

<table>
<thead>
<tr>
<th>Dose</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5–5 mg daily</td>
<td></td>
</tr>
</tbody>
</table>

### PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight</td>
<td>435.5 daltons</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>No data</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>80–90</td>
</tr>
<tr>
<td>Volume of distribution</td>
<td>0.5–0.8 L/kg</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>9/Increased</td>
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</tbody>
</table>

### DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>40–50</td>
<td>Start at low dose and adjust according to response</td>
</tr>
<tr>
<td>10–40</td>
<td>Start at low dose and adjust according to response</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Start at low dose and adjust according to response</td>
</tr>
</tbody>
</table>

### DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Modality</th>
<th>Dose/Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–40 mL/min</td>
</tr>
</tbody>
</table>

### IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs

- Anaesthetics: enhanced hypotensive effect
- Ciclosporin: decreased renal function and increased risk of hyperkalaemia
- NSAIDs: antagonism of hypotensive effect and increased risk of renal failure; hyperkalaemia
- Diuretics: enhanced hypotensive effect; hyperkalaemia with potassium-sparing diuretics
- Epoetin: increased risk of hyperkalaemia
- Lithium: ACE inhibitors reduce excretion of lithium (increased plasma lithium concentration)
- Potassium salts: hyperkalaemia
- Tacrolimus: decreased renal function and increased risk of hyperkalaemia

### ADMINISTRATION

#### RECONSTITUTION

- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  -
- **COMMENTS**
  - Take dose about the same time each day

### OTHER INFORMATION

- Data refer to active drug – cilazaprilat
- Symptomatic hypotension reported in patients with sodium or volume depletion, i.e. sickness, diarrhoea, on diuretics, low sodium diet or post dialysis
- Renal failure has been associated with ACE inhibitors in patients with renal artery stenosis, post renal transplant, and congestive heart failure.
- A high incidence of anaphylactoid reactions has been reported in patients dialysed with high-flux polyacrylonitrile membranes and treated concomitantly with an ACE inhibitor – this combination should therefore be avoided
- Hyperkalaemia and other side effects are more common in patients with impaired renal function
- Close monitoring of renal function during therapy is necessary in those with renal insufficiency
Cilostazol

CLINICAL USE
Intermittent claudication

DOSE IN NORMAL RENAL FUNCTION
100 mg twice daily, 30 minutes before or 2 hours after food

PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>369.5</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>95–98</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;2 as dehydro-cilostazol (74% as metabolites)</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>No data</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>10.5–13/unchanged</td>
</tr>
</tbody>
</table>

DOSE IN RENAL IMPAIRMENT

GFR (mL/min)

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>25–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–25</td>
<td>Dose as in normal renal function.</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function.</td>
</tr>
</tbody>
</table>

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Therapeutic modality</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be dialysed. Dose as in GFR=10–25mL/min</td>
</tr>
</tbody>
</table>

IMPORTANT DRUG INTERACTIONS

- Potentially hazardous interactions with other drugs
  - Anagrelide: avoid concomitant use
  - Antibacterials: concentration increased by erythromycin; also concentration of erythromycin reduced – avoid concomitant use.
  - Antifungals: concentration possibly increased by ketoconazole – avoid concomitant use.
  - Antivirals: concentration possibly increased by amprenavir, indinavir, lopinavir, nelfinavir, ritonavir and saquinavir – avoid concomitant use
  - Calcium-channel blockers: concentration increased by diltiazem – avoid concomitant use
  - Ulcer-healing drugs: concentration possibly increased by cimetidine and lansoprazole – avoid concomitant use; concentration increased by omeprazole – avoid concomitant use

ADMINISTRATION

RECONSTITUTION
- ROUTE
  - Oral

RATE OF ADMINISTRATION
- COMMENTS
  - OTHER INFORMATION
  - There are two major metabolites, a dehydro-cilostazol and a 4'-trans-hydroxy cilostazol, both of which have similar apparent half-lives. The dehydro metabolite is 4–7 times as active a platelet anti-aggregant as the parent compound, and the 4'-trans-hydroxy metabolite is one fifth as active
  - In subjects with severe renal impairment, the free fraction of cilostazol was 27% higher and both Cmax and AUC were 29% and 39% lower respectively than in subjects with normal renal function. The Cmax and AUC of the dehydro metabolite were 41% and 47% lower respectively in the severely renally impaired subjects compared to subjects with normal renal function. The Cmax and AUC of 4'-trans-hydroxy cilostazol were 173% and 209% greater in subjects with severe renal impairment. The drug should be used with great caution if administered to patients with a creatinine clearance <25mL/min
  - Contraindicated in patients with heart failure
  - Cilostazol is under investigation for its antiplatelet effect after coronary stent implantation
  - Dose can also be reduced to 50mg twice daily if used with drugs which affect its clearance
Cimetidine

**CLINICAL USE**

H₂ antagonist:
- Conditions associated with hyperacidity
- Refractory uraemic pruritus (unlicensed use)

**DOSE IN NORMAL RENAL FUNCTION**

- Oral: duodenal and gastric ulceration treatment: 800 mg at night, or 400 mg twice daily; rarely, up to 1.6 g daily
- Prophylaxis: 400 mg at night or 400 mg twice daily
- Prophylaxis of stress ulceration: 200–400 mg every 4–6 hours
- Reflux oesophagitis: 400 mg every 6 hours
- IM/IV: 200 mg every 4–6 hours, maximum 2.4 g daily
- IV Infusion: 200–400 mg every 4–6 hours intermittent or 50–100 mg/hour continuous, maximum 2.4 g daily
- Zollinger-Ellison syndrome: 400 mg every 4–6 hours

**PHARMACOKINETICS**

- Molecular weight (daltons) 252.3
- % Protein binding 20
- % Excreted unchanged in urine 50–75
- Volume of distribution (L/kg) 1–1.3
- Half-life – normal/ESRF (hrs) 2–3/5

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
<th>50% of normal dose</th>
<th>50% of normal dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>50% of normal dose</td>
<td></td>
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</tr>
<tr>
<td>&lt;10</td>
<td>50% of normal dose</td>
<td></td>
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</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD** Not dialysed. Dose as in GFR<10 mL/min
- **HD** Dialysed. Dose as in GFR<10 mL/min
- **HDF/High flux** Dialysed. Dose as in GFR<10 mL/min
- **CAV/VVHHD** Not dialysed. 300 mg every 8 hours

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Alpha-blockers: effects of tolazoline antagonised
- Anti-arrhythmics: increased concentration of amiodarone, flecaïnide, lidocaine, procainamide and propafenone
- Anticoagulants: enhanced effect of coumarins
- Anti-epileptics: metabolism of carbamazepine, phenytoin and valproate inhibited.
- Antifungals: absorption of itraconazole and ketoconazole reduced; posaconazole concentration reduced; terbinafine concentration increased
- Antimalarials: avoid concomitant use with artemether/lumefantrine; metabolism of chloroquine, hydroxychloroquine and quinine inhibited
- Antipsychotics: possibly enhanced effect of antipsychotics, chlorpromazine and clozapine; increased risk of ventricular arrhythmias with sertindole – avoid concomitant use
- Ciclosporin: possibly increased ciclosporin levels
- Cilostazol: possibly increased cilostazol concentration – avoid concomitant use
- Cytotoxics: concentration of epirubicin and fluorouracil increased
Ergot alkaloids: increased risk of ergotism
- avoid concomitant use
Theophylline: metabolism of theophylline inhibited

**ADMINISTRATION**

**RECONSTITUTION**

**ROUTE**
- Oral, IM, IV

**RATE OF ADMINISTRATION**
- IV Infusion: 400 mg in 100 mL sodium chloride 0.9% or glucose 5% over 30–60 minutes
- IV bolus: 200 mg over at least 5 minutes. Dilute larger doses to 10 mL and give over at least 10 minutes
- Continuous IV Infusion: 50–100 mg/hour

**COMMENTS**
- Avoid bolus if possible

**OTHER INFORMATION**

- Inhibits tubular secretion of creatinine
- Uraemic patients susceptible to mental confusion

References:
1. Dose from CVVH Initial Drug Dosing Guidelines on [www.thedrugmonitor.com](http://www.thedrugmonitor.com)
Cinacalcet

**CLINICAL USE**
Calcimimetic agent:
- Treatment of secondary hyperparathyroidism in patients with CKD 5 on dialysis
- Treatment of hypercalcaemia in patients with parathyroid carcinoma

**DOSE IN NORMAL RENAL FUNCTION**
Secondary hyperparathyroidism: 30–180 mg once daily
Parathyroid carcinoma: 30 mg twice daily increasing to a maximum of 90 mg 4 times a day

**PHARMACOKINETICS**
- Molecular weight (daltons): 393.9 as hydrochloride
- % Protein binding: 93–97
- % Excreted unchanged in urine: 80
- Volume of distribution (L/kg): 1000 litres

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/MIN)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAP: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unlikely to be dialysed. Dose as normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antifungals: metabolism inhibited by ketoconazole
- Tobacco: metabolism increased by tobacco

**ADMINISTRATION**
- RECONSTITUTION
  - ROUTE
  - Oral
  - RATE OF ADMINISTRATION
  - COMMENTS
  - Take with food or shortly after a meal

**OTHER INFORMATION**
- Adjust dose according to response
- Monitor calcium levels to prevent hypocalcaemia
- Can be used in combination with vitamin D analogues and phosphate binders
- Steady state is achieved after 7 days
- Metabolised by cytochrome P450 2D6, CYP3 A4 and CYP1 A2

RETURN TO CONTENTS
Cinnarizine

**CLINICAL USE**
- Vestibular disorders
- Motion sickness

**DOSE IN NORMAL RENAL FUNCTION**
- Vestibular disorders: 30 mg 3 times a day
- Motion sickness: 30 mg 2 hours before travel then 15 mg every 8 hours when required

**PHARMACOKINETICS**
- Molecular weight (daltons): 368.5
- % Protein binding: 80
- % Excreted unchanged in urine: <20
- Volume of distribution (L/kg): No data

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Unlikely to be dialysed. Dose as in normal renal function
- HDF/High Flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**
- RECONSTITUTION
  - 
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - 
- COMMENTS
  - 

It is not licensed for use by anyone else.
Ciprofibrate

**CLINICAL USE**
Hyperlipidaemia

**DOSE IN NORMAL RENAL FUNCTION**
100 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 289.2
- % Protein binding: 95–99
- % Excreted unchanged in urine: 20–25
- Volume of distribution (L/kg): 12 litres
- Half-life – normal/ESRF (hrs): 38–86/171.9

**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**
- 20–50: Dose as in normal renal function
- 10–20: 100 mg every 48 hours
- <10: Avoid. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Avoid
- HD: Not dialysed. Avoid
- HDF/High flux: Unknown dialysability. Avoid
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Antibacterials: increased risk of myopathy with daptomycin – try to avoid concomitant use
  - Anticoagulants: enhances effect of coumarins and phenindione. Dose of anticoagulant should be reduced by up to 50% and readjusted by monitoring INR
  - Antidiabetics: may improve glucose tolerance and have an additive effect with insulin or sulphonylureas
  - Lipid-regulating drugs: increased risk of myopathy in combination with statins (do not exceed 10 mg of simvastatin) and ezetimibe – avoid concomitant use with ezetimibe

**ADMINISTRATION**

**RECONSTITUTION**
- 
  **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- 
  **COMMENTS**
- 

**OTHER INFORMATION**
- Increased risk of rhabdomyolysis in doses of 200 mg or greater
- Approximately 30–75% of a single dose administered to volunteers was excreted in the urine in 72 hours, either as unchanged ciprofibrate (20–25% of the total excreted) or as a conjugate. Subjects with moderate renal impairment excreted on average 7% of a single dose as unchanged ciprofibrate over 96 hours, compared with 6.9% in normal subjects. In subjects with severe insufficiency this was reduced to 4.7%

References:
1. MHRA. Drug Safety Update. 2008, Jan; 1(6): 2–4
Ciprofloxacin

CLINICAL USE
Antibacterial agent

DOSE IN NORMAL RENAL FUNCTION
Oral: 250–750 mg every 12 hours
IV: 100–400 mg every 12 hours

PHARMACOKINETICS
Molecular weight (daltons) 331.3
% Protein binding 20–40
% Excreted unchanged in urine 40–70
Volume of distribution (L/kg) 2.5
Half-life – normal/ESRF (hrs) 3–5/8

DOSE IN RENAL IMPAIRMENT
GFR (mL/MIN)
20–50 Dose as in normal renal function
10–20 50–100% of normal dose
<10 50% of normal dose. (100% dose may be given for short periods under exceptional circumstances)

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Not dialysed. Oral: 250 mg every 8–12 hours. IV: 200 mg every 12 hours
HD Not dialysed. Oral: 250–500 mg every 12 hours. IV: 200 mg every 12 hours
HDF/High flux Unknown dialysability. Oral: 250–500 mg every 12 hours. IV: 200 mg every 12 hours
CAV/VVHD Dialysed. Oral: 500–750 mg every 12 hours. IV: 200–400 mg every 12 hours

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Analgesics: increased risk of convulsions with NSAIDs; avoid premedication with opioid analgesics
- Anticoagulants: anticoagulant effect of coumarins enhanced
- Antidepressants: metabolism of duloxetine inhibited
- Antimalarials: manufacturer of artemether with lumefantrine advises avoid concomitant use
- Antipsychotics: possibly increased concentration of olanzapine and clozapine
- Ciclosporin: variable response; no interaction seen locally; some reports of increased nephrotoxicity
- Muscle relaxants: tizanidine concentration increased – avoid concomitant use
- Tacrolimus: increased levels (anecdotally)
- Theophylline: possibly increased risk of convulsions; increased plasma levels of theophylline

ADMINISTRATION
RECONSTITUTION
- ROUTE
  - Oral, IV
- RATE OF ADMINISTRATION
  - Infusion: over 30–60 minutes
- COMMENTS
  - Swallow tablets whole, do not chew
  - Do not take milk, iron preparations, indigestion remedies or phosphate binders at the same time as ciprofloxacin orally

OTHER INFORMATION
- Intraperitoneal ciprofloxacin in CAPD, dose range 25 mg/L to 100 mg/L
- In CAPD peritonitis oral ciprofloxacin up to 500 mg twice daily may be administered
- Oral bioavailability is 70–80%
- Only very small amounts removed by dialysis
Cisplatin

**CLINICAL USE**

Antineoplastic agent:
- Testicular and metastatic ovarian tumours
- Cervical tumours
- Lung carcinoma
- Bladder cancer

**DOSE IN NORMAL RENAL FUNCTION**

- Single agent therapy: 50–120 mg/m² as a single dose every 3–4 weeks or 15–20 mg/m² daily for 5 days every 3–4 weeks
- Combination therapy: 20 mg/m² and upward, every 3–4 weeks

**PHARMACOKINETICS**

- Molecular weight (daltons): 300
- % Protein binding: >90
- % Excreted unchanged in urine: 27–45
- Volume of distribution (L/kg): 0.5
- Half-life – normal/ESRF (hrs): 0.3–1 (terminal T½) 2–5 days

**DOSE IN RENAL IMPAIRMENT**

- **GFR (mL/min)**
  - 20–50: See ‘Other Information’
  - 10–20: See ‘Other Information’
  - <10: See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**: Unknown dialysability. Dose as in GFR<10 mL/min
- **HD**: Not dialysed. Dose as in GFR<10 mL/min
- **HDF/High flux**: Dialysed. Dose as in GFR<10 mL/min
- **CAV/VVHD**: GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**

- Antipsychotics: avoid concomitant use with clozapine, increased risk of agranulocytosis
- Cytotoxics: increased pulmonary toxicity with bleomycin and methotrexate

**ADMINISTRATION**

**RECONSTITUTION**

- Water for injection to form a 1 mg/mL solution

**ROUTE**

- IV infusion

**RATE OF ADMINISTRATION**

- Over 6–8 hours

**COMMENTS**

- Pre-treatment hydration, with 1–2 litres of fluid infused for 8–12 hours prior to cisplatin dose, is recommended in order to initiate diuresis. The drug is then well diluted in 2 litres sodium chloride 0.9% or glucose-saline solutions to ensure hydration and maintain urine output. Adequate hydration must be maintained during the following 24 hours, with potassium and magnesium supplementation given as necessary
- Cisplatin solutions react with aluminium – do not use equipment containing aluminium

**OTHER INFORMATION**

- Dose modification depends not only on the degree of renal dysfunction, but also on the intended dose and the therapeutic end-point. In general, any patient with a GFR<70 mL/min should be highlighted as ‘at risk’ from cisplatin renal toxicity.
- Non-enzymatically transformed into multiple metabolites. Good uptake of cisplatin in the kidneys, liver and intestine.
Distributes into third spaces such as ascites and pleural fluid. Elimination of intact drug and metabolites is via the urine. In the first 24 hrs 20–80% is excreted.

- Ototoxicity, nephrotoxicity and myelosuppression reported. Check hearing, renal function and haematology before treatment and before each subsequent course.
- Toxicity is also associated with cumulative doses of cisplatin.
- Hypomagnesaemia, hypocalcaemia and hyperuricaemia observed.
- The addition of mannitol to the infusion may aid diuresis and protect the kidneys.

RETURN TO CONTENTS
Citalopram

**CLINICAL USE**
SSRI antidepressant:
- Depressive illness
- Panic disorder

**DOSE IN NORMAL RENAL FUNCTION**
10–60 mg daily
Oral drops: 8–48 mg (4 drops = 8 mg liquid = 10 mg tablet)

**PHARMACOKINETICS**
- Molecular weight: 324.4 daltons
- % Protein binding: <80%
- % Excreted unchanged in urine: 12%
- Volume of distribution (L/kg): 12.3
- Half-life – normal/ESRF (hrs): 36/49.5

**DOSE IN RENAL IMPAIRMENT**

- **GFR (mL/Min)**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function. Use with caution

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**: Unlikely to be dialysed. Dose as in GFR<10mL/min
- **HD**: Not dialysed. Dose as in GFR<10mL/min
- **HDF/High flux**: Not dialysed. Dose as in GFR<10mL/min
- **CAV/VVHD**: Unlikely to be dialysed. Dose as in GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Analgesics: increased risk of bleeding with aspirin and NSAIDs; risk of CNS toxicity increased with tramadol
  - Anticoagulants: effect of coumarins possibly enhanced
  - Antidepressants: avoid concomitant use with MAOIs and moclobemide, increased risk of toxicity; avoid concomitant use with St John’s wort; possibly enhanced serotonergic effects with duloxetine; can increase tricyclics antidepressant concentration; increased agitation and nausea with tryptophan
  - Anti-epileptics: convulsive threshold lowered
  - Antimalarials: avoid concomitant use with artemether/lumefantrine
  - Antipsychotics: possibly increased clozapine concentration
  - Antivirals: concentration possibly increased by ritonavir
  - Dopaminergics: use selegiline with caution; increased risk of CNS toxicity with rasagiline
  - 5 HT1 agonist: increased risk of CNS toxicity with sumatriptan; possibly increased risk of serotonergic effects with frovatriptan
  - Linezolid: use with care, possibly increased risk of side effects
  - Lithium: increased risk of CNS effects
  - Sibutramine: increased risk of CNS toxicity (avoid concomitant use)

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- Only 1% of drug is removed by haemodialysis
- There is reduced clearance of Citalopram in severe renal failure
Cladribine

CLINICAL USE
Antineoplastic agent:
- Hairy cell leukaemia (HCL)
- Chronic lymphocytic leukaemia (CLL)

DOSE IN NORMAL RENAL FUNCTION
Leustat:
- HCL: 0.09 mg/kg (3.6 mg/m²) daily for 7 days
- CLL: 0.12 mg/kg (4.8 mg/m²) daily for 2 hours on days 1 to 5 of a 28 day cycle
Litak:
- HCL: 0.14 mg/kg/day for 5 days by subcutaneous injection

PHARMACOKINETICS
- Molecular weight (daltons): 285.7
- % Protein binding: 20
- % Excreted unchanged in urine: 18
- Volume of distribution (L/kg): 9
- Half-life – normal/ESRF (hrs): 3–22/No data

DOSE IN RENAL IMPAIRMENT
GFR (mL/MIN)
- 20–50 Use with caution. See ‘Other Information’
- 10–20 Use with caution See ‘Other Information’
- <10 Use with caution See ‘Other Information’

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD Unknown dialysability. Dose as in GFR<10mL/min
- HD Unknown dialysability. Dose as in GFR<10mL/min
- HDF/High flux Unknown dialysability. Dose as in GFR<10mL/min
- CAV/VVHD Unknown dialysability. Dose as in GFR=10–20mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs:
- Caution when administering with any other immunosuppressive or myelosuppressive therapy

ADMINISTRATION
RECONSTITUTION
- ROUTE SC, IV infusion
- RATE OF ADMINISTRATION 24 hours or 2 hours depending on condition being treated
COMMENTS
- Add to 100–500 mL of sodium chloride 0.9%

OTHER INFORMATION
- Prodrug – activated by intracellular phosphorylation. The nucleotide that is formed accumulates in the cell and is incorporated into the DNA.
- Regular monitoring is recommended in renal failure
- Acute renal insufficiency has developed in some patients receiving high-dose cladribine
- Inadequate data on dosing of patients with renal insufficiency therefore use according to clinical need
- Study showed that <10% of dose is excreted in urine as metabolites and <20% as parent drug

RETURN TO CONTENTS
Clarithromycin

**CLINICAL USE**
Antibacterial agent:
- Adjunct in treatment of duodenal ulcers by eradication of *Helicobacter pylori*

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: 250–500 mg every 12 hours
- IV: 500 mg every 12 hours

**PHARMACOKINETICS**
- Molecular weight: 748 daltons
- % Protein binding: 80
- % Excreted unchanged in urine: 15–40
- Volume of distribution (L/kg): 2–4
- Half-life – normal/ESRF (hrs): 3–7/Prolonged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose (mg every 12 hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–30</td>
<td>Oral: 250–500 mg</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Oral: 250–500 mg</td>
</tr>
</tbody>
</table>

See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose (mg every 12 hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High Flux</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/ VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–30mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
- Anti-coagulants: effect of coumarins potentially enhanced
- Antidepressants: avoid concomitant use with reboxetine
- Anti-epileptics: increased carbamazepine and phenytoin concentration.
- Antihistamines: metabolism of mizolastine inhibited – avoid concomitant use
- Antimalarials: avoid concomitant administration with artemether/lumefantrine
- Antimuscarinics: avoid concomitant use with tolterodine
- Antipsychotics: increased risk of arrhythmias with pimozide and sertindole – avoid concomitant use; possibly increased quetiapine concentration
- Antivirals: concentration of both drugs increased with atazanavir; increased risk of rash with efavirenz; oral clarithromycin reduces absorption of zidovudine; concentration increased by ritonavir and tipranavir; also concentration of tipranavir increased – reduce dose of clarithromycin in renal impairment
- Anxiolytics: metabolism of midazolam inhibited
- Calcium-channel blockers: possibly inhibits verapamil concentration
- Ciclosporin: increased ciclosporin concentration (although may take ≅ 5 days after starting clarithromycin before increase in ciclosporin levels is seen)
- Colchicine: treatment with both agents has been shown in a study to increase the risk of fatal colchicine toxicity, especially in patients with renal impairment.
- Diuretics: increased eplerenone concentration – avoid concomitant use
- Ergot alkaloids: increased risk of ergotism – avoid concomitant use
- 5 HT1 agonists: increased eletriptan concentration – avoid concomitant use
- Ivabradine: increased ivabradine concentration – avoid concomitant use
- Lipid-lowering drugs: increased risk of myopathy with atorvastatin and simvastatin, avoid with simvastatin and max dose of atorvastatin 20 mg.
- Sirolimus: possibly increased sirolimus concentration – avoid concomitant use
- Tacrolimus: increased tacrolimus levels
- Theophylline: increased theophylline concentration

- Anti-arrhythmics: possibly increased disopyramide concentration
- Antibacterials: increased rifabutin concentration – reduce rifabutin dose; clarithromycin concentration reduced by rifamycins
- Anticoagulants: effect of coumarins potentially enhanced
- Antidepressants: avoid concomitant use with reboxetine
- Anti-epileptics: increased carbamazepine and phenytoin concentration.
- Antihistamines: metabolism of mizolastine inhibited – avoid concomitant use
- Antimalarials: avoid concomitant administration with artemether/lumefantrine
- Antimuscarinics: avoid concomitant use with tolterodine
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- Ivabradine: increased ivabradine concentration – avoid concomitant use
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- Sirolimus: possibly increased sirolimus concentration – avoid concomitant use
- Tacrolimus: increased tacrolimus levels
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- Antihistamines: metabolism of mizolastine inhibited – avoid concomitant use
- Antimalarials: avoid concomitant administration with artemether/lumefantrine
- Antimuscarinics: avoid concomitant use with tolterodine
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- Ergot alkaloids: increased risk of ergotism – avoid concomitant use
- 5 HT1 agonists: increased eletriptan concentration – avoid concomitant use
- Ivabradine: increased ivabradine concentration – avoid concomitant use
- Lipid-lowering drugs: increased risk of myopathy with atorvastatin and simvastatin, avoid with simvastatin and max dose of atorvastatin 20 mg.
- Sirolimus: possibly increased sirolimus concentration – avoid concomitant use
- Tacrolimus: increased tacrolimus levels
- Theophylline: increased theophylline concentration
### ADMINISTRATION

**RECONSTITUTION**
- Add 10 mL water for injection to vial (500 mg). Add reconstituted product to 250 mL glucose 5% or sodium chloride 0.9%. (Stable in 100 mL, but more likely to cause phlebitis, pain and inflammation at the injection site)

**ROUTE**
- IV infusion into one of the larger proximal veins
- Not to be administered by bolus or IM injection

**RATE OF ADMINISTRATION**
- Over 60 minutes

### OTHER INFORMATION

- Use with caution in renal or hepatic failure
- Oral bioavailability is 55%
- Patients with GFR<10 mL/min, vomiting may be a problem with high doses

**REFERENCES**
2. MHRA. *Drug Safety Update.* 2008, Jan; 1(6): 2–4
Clindamycin

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
Oral: 150–450 mg every 6 hours,
Endocarditis prophylaxis: 600 mg 1 hour before procedure
IV/IM: 0.6–4.8 g daily in 2–4 divided doses,
Prophylaxis: 300 mg 15 minutes before procedure then 150 mg 6 hours later

**PHARMACOKINETICS**
- Molecular weight
  - As hydrochloride: 461.4 da (daltons)
  - As phosphate: 505 da
- % Protein binding
  - >90%
- % Excreted unchanged in urine
  - 10%
- Volume of distribution
  - (L/kg)
  - 0.6–1.2
- Half-life – normal/ESRF (hrs)
  - 2–3/3–5

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50 Dose as in normal renal function
  - 10–20 Dose as in normal renal function
  - <10 Dose as in normal renal function. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Not dialysed. Dose as in normal renal function
- HD Not dialysed. Dose as in normal renal function
- HDF/High flux Unknown dialysability. Dose as in normal renal function
- CAV/ VVHD Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Ciclosporin: may cause reduced ciclosporin levels
- Erythromycin: antagonism demonstrated in vitro; manufacturers recommend that the two drugs should not be administered concurrently
- Muscle relaxants: enhanced neuromuscular blockade

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral, IV, IM
- RATE OF ADMINISTRATION
  - 10–60 minutes
- COMMENTS
  - Dilute prior to IV administration: up to 900 mg, in at least 50 mL of diluent; over 900 mg, in 100 mL of diluent. Compatible with sodium chloride 0.9% or glucose 5%
  - Administration of more than 1200 mg in a single 1 hour infusion is not recommended
  - Doses greater than 600 mg should be given as IV infusions

**OTHER INFORMATION**
- Capsules should be swallowed whole with a glass of water
- Pseudomembranous colitis may occur
- Periodic kidney and liver function tests should be carried out during prolonged therapy
- Dosage may require reduction in patients with severe renal impairment due to prolonged half-life
Clobazam

**CLINICAL USE**

Benzodiazepine:
- Anticonvulsant
- Anxiolytic

**DOSE IN NORMAL RENAL FUNCTION**

20–30 mg daily; maximum 60 mg daily (doses may be divided for anxiety and can go up to 80 mg)

**PHARMACOKINETICS**

Molecular weight (daltons) 300.7

% Protein binding 85%

% Excreted unchanged in urine 87 (unchanged drug and metabolite)

Volume of distribution (L/kg) 0.87–1.83

Half-life – normal/ESRF (hrs) 11–77 (42 hours for metabolite)/–

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function. Start with low doses</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Dialysis Type</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Antibacterials: metabolism possibly increased by rifampicin
- Antipsychotics: increased sedative effects
- Antivirals: concentration possibly increased by ritonavir
- Disulfiram: metabolism of clobazam inhibited; increased sedative effects
- Sodium oxybate: enhanced effects of sodium oxybate – avoid

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**

- **COMMENTS**

**OTHER INFORMATION**

- Syrup is available
- Metabolised to active N-desmethylclobazam which may accumulate
- Causes less sedation than clonazepam
- There is a case report of clobazam being used to treat phantom limb pain at a dose of 10 mg 3 times a day. (Rice-Oxley CP. The limited list: clobazam for phantom limb pain. *BMJ*. 1986; 293: 1309)
Clofazimine

**CLINICAL USE**
Treatment of leprosy

**DOSE IN NORMAL RENAL FUNCTION**
Multibacillary leprosy: 300 mg once monthly (supervised) or 50 mg daily or 100 mg alternate days (unsupervised)
Lepromatous lepra reactions: 300 mg daily

**PHARMACOKINETICS**
Molecular weight (daltons) 473.4
% Protein binding Low
% Excreted unchanged in urine <1
Volume of distribution (L/kg) High
Half-life – normal/ESRF (hrs) 10–70 days/Unchanged

**DOSE IN RENAL IMPAIRMENT**
GFR (mL/MIN)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
CAPD Not dialysed. Dose as in normal renal function
HD Not dialysed. Dose as in normal renal function
HDF/High flux Unknown dialysability. Dose as in normal renal function
CAV/ VVHD Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
None known

**ADMINISTRATION**

**RECONSTITUTION**
–

**ROUTE**
– Oral

**RATE OF ADMINISTRATION**
–

**COMMENTS**
–

**OTHER INFORMATION**
– In the sunlight a red/brown discolouration may appear on the skin
– Secretions may also become a red/brown colour
– Available on a named patient basis

References:
Clomethiazole (chlormethiazole)

**CLINICAL USE**
- Alcohol withdrawal
- Insomnia
- Restlessness and agitation

**DOSE IN NORMAL RENAL FUNCTION**
- Alcohol withdrawal: 2–4 capsules stat, then:
  - Day 1: 3 capsules 3 or 4 times daily
  - Day 2: 2 capsules 3 or 4 times daily
  - Day 3: 1 capsule 4 times daily
  - Reduce over a further 4–6 days; give a total treatment of not more than 9 days
- Insomnia: 1–2 capsules at night
- Restlessness and agitation: 1 capsule 3 times daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 161.7
- % Protein binding: 65
- % Excreted unchanged in urine: 0.1–5
- Volume of distribution (L/kg): 4–16

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Dialysed. Dose as in normal renal function
- HDF/High flux: Dialysed. Dose as in normal renal function
- CAV/VVHD: Dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs:
  - Antipsychotics: enhanced sedative effects
  - Antivirals: concentration possibly increased by ritonavir
  - Cimetidine: inhibits metabolism of clomethiazole

**ADMINISTRATION**
- RECONSTITUTION
  - ROUTE: Oral
  - RATE OF ADMINISTRATION
  - COMMENTS: Syrup should be stored in a fridge

**OTHER INFORMATION**
- Clomethiazole has a high hepatic extraction ratio
- Increased cerebral sensitivity in renal impairment
- Manufacturers recommend caution should be observed in patients with chronic renal disease
Clomipramine hydrochloride

**CLINICAL USE**
- Depressive illness
- Phobic and obsessional states
- Adjunctive treatment of cataplexy associated with narcolepsy

**DOSE IN NORMAL RENAL FUNCTION**
- 10–250 mg daily
- Cataplexy: 10–75 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 351.3
- % Protein binding: 97.6
- % Excreted unchanged in urine: 2
- Volume of distribution (L/kg): 12–17
- Half-life – normal/ESRF (hrs): 12–36/

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Start at lower doses and increase according to response
  - <10: Start at lower doses and increase according to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Not dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
- Anti-arrhythmics: increased risk of ventricular arrhythmias with amiodarone – avoid concomitant use; increased risk of ventricular arrhythmias with drugs that prolong the QT interval; increased risk of arrhythmias with propafenone
- Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin – avoid concomitant use; concentration possibly reduced by rifampicin
- Anticoagulants: may alter anticoagulant effect of coumarins
- Antidepressants: possibly increased serotonergic effects with duloxetine; enhanced CNS excitation and hypertension with MAOIs and moclobemide; concentration possibly increased with SSRIs
- Anti-epileptics: convulsive threshold lowered; concentration reduced by carbamazepine, primidone, barbiturates and possibly phenytoin
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: increased risk of ventricular arrhythmias especially with pimozide; increased antimuscarinic effects with clozapine and phenothiazines; concentration increased by antipsychotics
- Antivirals: increased tricyclic side effects with amipavir; concentration possibly increased with ritonavir
- Atomoxetine: increased risk of ventricular arrhythmias and possibly convulsions
- Beta-blockers: increased risk of ventricular arrhythmias with sotalol
- Clonidine: tricyclics antagonise hypotensive effect; increased risk of hypertension on clonidine withdrawal
- Dopaminergics: avoid use with entacapone; CNS toxicity reported with selegiline and rasagiline
- Pentamidine: increased risk of ventricular arrhythmias
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use.
- Sympathomimetics: increased risk of hypertension and arrhythmias with adrenaline and noradrenaline; metabolism possibly inhibited by methylphenidate
### ADMINISTRATION

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

### OTHER INFORMATION

- Normal doses have been used in dialysis patients long term, but caution as parent drug and active metabolites may accumulate
Clonazepam

**CLINICAL USE**

Benzodiazepine:
- Anticonvulsant
- Anxiolytic
- Restless legs syndrome

**DOSE IN NORMAL RENAL FUNCTION**

- Oral: 0.5–20 mg daily in 3–4 divided doses or as a single dose at night once on maintenance therapy; normal maintenance dose: 4–8 mg daily
- IV: 1 mg, repeated if necessary
- Restless legs syndrome: 0.5–4 mg at night

**PHARMACOKINETICS**

- Molecular weight (daltons): 315.7
- % Protein binding: 86
- % Excreted unchanged in urine: <0.5
- Volume of distribution (L/kg): 3
- Half-life – normal/ESRF (hrs): 20–60/–

**DOSE IN RENAL IMPAIRMENT**

- GFR (mL/min):
  - 20–50: Start at low dose and increase according to response
  - 10–20: Start at low dose and increase according to response
  - <10: Start at low dose and increase according to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as GFR<10 mL/min
- CAV/VVHD: Not dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Antibacterials: metabolism possibly increased by rifampicin
- Antipsychotics: increased sedative effects
- Antivirals: increased risk of prolonged sedation with ampranavir; concentration possibly increased by ritonavir
- Disulfiram: metabolism inhibited, increased sedative effects
- Sodium oxybate: metabolism inhibited, increased sedative effects

**ADMINISTRATION**

**RECONSTITUTION**

- IV bolus: reconstitute with 1 mL diluent (water for injection) to give 1 mg in 1 mL solution.
- IV infusion: up to 3 mg (3 amps) added to 250 mL sodium chloride 0.9% or glucose 5%

**ROUTE**

- Oral, IV bolus or infusion

**RATE OF ADMINISTRATION**

- IV bolus: 0.25–0.5 mg over 1 minute

**COMMENTS**

- IV infusion of clonazepam is potentially hazardous (especially if prolonged), calling for close and constant observation; best carried out in specialist centres with ICU facilities. Risks include apnoea, hypotension and deep unconsciousness

**OTHER INFORMATION**

- In long-term administration, active metabolites may accumulate and lower doses should be used
- Clonazepam is one of several agents that are used in restless leg syndrome, and has also been tried in the management of intractable hiccup where chlorpromazine has failed
Clonidine hydrochloride

### Clinical Use
- Hypertension
- Migraine
- Gilles de la Tourette syndrome
- Menopausal flushing

### Dose in Normal Renal Function
- Hypertension: 50–100 mcg 3 times a day, increasing gradually to 1.2 mg daily
- Slow IV: 150–300 mcg; maximum 750 mcg in 24 hours
- Migraine, menopausal flushing, Gilles de la Tourette syndrome: 50–75 mcg twice daily

### Pharmacokinetics
- Molecular weight: 266.6
- % Protein binding: 30–40
- % Excreted: 40–60
- Volume of distribution (L/kg): 3–6
- Half-life – normal/ESRF (hrs): 10–20/41

### Dose in Renal Impairment

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose in Normal Renal Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

### Administration
- **Reconstitution**
  - Route
    - Oral, IV
- **Rate of Administration**
  - Slow IV injection
- **Comments**
  - Minimum volume for infusion 6–50 mcg/mL in sodium chloride 0.9% or glucose 5% (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006)

### Other Information
- Use in renal impairment: clonidine plasma concentrations for a given dose are 2–3 times higher in patients with severe renal impairment; however, blood pressure control appears satisfactory and adverse effects are not increased
- Clonidine withdrawal: rebound hypertension if drug is abruptly withdrawn
- Tricyclic antidepressants may decrease efficacy

### Important Drug Interactions
Potentially hazardous interactions with other drugs
- Antidepressants: tricyclics antagonise hypotensive effect and also increase risk of hypertension on clonidine withdrawal; increased hypotensive effect with MAOIs
- Beta-adrenoceptor antagonists: increased risk of hypertension on withdrawal
- Ciclosporin: may increase ciclosporin levels
- Sympathomimetics: possibly increased risk of hypertension with adrenaline and noradrenaline; serious adverse effects reported with methylphenidate
Clopidogrel

CLINICAL USE
Antiplatelet agent

DOSE IN NORMAL RENAL FUNCTION
75 mg daily
Acute coronary syndrome and post-MI: 300 mg loading dose then 75 mg daily (with aspirin 75–325 mg daily)

PHARMACOKINETICS
Molecular weight (daltons) 419.9 (as hydrogen sulphate)
% Protein binding 98
% Excreted unchanged in urine 50
Volume of distribution (L/kg) No data
Half-life – normal/ESRF (hrs) 8 (active metabolite)/–

DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unlikely to be dialysed. Dose as in normal renal function
HD Unlikely to be dialysed. Dose as in normal renal function
HDF/High flux Unknown dialysability. Dose as in normal renal function
CAV/VVHD Unlikely to be dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Anticoagulants: enhanced anticoagulant effect with coumarins and phenindione; manufacturer advises to avoid concomitant use with warfarin
- Heparin: increased risk of bleeding

ADMINISTRATION
RECONSTITUTION –
ROUTE
- Oral
RATE OF ADMINISTRATION –
COMMENTS –

RETURN TO CONTENTS
Clozapine

**CLINICAL USE**
Atypical antipsychotic:
- Schizophrenia
- Psychosis in Parkinson's disease

**DOSE IN NORMAL RENAL FUNCTION**
- Schizophrenia: 200–450 mg daily in divided doses, maximum 900 mg daily
- Psychosis in Parkinson's disease: 25–37.5 mg daily at night, maximum 100 mg daily in 1–2 divided doses

**PHARMACOKINETICS**
- Molecular weight (daltons): 326.8
- % Protein binding: 95–97
- % Excreted unchanged in urine: Minimal (50% as metabolites)
- Volume of distribution (L/kg): 1.6–6
- Half-life – normal/ESRF (hrs): 6–26

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function; use with caution</th>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function; use with caution</th>
<th>GFR (mL/min)</th>
<th>Start with a low dose and titrate slowly</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td>10–20</td>
<td></td>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose as in GFR&lt;10 mL/min</th>
<th>Dose as in GFR&lt;10 mL/min</th>
<th>Dose as in GFR&lt;10 mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed.</td>
<td>Unlikely to be dialysed.</td>
<td>Unknown dialysability.</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed.</td>
<td>Unlikely to be dialysed.</td>
<td>Unknown dialysability.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability.</td>
<td>Unknown dialysability.</td>
<td>Unknown dialysability.</td>
</tr>
<tr>
<td>CAV/ VVHD</td>
<td>GFR=10–20 mL/min</td>
<td>GFR=10–20 mL/min</td>
<td>GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
- Analgesics: avoid concomitant use with azapropazone; increased risk of convulsions with tramadol; enhanced hypotensive and sedative effects with opioids
- Anti-arrhythmics: increased risk of ventricular arrhythmias with anti-arrhythmics that prolong the QT interval; increased risk of arrhythmias with flecainide
- Antibacterials: concentration possibly increased by erythromycin (possible increased risk of convulsions); concentration increased by ciprofloxacin; concentration possibly reduced by rifampicin; avoid concomitant use with chloramphenicol and sulphonamides (increased risk of agranulocytosis)
- Antidepressants: concentration possibly increased by citalopram, fluoxetine, fluvoxamine, sertraline and venlafaxine (increased risk of toxicity); possibly increased CNS effects of MAOIs; possibly increased antimuscarinic effects with tricyclics; increased plasma level of tricyclics
- Anti-epileptics: antagonises anticonvulsant effect; metabolism accelerated by carbamazepine and phenytoin; avoid concomitant use with drugs known to cause agranulocytosis
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: avoid concomitant use with depot formulations (cannot be withdrawn quickly if neutropenia occurs)
- Antivirals: concentration possibly increased by amiprenavir; concentration increased by ritonavir – avoid concomitant use
- Anxiolytics and hypnotics: increased sedative effects
- Cytotoxics: increased risk of agranulocytosis – avoid concomitant use
- Lithium: increased risk of extrapyramidal side effects and possibly neurotoxicity
- Penicillamine: increased risk of agranulocytosis – avoid concomitant use
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use
- Ulcer-healing drugs: effects possibly enhanced by cimetidine; concentration possibly reduced by omeprazole

RETURN TO CONTENTS
<table>
<thead>
<tr>
<th>ADMINISTRATION</th>
<th>OTHER INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>RECONSTITUTION</td>
<td>● Patient must be registered with appropriate company monitoring scheme</td>
</tr>
<tr>
<td>ROUTE</td>
<td>● Associated with myocarditis (increased risk in the first 2 months) and cardiomyopathy</td>
</tr>
<tr>
<td>● Oral</td>
<td>● Potentially fatal agranulocytosis and neutropenia have been reported. WCC has to be monitored at least weekly for the first 18 weeks then 2 weekly for weeks 18–52 and then at least 4 weekly</td>
</tr>
<tr>
<td>RATE OF ADMINISTRATION</td>
<td>● Increased risk of side effects especially seizures in doses above 450 mg daily</td>
</tr>
<tr>
<td>COMMENTS</td>
<td>● Rarely interstitial nephritis has been reported with clozapine</td>
</tr>
<tr>
<td></td>
<td>● Dose in severe renal impairment taken from personal experience</td>
</tr>
</tbody>
</table>
Co-amoxiclav (amoxicillin/clavulanic acid)

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
- IV: 1.2 g every 8 hours (increasing to every 6 hours in severe infections)
- Oral: 375–625 mg 3 times daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th></th>
<th>Amoxycillin</th>
<th>Clavulanic acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>365.4</td>
<td>199.2</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>20</td>
<td>25</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>60</td>
<td>40</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1–1.5/7–20</td>
<td>1/3–4</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td></td>
</tr>
<tr>
<td>10–30</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>IV: 1.2 g every 12 hours</td>
</tr>
<tr>
<td></td>
<td>Oral: Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapies</th>
<th>Dose as in GFR &lt;10 mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Dialysed</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: effects of coumarins are potentially enhanced
- Oral contraceptives: potentially reduced efficacy
- Methotrexate: reduced excretion thereby increasing risk of toxicity

**ADMINISTRATION**

**RECONSTITUTION**
- 600 mg with 10 mL water for injection; 1.2 g with 20 mL water for injection

**ROUTE**
- Oral, IV

**RATE OF ADMINISTRATION**
- IV bolus: over 3–4 minutes
- Infusion: infuse over 30–40 minutes in 50–100 mL sodium chloride 0.9%

**COMMENTS**
- IV preparation is less stable in infusion solutions containing glucose, dextran or bicarbonate. May be injected into drip tubing over period of 3–4 minutes
- Do not mix with aminoglycosides

**OTHER INFORMATION**
- CSM has advised that cholestatic jaundice may occur if treatment exceeds a period of 14 days or up to 6 weeks after treatment has been stopped. The incidence of cholestatic jaundice occurring with co-amoxiclav is higher in males than in females, and prevalent particularly in men over the age of 65 years
- The probability of co-amoxiclav associated cholestatic jaundice is 6 times more common than with amoxicillin, and with higher doses of clavulanic acid
- Each 1.2 g vial contains: sodium 2.7 mmol, potassium 1 mmol

---

CSM has advised that cholestatic jaundice may occur if treatment exceeds a period of 14 days or up to 6 weeks after treatment has been stopped. The incidence of cholestatic jaundice occurring with co-amoxiclav is higher in males than in females, and prevalent particularly in men over the age of 65 years

- The probability of co-amoxiclav associated cholestatic jaundice is 6 times more common than with amoxicillin, and with higher doses of clavulanic acid
- Each 1.2 g vial contains: sodium 2.7 mmol, potassium 1 mmol
Co-beneldopa (Madopar)

**CLINICAL USE**
Treatment of Parkinsonism

**DOSE IN NORMAL RENAL FUNCTION**
150–800 mg daily in divided doses after meals (expressed as levodopa)

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Benserazide</th>
<th>Levodopa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>293.7 (as HCl)</td>
<td>197.2</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>0</td>
<td>10–30</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>0 (64 as metab), levodopa: &lt;1</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>no data, levodopa: 0.36–1.6</td>
<td>0.36–1.6</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1.5/Increased, levodopa: 1.5/Increased by 25%</td>
<td>1.5/Increased by 25%</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed.</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysed.</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unknown dialysability.</td>
</tr>
<tr>
<td>VVHD</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Anaesthetics: risk of arrhythmias with volatile liquid anaesthetics such as halothane
- Antidepressants: hypertensive crisis with MAOIs and linezolid (including moclobemide) – avoid for at least 2 weeks after stopping MAOI
- Bupropion: increased risk of side effects of levodopa
- Ferrous sulphate: reduces AUC of levodopa by 30–50%, clinically significant in some but not all patients

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- Can be used to treat restless legs syndrome at a dose of 62.5–125 mg
- Urine may be red-tinged and turn dark on standing, due to metabolites
- Serum uric acid and blood urea nitrogen levels are occasionally elevated

RETURN TO CONTENTS
Co-careldopa (Sinemet)

**CLINICAL USE**
Treatment of Parkinsonism

**DOSE IN NORMAL RENAL FUNCTION**
75–800 mg carbidopa daily in divided doses after meals

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Carbidopa</th>
<th>Levodopa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>244.2</td>
<td>197.2</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>36%</td>
<td>10–30%</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>30%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>No data</td>
<td>0.36–1.6</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>2–3</td>
<td>0.6–1.3/Unknown</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

GFR (mL/min)
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: risk of arrhythmias with volatile liquid anaesthetics such as halothane
- Antidepressants: hypertensive crisis with MAOIs and linezolid (including moclobemide) – avoid for at least 2 weeks after stopping MAOI
- Bupropion: increased risk of side effects of levodopa
- Ferrous sulphate: reduces AUC of levodopa by 30–50%, clinically significant in some but not all patients

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- Can be used to treat restless legs syndrome
- May cause dark urine
Co-codamol (paracetamol and codeine phosphate)

**CLINICAL USE**
Analgesic

**DOSE IN NORMAL RENAL FUNCTION**
1–2 tablets up to 4 times a day

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Paracetamol</th>
<th>Codeine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>151.2</td>
<td>317.4</td>
</tr>
<tr>
<td>(codeine phosphate 406.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Protein binding</td>
<td>20–30</td>
<td>7</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;5</td>
<td>0</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1–1.2</td>
<td>3–4</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1–4</td>
<td>2.5–4/13</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed.</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability.</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed.</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
  - Available in 2 strengths: (1) 8/500; 8 mg codeine phosphate/500 mg paracetamol, (2) 30/500; 30 mg codeine phosphate/500 mg paracetamol
  - 30/500 formulation: may cause drowsiness, due to increased cerebral sensitivity in patients with renal failure

**OTHER INFORMATION**

- Effervescent formulations of Solpadol and Tylex (30/500) should be avoided in renal impairment. They contain 16.9 mmol and 13.6 mmol sodium per tablet respectively
- In renal impairment, opioid analgesics may produce a prolonged effect with increased cerebral sensitivity
- Increased risk of constipation in ERF especially with 30/500 preparation
# Codeine phosphate

## CLINICAL USE
- Analgesic
- Antidiarrhoeal
- Cough suppressant

## DOSE IN NORMAL RENAL FUNCTION
- 30–60 mg up to every 4 hours

## PHARMACOKINETICS
- Molecular weight (daltons): 406.4
- % Protein binding: 7
- % Excreted unchanged in urine: 0
- Volume of distribution (L/kg): 3–4
- Half-life – normal/ESRF (hrs): 2.5–4/13

## DOSE IN RENAL IMPAIRMENT
- **GFR (mL/min)**
  - 20–50: Dose as in normal renal function
  - 10–20: 30 mg up to every 4 hours. Increase if tolerated
  - <10: 30 mg up to every 6 hours. Increase if tolerated

## DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- **CAPD**: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- **HD**: Not dialysed. Dose as in GFR<10 mL/min
- **HDF/High flux**: Unknown dialysability. Dose as in GFR<10 mL/min
- **CAV/VVHD**: Not dialysed. Dose as in GFR=10–20 mL/min

## IMPORTANT DRUG INTERACTIONS
- Potentially hazardous interactions with other drugs
  - None known

## ADMINISTRATION
- **REconstitution**
  - **route**
    - Oral, IV, IM, SC
  - **rate of administration**
    - IV bolus
- **comments**

## OTHER INFORMATION
- Increased risk of drowsiness due to increased cerebral sensitivity in patients with renal failure
- Increased risk of constipation – caution in patients on peritoneal dialysis
Co-dydramol (paracetamol and dihydrocodeine)

CLINICAL USE
Analgesic

DOSE IN NORMAL RENAL FUNCTION
1–2 tablets up to 4 times a day

PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Paracetamol</th>
<th>Dihydrocodeine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>151.2</td>
<td>451.5</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>20–30</td>
<td>–</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;5</td>
<td>13–22</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1–2</td>
<td>1.1</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1–4/Unchanged</td>
<td>3.5–5/6+</td>
</tr>
</tbody>
</table>

DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>20–50</th>
<th>50–100% of dose every 6 hours</th>
<th>10–20</th>
<th>50–100% of dose every 6–8 hours</th>
<th>&lt;10</th>
<th>50–100% of dose every 6–8 hours</th>
</tr>
</thead>
</table>

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unknown dialysability. Dose as in GFR=10–20mL/min</td>
</tr>
<tr>
<td>VVHD</td>
<td>GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs
- None known

ADMINISTRATION

RECONSTITUTION
- ROUTE
  - Oral
  - RATE OF ADMINISTRATION
  - COMMENTS
  -

OTHER INFORMATION

- Active metabolites of dihydrocodeine accumulate in renal impairment (drowsiness/lightheadedness/constipation). Increased cerebral sensitivity in patients with renal failure

RETURN TO CONTENTS
Colchicine

**CLINICAL USE**
- Acute gout
- Short-term prophylaxis during initial therapy with allopurinol and uricosuric drugs
- Prophylaxis of familial Mediterranean fever (unlicensed)

**DOSE IN NORMAL RENAL FUNCTION**
- Acute: 1 mg then 500 micrograms every 4 hours until pain relieved or vomiting/diarhoea occurs. Maximum of 6 mg per course. Do not repeat course within 3 days
- Short-term prophylaxis: 500 micrograms 2–3 times per day
- Prophylaxis of familial Mediterranean fever: 0.5–2 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 399.4
- % Protein binding: 30–50%
- % Excreted unchanged in urine: 5–20%
- Volume of distribution (L/kg): 1–2
- Half-life – normal/ESRF (hrs): 4.4/18.8

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/MIN)**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: 500 mcg 3–4 times a day; maximum total dose of 3 mg

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Antibacterials: increased toxicity with clarithromycin and erythromycin
  - Ciclosporin: risk of myopathy or rhabdomyolysis, also increased blood-ciclosporin concentrations and nephrotoxicity

**ADMINISTRATION**
- RECONSTITUTION
  - ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - COMMENTS
  -

**OTHER INFORMATION**
- If nausea, vomiting or diarrhoea occur, stop therapy
- In CKD 5, colchicine can be administered concurrently with allopurinol, but seek specialist advice
Colestipol hydrochloride

**CLINICAL USE**
Hyperlipidaemias, particularly type IIa

**DOSE IN NORMAL RENAL FUNCTION**
5g once or twice daily, increased if necessary at intervals of 1–2 months, to a maximum of 30g daily

**PHARMACOKINETICS**
- Molecular weight (daltons) –
- % Protein binding 0
- % Excreted unchanged in urine 0
- Volume of distribution (L/kg) Not absorbed
- Half-life – normal/ESRF (hrs) Not absorbed

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD** Not dialysed. Dose as in normal renal function
- **HD** Not dialysed. Dose as in normal renal function
- **HDF/High flux** Not dialysed. Dose as in normal renal function
- **CAV/VVHD** Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: may enhance or reduce effects of coumarins and phenindione
- Ciclosporin: No reports of an interaction; however, ciclosporin levels should be carefully monitored if colestipol and ciclosporin are prescribed concurrently, as colestipol may interfere with ciclosporin absorption

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE Oral
- RATE OF ADMINISTRATION
- COMMENTS
- Other drugs should be taken at least 1 hour before or 4–6 hours after colestipol to reduce possible interference with absorption
- Colestipol granules may be administered as a suspension in water or a flavoured vehicle
- Colestipol orange contains 32.5mg aspartame (18.2mg phenylalanine) per sachet

**OTHER INFORMATION**
- Colestipol may interfere with the absorption of fat soluble vitamins
# Colestyramine (cholestyramine)

## CLINICAL USE
- Hyperlipidaemias
- Pruritus associated with partial biliary obstruction and primary biliary cirrhosis
- Diarrhoeal disorders

## DOSE IN NORMAL RENAL FUNCTION

- **Lipid reduction**: 12–24 g daily (in single or up to 4 divided doses). Maximum 36 g daily
- **Pruritus**: 4–8 g daily
- **Diarrhoeal disorders**: 12–24 g daily. Maximum 36 g daily

## PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>–</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>0</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>0</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>Not absorbed</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>Not absorbed</td>
</tr>
</tbody>
</table>

## IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Anticoagulants: effect of coumarins and phenindione may be enhanced or reduced
- Ciclosporin: may interact unpredictably with ciclosporin. Take ciclosporin at least 1 hour before or 4–6 hours after to prevent problems with absorption
- Leflunomide: avoid concomitant use
-Raloxifene, thyroid hormones, bile acids, valproate, cardiac glycosides and mycophenolate mofetil: absorption reduced

## ADMINISTRATION

### RECONSTITUTION
- Mix with water, or a suitable liquid such as fruit juice, and stir to a uniform consistency
- May also be mixed with skimmed milk, thin soups, apple sauce, etc

### ROUTE
- Oral

### RATE OF ADMINISTRATION
- 

## COMMENTS
- Do not take in dry form
- Administer other drugs at least one hour before or 4–6 hours after colestyramine
- Prepare powder immediately prior to administration

## OTHER INFORMATION
- Hyperchloraemic acidosis occasionally reported on prolonged use of colestyramine
- On chronic use, an increased bleeding tendency may occur associated with vitamin K deficiency

## DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

## DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Therapeutic Modality</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/ VVHD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

RETURN TO CONTENTS
Colistin

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
- Oral for bowel sterilisation or gram negative GI infections: 1.5–3 million units every 8 hours
- IV: <60 kg: 50,000–75,000 units/kg in 3 divided doses
- >60 kg 1–2 million units every 8 hours
- Nebulised solution: 1–2 million units every 12 hours

**PHARMACOKINETICS**
- Molecular weight (daltons) Approximtely 1748 (as colistimethate sodium)
- % Protein binding 55%
- % Excreted unchanged in urine 80
- Volume of distribution (L/kg) 0.09–0.34
- Half-life – normal/ESRF (hrs) 1.5–8/13–20 (IV), 6.8–14 (Nebulised)

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50 IV: 1–2 million units every 8 hours. Oral: Dose as in normal renal function; use with caution
  - 10–20 IV: 1 million units every 12–18 hours or 50% of dose. Oral: Dose as in normal renal function; use with caution
  - <10 IV: 1 million units every 18–24 hours or 30% of dose. Oral: Dose as in normal renal function; use with caution

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Dialysed. Dose as in GFR<10mL/min
- HD Not dialysed. Dose as in GFR<10mL/min
- HDF/High flux Dialysed. Dose as in GFR<10mL/min
- CAV/ VVHD Not dialysed. 2 million units every 48 hours

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: increased risk of nephrotoxicity with aminoglycosides and capreomycin; increased risk of nephrotoxicity and ototoxicity with teicoplanin and vancomycin
- Ciclosporin: increased risk of nephrotoxicity
- Cytotoxics: increased risk of nephrotoxicity and possibly ototoxicity with platinum agents
- Diuretics: increased risk of ototoxicity with loop diuretics
- Muscle relaxants: polymyxins enhance the effect of non-depolarising muscle relaxants and suxamethonium
- Parasympathomimetics: polymyxins antagonise the effect of neostigmine and pyridostigmine

**ADMINISTRATION**
- **RECONSTITUTION**
  - Sodium chloride 0.9% or water for injection
- **ROUTE**
  - Oral, IV, Nebulised, Topical
- **RATE OF ADMINISTRATION**
  - Infusion: over 30 minutes
  - Bolus: over 5 minutes (only if patient has a totally implantable venous access device, TIVAD)
- **COMMENTS**
  - IV: Give in 10–50mL sodium chloride 0.9% or water for injection
  - Inhalation: Dissolve in 2–4mL sodium chloride 0.9% or water for injection

**OTHER INFORMATION**
- Less than 0.5mmol/L sodium per 0.5–2 million unit vial (before reconstitution)
- Can cause renal failure, muscle weakness and apnoea in overdose. Risk factors are usually the IV route, high doses, concomitant use with other nephrotoxic agents, and if the dose is not reduced appropriately in renal failure
- No systemic absorption from oral administration in adults

RETURN TO CONTENTS
In renal impairment, neonates, and cystic fibrosis patients, plasma concentrations of 10–15 mg/L (125–200 units/mL) are usually adequate.

Dosage schedules in renal impairment vary according to which preparation is being used. Doses in the following table are from Dollery (1999) and Colomycin SPC:

- **Promixin SPC (IV):**
  - GFR: 40–75 mL/min: 1–1.5 MIU twice daily
  - 25–40 mL/min: 0.8–2 MIU once or twice daily
  - <25 mL/min: 1–1.5 MIU every 36 hours

- **Promixin SPC (nebulised):**
  - GFR: 40–75 mL/min: 1–1.5 MIU twice daily
  - 25–40 mL/min: 1 MIU once or twice daily
  - <25 mL/min: 1–1.5 MIU every 36 hours

References:
Cortisone acetate

**CLINICAL USE**
Glucocorticoid replacement in adrenocortical insufficiency

**DOSE IN NORMAL RENAL FUNCTION**
25–37.5 mg daily in divided doses

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>402.5</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>90</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>0</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.3</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>0.5/3.5</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Type</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

- Antifungals: increased risk of hypokalaemia with amphotericin – avoid concomitant use; metabolism possibly inhibited by itraconazole and ketoconazole.
- Antivirals: concentration possibly increased by ritonavir
- Ciclosporin: rare reports of convulsions in patients on ciclosporin and high-dose corticosteroids
- Cytotoxics: increased risk of haematological toxicity with methotrexate
- Diuretics: enhanced hypokalaemic effects of acetazolamide, loop diuretics and thiazide diuretics
- Vaccines: high-dose corticosteroids can impair immune response to vaccines; avoid concomitant use with live vaccines

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**

- **COMMENTS**

**OTHER INFORMATION**

- Treatment of adrenocortical insufficiency with hydrocortisone is now generally preferred since cortisol itself is inactive. It must be converted by the liver to hydrocortisone, its active metabolite, and hence, in some liver disorders, its bioavailability is less reliable
- Mineralocorticoid activity is usually supplemented by oral fludrocortisone acetate
- Cortisone acetate has been used in the treatment of many allergic and inflammatory disorders, but prednisolone or other synthetic glucocorticoids are generally preferred because of their reduced sodium retaining properties
Co-trimoxazole (trimethoprim + sulfamethoxazole)

**CLINICAL USE**

Antibacterial agent:
- Treatment and prophylaxis of *Pneumocystis jiroveci* pneumonia (PCP)
- Acute exacerbations of chronic bronchitis
- Urinary tract infections, on microbiological advice

**DOSE IN NORMAL RENAL FUNCTION**

- PCP: 120 mg/kg/day in 2–4 divided doses
- Oral prophylaxis: 480–960 mg daily or 960 mg on alternate days
- Acute exacerbations of chronic bronchitis and urinary tract infections on microbiological advice:
  - IV: 960 mg – 1.44 g of co-trimoxazole twice a day
  - Oral: 960 mg of co-trimoxazole twice a day

**PHARMACOKINETICS**

- Molecular weight (daltons)
  - Sulfamethoxazole: 253.3; trimethoprim: 290.3
- % Protein binding
  - Sulfamethoxazole: 70; trimethoprim: 45
- % Excreted unchanged in urine
  - Sulfamethoxazole: 15–30; trimethoprim: 40–60
- Volume of distribution (L/kg)
  - Sulfamethoxazole: 0.28–0.38; trimethoprim: 1–2.2
- Half-life – normal/ESRF (hrs)
  - Sulfamethoxazole: 6–12/20–50; trimethoprim: 8–10/20–49

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>30–50</th>
<th>15–30</th>
<th>&lt;15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose as in normal renal function</td>
<td>50% of dose; PCP: 60 mg/kg twice daily for 3 days then 30 mg/kg twice daily</td>
<td>50% of dose; PCP: 30 mg/kg twice daily. (This should only be given if haemodialysis facilities are available)</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

| CAPD | Not dialysed. Dose as in GFR<15 mL/min |
| HD | Dialysed. Dose as in GFR<15 mL/min |
| HDF/High flux | Dialysed. Dose as in GFR<15 mL/min |
| CAV/VVHD | Dialysed. Dose as in GFR=15–30 mL/min |

**IMPORTANT DRUG INTERACTIONS**

- Potentially hazardous interactions with other drugs
  - Anti-arrhythmics: increased risk of ventricular arrhythmias with amiodarone – avoid concomitant use; concentration of procainamide increased
  - Antibacterials: increased risk of crystalluria with methenamine
  - Anticoagulants: effect of coumarins enhanced
  - Anti-epileptics: antifolate effect and concentration of phenytoin increased
  - Antimalarials: increased risk of antifolate effect with pyrimethamine
  - Antipsychotics: avoid concomitant use with clozapine, increased risk of agranulocytosis
  - Ciclosporin: increased risk of nephrotoxicity; possibly reduced ciclosporin levels
  - Cytotoxics: increased risk of haematological toxicity with azathioprine and mercaptopurine. Antifolate effect of methotrexate increased

**ADMINISTRATION**

- **RECONSTITUTION**
  - **ROUTE**
    - IV, oral
  - **RATE OF ADMINISTRATION**
    - Over 60–90 minutes
    - Alternatively: 2–3 hours for high doses as undiluted solution via central line (unlicensed)
COMMENTS
- For an IV infusion dilute each 5 mL co-
  trimoxazole strong solution with 125 mL
  sodium chloride 0.9% or glucose 5%
- Glaxo Smith Kline: dilute 5 mL to 75 mL
  glucose 5% and administer over 1 hour if
  fluid restricted

OTHER INFORMATION
- Alternative dosing (for acute exacerbations
  of chronic bronchitis and urinary tract
  infections) on microbiological advice only;
  not PCP
- After 2–3 days, plasma samples collected
  12 hours post dose should have levels of
  sulfamethoxazole not higher than 150
  micrograms/mL. If higher, stop treatment
  until levels fall below 120 micrograms/mL.
- Plasma levels of trimethoprim should be
  5 micrograms/mL or higher, for optimum
  efficacy for PCP
- Folic acid supplementation may be
  necessary during chronic therapy.
- Monthly blood counts advisable
Cyclizine

### CLINICAL USE
- Nausea and vomiting
- Vertigo
- Motion sickness
- Labyrinthine disorders

### DOSE IN NORMAL RENAL FUNCTION
50 mg up to 3 times daily

#### PHARMACOKINETICS
- **Molecular weight (daltons):** 266.4
- **% Protein binding:** No data
- **% Excreted unchanged in urine:** <1
- **Volume of distribution (L/kg):** No data
- **Half-life – normal/ESRF (hrs):** 20/-

#### DOSE IN RENAL IMPAIRMENT
- **GFR (mL/MIN):**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

### IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- None known

### ADMINISTRATION
- **RECONSTITUTION**
- **ROUTE**
  - IV, IM, oral
- **RATE OF ADMINISTRATION**
  - Slow IV
- **COMMENTS**
  - Increased cerebral sensitivity in patients with renal failure

### DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- **CAPD:** Unknown dialysability. Dose as in normal renal function
- **HD:** Unknown dialysability. Dose as in normal renal function
- **HDF/High flux:** Unknown dialysability. Dose as in normal renal function
- **CAV/VVHD:** Unknown dialysability. Dose as in normal renal function

RETURN TO CONTENTS
Cyclopenthiazide

**CLINICAL USE**
- Hypertension
- Heart failure
- Oedema

**DOSE IN NORMAL RENAL FUNCTION**
- Oedema: up to 500 mcg once daily
- Heart failure: 250 mcg – 1 mg once daily
- Hypertension: 250–500 mcg once daily

**PHARMACOKINETICS**
- Molecular weight: 379.9 (daltons)
- % Protein binding: No data
- % Excreted unchanged in urine: 100
- Volume of distribution: No data
- Half-life – normal/ESRF (hrs): 12/Increased

**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**
- 20–50: Dose as in normal renal function
- 10–20: Unlikely to work
- <10: Unlikely to work

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Unlikely to work
- HD: Unknown dialysability. Unlikely to work
- HDF/High flux: Unknown dialysability. Unlikely to work
- CAV/VVHD: Unknown dialysability. Unlikely to work

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Analgesics: increased risk of nephrotoxicity with NSAIDs; antagonism of diuretic effect
  - Anti-arrhythmics: hypokalaemia leads to increased cardiac toxicity; effects of lidocaine and mexiletine antagonised
  - Antibacterials: avoid administration with lymecycline
  - Antidepressants: increased risk of hypokalaemia with reboxetine; enhanced hypotensive effect with MAOIs; increased risk of postural hypotension with tricyclics
  - Anti-epileptics: increased risk of hyponatraemia with carbamazepine
  - Antifungals: increased risk of hypokalaemia with amphotericin
  - Antihypertensives: enhanced hypotensive effect; increased risk of first dose hypotension with post-synaptic alpha-blockers like prazosin; hypokalaemia increases risk of ventricular arrhythmias with sotalol
  - Antipsychotics: hypokalaemia increases risk of ventricular arrhythmias with amisulpride or sertindole; enhanced hypotensive effect with phenothiazines; hypokalaemia increases risk of ventricular arrhythmias with pimozide – avoid concomitant use
  - Atomoxetine: hypokalaemia increases risk of ventricular arrhythmias
  - Cardiac glycosides: increased toxicity if hypokalaemia occurs
  - Ciclosporin: increased risk of nephrotoxicity and possibly hypomagnesaemia
  - Lithium: excretion reduced, increased toxicity

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- Monitor for hypokalaemia
- Acts within 1–3 hours, peaks in 4–8 hours and lasts up to 12 hours

RETURN TO CONTENTS
Cyclophosphamide

**CLINICAL USE**

Alkylating agent:
- Immunosuppression of autoimmune diseases including rheumatoid arthritis
- Treatment of malignant disease

**DOSE IN NORMAL RENAL FUNCTION**

- **Autoimmune disease:**
  - Oral: 1–2.5 mg/kg/day
  - IV: Usually 0.5–1 g/m² or 10–15 mg/kg repeated at intervals, e.g. monthly (pulse therapy)

- **Malignant disease:**
  - Oral: 50–250 mg/m² daily or according to local protocol

**PHARMACOKINETICS**

- **Molecular weight (daltons):** 279.1
- **% Protein binding:** Parent drug 0–10: alkylating metabolites >60
- **% Excreted unchanged in urine:** 5–25
- **Volume of distribution (L/kg):** 0.78
- **Half-life – normal/ESRF (hrs):** 3–12/10

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>75–100% of normal dose depending on clinical indication and local protocol</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>50–100% of normal dose depending on clinical indication and local protocol</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**: Dialysed. Dose as in GFR<10 mL/min. Following dose, do not perform CAPD exchange for 12 hours
- **HD**: Dialysed. Dose as in GFR<10 mL/min. Dose at minimum of 12 hours before HD session
- **HDF/High flux**: Dialysed. Dose as in GFR<10 mL/min. Dose at minimum of 12 hours before HDF session

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Antipsychotics: avoid concomitant use with clozapine, increased risk of agranulocytosis
- Cytotoxics: increased toxicity with high-dose cyclophosphamide and pentostatin – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**

- Add 5 mL water for injection to each 100 mg (sodium chloride 0.9% for Endoxana)

**ROUTE**

- Oral, IV

**RATE OF ADMINISTRATION**

- Directly into vein over 2–3 minutes, OR directly into tubing of fast running IV infusion with patient supine

**COMMENTS**

- IV route occasionally used for pulse therapy. Can be administered as an IV infusion
- Injection can be administered orally down an NG tube

**OTHER INFORMATION**

- Prodrug – converted by hepatic microsomal enzymes to alkylating metabolites (great inter-patient variability in metabolism). Excretion primarily renal.
- Reduce IV dose to 75% of oral dose, bioavailability is 75%
- Cyclophosphamide and its alkylating metabolites can be eliminated by dialysis
- Patients receiving chronic indefinite therapy may be at increased risk of developing urothelial carcinoma
- If patient is anuric and on dialysis, neither cyclophosphamide or its metabolites, nor Mesna should appear in the urinary tract. The use of Mesna may therefore be unnecessary, although this would be a clinical decision
- If the patient is still passing urine, Mesna should be given to prevent urothelial toxicity
Cycloserine

**CLINICAL USE**
Antibacterial agent:
- Tuberculosis

**DOSE IN NORMAL RENAL FUNCTION**
Initially 250 mg every 12 hours for 2 weeks; then increased according to blood concentration and response to maximum 500 mg every 12 hours

**PHARMACOKINETICS**
- Molecular weight: 102.1 daltons
- % Protein binding: <20
- % Excreted unchanged in urine: 50–70
- Volume of distribution (L/kg): 0.11–0.26
- Half-life – normal/ESRF (hrs): 8–12/Increased

**DOSE IN RENAL IMPAIRMENT**
<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Frequency</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>250–500 mg every 12–24 hours.</td>
<td>Monitor blood levels weekly</td>
<td>Monitor blood levels weekly</td>
</tr>
<tr>
<td>10–20</td>
<td>250–500 mg every 12–24 hours.</td>
<td>Monitor blood levels weekly</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>250–500 mg every 24 hours.</td>
<td>Monitor blood levels weekly</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR<10 mL/min
- HD: Dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Likely dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Alcohol: Increased risk of seizures

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**
- May cause drowsiness – increased cerebral sensitivity in patients with renal impairment
- Blood concentration monitoring is required, especially in renal impairment, if dose exceeds 500 mg daily, or if signs of toxicity. Blood concentration should not exceed 30 mg/L
- Contraindicated in severe renal insufficiency
- Can cause CNS toxicity
- Pyridoxine has been used in an attempt to treat or prevent neurological reactions, but its value is unproven
Cyproterone acetate

CLINICAL USE
- Control of libido in severe hypersexuality and sexual deviation in adult male
- Management of patients with prostatic cancer (LHRH ‘flare’, palliative treatment)
- Hot flushes post orchidectomy

DOSE IN NORMAL RENAL FUNCTION
- Control of hypersexuality: 50mg twice daily
- Prostatic cancer: 200–300mg/day in 2–3 divided doses
- Hot flushes: 50–150mg daily in 1–3 divided doses

PHARMACOKINETICS
Molecular weight (daltons) 416.9
% Protein binding Approx 96
% Excreted unchanged in urine <1
Volume of distribution (L/kg) 10–30
Half-life – normal/ESRF (hrs) 32.1–56.7/–

DOSE IN RENAL IMPAIRMENT
GFR (mL/MIN)
20–50  Dose as in normal renal function
10–20  Dose as in normal renal function
<10  Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD  Unknown dialysability. Dose as in normal renal function
HD  Unknown dialysability. Dose as in normal renal function
HDF/High flux  Unknown dialysability. Dose as in normal renal function
CAV/ VVHD  Unknown dialysability. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- None known

ADMINISTRATION
RECONSTITUTION
- ROUTE
- Oral
RATE OF ADMINISTRATION
- COMMENTS
- OTHER INFORMATION
- May cause drowsiness – increased CNS sensitivity in patients with renal impairment
- CSM has advised that in view of the hepatotoxicity associated with long-term doses of 300mg daily, the use of cyproterone acetate in prostatic cancer should be restricted to short courses, to cover testosterone ‘flare’ associated with gonadorelin analogues, treatment of hot flushes after orchidectomy or gonadorelin analogues, and for patients who have not responded to (or are intolerant of) other treatments
- Direct hepatic toxicity including jaundice, hepatitis and hepatic failure have been reported. Liver function tests should be performed before treatment and whenever symptoms suggestive of hepatotoxicity occur
Cytarabine

**CLINICAL USE**
Antineoplastic agent:
- Acute leukaemias
- Lymphomatous meningitis

**DOSE IN NORMAL RENAL FUNCTION**
- High-dose (infusional) therapy: 1–3 g/m\(^2\) every 12 hours
- Low dose (conventional) therapy: 100 mg/m\(^2\)
- Lymphomatous meningitis: 50 mg (intrathecal) every 14–28 days. See SPC for more information, depends on formulation
- Or according to local policy

**PHARMACOKINETICS**
- Molecular weight (daltons) 243.2
- % Protein binding 13
- % Excreted unchanged in urine 5.8–10
- Volume of distribution (L/kg) 2.6
- Half-life – normal/ESRF (hrs) 1–3 (Intrathecal liposomal: 100–263)/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>% of conventional low dose regime. For high dose, see ‘Other Information’</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>100%</td>
</tr>
<tr>
<td>10–20</td>
<td>100%</td>
</tr>
<tr>
<td>&lt;10</td>
<td>100%</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

| CAPD | Not dialysed. Dose as in GFR<10mL/min |
| HD   | Not dialysed. Dose as in GFR<10mL/min |
| HDF/High flux | Dialysed. Dose as in GFR<10mL/min |
| CAV/ VVHD | Unknown dialysability. Dose as in GFR=10–20mL/min |

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antipsychotics: avoid concomitant use with clozapine, increased risk of agranulocytosis

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - IV infusion, IV injection, SC, intrathecal
- **RATE OF ADMINISTRATION**
  - IV injection: rapid
  - IV infusion: 1–24 hours

**COMMENTS**
- Patients generally tolerate higher doses when medication given by rapid IV injection (compared with slow infusion), due to the rapid metabolism of cytarabine and the consequent short duration of action of the high dose

**OTHER INFORMATION**
- Cytarabine is concentrated in the liver. A major fraction of dose is inactivated by cytidine deaminase in the liver and other body tissues. After 24 hrs, 80% of dose has been eliminated either as the inactive metabolite or as unchanged cytarabine, mostly in the urine, but some in the bile
- Elevated baseline serum creatinine (>1.2 mg/dl) is an independent risk factor for the development of neurotoxicity during treatment with high-dose cytarabine.
- Retrospective analysis implicates impaired renal function as an independent risk factor for high-dose cytarabine-induced cerebral and cerebellar toxicity.
- The incidence of neurotoxicity was 86–100% following administration of high-dose cytarabine to patients with CrCl <40 mL/min and 60–76% following administration to patients with CrCl <60 mL/min. In contrast, when patients with CrCl >60 mL/min received high-dose cytarabine, the incidence of neurotoxicity was found to be 8%, which correlates with the overall incidence of this adverse effect.
- Accordingly, it has been suggested that high-dose cytarabine should be used with
caution in patients with impaired renal function:

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>45–60</td>
<td>60%</td>
<td>30–45</td>
<td>50%</td>
</tr>
<tr>
<td>&lt;30</td>
<td>Avoid</td>
<td>&lt;30</td>
<td>Avoid</td>
</tr>
</tbody>
</table>

- Anecdotally, an initial dose of 25% of the normal dose has been given to patients with a GFR < 20 mL/min, with subsequent doses escalated according to tolerance.
Cytomegalovirus (CMV) human immunoglobulin (unlicensed product)

**CLINICAL USE**
- Prophylaxis for renal transplant recipients at risk of primary cytomegalovirus (CMV) disease
- Treatment of CMV disease (usually with ganciclovir)

**DOSE IN NORMAL RENAL FUNCTION**
See local protocols

**PHARMACOKINETICS**
- Molecular weight (daltons): 150
- % Protein binding: N/A
- % Excreted unchanged in urine: 0
- Volume of distribution (L/kg): 1
- Half-life – normal/ESRF (hrs): 50

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Ciclosporin: no effect on efficacy of CMV immunoglobulin

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
- IV peripherally or centrally

**RATE OF ADMINISTRATION**
- COMMENTS
- Follow guidelines supplied by company

**OTHER INFORMATION**
- Can give 10 mg IV chlorphenamine 1 hour before administration
- Monitor for anaphylaxis, have epinephrine available
- Do not mix with any other drugs or infusion fluids
## Dacarbazine

### CLINICAL USE

Antineoplastic agent:
- Metastatic melanoma
- Hodgkin's disease
- Soft tissue sarcomas

### DOSE IN NORMAL RENAL FUNCTION

- Single agent: 2–4.5 mg/kg daily for 10 days, repeated every 4 weeks or 200–250 mg/m² daily for 5 days, repeated every 3 weeks or 850 mg/m² on day 1 then once every 3 weeks
- Hodgkin's disease: 150 mg/m² daily for 5 days, repeated every 4 weeks (or 375 mg/m² every 15 days in combination)

### PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>182.2</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>0–5</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>20–50</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1.49</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>0.5–5/Increased</td>
</tr>
</tbody>
</table>

### DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>% of dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>45–60</td>
<td>80%</td>
</tr>
<tr>
<td>30–45</td>
<td>75%</td>
</tr>
<tr>
<td>&lt;30</td>
<td>70%</td>
</tr>
</tbody>
</table>

### DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose as in</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>GFR&lt;30 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>GFR&lt;30 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>GFR&lt;30 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>GFR&lt;30 mL/min</td>
</tr>
</tbody>
</table>

### IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs
- None known

### ADMINISTRATION

#### RECONSTITUTION

- 10 mL water for injection per 100 mg vial (50 mL for 1 g vial)

#### ROUTE

- IV

#### RATE OF ADMINISTRATION

- Bolus: 1–2 minutes
- Infusion: 15–30 minutes

#### COMMENTS

- For infusion can be diluted with up to 125–300 mL glucose 5% or sodium chloride 0.9%
- Avoid contact with skin and mucous membranes
- Protect from light
- Doses above 200 mg/m² should be given as infusions

### OTHER INFORMATION

- Nadir for white cell count usually occurs 21–25 days after a dose
- Dacarbazine (DTIC) is assumed to be inactive. Microsomal metabolism in the liver produces main metabolite; 5-aminoimidazole-4-carboxamide (AIC). Approximately 50% DTIC is renally cleared. Half of this is unchanged DTIC and approximately 50% is AIC. DTIC is secreted via the renal tubules, rather than filtered at the glomerulus
Daclizumab

**CLINICAL USE**

Humanised murine/human monoclonal anti-CD25 antibody:
- Prophylaxis of acute allograft rejection, in combination with maintenance immunosuppressants

**DOSE IN NORMAL RENAL FUNCTION**

1 mg/kg within 24 hours of transplantation, then 1 mg/kg every 14 days for 5 doses. See ‘Other Information’

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>144,000</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>No data</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>No data</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>5.3 litres</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>270–919/–</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
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<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability.</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be dialysed.</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- IV infusion

**RATE OF ADMINISTRATION**
- Over 15 minutes

**COMMENTS**
- Add required dose to 50 mL of sodium chloride 0.9%
- Stable for 24 hours at 2–8°C if prepared aseptically

**OTHER INFORMATION**
- An alternative dosing regimen that may be used is 2 mg/kg every 14 days for 2 doses
Dactinomycin

**CLINICAL USE**
Antineoplastic antibiotic

**DOSE IN NORMAL RENAL FUNCTION**
Dose varies according to patient tolerance, size and location of neoplasm
Maximum dose: 15 mcg/kg or 400–600 mcg/m² daily for 5 days per 2 week cycle

**PHARMACOKINETICS**
- Molecular weight: 1255.4 (daltons)
- % Protein binding: 5
- % Excreted unchanged in urine: 30
- Volume of distribution (L/kg): >12.1
- Half-life – normal/ESRF (hrs): 36/–

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Use with caution Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
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<tr>
<td>&lt;10</td>
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</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function</th>
<th>Use with caution Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
<td></td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
<td></td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–20mL/min</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- 1.1 mL water for injection without preservative

**ROUTE**
- IV

**RATE OF ADMINISTRATION**
- 15 minutes

**COMMENTS**
- Add to 50 mL glucose 5% or sodium chloride 0.9% (maximum concentration 10mg/mL) or to a fast running IV infusion
- Avoid direct contact with the skin

**OTHER INFORMATION**
- Nadir for platelet and white cell count usually occurs after 14–21 days, with recovery in 21–25 days
- 15% eliminated by hepatic metabolism. Approximately 30% of the dose was recovered in the urine and faeces in 1 week.
- Can cause renal abnormalities
Dalteparin sodium (LMWH)

**CLINICAL USE**

1. Peri- and postoperative surgical and medical thromboprophylaxis
2. Prevention of clotting in extracorporeal circuits
3. Treatment of DVT
4. Acute coronary syndrome

**DOSE IN NORMAL RENAL FUNCTION**

- Dose according to risk of thrombosis:
  - Moderate risk: 2500 IU daily
  - High risk and medical: 5000 IU daily
- Dose for >4 hour session: IV bolus of 30–40 IU/kg, followed by infusion of 10–15 IU/kg/hour
  - Dose for <4 hour session: as above or single IV bolus injection of 5000 IU
  - If at increased risk of bleeding: IV bolus of 5–10 IU/kg, followed by infusion of 4–5 IU/kg/hour
- 200 IU/kg daily (maximum 18 000 units as a single dose) or 100 IU/kg twice daily
- 120 IU/kg every 12 hours maximum 10 000 IU twice daily for 5–8 days

**PHARMACOKINETICS**

- Molecular weight (daltons): Average 6000
- % Protein binding: No data
- % Excreted unchanged in urine: No data
- Volume of distribution (L/kg): 0.04–0.06
- Half-life – normal/ESRF (hrs): IV: 2; SC: 3.5–4/Prolonged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose as in normal renal function</th>
<th>Dose as in normal renal function only for prophylaxis doses. See 'Other Information'</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Not dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs

- Analgesics: increased risk of bleeding with NSAIDs, avoid concomitant use with IV diclofenac; increased risk of haemorrhage with ketorolac – avoid concomitant use
- Nitrates: anticoagulant effect reduced by infusions of glyceryl trinitrate
- Drotrecogin alfa: manufacturer advises to avoid use of high doses of heparin with drotrecogin alfa
- Use with care in patients receiving oral anticoagulants, platelet aggregation inhibitors, aspirin or dextran

**ADMINISTRATION**

- **RECONSTITUTION**
  - **ROUTE**
    - SC injection into abdominal wall (prefilled syringes)
    - IV bolus/infusion (ampoules)
- **RATE OF ADMINISTRATION**
  - **COMMENTS**
    - Dalteparin solution for injection (ampoules) is compatible with sodium chloride 0.9% and glucose 5%

**OTHER INFORMATION**

- Low molecular weight heparins are renally excreted and hence accumulate in severe renal impairment. While the doses recommended for prophylaxis against DVT and prevention of thrombus formation in extracorporeal circuits are well tolerated in patients with ERF, the doses recommended for treatment of DVT and PE have been associated with severe, sometimes fatal, bleeding episodes in such
patients. Hence the use of unfractionated heparin would be preferable in these instances.

- In patients with GFR ≤ 30 mL/min, monitoring for anti-Xa levels is recommended to determine the appropriate dalteparin dose. Target anti-Xa range is 0.5-1.5 IU/mL.

- When monitoring anti-Xa in these patients, sampling should be performed 4–6 hrs after dosing and only after the patient has received 3–4 doses.

- Antifactor-Xa levels should be regularly monitored in new patients on haemodialysis, during the first weeks; later, less frequent monitoring is generally required. Consult manufacturer’s literature for details.

- Additional doses may be required if using LMWHs for anticoagulation in HDF.

- Bleeding may occur especially at high doses corresponding with antifactor-Xa levels greater than 1.5 IU/mL.

- The prolongation of the APTT induced by dalteparin is fully neutralised by protamine, but the anti-Xa activity is only neutralised to about 25–50%.

- 1 mg of protamine inhibits the effect of 100 IU (antifactor-Xa) of dalteparin.

- Heparin can suppress adrenal secretion of aldosterone leading to hypercalcaemia, particularly in patients with chronic renal impairment and diabetes mellitus.
Danaparoid sodium

**CLINICAL USE**
- Prophylaxis of DVT and PE
- Thromboembolic disease requiring parenteral anticoagulation in patients with heparin induced thrombocytopenia (HIT)
- Anticoagulation for haemodialysis

**DOSE IN NORMAL RENAL FUNCTION**
- Prophylaxis, DVT and PE: 750 units twice daily for 7–10 days (SC)
- HIT: 2500 units IV bolus (Wt<55 kg: 1250 units; >90 kg: 3750 units) then an IV infusion of 400 units/hour for 2 hours, 300 units/hour for 2 hours, then 200 units/hour for 5 days
- Haemodialysis: see ‘Other Information’

**PHARMACOKINETICS**
- Molecular weight (daltons): Approx 6500
- % Protein binding: No data
- % Excreted unchanged in urine: 40–50
- Volume of distribution (L/kg): 8–9
- Half-life – normal/ESRF (hrs): 25/>31

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Use with caution
  - <10: Use with caution. Reduce second and subsequent doses for thromboembolism prophylaxis

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Not dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Enhances effects of oral anticoagulants
  - Interferes with laboratory monitoring of prothrombin time – monitor anticoagulation closely

**ADMINISTRATION**

**RECONSTITUTION**
- Glucose 5% or sodium chloride 0.9%

**ROUTE**
- SC, IV

**RATE OF ADMINISTRATION**
- SC, IV

**COMMENTS**

**OTHER INFORMATION**
- Pharmacokinetic information is from Pharm Update. 1997, Nov/Dec; www.cc.nih.gov/phar/updates/97novdec.html
- Monitor anti-Xa activity in patients >90 kg and with renal impairment
- Can also be used for haemodialysis anticoagulation: 2/3 times a week dialysis:
  - 1st and 2nd dialysis: 3750 units IV bolus prior to dialysis. (If patient weighs <55 kg then give 2500 unit IV bolus.)
  - Subsequent dialysis: 3000 units by IV bolus prior to dialysis, provided there are no fibrin threads in the bubble chamber. (If patient weighs <55 kg then give 2000 unit IV bolus.)
- Daily dialysis:
  - 1st dialysis: 3750 units IV bolus prior to dialysis; if patient <55 kg give 2500 units
  - 2nd dialysis: 2500 units IV bolus prior to dialysis; if patient <55 kg give 2000 units
  - Prior to the second and subsequent dialysis a specimen should be drawn for plasma anti-Xa levels (to be used for dosing a third and subsequent dialysis)
- Expected pre-dialysis ranges of anti-Xa levels:
  - If plasma anti-Xa levels are <0.3 U/mL, then 3rd or subsequent dialysis dose should be 3000 units. For patients weighing <55 kg use 2000 units
  - If plasma anti-Xa levels are 0.3–0.35 U/mL, then 3rd or subsequent dialysis dose should be 2500 units. For patients weighing <55 kg use 1500 units
  - If plasma anti-Xa levels are 0.35–0.4 U/mL, then 3rd or subsequent dialysis dose should be 2000 units. For patients weighing <55 kg use 1500 units

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If plasma anti-Xa levels are >0.4 U/mL, then do not give any danaparoid before dialysis. However, if fibrin threads form in the bubble chamber, then the patient may be given 1500 units IV bolus (irrespective of the patient’s weight).

- During dialysis the plasma anti-Xa level should be between 0.5–0.8 U/mL.
- If needed take a blood sample prior to every dialysis and during dialysis (at 30 minutes and at 4 hours).
- Alternative regime for HD (New Zealand data sheet): infusion of 600 units/hour for 4 hours then 200–600 units/hour to maintain anti-Xa levels of 0.5–1 U/mL. If patient <55 kg then use 400 units/hour for 4 hours then 150–400 units/hour.
- Protamine is no use as an antidote for bleeding complications. If no anti-Xa monitoring is available then the first 4 dialysis sessions should have pre-dialysis IV bolus of 3750, 3750, 3000 and 2500 units respectively, then 2500 units thereafter. Take blood sample prior to 4th and 7th dialysis to ensure there is no accumulation.
- Oozing from puncture sites has been noted 24–36 hours post dose.
- For CVVH, an initial bolus of 750 units followed by an infusion of 0.7–2 units/kg/hr can be given. (Wester JP). Guidelines for anticoagulation with danaparoid sodium and lepirudin in continuous venovenous hemofiltration. Neth J Crit Care. 2004; 8(4):293–301). Although there are many different regimes this one uses the least amount of danaparoid.
Dapsone

**CLINICAL USE**
- Treatment and prophylaxis of leprosy
- Dermatitis herpetiformis
- *Pneumocystis jiroveci* pneumonia (PCP)
- Malaria prophylaxis

**DOSE IN NORMAL RENAL FUNCTION**
- Leprosy: 1–2 mg/kg or 100 mg daily
- PCP: 100 mg daily in 1 or 2 divided doses
- Dermatitis herpetiformis: 50–300 mg daily
- Malaria prophylaxis: 100 mg weekly in combination with pyrimethamine 12.5 mg weekly

**PHARMACOKINETICS**
- Molecular weight (daltons): 248.3
- % Protein binding: 50–80
- % Excreted unchanged in urine: 20
- Volume of distribution (L/kg): 1–1.5

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in renal function</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function, use with caution</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>50–100 mg daily, use with caution. No dose reduction is required for malaria prophylaxis. See ‘Other Information’</td>
<td></td>
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**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Technique</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Likely dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Likely dialysability. Dose as in GFR=10–20 mL/min</td>
</tr>
<tr>
<td>VVHD</td>
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</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - COMMENTS

**OTHER INFORMATION**
- Greater risk of haemolytic side effects in patients with glucose-6-phosphate-dehydrogenase deficiency
- Regular blood counts are recommended in patients with severe anaemia or renal impairment: weekly for the 1st month, then monthly for 6 months, then semi-annually
- Almost all patients lose 1–2 g of haemoglobin
- The dose for herpetiformis can be reduced if the patient is on a gluten free diet
- One study used dapsone in a haemodialysis patient for bullous dermatosis: therapy was initiated at 100 mg but the dose had to be reduced to 50 mg due to haemolytic effects. (Serwin AB, Mysliwiec H, Laudanska H, et al. Linear IgA bullous dermatosis in a diabetic patient with chronic renal failure. *Int J Dermatol*. 2002, Nov; 41(11): 778–80)
Daptomycin

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
4–6 mg/kg once daily for 7 to 14 days depending on indication

**PHARMACOKINETICS**
- Molecular weight (daltons): 1620.7
- % Protein binding: 90–92
- % Excreted: Approximately 50%
- Volume of distribution (L/kg): 0.092–0.104
- Half-life – normal/ESRF (hrs): 8.1–9/29.4

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min):
  - 30–50: Dose as in normal renal function
  - <30: 4 mg/kg every 48 hours

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<30 mL/min
- HD: Not dialysed. Dose as in GFR<30 mL/min
- HDF/High flux: Dialysed. Dose as in GFR<30 mL/min
- CAV/VVHD/VVHDF: Slightly dialysed. 4–6 mg/kg every 48 hours

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Warfarin: Monitor INR when on daptomycin
  - Ciclosporin: increased risk of myopathy – try to avoid concomitant use
  - Lipid-regulating drugs: increased risk of myopathy with fibrates and statins – try to avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- 7 mL sodium chloride 0.9% or water for injection to give a solution of 50 mg/mL

**ROUTE**
- IV infusion

**RATE OF ADMINISTRATION**
- Over 30 minutes

**COMMENTS**
- Once reconstituted, stable for 12 hours at room temperature and 48 hours refrigerated
- Add to 50 mL sodium chloride 0.9% before administration. Stable for 12 hours at room temperature or 24 hours refrigerated
- Incompatible with dextrose solutions
- Compatible with solutions containing aztreonam, ceftazidime, ceftriaxone, gentamicin, fluconazole, levofloxacin, dopamine, heparin and lidocaine

**OTHER INFORMATION**
- May cause renal impairment
- Vials do not contain any bacteriostatic or fungiostatic agents
- Company advises to administer post dialysis
- Monitor creatinine phosphokinase levels, muscle pain or weakness
- Increased risk of myopathy in severe renal failure due to increased daptomycin levels
- 15% of dose is removed by 4 hours of haemodialysis and 11% over 48 hours by peritoneal dialysis
- Therapeutic concentrations of daptomycin are unlikely due to low PD clearance of drug therefore systemic use for peritonitis is unlikely to work.

References:
Darbepoetin alfa

**CLINICAL USE**
Treatment of anaemia associated with chronic renal failure, and with non-haematological malignancies in adult cancer patients receiving chemotherapy

**DOSE IN NORMAL RENAL FUNCTION**
- Renal failure: 0.45 micrograms/kg once a week; dose is adjusted by 25% every 4 weeks according to response; maintenance every 1–2 weeks
- Patients not on dialysis: 0.75 mcg every 2 weeks; maintenance may be every 1–4 weeks
- Cancer: 2.25 mcg/kg once a week, or 6.75 mcg/kg every 3 weeks; adjust doses by 50% every 4 weeks according to response

**PHARMACOKINETICS**
- Molecular weight (daltons) 30 000–37 000
- % Protein binding No data
- % Excreted unchanged in urine No data
- Volume of distribution (L/kg) 0.05
- Half-life – normal/ESRF (hrs) 21 (IV), 73 (SC)/Unchanged

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50 Dose as in normal renal function
- 10–20 Dose as in normal renal function
- <10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Not dialysed. Dose as in normal renal function
- HD Not dialysed. Dose as in normal renal function
- HDF/High flux Not dialysed. Dose as in normal renal function
- CAV/VVHD Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Ciclosporin and tacrolimus: monitor ciclosporin and tacrolimus levels; since these drugs are bound to red blood cells there is a potential risk of a drug interaction as haemoglobin concentration increases
- ACE inhibitors and angiotensin-II antagonists: increased risk of hyperkalaemia

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - SC, IV
- RATE OF ADMINISTRATION
  - COMMENTS
  -

**OTHER INFORMATION**
- To convert to darbepoetin from epoetin, divide total weekly epoetin dose by 200 although that may slightly overestimate the darbepoetin dose
- Same dose may be given either SC or IV – monitor response
- Use with caution in patients with a history of epilepsy as convulsions have been reported in patients with CKD
- Once a pre-filled pen has been removed from the fridge and brought to room temperature it must be used within 7 days
- Pre-treatment checks and appropriate correction/treatment needed for iron, folate and B12 deficiency, infection, inflammation or aluminium toxicity to produce optimum response to therapy
- Concomitant iron therapy (200–300 mg elemental oral iron) needed daily. IV iron may be needed for patients with very low serum ferritin (<100 nanograms/mL)
- May increase heparin requirement during HD
- Reported association of pure red cell aplasia (PRCA) with epoetin therapy. This is a very rare condition; due to failed production of red blood cell precursors in the bone marrow, resulting in profound anaemia. Possibly due to an immune response to the protein backbone of R-HuEPO. Resulting antibodies render the patient unresponsive to the therapeutic effects of all epoetins and darbepoetin
Darifenacin

**CLINICAL USE**
Symptomatic treatment of urinary incontinence, frequency or urgency

**DOSE IN NORMAL RENAL FUNCTION**
7.5–15 mg once daily

**PHARMACOKINETICS**
- Molecular weight: 426.6 (507.5 as hydrobromide)
- % Protein binding: 98
- % Excreted unchanged in urine: 3
- Volume of distribution: 163 litres

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux: Unlikely to be dialysed. Dose as in normal renal function
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antifungals: concentration increased by ketoconazole – avoid concomitant use
- Antivirals: avoid concomitant use with amprenavir, atazanavir, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir and tipranavir
- Calcium-channel blockers: avoid concomitant use with verapamil
- Ciclosporin: avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
  - **RATE OF ADMINISTRATION**
  - 
  - **COMMENTS**
  - 

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Darunavir

CLINICAL USE
Protease inhibitor:
- Treatment of HIV infection with 100 mg of ritonavir, in combination with other antiretroviral medication

DOSE IN NORMAL RENAL FUNCTION
600 mg twice daily

PHARMACOKINETICS
Molecular weight (daltons) 593.7 (as ethanolate)
% Protein binding 95
% Excreted unchanged in urine 7.7
Volume of distribution (L/kg) 29.1–147.1 litres (81.1–180.9 litres with ritonavir)
Half-life – normal/ESRF (hrs) 15 (with ritonavir)/Unchanged

DOSE IN RENAL IMPAIRMENT GFR (mL/Min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAP Unlikely to be dialysed. Dose as in normal renal function
HD Unlikely to be dialysed. Dose as in normal renal function
HDF/High flux Unlikely to be dialysed. Dose as in normal renal function
CAV/VVHD Unlikely to be dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Antibacterials: rifabutin concentration increased – reduce dose of rifabutin; darunavir concentration reduced by rifampicin – avoid concomitant use
- Antidepressants: possibly reduced concentration of paroxetine and sertraline; darunavir concentration reduced by St John’s wort – avoid concomitant use

ADMINISTRATION
RECONSTITUTION
- ROUTE Oral
RATE OF ADMINISTRATION
- COMMENTS
-
Dasatinib

**CLINICAL USE**
- Chronic myeloid leukaemia (CML) in patients who have resistance or intolerance to previous therapy, including imatinib
- Philadelphia chromosome-positive acute lymphoblastic leukaemia in adults who are resistant to or intolerant of prior therapy

**DOSE IN NORMAL RENAL FUNCTION**
- Chronic CML: 100 mg once daily
- All other indications: 70 mg twice daily; dose can be increased in 20 mg steps. Maximum: 140 mg once daily in patients with chronic phase CML, and up to 100 mg twice daily in advanced phase or with ALL

**PHARMACOKINETICS**
- Molecular weight (daltons) 488
- % Protein binding 96
- % Excreted unchanged in urine 0.1
- Volume of distribution (L/kg) 2505 litres
- Half-life – normal/ESRF (hrs) 5–6/

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/min)**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Use with caution

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**: Unlikely to be dialysed. Dose as in GFR<10mL/min
- **HD**: Unlikely to be dialysed. Dose as in GFR<10mL/min
- **HDF/High flux**: Unlikely to be dialysed. Dose as in GFR<10mL/min
- **CAV/VVHD**: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Antibacterials: metabolism accelerated by rifampicin – avoid concomitant use
  - Antipsychotics: avoid concomitant use with clozapine, increased risk of agranulocytosis

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- No studies have been done with dasatinib in renal impairment but due to the low renal excretion there is unlikely to be a reduction in clearance
- Extensively metabolised in humans with multiple enzymes involved in the generation of the metabolites – CYP3A4 is a major enzyme. In healthy subjects administered 100 mg of [14C]-labelled dasatinib, unchanged dasatinib represented 29% of circulating radioactivity in plasma. Plasma concentration and measured in vitro activity indicate that metabolites are unlikely to play a major role in the observed pharmacology of the product
- Elimination is predominantly in the faeces, mostly as metabolites. Following a single oral dose of [14C]-labelled dasatinib, approximately 89% of the dose was eliminated within 10 days, with 4% and 85% of the radioactivity recovered in the urine and faeces, respectively. Unchanged dasatinib accounted for 0.1% and 19% of the dose in urine and faeces, respectively, with the remainder of the dose as metabolites
- Most common adverse effects of dasatinib include fluid retention, gastrointestinal disturbances, and bleeding. Fluid retention may be severe, and can result in pleural and pericardial effusion, pulmonary oedema and ascites
Daunorubicin

**CLINICAL USE**
Antineoplastic agent:
- Acute leukaemias

**DOSE IN NORMAL RENAL FUNCTION**
30–45 mg/m², or as for local protocol

**PHARMACOKINETICS**
- Molecular weight: 564 (as hydrochloride) (daltons)
- % Protein binding: 50–90
- % Excreted unchanged in urine: 5–18
- Volume of distribution (L/kg): 39.2
- Half-life – normal/ESRF (hrs): 18.5; Liposomal: 4–5.2/

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function.</th>
<th>See ‘Other Information’</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
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<tr>
<td>10–20</td>
<td></td>
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<tr>
<td>&lt;10</td>
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</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

| CAPD       | Unlikely to be dialysed. Dose as GFR<10 mL/min |
| HD         | Unlikely to be dialysed. Dose as GFR<10 mL/min |
| HDF/High flux | Unknown dialysability. Dose as GFR<10 mL/min |
| CAV        | Unlikely to be dialysed. Dose as GFR=10–20 mL/min |
| VVHD       |                                                  |

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- Reconstitute 20 mg vial with 4 mL water for injection giving a concentration of 5 mg/mL. Dilute calculated dose of daunorubicin further in sodium chloride 0.9% to give a final concentration of 1 mg/mL

**ROUTE**
- IV

**RATE OF ADMINISTRATION**
- 1 mg/mL solution should be infused over 20 minutes into the tubing or a side arm of a rapidly flowing IV infusion of sodium chloride 0.9%

**COMMENTS**
- Potentially cardiotoxic
- Monitor blood uric acid and urea levels
- Rapidly taken up by the tissues, especially by the kidneys, liver, spleen and heart. Subsequent release of drug and metabolites is slow (T½ ~55 hrs). Rapidly metabolised in the liver, and the major metabolite daunorubicinol is also active. It is excreted slowly in the urine, mainly as metabolites with 25% excreted within 5 days. Biliary excretion accounts for 40–50% elimination
- Manufacturer’s literature suggests that in patients with a serum creatinine of 105–265 µmol/L the dose should be reduced to 75% of normal; if the creatinine is >265 µmol/L, the dose should be 50% of normal
- A liposomal formulation of daunorubicin is now available (DaunoXome). Dilute to 0.2–1 mg/mL with glucose 5% and administer over 30–60 minutes
Deferasirox

**CLINICAL USE**
Treatment of iron overload

**DOSE IN NORMAL RENAL FUNCTION**
10–30 mg/kg once daily rounded to the nearest whole tablet

**PHARMACOKINETICS**
- Molecular weight (daltons): 373.4
- % Protein binding: 99
- % Excreted unchanged in urine: 8
- Volume of distribution (L/kg): 14 litres
- Half-life – normal/ESRF (hrs): 8–16

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50: Avoid. See 'Other Information'
- 10–20: Avoid. See 'Other Information'
- <10: Avoid. See 'Other Information'

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Avoid
- HD: Dialysed. Avoid
- HDF/High flux: Dialysed. Avoid
- CAV/VVHD: Unlikely to be dialysed. Avoid

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Aluminium-containing antacids: avoid concomitant use
- Other nephrotoxic agents: avoid concomitant therapy

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - 
- **COMMENTS**
  - Take on an empty stomach
  - Disperse in a glass of water, orange or apple juice

**OTHER INFORMATION**
- During clinical trials, increases in serum creatinine of >33% on 2 consecutive occasions (sometimes above the upper limit of the normal range) occurred in about 36% of patients. These were dose-dependent. Cases of acute renal failure have been reported following post-marketing use of deferasirox
- Patients with pre-existing renal conditions and patients who are receiving medicinal products that depress renal function may be more at risk of complications
- Tests for proteinuria should be performed monthly. Other markers of renal tubular function may also be monitored (e.g., glycosuria in non-diabetics and low levels of serum potassium, phosphate, magnesium or urate, phosphaturia, aminoaciduria)
- If, despite dose reduction and interruption, the serum creatinine remains significantly elevated and there is also persistent abnormality in another marker of renal function (e.g., proteinuria, Fanconi's Syndrome), the patient should be referred to a renal specialist, and further specialised investigations (such as renal biopsy) may be considered
Deferiprone

CLINICAL USE
Orally administered chelator:
- Treatment of transfusional iron overload

DOSE IN NORMAL RENAL FUNCTION
25 mg/kg 3 times daily. Maximum 100 mg/kg daily

PHARMACOKINETICS
Molecular weight (daltons) 139.2
% Protein binding No data
% Excreted unchanged in urine Information
Volume of distribution (L/kg) 1.55–1.73
Half-life – normal/ESRF (hrs) 2–3/Unknown

DOSE IN RENAL IMPAIRMENT
GFR (mL/Min)
20–50 Dose as in normal renal function
10–20 Give 50% of dose and monitor
<10 Give 50% of dose and monitor

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unknown dialysability. Dose as in GFR<10 mL/min
HD Dialysed. Dose as in GFR<10 mL/min
HDF/Highflux Dialysed. Dose as in GFR<10 mL/min
CAV/VVHD Dialysed. Dose as in GFR=10–20 mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- None known

ADMINISTRATION
RECONSTITUTION
- ROUTE
- Oral
RATE OF ADMINISTRATION
- COMMENTS
- OTHER INFORMATION
- Deferiprone is hepatically metabolised (>85%) to predominantly glucuronide conjugates (no chelating activity). Deferiprone, the glucuronide conjugates, and deferiprone-complexed iron are cleared principally by the kidney, with 80% of the dose recovered in the urine
- Side effects include reversible neutropenia, agranulocytosis, musculoskeletal and joint pain, subclinical ototoxicity, plus case reports of systemic vasculitis and fatal SLE
- Can cause subnormal serum zinc levels
- Reddish-brown discolouration of the urine reported in 40% of thalassaemia patients undergoing deferiprone therapy
- Deferiprone removed aluminium in vitro from blood samples of 46 patients undergoing chronic haemodialysis. Only patients with serum aluminium concentrations >80 mcg/mL were included. Deferiprone removed the aluminium faster and more effectively from higher molecular weight proteins than desferrioxamine. (Canteros-Picotto MA, Fernández-Martin JL, Cannata-Ortiz MJ, et al. Effectiveness of deferiprone (L1) releasing the aluminium bound to plasma proteins in chronic renal failure. Nephrol Dial Transplant. 1996; 11(7): 1488–9)
Deflazacort

**CLINICAL USE**

Glucocorticoid:
- Suppression of inflammatory and allergic disorders

**DOSE IN NORMAL RENAL FUNCTION**

3–18 mg daily
(Acute disorders up to 120 mg daily initially)

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>441.5</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>40%</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>70%</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1.2</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1.1–1.9/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Antibacterials: metabolism accelerated by rifampicin; metabolism possibly inhibited by erythromycin
- Anticoagulants: efficacy of coumarins may be altered
- Anti-epileptics: metabolism accelerated by carbamazepine, barbiturates, phenytoin and primidone
- Antifungals: increased risk of hypokalaemia with amphotericin – avoid concomitant use; metabolism possibly inhibited by itraconazole and ketoconazole.
- Antivirals: concentration possibly increased by ritonavir
- Ciclosporin: rare reports of convulsions in patients on ciclosporin and high-dose corticosteroids; increased half-life of deflazacort
- Cytotoxics: increased risk of haematological toxicity with methotrexate
- Diuretics: enhanced hypokalaemic effects of acetazolamide, loop diuretics and thiazide diuretics
- Vaccines: high dose corticosteroids can impair immune response to vaccines; avoid concomitant use with live vaccines

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**

- 6 mg of deflazacort is equivalent to 5 mg prednisolone
Demeclocycline hydrochloride

**CLINICAL USE**
Antibacterial agent:
- Treatment of syndrome of inappropriate antidiuretic hormone secretion

**DOSE IN NORMAL RENAL FUNCTION**
- 150 mg 4 times a day or 300 mg twice daily
- Syndrome of inappropriate antidiuretic hormone: 900–1200 mg daily in divided doses
- Maintenance: 600–900 mg daily in divided doses

**PHARMACOKINETICS**
- Molecular weight (daltons): 501.3
- % Protein binding: 41–90
- % Excreted unchanged in urine: 42
- Volume of distribution (L/kg): 1.7

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/MIN)
  - 20–50: Dose as in normal renal function
  - 10–20: 600 mg every 24–48 hours
  - <10: 600 mg every 24–48 hours

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. 600 mg every 48 hours
- HD: Dialysed. 600 mg post dialysis
- HDF/High flux: Dialysed. 600 mg post dialysis
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs:
- Anticoagulants: possibly enhanced anticoagulant effect of coumarins and phenindione
- Oestrogens: possibly reduced contraceptive effects of oestrogens (risk probably small)
- Retinoids: possible increased risk of benign intracranial hypertension, avoid concomitant use

**ADMINISTRATION**
- RECONSTITUTION
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - COMMENTS

**OTHER INFORMATION**
- Avoid if possible in renal impairment due to its potential nephrotoxicity
- May be administered to anuric patients every 3–4 days
Desferrioxamine mesilate

**CLINICAL USE**

Chelating agent:
- Acute iron poisoning
- Chronic iron or aluminium overload

**DOSE IN NORMAL RENAL FUNCTION**

- SC/IV: Initially 500 mg then 20–60 mg/kg/day 3–7 times a week. Exact dosages should be determined for each individual
- IM: 0.5–1 g daily as 1 or 2 injections, maintenance dose as per response
- Oral: acute iron poisoning: 5–10 g should be dissolved in 50–100 mL water
- Aluminium overload in HD: (IV) 5 mg/kg weekly over last hour of dialysis
- PD: (SC, IM, IV, IP) 5 mg/kg weekly before the final exchange of the day

**PHARMACOKINETICS**

- Molecular weight (daltons) 656.8
- % Protein binding <10
- % Excreted unchanged in urine 22
- Volume of distribution (L/kg) 2–2.5
- Half-life – normal/ESRF (hrs) 6/–

**DOSE IN RENAL IMPAIRMENT**

- GFR (mL/Min) 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Dialysed. Treatment of aluminium overload: 1 g once or twice each week prior to final exchange of the day by slow IV infusion, IM, SC or IP
- HD: Dialysed. Treatment of aluminium overload: 1 g once each week administered during the last hour of dialysis as a slow IV infusion
- HDF/High flux: Dialysed. Treatment of aluminium overload: 1 g once each week administered during the last hour of dialysis as a slow IV infusion

** IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Avoid prochlorperazine, methotrimeprazine (prolonged unconsciousness)
- Do not administer with blood

**ADMINISTRATION**

**RECONSTITUTION**

Dissolve contents of one vial (500 mg) in 5 mL of water for injection =10% solution. If for IV administration, the 10% solution can be diluted with sodium chloride 0.9%, glucose 5% or glucose/sodium chloride

**ROUTE**

- IV, SC (bolus or continuous infusion), IM, IP, oral

**RATE OF ADMINISTRATION**

- IV (acute overdose): Maximum 15 mg/kg/hour. Reduce after 4–6 hours so that total dose does not exceed 80 mg/kg/24 hours
- SC: Infuse over 8–24 hours. Local irritation may occur

**COMMENTS**

- The urine may appear orange/red in patients treated with desferrioxamine for severe iron intoxication
- SC infusion is about 90% as effective as IV administration, which is now the route of choice in transfusion-related iron overload
- IM injection is less effective than SC

**OTHER INFORMATION**

- Studies suggest that during HD only a small amount of plasma desferrioxamine crosses the dialysis membrane
- Contraindicated in patients with severe renal disease except those on dialysis
- 100 mg desferrioxamine mesilate can bind 4.1 mg Al³⁺
- Desferrioxamine may predispose to development of infection with *Yersinia* species
- In haemodialysis patients treated with desferrioxamine post dialysis, the half-life has been found to be extended to 19 hours between dialysis sessions

RETURN TO CONTENTS
Anecdotally, escalating doses of up to 2 g, 3 times a week have been successfully used for iron overload in patients on haemodialysis.

In treatment of acute iron poisoning, effectiveness of treatment is dependent on an adequate urine output. If oliguria or anuria develop, PD or HD may be necessary.
Desirudin (unlicensed product)

**CLINICAL USE**
Prophylaxis of DVT in patients undergoing orthopaedic surgery

**DOSE IN NORMAL RENAL FUNCTION**
15 mg 5–15 minutes before surgery then 15 mg twice daily for 9–12 days or until mobile

**PHARMACOKINETICS**
- Molecular weight: 6963.4 (daltons)
- % Protein binding: No data
- % Excreted: 40–50 unchanged in urine
- Volume of distribution: 0.25 (L/kg)
- Half-life – normal/ESRF (hrs): 2–3

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 31–60: Initially 5 mg twice daily. Aim for APTT <0.85 seconds
  - <31: Initially 1.7 mg twice daily and monitor APTT

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<31 mL/min
- HD: Not dialysed. Dose as in GFR<31 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<31 mL/min
- CAV/VVHD: Not dialysed. Dose as in GFR<31 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants, antiplatelets, fondaparinux, NSAIDs, heparin and dextran – increased risk of bleeding

**ADMINISTRATION**
- RECONSTITUTION
  - With diluent supplied
- ROUTE
  - SC
- RATE OF ADMINISTRATION
  - COMMENTS

**OTHER INFORMATION**
- The effect is poorly reversible
- APTT levels can be reduced by IV DDAVP
- Available on a named patient basis from Aventis Pharma
- 7% of dose is metabolised by the kidneys
Desloratadine

**CLINICAL USE**
Antihistamine:
- Symptomatic relief of allergy such as hay fever, urticaria

**DOSE IN NORMAL RENAL FUNCTION**
5 mg daily

**PHARMACOKINETICS**
- Molecular weight: 310.8 (daltons)
- % Protein binding: 83–87
- % Excreted unchanged in urine: 40.6 (as active metabolites)
- Volume of distribution: No data
- Half-life – normal/ESRF: 27/Increased

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**
- RECONSTITUTION
  -
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
  -
- COMMENTS
  -

**OTHER INFORMATION**
- Desloratadine is an active metabolite of loratadine
- Full dose may result in increased sedation in patients with GFR<10 mL/min
Desmopressin (DDAVP)

**CLINICAL USE**
- Diabetes insipidus
- Nocturnal enuresis
- Post-biopsy bleeding (unlicensed indication)
- Pre-biopsy prophylaxis (unlicensed indication)

**DOSE IN NORMAL RENAL FUNCTION**
- Diabetes insipidus: Oral: 0.2–1.2 mg daily in 3 divided doses. IV: 1–4 mcg daily. Inhaled: 10–40 mcg in 1 or 2 divided doses. Sub-lingual: 120–720 mcg daily
- Nocturnal enuresis: Oral: 200–400 mcg at bedtime,
- Biopsy: Males – 16 mcg; Females – 12 mcg or 300–400 nanograms/kg
- Pre-biopsy prophylaxis in uraemic patients: 20 mcg (IV) over 30 minutes

**PHARMACOKINETICS**
- Molecular weight (daltons) 1069.2
- % Protein binding 0
- % Excreted unchanged in urine 45
- Volume of distribution (L/kg) 0.2–0.41
- Half-life – normal/ESRF (hrs) Inhaled: 55 minutes; Oral: 2.8 hours; IV: 51–158 minutes

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Unlikely to be dialysed. Dose as in normal renal function
- HD Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux Unknown dialysability. Dose as in normal renal function
- CAV/VVHD Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**
- Reconstitution
  - Dilute dose to 50 mL with sodium chloride 0.9%
  - IV, intranasally, oral, SC, IM, SL
- Rate of Administration
  - Over 20–60 minutes
- Comments
  - Do not inject at a faster rate – greater risk of tachyphylaxis
  - In patients with ischaemic heart disease, infuse more slowly – increased risk of acute ischaemic event

**OTHER INFORMATION**
- Emergency treatment of more generalised bleeding unresponsive to normal treatments: 0.1–0.5 micrograms/kg 4 times a day + IV conjugated oestrogens (premarin) 0.6 mg/kg/day for up to 5 days
- DDAVP works as a haemostatic by stimulating factor VIII production
- Onset of action less than 1 hour. Duration of effect 4–8 hours
Dexamethasone

**CLINICAL USE**
Corticosteroid:
- Cerebral oedema
- Suppression of inflammatory and allergic disorders
- Rheumatic disease
- Congenital adrenal hyperplasia
- Anti-emetic (unlicensed indication)

**DOSE IN NORMAL RENAL FUNCTION**
- Cerebral oedema: 10 mg IV followed by 4 mg IM every 6 hours
- Rheumatic disease:
  - intra-articular, intrasynovial: 0.4–4 mg (as dexamethasone phosphate)
  - soft tissue infiltration: 2–6 mg
- Oral: 0.5–10 mg daily, IV/IM: 0.5–24 mg

**PHARMACOKINETICS**
- Molecular weight (daltons): 392.5 (472.4 as phosphate)
- % Protein binding: 77
- % Excreted unchanged in urine: 65
- Volume of distribution (L/kg): 0.8–1
- Half-life – normal/ESRF (hrs): 3.5–4.5/

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Removal unlikely. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: metabolism accelerated by rifampicin; metabolism possibly inhibited by erythromycin
- Anticoagulants: efficacy of coumarins may be altered
- Anti-epileptics: metabolism accelerated by carbamazepine, barbiturates, phenytoin and primidone
- Antifungals: increased risk of hypokalaemia with amphotericin – avoid concomitant use; metabolism possibly inhibited by itraconazole and ketoconazole; caspofungin concentration possibly reduced (may need to increase dose).
- Antivirals: concentration of indinavir, lopinavir and saquinavir possibly reduced; concentration possibly increased by ritonavir
- Ciclosporin: rare reports of convulsions in patients on ciclosporin and high-dose corticosteroids
- Cytotoxics: increased risk of haematological toxicity with methotrexate
- Diuretics: enhanced hypokalaemic effects of acetazolamide, loop diuretics and thiazide diuretics
- Vaccines: high dose corticosteroids can impair immune response to vaccines; avoid concomitant use with live vaccines

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral, IV, IM, intra-articular, intrasynovial
  - **RATE OF ADMINISTRATION**
  - IV slowly over not less than 5 minutes.
  - If underlying cardiac pathology, infusion over 20–30 minutes advised

**COMMENTS**
- **OTHER INFORMATION**
  - Dexamethasone sodium phosphate 1.3 mg = dexamethasone 1 mg
  - 750 mcg of dexamethasone is equivalent to 5 mg prednisolone
  - Injection solution can be administered orally or via naso-gastric tube
  - Tablets will disperse in water

*It is not licensed for use by anyone else.*
Dexibuprofen

**CLINICAL USE**

NSAID and analgesic

**DOSE IN NORMAL RENAL FUNCTION**

Initially: 600–900 mg daily in divided doses, after food; Maximum 1.2 g daily (900 mg daily for dysmenorrhoea); Maximum single dose: 400 mg (300 mg for dysmenorrhoea)

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>206.3</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>&gt;99</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>82 (mainly as inactive metabolites)</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>10–11 litres</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1.6–1.9/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function, but avoid if possible</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function, but avoid if possible</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function, but only use if on dialysis</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapeutic Modality</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:

- ACE inhibitors and angiotensin-II antagonists: antagonism of hypotensive effect, increased risk of nephrotoxicity and hyperkalaemia
- Analgesics: avoid concomitant use of 2 or more NSAIDs, including aspirin (increased side effects); avoid with ketorolac (increased risk of side effects and haemorrhage)

- Antibacterials: possibly increased risk of convulsions with quinolones
- Anticoagulants: effects of coumarins enhanced; possibly increased risk of bleeding with heparins and coumarins
- Antidepressants: increased risk of bleeding with SSRIs and venlafaxine
- Antidiabetic agents: effects of sulphonylureas enhanced
- Anti-epileptics: possibly increased phenytoin concentration
- Antivirals: increased risk of haematological toxicity with zidovudine; concentration possibly increased by ritonavir
- Ciclosporin: may potentiate nephrotoxicity
- Cytotoxic agents: reduced excretion of methotrexate; increased risk of bleeding with erlotinib
- Diuretics: increased risk of nephrotoxicity; antagonism of diuretic effect; hyperkalaemia with potassium-sparing diuretics
- Lithium: excretion decreased
- Pentoxifylline: increased risk of bleeding
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**

- **COMMENTS**

**OTHER INFORMATION**

- S (+)– enantiomer of racemic ibuprofen
- Inhibition of renal prostaglandin synthesis by NSAIDs may interfere with renal function, especially in the presence of existing renal disease – avoid if possible; if not, check serum creatinine 48–72 hours after starting NSAID – if raised, discontinue NSAID therapy.
- Use normal doses in patients with CKD 5 on dialysis
- Use with caution in renal transplant recipients – can reduce intrarenal autacoid synthesis

RETURN TO CONTENTS
Dexketoprofen

**CLINICAL USE**
NSAID and analgesic

**DOSE IN NORMAL RENAL FUNCTION**
12.5 mg every 4–6 hours
or 25 mg every 8 hours

**PHARMACOKINETICS**
<table>
<thead>
<tr>
<th>Molecular weight (daltons)</th>
<th>254.3</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Protein binding</td>
<td>99%</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;10%</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.24</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1.65/Increased</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function but use with caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function but avoid if possible</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function but only if on dialysis</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>CAPD</th>
<th>Dialysed. Dose as in normal renal function. See ‘Other Information’</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in normal renal function. See ‘Other Information’</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in normal renal function. See ‘Other Information’</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose as for GFR=10–20 mL/min.</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- ACE inhibitors and angiotensin-II antagonists: antagonism of hypotensive effect; increased risk of nephrotoxicity and hyperkalaemia
- Analgesics: avoid concomitant use of 2 or more NSAIDs, including aspirin (increased side effects); avoid with ketorolac (increased risk of side effects and haemorrhage)
- Antibacterials: possibly increased risk of convulsions with quinolones
- Anticoagulants: effects of coumarins enhanced; possibly increased risk of bleeding with heparins and coumarins
- Antidepressants: increased risk of bleeding with SSRI and venlafaxine
- Antidiabetic agents: effects of sulphonylureas enhanced
- Anti-epileptics: possibly increased phenytoin concentration
- Antiviral: increased risk of haematological toxicity with zidovudine; concentration possibly increased by ritonavir
- Ciclosporin: may potentiate nephrotoxicity
- Cytotoxic agents: reduced excretion of methotrexate; increased risk of bleeding with erlotinib
- Diuretics: increased risk of nephrotoxicity; antagonism of diuretic effect, hyperkalaemia with potassium-sparing diuretics
- Lithium: excretion decreased
- Pentoxifylline: increased risk of bleeding
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**
- Inhibition of renal prostaglandin synthesis by NSAIDs may interfere with renal function, especially in the presence of existing renal disease – avoid if possible; if not, check serum creatinine 48–72 hours after starting NSAID – if raised, discontinue NSAID therapy
- Use normal doses in patients with ERF on dialysis if they do not pass any urine
- Use with caution in renal transplant recipients – can reduce intrarenal autochoid synthesis
- Dexketoprofen should be used with caution in uraemic patients predisposed to gastrointestinal bleeding or uraemic coagulopathies

RETURN TO CONTENTS
Diamorphine hydrochloride

**CLINICAL USE**

Opiate analgesic:
- Control of severe pain
- Pain relief in myocardial infarction (MI)
- Acute pulmonary oedema

**DOSE IN NORMAL RENAL FUNCTION**

- Severe pain: Oral/SC/IM: 5–10 mg 4 hourly, increasing dose as necessary
- Acute MI, pulmonary oedema: IV: 2.5–5 mg. Elderly patients – reduce dose by half

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Molecular weight (daltons)</th>
<th>423.9</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Protein binding</td>
<td>35</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>0.1</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>40–50 litres</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1.7–5.3 minutes/–</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Use small doses, e.g. 2.5 mg SC/IM approx 6 hourly and titrate to response</td>
</tr>
<tr>
<td>10–20</td>
<td>Use small doses, e.g. 2.5 mg SC/IM approx 8 hourly and titrate to response</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Use small doses, e.g. 2.5 mg SC/IM approx 8 hourly and titrate to response</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Modality</th>
<th>Dose as in GFR&lt;10mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Anti-arrhythmics: delayed absorption of mexiletine
- Antidepressants: possible CNS excitation or depression with MAOIs – avoid concomitant use and for 2 weeks after stopping MAOI; possible CNS excitation or depression with moclobemide; increased sedative effects with tricyclics
- Antipsychotics: enhanced sedative and hypotensive effect
- Sodium oxybate: enhanced effect of sodium oxybate – avoid concomitant use

**ADMINISTRATION**

- IV, IM, SC, oral

**RECONSTITUTION**

- 1 mL water for injection or sodium chloride 0.9% (less may be used, e.g. for SC injection use 0.1 mL for 10 mg)

**RATE OF ADMINISTRATION**

- IV: 1 mg/minute

**COMMENTS**

- Monitor BP and respiratory rates

**OTHER INFORMATION**

- Increased cerebral sensitivity in renal impairment which can result in excessive sedation and serious respiratory depression necessitating ventilation
- More rapid onset and shorter duration of action than morphine
- Extreme caution with regular dosing – accumulation of active metabolites may occur
- Naloxone must be readily available for reversal if required
Diazepam

**CLINICAL USE**
Benzodiazepine:
- Perioperative sedation (IV)
- Anxiolytic
- Muscle relaxant
- Status epilepticus

**DOSE IN NORMAL RENAL FUNCTION**
- Pre-med: Oral: 5 mg, IV: 10–20 mg or 100–200 mcg/kg; PR: 500 mcg/kg repeated after 12 hours as rectal solution
- Anxiety: Oral: 2 mg 3 times a day, increasing if necessary to 15–30 mg daily in divided doses; PR: 10–30 mg daily in divided doses
- IM/IV: 5–10 mg repeated after not less than 4 hours
- Insomnia: 5–15 mg at night
- Status epilepticus: IV: 10 mg, repeated after 10 minutes if required; PR: 500 mcg/kg

**PHARMACOKINETICS**
- Molecular weight (daltons): 284.7
- % Protein binding: 95–99
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): 0.95–2

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/Min)**
  - 20–50: Dose as in normal renal function
  - 10–20: Use small doses and titrate to response
  - <10: Use small doses and titrate to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Not dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: metabolism enhanced by rifampicin; metabolism inhibited by isoniazid
- Antipsychotics: increased sedative effects; increased risk of hypotension, bradycardia and respiratory depression with parenteral diazepam and IM olanzapine; concentration of zotepine increased
- Antivirals: increased risk of prolonged sedation with amprenavir; concentration possibly increased by ritonavir
- Sodium oxybate: enhanced effects of sodium oxybate – avoid

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - IV injection, infusion, oral, PR
  - RATE OF ADMINISTRATION
    - 5 mg (1 mL)/minute
  - **COMMENTS**
    - Injection can be mixed with sodium chloride 0.9% or glucose 5% to 40 mg in 500 mL

**OTHER INFORMATION**
- Active metabolites renally excreted; therefore accumulate in renal impairment
- Increased cerebral sensitivity in renal impairment which may result in excessive sedation and encephalopathy
- Always have flumazenil available to reverse effect
- Protein binding decreased in ERF
- Volume of distribution increased in ERF
- IV emulsion formulation (Diazemuls) less likely to cause thrombophlebitis
Diazoxide

CLINICAL USE
- Treatment of hypertensive emergencies including severe hypertension associated with renal disease
- Hypoglycaemia

DOSE IN NORMAL RENAL FUNCTION
- Hypertension: IV: 1–3 mg/kg; maximum single dose: 150 mg, repeat after 5–15 minutes
- Hypoglycaemia: Oral: 3–5 mg/kg in 2–3 divided doses; adjust according to response, usually 3–8 mg/kg; total doses up to 1 g have been used

PHARMACOKINETICS
Molecular weight (daltons) 230.7
% Protein binding >90
% Excreted unchanged in urine 50
Volume of distribution (L/kg) 0.2–0.3
Half-life – normal/ESRF (hrs) 20–45/30–60

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Start with a lower dose and increase gradually according to response. Use with caution

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD Dialysed. Dose as in GFR<10mL/min
- HD Dialysed. Dose as in GFR<10mL/min
- HDF/High flux Dialysed. Dose as in GFR<10mL/min
- CAV/VVHD Unknown dialysability. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Antihypertensives and vasodilators: enhanced hypotensive effect
- MAOIs: withdraw at least 14 days before starting diazoxide
- Phenytoin: may reduce phenytoin levels

ADMINISTRATION
RECONSTITUTION
- ROUTE
  - IV bolus, oral
RATE OF ADMINISTRATION
- <30 seconds
COMMENTS
- OTHER INFORMATION
  - Single doses above 300 mg have been associated with angina and myocardial and cerebral infarction.
  - Can cause sodium and water retention
Diclofenac sodium

**CLINICAL USE**
NSAID and analgesic

**DOSE IN NORMAL RENAL FUNCTION**
75–150 mg daily in divided doses

**PHARMACOKINETICS**
- Molecular weight (daltons): 318.1
- % Protein binding: 99.7
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): 0.12–0.17

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min): 20–50 Dose as in normal renal function
- GFR (mL/min): 10–20 Dose as in normal renal function, but avoid if possible
- GFR (mL/min): <10 Dose as in normal renal function, but only use if on dialysis

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function. See 'Other Information'
- HD: Not dialysed. Dose as in normal renal function. See 'Other Information'
- HDF/High flux: Not dialysed. Dose as in normal renal function. See 'Other Information'
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- ACE inhibitors and angiotensin-II antagonists: antagonism of hypotensive effect; increased risk of nephrotoxicity and hyperkalaemia
- Analgesics: avoid concomitant use of 2 or more NSAIDs, including aspirin (increased side effects); avoid with ketorolac (increased risk of side effects and haemorrhage)
- Antibacterials: possibly increased risk of convulsions with quinolones
- Anticoagulants: effects of coumarins enhanced; possibly increased risk of bleeding with heparins and coumarins; increased risk of haemorrhage with IV diclofenac – avoid concomitant use
- Antidepressants: increased risk of bleeding with SSRIs and venlafaxine
- Antidiabetic agents: effects of sulphonylureas enhanced
- Anti-epileptics: possibly increased phenytoin concentration
- Antivirals: increased risk of haematological toxicity with zidovudine; concentration possibly increased by ritonavir
- Ciclosporin: may potentiate nephrotoxicity; concentration increased by ciclosporin
- Cytotoxic agents: reduced excretion of methotrexate; increased risk of bleeding with erlotinib
- Diuretics: increased risk of nephrotoxicity; antagonism of diuretic effect; hyperkalaemia with potassium-sparing diuretics
- Lithium: excretion decreased
- Pentoxifylline: increased risk of bleeding
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral, IV, IM, PR
- **RATE OF ADMINISTRATION**
  - 25–50 mg over 15–60 minutes; 75 mg over 30–120 minutes
- **Continuous infusion of 5 mg/hour**

**COMMENTS**
- Dilute 75 mg in 100–500 mL of sodium chloride 0.9% or glucose 5% buffered with 0.5 mL sodium bicarbonate 8.4%

**OTHER INFORMATION**
- **Diclofenac should be used with caution in uraemic patients predisposed to gastrointestinal bleeding or uraemic coagulopathies**
- **Inhibition of renal prostaglandin synthesis by NSAIDs may interfere with renal function, especially in the presence of**
existing renal disease – avoid if possible; if not, check serum creatinine 48–72 hours after starting NSAID – if raised, discontinue NSAID therapy.

- Use normal doses in patients with ERF on dialysis if they do not pass any urine
- Use with great caution in renal transplant recipients – can reduce intrarenal autocoid synthesis
Didanosine

**CLINICAL USE**

Nucleoside reverse transcriptase inhibitor:
- Treatment of HIV in combination with other antiretroviral drugs

**DOSE IN NORMAL RENAL FUNCTION**

<table>
<thead>
<tr>
<th>Weight</th>
<th>Daily Dose</th>
<th>Divided Doses</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;60 kg</td>
<td>400 mg</td>
<td>1–2</td>
</tr>
<tr>
<td>&lt;60 kg</td>
<td>250 mg</td>
<td>1–2</td>
</tr>
</tbody>
</table>

**PHARMACOKINETICS**

- Molecular weight: 236.2 daltons
- % Protein binding: <5
- % Excreted unchanged in urine: 20
- Volume of distribution (L/kg): 1
- Half-life – normal/ESRF (hrs): 1.4/4.1

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>&lt;60 kg</th>
<th>&gt;60 kg</th>
<th>10–29</th>
<th>&lt;10</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–59</td>
<td>150 mg</td>
<td>200 mg</td>
<td>100 mg</td>
<td>75 mg</td>
</tr>
<tr>
<td>10–29</td>
<td>100 mg</td>
<td>150 mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>75 mg</td>
<td>100 mg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Type</th>
<th>Dose Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose as in GFR=10–29mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Antibacterials: ciprofloxacin, tetracyclines, and other antibiotics affected by indigestion remedies – do not administer within 2 hours of didanosine
- Antivirals: concentration increased by ganciclovir and tenofovir – avoid with tenofovir; increased risk of side effects with ribavirin and stavudine; concentration reduced by tipranavir
- Cytotoxics: increased risk of toxicity with hydroxyx carbamide – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - 
- **COMMENTS**
  - Give dose after dialysis on dialysis days, and at the same time on non-dialysis days

**OTHER INFORMATION**

- Haemodialysis removes 20–35% of the dose
- Administer 30 minutes to 2 hours before meals (depends on formulation)
- Magnesium content of tablets 8.6 mEq.
- Chew, crush tablet or disperse in at least 30mL of water
- Can be diluted in apple juice
- Ingestion with food decreases absorption by 55%
**Digitoxin**

**CLINICAL USE**
- Heart failure
- Supraventricular arrhythmias

**DOSE IN NORMAL RENAL FUNCTION**
Maintenance dose: 100 mcg daily or on alternate days; may be increased to 200 mcg daily if necessary

**PHARMACOKINETICS**
- Molecular weight: 764.9 daltons
- % Protein binding: >90%
- % Excreted unchanged in urine: 25%
- Volume of distribution: 0.6 L/kg
- Half-life – normal/ESRF (hrs): 7.5 days/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/Min)**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Give 50–75% of normal dose

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**
  - Not dialysed. Dose as in GFR<10mL/min
- **HD**
  - Not dialysed. Dose as in GFR<10mL/min
- **HDF/High flux**
  - Not dialysed. Dose as in GFR<10mL/min
- **CAV/VVHD**
  - Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Antifungals: increased toxicity if hypokalaemia occurs with amphotericin
  - Diuretics: increased digitoxin toxicity if hypokalaemia occurs; concentration possibly increased by spironolactone

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - Comments

**OTHER INFORMATION**
- Volume of distribution is decreased by uraemia
- Largely metabolised in the liver where 8–10% is converted to digoxin. More digitoxin is converted to digoxin in severe renal impairment
Digoxin

CLINICAL USE
- Supraventricular arrhythmias
- Heart failure

DOSE IN NORMAL RENAL FUNCTION
Digitalisation: 1–1.5 mg in divided doses over 24 hours, followed by 62.5–500 mcg daily, adjusted according to response
Emergency loading (IV): 0.75–1 mg over at least 2 hours

PHARMACOKINETICS
Molecular weight (daltons) 780.9
% Protein binding 25
% Excreted unchanged in urine 50–75
Volume of distribution (L/kg) 5–8
Half-life – normal/ESRF (hrs) 30–40/100

DOSE IN RENAL IMPAIRMENT
GFR (mL/MIN)
20–50 125–250 micrograms per day
10–20 125–250 micrograms per day. Monitor levels
<10 Dose commonly 62.5 micrograms alternate days, or 62.5 micrograms daily. Monitor levels

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Not dialysed. Dose as in GFR<10mL/min
HD Not dialysed. Dose as in GFR<10mL/min
HDF/High flux Not dialysed. Dose as in GFR<10mL/min
CAV/VVHD Not dialysed. Dose as in GFR=10–20mL/min

IMPORTANT DRUG INTERACTIONS
- Antidepressants: concentration reduced by St John’s wort – avoid concomitant use
- Antifungals: increased toxicity if hypokalaemia occurs with amphotericin; concentration increased by itraconazole
- Antimalarials: concentration possibly increased by quinine, hydroxychloroquine and chloroquine; increased risk of bradycardia with mefloquine
- Calcium-channel blockers: concentration increased by diltiazem, lercanidipine, nicardipine, verapamil and possibly nifedipine; increased risk of AV block and bradycardia with verapamil
- Ciclosporin: concentration increased by ciclosporin
- Diuretics: increased toxicity if hypokalaemia occurs; concentration increased by spironolactone

ADMINISTRATION
RECONSTITUTION
- ROUTE
- Oral, IV
- RATE OF ADMINISTRATION
- Loading dose: infuse over 10–20 minutes
- COMMENTS
- IV administration: dilute dose to 4 times volume with sodium chloride 0.9% or glucose 5%
- IV dosing may be used for very rapid control

OTHER INFORMATION
- Complex kinetics in renal impairment: Volume of distribution and total body clearance reduced in CKD 5
- Steady-state plasma monitoring advisable: normal range 0.8–2 nanograms/mL. take at least 8 hours post-dose, ideally before dose in the morning
- If changing from oral to IV reduce dose by a third
- Hypokalaemia, hypomagnesaemia, marked hypercalcaemia and hypothyroidism increase toxicity
- Increases uraemic gastrointestinal symptoms
- Only 3% of dose is removed after a 5 hour HD session
- Concomitant administration of phosphate binders reduces GI absorption by up to 25%
- Digitalisation using 750 micrograms – 1 mg. Interval between normal or reduced doses may need to be lengthened

RETURN TO CONTENTS
Dihydrocodeine tartrate

**CLINICAL USE**
Analgesia

**DOSE IN NORMAL RENAL FUNCTION**
Oral: 30 mg every 4–6 hrs
SC/IM: up to 50 mg every 4–6 hrs

**PHARMACOKINETICS**
- Molecular weight: 451.5 (daltons)
- % Protein binding: No data
- % Excreted unchanged in urine: 13–22
- Volume of distribution: 1.1 (L/kg)
- Half-life – normal/ESRF (hrs): 3.5–5/>6

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/Min)**
  - 20–50: Dose as in normal renal function
  - 10–20: Use small doses and titrate to response
  - <10: Use small doses and titrate to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR<10mL/min
- HD: Unknown dialysability. Dose as in GFR<10mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10mL/min
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral, IM, SC

**COMMENTS**
- Increased and prolonged effect in renal impairment, enhancing respiratory depression and constipation
- Increased CNS sensitivity in renal impairment.
- Accumulation of active metabolites can occur – caution
- Effects can be reversed by naloxone

**OTHER INFORMATION**
- Increased and prolonged effect in renal impairment, enhancing respiratory depression and constipation
- Increased CNS sensitivity in renal impairment.
- Accumulation of active metabolites can occur – caution
- Effects can be reversed by naloxone
Diltiazem hydrochloride

**CLINICAL USE**
Calcium-channel blocker:
- Prophylaxis and treatment of angina
- Hypertension

**DOSE IN NORMAL RENAL FUNCTION**
180–500 mg in up to 3 divided doses

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight</td>
<td>451 (daltons)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>80–85%</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>5%</td>
</tr>
<tr>
<td>Volume of distribution</td>
<td>3–8 (L/kg)</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>2–11/5–8/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
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</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

- Potentially hazardous interactions with other drugs:
  - Anesthetics: enhanced hypotensive effect
  - Anti-arrhythmics: increased risk of bradycardia, AV block and myocardial depression with amiodarone
  - Antibacterials: metabolism increased by rifampicin
  - Anti-epileptics: effect probably reduced by barbiturates, phenytoin, and primidone; enhanced effect of carbamazepine; increased levels of phenytoin
  - Antihypertensives: enhanced hypotensive effect; increased risk of first dose hypotensive effect of post-synaptic alpha-blockers
  - Antivirals: concentration increased by amprenavir, atazanavir and ritonavir – reduce dose of diltiazem with atazanavir; concentration reduced by efavirenz
  - Beta-blockers: risk of bradycardia and AV block if co-prescribed with beta-blockers
  - Cardiac glycosides: increased digoxin concentration
  - Ciclosporin: increased ciclosporin concentrations
  - Cilostazol: increased cilostazol concentration – avoid concomitant use
  - Ivabradine: avoid concomitant use
  - Sirolimus: sirolimus concentration increased
  - Statins: increased myopathy with simvastatin. Do not exceed 40 mg of simvastatin with diltiazem.
  - Tacrolimus: increased tacrolimus concentration
  - Theophylline: enhanced effect of theophylline

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**

- **COMMENTS**

**OTHER INFORMATION**

- Active metabolites
- Monitor heart rate early on in therapy. If falls below 50 beats/minute, do not increase dose
- Maintain patient on same brand

References:
Dipyridamole

**CLINICAL USE**
Antiplatelet agent

**DOSE IN NORMAL RENAL FUNCTION**
100–200 mg 3 times daily
Modified release: 200 mg twice daily

**PHARMACOKINETICS**
<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>504.6</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>97–99</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>1–5</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1.33–3.53</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>9–12/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>VVHD</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anti-arrrhythmics: effects of adenosine enhanced and extended
- Anticoagulants: anticoagulant effect of coumarins, phenindione and heparin enhanced

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
-
## Disodium etidronate

### CLINICAL USE

**Bisphosphonate:**
- Paget’s disease of bone
- Vertebral osteoporosis (Didronel PMO)

### DOSE IN NORMAL RENAL FUNCTION

- Paget’s disease: 5–20 mg/kg daily for 3–6 months
- Vertebral osteoporosis: 400 mg daily for 14 days followed by 76 days of calcium carbonate 1.25 g (= 500 mg calcium)

### PHARMACOKINETICS

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>250</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>Depends on calcium concentration and pH</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>50</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.3–1.3</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1–6/–</td>
</tr>
</tbody>
</table>

### DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Maximum dose = 5 mg/kg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Maximum dose = 5 mg/kg/day – use with caution. (May also use Didronel PMO for osteoporosis.)</td>
</tr>
</tbody>
</table>

### DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>CAPD</th>
<th>Unknown dialysability. Dose as in GFR&lt;10 mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

### IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs
- Do not give iron and mineral supplements, antacids or phosphate binders within 2 hours of an etidronate

### ADMINISTRATION

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  -
- **COMMENTS**
  - Take on an empty stomach. Recommended that patients take with water at the midpoint of a 4 hour fast (i.e. 2 hours before and 2 hours after food)
  - Oral bioavailability is very low; only about 4% of dose is absorbed

### OTHER INFORMATION

- Renal clearance of etidronate is 1.2 mL/minute/kg, whilst the total body clearance is 2.2 mL/minute/kg
- Elimination is likely to be reduced in patients with renal impairment and elderly with reduced renal function necessitating caution. Uptake of etidronate by bone represents non-renal clearance
## Disodium pamidronate

### CLINICAL USE

Bisphosphonate:
- Hypercalcaemia
- Bone pain
- Paget’s disease

### DOSE IN NORMAL RENAL FUNCTION

- Hypercalcaemia: depends on serum calcium – 15–90 mg in single or divided doses
- Bone pain: 90 mg every 4 weeks
- Paget’s disease: 30 mg weekly for 6 weeks, or 30 mg first dose then 60 mg every other week

### PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>369.1</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>54</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>20–55</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.5–0.6</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>0.8–27/Unchanged</td>
</tr>
</tbody>
</table>

### DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Serum calcium &gt;4.0, give 60 mg.</td>
<td>Serum calcium &lt;4.0, give 30 mg.</td>
</tr>
</tbody>
</table>

### DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

### IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs
- None known

### ADMINISTRATION

**RECONSTITUTION**
- 15 mg in 5 mL water for injection
- 30 or 90 mg in 10 mL water for injection
- Final concentration should not exceed
  - 30 mg per 125 mL sodium chloride 0.9%

**ROUTE**
- IV

**RATE OF ADMINISTRATION**
- Maximum 20 mg/hour in patients with impaired renal function

### OTHER INFORMATION

- If pamidronate is not excreted adequately, kidney stones may be formed
- In dialysis patients there is increased risk of asymptomatic hypocalcaemia with 90 mg doses (anecdotal)
**Disopyramide**

**CLINICAL USE**
Ventricular and supraventricular arrhythmias

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: 300–800 mg daily in divided doses
- IV: 2 mg/kg over 5 minutes to a maximum of 150 mg
- Infusion: 400 mcg/kg/hour, maximum 300 mg in 1st hour and 800 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons) 339.5
- % Protein binding 50–65
- % Excreted unchanged in urine 50–75
- Volume of distribution (L/kg) 0.8–2.6
- Half-life – normal/ESRF (hrs) 5–8/12–22

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Oral Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>100 mg every 8 hours or 150 mg every 12 hours</td>
</tr>
<tr>
<td>10–20</td>
<td>100 mg every 12 hours</td>
</tr>
<tr>
<td>&lt;10</td>
<td>150 mg every 24 hours (monitor levels)</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
- Antibacterials: concentration possibly increased by clarithromycin and erythromycin (risk of toxicity); increased risk of ventricular arrhythmias with moxifloxacin and quinupristin/dalfopristin – avoid concomitant use; concentration reduced by rifampicin
- Antidepressants: increased risk of ventricular arrhythmias with tricyclics
- Antifungals: increased risk of ventricular arrhythmias with ketoconazole – avoid concomitant use
- Antihistamines: increased risk of ventricular arrhythmias with mizolastine
- Antihypertensives: increased myocardial depression and asystole with beta-blockers or verapamil; increased risk of ventricular arrhythmias with sotalol – avoid
- Antimalarial: avoid concomitant use with arteether/lumefantrine
- Antipsychotics: increased risk of ventricular arrhythmias with antipsychotics that prolong the QT interval and phenothiazines; increased risk of ventricular arrhythmias with amisulpride, pimozide and sertindole – avoid concomitant use
- Antivirals: concentration possibly increased by ritonavir, increased risk of toxicity
- Atomoxetine: increased risk of ventricular arrhythmias
- Ciclosporin: may increase risk of nephrotoxicity with ciclosporin
- Diuretics: increased cardiac toxicity if hypokalaemia occurs
- 5HT3 antagonists: increased risk of ventricular arrhythmias with dolasetron – avoid concomitant use; use tropisetron with caution
- Ivabradine: increased risk of ventricular arrhythmias

**ADMINISTRATION**
**RECONSTITUTION**
- **ROUTE**
  - Oral, IV
- **RATE OF ADMINISTRATION**
  - 20–30 mg/hour (0.4 mg/kg/hour)
- **COMMENTS**
  - May be given by peripheral IV infusion in glucose 5%, sodium chloride 0.9% or compound sodium lactate

**RETURN TO CONTENTS**
OTHER INFORMATION

- Use with caution in patients with impaired renal function
- Do not give renally impaired patients sustained release preparations
- Optimum therapeutic plasma level 2–6 mg/L
- Haemoperfusion can be used in cases of severe poisoning
Disulfiram

**CLINICAL USE**
Adjunct in the treatment of chronic alcohol dependence

**DOSE IN NORMAL RENAL FUNCTION**
800mg on day 1 reducing over 5 days to 100–200mg daily

**PHARMACOKINETICS**
- Molecular weight: 296.5 daltons
- % Protein binding: 96
- % Excreted unchanged in urine: 70–76 (as metabolites)
- Volume of distribution: No data
- Half-life – normal/ESRF (hrs): 12/–

**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**
- 20–50: Dose as in normal renal function
- 10–20: Use with caution
- <10: Avoid

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Avoid
- HD: Unlikely to be dialysed. Avoid
- HDF/High flux: Unlikely to be dialysed. Avoid
- CAV: Unlikely to be dialysed. Dose as in GFR=10–20mL/min
- VVHD: Unlikely to be dialysed. Avoid

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Alcohol: risk of severe disulfiram reaction
- Anticoagulants: enhanced anticoagulant effect with coumarins
- Anti-epileptics: inhibition of metabolism of phenytoin (increased risk of toxicity)
- Paraldehyde: increased risk of toxicity with paraldehyde

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- Review after 6 months
- Patients should be warned about severe nature of alcohol and disulfiram reaction
- Contraindicated in cardiovascular disease, psychoses or severe personality disorders
- Disulfiram blocks the metabolism of alcohol and leads to an accumulation of acetaldehyde in the bloodstream. Use with caution in diabetics
- Disulfiram is rapidly metabolised to diethyldithiocarbamic acid (DDC); is conjugated with glucuronic acid, oxidised to sulphate, methylated, and decomposed to diethylamine and carbon disulphide. Excretion is primarily through the kidneys.
Dobutamine

**CLINICAL USE**
Inotropic agent

**DOSE IN NORMAL RENAL FUNCTION**
2.5–10 micrograms/kg/minute, increasing up to 40 micrograms/kg/minute according to response

**PHarmacokinetics**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>301.4; 337.8 (as hydrochloride)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>No data</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.12–0.28</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>2–4 minutes/−</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed.</td>
</tr>
</tbody>
</table>

**IMPORTANT Drug interactions**
Potentially hazardous interactions with other drugs
- Beta-blockers: possibly severe hypotension with beta-blockers
- Dopaminergic: effects possibly enhanced by entacapone; avoid concomitant use with rasagiline

**Administration**

**Reconstitution**
- **Route**
  - Continuous IV infusion centrally via CRIP (or peripherally via a large vein)
  - Rate of administration
    - Varies with dose
  - Comments
    - Dilute to at least 50 mL with sodium chloride 0.9% or glucose 5% (less than 5 mg/mL, ideally 0.5–1 mg/mL)
    - 250 mg may be diluted in as little as 50 mL diluent
    - Minimum volume 10 mg/mL or even undiluted; give strong solution via central line (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006)

**Other Information**
- Cardiac and BP monitoring advised
- Sodium bicarbonate rapidly inactivates dobutamine
- Solution may turn pink, but potency is unaffected
- Can cause hypokalaemia
# Docetaxel

## CLINICAL USE

Antineoplastic agent:
- Treatment of breast cancer, prostate cancer and non-small cell lung cancer unresponsive to alternative therapies

## DOSE IN NORMAL RENAL FUNCTION

- Breast cancer: 100 mg/m² every 3 weeks
- In combination for breast cancer, non-small cell lung cancer, prostate cancer: 75 mg/m² every 3 weeks

## PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>807.9</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>&gt;95</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>6</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>113 litres</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>4 min(α)/36 min(β)/11.1 hr(γ)</td>
</tr>
</tbody>
</table>

## DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

## DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed.</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unlikely to be dialysed.</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be dialysed.</td>
</tr>
</tbody>
</table>

## IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs
- Antipsychotics: avoid concomitant use with clozapine – increased risk of agranulocytosis
- Ciclosporin: possibly inhibits metabolism of ciclosporin

## ADMINISTRATION

### RECONSTITUTION

- With diluent provided
- IV

### RATE OF ADMINISTRATION

- Over 1 hour

### COMMENTS

- Allow vials to come to room temperature for 5 minutes
- Doses of up to 200 mg can be added to 250 mL infusion bags of glucose 5% or sodium chloride 0.9%
- Doses greater than 200 mg should be diluted to a concentration of 0.74 mg/mL
- Administer within 4 hours of dilution

## OTHER INFORMATION

- Give premedication with oral dexamethasone 16 mg daily for 3 days, starting 1 day before commencing chemotherapy
- Cytochrome P–450 mediated metabolism. In animal studies, drug distributed to all tissues and organs except the brain. 6% and 75% of the dose is excreted via the renal and faecal route respectively within 7 days
**Dolasetron mesilate**

**CLINICAL USE**

**Anti-emetic:**
- Cancer chemotherapy
- Postoperative nausea and vomiting (PONV)

**DOSE IN NORMAL RENAL FUNCTION**

- **Chemotherapy:**
  - IV bolus or infusion: 100 mg 30 minutes before chemotherapy
  - Oral: 200 mg 1 hour before chemotherapy, then 200 mg daily to prevent delayed nausea and vomiting
- **PONV:**
  - IV bolus or infusion: 12.5 mg
  - Oral: 50 mg before induction of anaesthesia

**PHARMACOKINETICS**

- Molecular weight (daltons) 420.5
- % Protein binding 69–77
- % Excreted unchanged in urine 50–60
- Volume of distribution (L/kg) 5–7.9
- Half-life – normal/ESRF (hrs) 7–9/Increased

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD** Unknown dialysability. Dose as in normal renal function
- **HD** Unknown dialysability. Dose as in normal renal function
- **HDF/High flux** Unknown dialysability. Dose as in normal renal function
- **CAV/VVHD** Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Anti-arrhythmics: increased risk of ventricular arrhythmias – avoid concomitant use
- Beta-blockers: increased risk of ventricular arrhythmias with sotalol – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral, IV bolus, IV infusion
- **RATE OF ADMINISTRATION**
  - Bolus: over 30 seconds
  - Infusion: over 15 minutes
- **COMMENTS**
  - Can be added to 50 mL sodium chloride 0.9%, glucose 5% or compound sodium lactate

**OTHER INFORMATION**

- Peak concentrations occur 1 hour after oral and 0.6 hour after IV doses
- Oral bioavailability of 75%
- Active metabolite is renally excreted (approximately 30%)
- In patients with severe renal impairment (creatinine clearance <10 mL/min), maximum plasma levels of metabolite are increased 17% or 34%, respectively, after intravenous or oral administration of dolasetron, and systemic exposure is increased approximately 2-fold
Domperidone

CLINICAL USE
- Acute nausea and vomiting (including that caused by levodopa and bromocriptine)
- Gastro-oesophageal reflux
- Dyspepsia

DOSE IN NORMAL RENAL FUNCTION
Nausea and vomiting: Adults 10–20 mg orally 3–4 times daily, maximum 80 mg daily
PR: 60 mg twice daily

PHARMACOKINETICS
Molecular weight (daltons) 425.9
% Protein binding >90
% Excreted unchanged in urine <1
Volume of distribution (L/kg) 5.7
Half-life – normal/ESRF (hrs) 7–9/Increased

DOSE IN RENAL IMPAIRMENT
GFR (mL/MIN)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unlikely to be dialysed. Dose as in normal renal function
HD Unlikely to be dialysed. Dose as in normal renal function
HDF/High flux Unlikely to be dialysed. Dose as in normal renal function
CAV/VVHD Unknown dialysability. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Antifungals: possibly increased risk of arrhythmias with ketoconazole

ADMINISTRATION
RECONSTITUTION
- ROUTE
  - Oral, PR
  - RATE OF ADMINISTRATION
    - COMMENTS
      - Treatment of acute nausea and vomiting: maximum period of treatment is 12 weeks
      - Treatment of dyspepsia: administer before food; maximum period of treatment is 12 weeks

OTHER INFORMATION
- Domperidone has the advantage over metoclopramide and phenothiazines of being less likely to cause central effects, such as sedation and dystonic reactions, as it does not readily cross the blood brain barrier
# Donepezil hydrochloride

## Clinical Use
Treatment of dementia in mild to moderate Alzheimer's disease

## Dose in Normal Renal Function
5–10 mg daily

## Pharmacokinetics
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>416</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>95</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>17</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>12</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>70/Unchanged</td>
</tr>
</tbody>
</table>

## Dose in Renal Impairment

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

## Dose in Patients Undergoing Renal Replacement Therapies

<table>
<thead>
<tr>
<th>Therapies</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

## Important Drug Interactions
Potentially hazardous interactions with other drugs
- None known

## Administration

### Reconstitution
- 

### Route
- Oral

### Rate of Administration
- 

### Comments
- 

## Other Information
- Metabolised via CYP450 3A4 and 2D6 so may interact with other drugs metabolised by these pathways
Dopamine hydrochloride

**CLINICAL USE**
Cardiogenic shock in infarction or cardiac surgery

**DOSE IN NORMAL RENAL FUNCTION**
Initially 2–5 mcg/kg/minute

**PHARMACOKINETICS**
- Molecular weight: 189.6 (daltons)
- % Protein binding: No data
- % Excreted unchanged in urine: Minimal
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 2 min/

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/MIN)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Not dialysed. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Alpha-blockers: avoid concomitant use with tolazoline
- Antidepressants: risk of hypertensive crisis with MAOIs and moclobemide
- Ciclosporin: may reduce risk of ciclosporin nephrotoxicity
- Dopaminergics: effects possibly enhanced by entacapone; avoid concomitant use with rasagiline; risk of hypertensive crisis with selegiline

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- IV peripherally into large vein (centrally for inotropic dose). Central route always preferable

**RATE OF ADMINISTRATION**
- Via CRIP as indicated below

**COMMENTS**
- Minimum dilution 200 mg in 50 mL
- Not compatible with sodium bicarbonate – rapid deactivation of dopamine

**OTHER INFORMATION**
- Renal dose is 2–5 mcg/kg/min but little evidence that it can improve renal function
- Causes renal vasoconstriction at inotropic dose
- Cardiac and BP monitoring advised
- Very severe tissue damage caused by extravasation
Dopexamine hydrochloride

**CLINICAL USE**
Inotropic support in exacerbations of heart failure and heart failure associated with cardiac surgery.

**DOSE IN NORMAL RENAL FUNCTION**
IV infusion: 0.5 – 1 mcg/kg/minute and then in increments (0.5 – 1 micrograms/kg/minute) up to 6 micrograms/kg/minute at not less than 15 minute intervals.

**PHARMACOKINETICS**
- Molecular weight: 429.4 (daltons)
- % Protein binding: No data
- % Excreted unchanged in urine: 10
- Volume of distribution (L/kg): 0.45
- Half-life – normal/ESRF (hrs): 6–11 minutes/–

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min):
  - 20–50: Dose as in normal renal function and adjust to response
  - 10–20: Dose as in normal renal function and adjust to response
  - <10: Dose as in normal renal function and adjust to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Unknown dialysability. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs:
- Antidepressants: risk of hypertensive crisis with MAOIs and moclobemide
- Beta-blockers: risk of severe hypertension
- Sympathomimetics: effects of adrenaline and noradrenaline possibly enhanced

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - By intravenous infusion into a central or large peripheral vein

**RATE OF ADMINISTRATION**
- See dosage instructions

**COMMENTS**
- IV infusion of 400 or 800 micrograms/mL in glucose 5% or sodium chloride 0.9%
- Peripheral administration: concentration of infusion solution must not exceed 1 mg/mL
- Central administration: concentration not >4 mg/mL
- Rate of administration and duration of therapy should be adjusted according to the patient’s response as determined by heart rate and rhythm, blood pressure, urine flow and measurement of cardiac output

**OTHER INFORMATION**
- Avoid abrupt withdrawal
Dornase alfa

**CLINICAL USE**
To improve pulmonary function in cystic fibrosis

**DOSE IN NORMAL RENAL FUNCTION**
2.5 mg (2500 u) daily via nebuliser can be increased to twice daily if over 21 years of age

**PHARMACOKINETICS**
- Molecular weight (daltons): 29249.6
- % Protein binding: No data
- % Excreted unchanged in urine: No data
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 11 (from lungs in rats)

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/MIN):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux: Unlikely to be dialysed. Dose as in normal renal function
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE:
  - Nebulised

**RATE OF ADMINISTRATION**
- COMMENTS:
  - <15% of dose is systemically absorbed

**OTHER INFORMATION**
- No pharmacokinetic data available; little systemic absorption therefore little accumulation expected
- Use undiluted, using recommended jet nebuliser/compressor system. Refer to data sheet
Dosulepin hydrochloride (dothiepin)

**CLINICAL USE**
Tricyclic antidepressant

**DOSE IN NORMAL RENAL FUNCTION**
50–225 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 331.9
- % Protein binding: 84
- % Excreted unchanged in urine: 56 (mainly as metabolites)
- Volume of distribution (L/kg): 45

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Start with small dose, and titrate according to response</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
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<tr>
<td>10–20</td>
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<tr>
<td>&lt;10</td>
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</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Modality</th>
<th>Dose as in GFR&lt;10 mL/min</th>
<th>Dose as in GFR&lt;10 mL/min</th>
<th>Dose as in GFR&lt;10 mL/min</th>
<th>Dose as in GFR&lt;10 mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
- Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin – avoid concomitant use; concentration reduced by rifampicin
- Anticoagulants: may alter anticoagulant effect of coumarins
- Antidepressants: enhanced CNS excitation and hypertension with MAOIs and moclobemide – avoid concomitant use; concentration possibly increased with SSRIs
- Anti-epileptics: convulsive threshold lowered; concentration reduced by carbamazepine, primidone, barbiturates and possibly phenytoin
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: increased risk of ventricular arrhythmias especially with pimozide; increased antimuscarinic effects with clozapine and phenothiazines; concentration increased by antipsychotics
- Antivirals: increased tricyclic side effects with amprenavir; concentration possibly increased with ritonavir
- Atomoxetine: increased risk of ventricular arrhythmias and possibly convulsions
- Beta-blockers: increased risk of ventricular arrhythmias with sotalol
- Clonidine: tricyclics antagonise hypotensive effect; increased risk of hypertension on clonidine withdrawal
- Dopaminergics: avoid use with entacapone; CNS toxicity reported with selegiline and rasagiline
- Pentamidine: increased risk of ventricular arrhythmias
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use
- Sympathomimetics: increased risk of hypertension and arrhythmias with adrenaline and noradrenaline; metabolism possibly inhibited by methylphenidate

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**
OTHER INFORMATION

- Metabolites are active and partly renally excreted
- Metabolites accumulate and cause excessive sedation
- 25–50 mg usually effective without too much sedation
Doxapram hydrochloride

**CLINICAL USE**
- Postoperative respiratory depression
- Acute respiratory failure

**DOSE IN NORMAL RENAL FUNCTION**
- Postoperative respiratory depression: IV injection 1–1.5 mg/kg repeated at hourly intervals, or IV infusion 2–3 mg/minute, adjusted according to response.
- Acute respiratory failure: 1.5–4 mg/minute as an IV infusion, adjusted according to response

**PHARMACOKINETICS**
- Molecular weight: 433 daltons
- % Protein binding: No data
- % Excreted unchanged in urine: <5
- Volume of distribution: 0.58–2.74 L/kg
- Half-life – normal/ESRF (hrs): 2.4–4.1/–

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Unknown dialysability. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - IV bolus, IV infusion
- RATE OF ADMINISTRATION
  - IV injection: over at least 30 seconds
  - IV infusion as indication
- COMMENTS
  - Doxapram has a narrow margin of safety; the minimum effective dosage should be used and maximum recommended dosages should not be exceeded

**OTHER INFORMATION**
- Unlike naloxone, doxapram does not reverse the other effects of opioid analgesics (i.e. analgesia)
Doxazosin

**CLINICAL USE**

Alpha-adrenoceptor blocker:
- Hypertension
- Benign prostatic hyperplasia (BPH)

**DOSE IN NORMAL RENAL FUNCTION**
- Hypertension: 1–16 mg daily
- BPH: 1–8 mg daily
- XL preparation: 4–8 mg once daily

**PHARMACOKINETICS**

- Molecular weight: 547.6 (as mesilate)
- % Protein binding: 98
- % Excreted: <5
- Volume of distribution: 1–1.7
- Half-life – normal/ESRF (hrs): 22/Unchanged

**DOSE IN RENAL IMPAIRMENT**

- GFR (mL/Min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Antidepressants: enhanced hypotensive effect with MAOIs
- Beta-blockers: enhanced hypotensive effect; increased risk of first dose hypotensive effect
- Calcium-channel blockers: enhanced hypotensive effect, increased risk of first dose hypotensive effect
- Diuretics: enhanced hypotensive effect, increased risk of first dose hypotensive effect
- Moxisylyte: possibly severe postural hypotension when used in combination
- Vardenafil, sildenafil and tadalafil: enhanced hypotensive effect, avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  -
- **COMMENTS**
  -

**CLINICAL USE**

Antineoplastic agent:
- Acute leukaemias
- Lymphomas
- Sarcomas
- Various solid tumours

**DOSE IN NORMAL RENAL FUNCTION**

Varies according to local protocol

**PHARMACOKINETICS**

- Molecular weight (daltons): 580
- % Protein binding: 50–85
- % Excreted: <15
- Volume of distribution (L/kg): >20–30
- Half-life – normal/ESRF (hrs): 30; (Liposomal: 55–75; Pegylated: 24–231)/Unchanged
Doxorubicin hydrochloride

**CLINICAL USE**

Antineoplastic agent:
- Acute leukaemias
- Lymphomas
- Sarcomas
- Various solid tumours

**DOSE IN NORMAL RENAL FUNCTION**

Varies according to local protocol

**PHARMACOKINETICS**

- Molecular weight (daltons): 580
- % Protein binding: 50–85
- % Excreted unchanged in urine: <15
- Volume of distribution (L/kg): >20–30
- Half-life – normal/ESRF (hrs): 30; (Liposomal: 55–75; Pegylated: 24–231)/Unchanged

**DOSE IN RENAL IMPAIRMENT**

- GFR (mL/MIN)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Antipsychotics: avoid concomitant use with clozapine, increased risk of agranulocytosis
- Ciclosporin: increased risk of neurotoxicity

**ADMINISTRATION**

RECONSTITUTION
- Reconstitute with water for injection or sodium chloride 0.9%, 10 mg in 5 mL, 50 mg in 25 mL

ROUTE
- IV, intra-arterial, intravesical (bladder instillation)

RATE OF ADMINISTRATION
- Via the tubing of a fast running intravenous infusion of sodium chloride 0.9% or glucose 5%
- 3–5 minutes for the injection
- 24 hours for continuous infusion

COMMENTS
- For bladder instillation, concentration of doxorubicin in bladder should be 50 mg per 50 mL. To avoid undue dilution in urine, the patient should be instructed not to drink any fluid in the 12 hours prior to instillation. This should limit urine production to approximately 50 mL per hour

**OTHER INFORMATION**

- A cumulative dose of 450–550 mg/m$^2$ should only be exceeded with extreme caution. Above this level, the risk of irreversible congestive cardiac failure increases greatly.
- Patients with impaired hepatic function have prolonged and elevated plasma concentrations of both the drug and its metabolites. Dose reduction is required
- Liposomal preparations available: up to 90 mg in 250 mL glucose 5%; if greater than 90 mg dilute in 500 mL glucose 5%
- Mainly metabolised in the liver. Rapidly cleared from plasma and slowly excreted in the urine and bile (50% of drug recoverable in the bile or faeces in 7 days)
Doxycycline

**CLINICAL USE**
Antibacterial agent
- Prophylaxis/treatment of malaria

**DOSE IN NORMAL RENAL FUNCTION**
- 200 mg on day 1, then 100 mg daily; severe infections 200 mg daily
- Late latent syphilis: 200 mg twice daily
- Malaria: treatment: 200 mg once daily; prophylaxis: 100 mg daily

**PHARMACOKINETICS**
- Molecular weight: 462.4 daltons
- % Protein binding: >90
- % Excreted unchanged in urine: 33–45
- Volume of distribution: 0.7 L/kg
- Half-life – normal/ESRF (hrs): 18/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
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</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability.</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed.</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: possibly enhanced anticoagulant effect of coumarins and phenindione
- Ciclosporin: possibly increases plasma-ciclosporin concentration
- Oestrogens: possibly reduced contraceptive effects of oestrogens (risk probably small)
- Retinoids: possible increased risk of benign intracranial hypertension – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
  - Do not take iron preparations, indigestion remedies or phosphate binders at the same time of day as doxycycline

RETURN TO CONTENTS
Drotrecogin alfa

CLINICAL USE
Treatment of adult patients with severe sepsis with multiple organ failure

DOSE IN NORMAL RENAL FUNCTION
24 micrograms/kg/hour for 96 hours

PHARMACOKINETICS
Molecular weight (daltons) Approx 55000
% Protein binding No data
% Excreted unchanged in urine No data
Volume of distribution 8.2–31.2 litres (L/kg)
Half-life – normal/ESRF (hrs) 13 minutes/

DOSE IN RENAL IMPAIRMENT
GFR (mL/MIN)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unlikely to be dialysed. Dose as in normal renal function
HD Unlikely to be dialysed. Dose as in normal renal function
HDF/High flux Unlikely to be dialysed. Dose as in normal renal function
CAV/VVHD Unlikely to be dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Heparin: avoid concomitant use with high dose heparin
- Thrombolytic therapy: avoid for 3 days before administering drotrecogin
- Oral anticoagulants, antiplatelets: avoid for 7 days before administering drotrecogin

ADMINISTRATION
RECONSTITUTION
- Water for injection
ROUTE
- IV infusion
RATE OF ADMINISTRATION
- 24 micrograms/kg/hour
COMMENTS
- Further dilute with sodium chloride 0.9% to a concentration of 100–200 mcg/mL
- Minimum volume: 20 mg in 50 mL. (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006)

OTHER INFORMATION
- No anticoagulation is required for haemofiltration as the drotrecogin acts as an anticoagulant
- Can be started 12 hours after major invasive procedures or surgery
- Clearance is reduced by 30% in renal impairment but no dose reduction is required
- Has a short half-life of 13 minutes and a β-half-life of 1.6 hours
- Plasma clearance:
  — Patients with sepsis: 41.8 L/hour
  — Healthy subjects: 28.1 L/hour
  — Haemodialysis patents: 30 L/hour
  — Peritoneal dialysis patients: 23 L/hour
Duloxetine

**CLINICAL USE**
- Moderate to severe stress urinary incontinence
- Depression
- Diabetic peripheral neuropathy

**DOSE IN NORMAL RENAL FUNCTION**
- Incontinence: 20–40 mg twice daily
- Depression and diabetic peripheral neuropathy: 60 mg daily

**PHARMACOKINETICS**
- Molecular weight: 333.9 (as hydrochloride)
- % Protein binding: 95–96
- % Excreted unchanged in urine: <1 (77% as metabolites)
- Volume of distribution: 1640 litres
- Half-life – normal/ESRF (hrs): 8–17/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 30–50: Dose as in normal renal function; start with a low dose
  - 10–30: Start at low dose and increase according to response
  - <10: Start at very low dose and increase according to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR <10 mL/min
- HD: Not dialysed. Dose as in GFR <10 mL/min
- HDF/High flux: Unlikely to be dialysed. Dose as in GFR <10 mL/min
- CAV: Not dialysed. Dose as in GFR
- VVHD: =10–30 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: metabolism inhibited by ciprofloxacin – avoid concomitant use
- Other CNS medication: enhanced effect
- Antidepressants: avoid concomitant use with MAOIs, moclobemide, St John’s wort, tryptophan, venlafaxine, amitriptyline, clomipramine and SSRIs due to increased risk of serotonin syndrome; increased risk of side effects with tricyclic antidepressants; fluvoxamine decreases the clearance of duloxetine by 77% – avoid concomitant use
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- In CKD 5 there is a 2-fold increase in $C_{\text{max}}$ and AUC. The renally excreted metabolites 4-hydroxy duloxetine glucuronide and 5-hydroxy, 6-methoxy duloxetine sulphate were 7–9 times higher than in people with normal renal function
- Contraindicated in uncontrolled hypertension due to potential risk of hypertensive crisis
Efalizumab

**CLINICAL USE**
Treatment of patients with moderate to severe chronic plaque psoriasis, who have failed to respond to other therapies or who are unable to take other therapies

**DOSE IN NORMAL RENAL FUNCTION**
Initially: 0.7 mg/kg followed by weekly injections of 1 mg/kg (maximum single dose should be <200 mg) for 12 weeks

**PHARMACOKINETICS**
- Molecular weight: 150,000 daltons
- % Protein binding: No data
- % Excreted unchanged in urine: No data
- Volume of distribution (L/kg): 0.058–0.11
- Half-life – normal/ESRF (hrs): 13–35 days

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Not dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Not dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Immunosuppressants: may potentiate the effect of immunosuppressants
  - Vaccines: do not administer live vaccines during treatment

**ADMINISTRATION**
- RECONSTITUTION
  - With solvent provided (water for injection)
- ROUTE
  - SC
- RATE OF ADMINISTRATION
  - COMMENTS
  -

**OTHER INFORMATION**
- Use with caution in patients with a history of recurrent infections
- Contraindicated in people who are immunosuppressed
Efavirenz

**CLINICAL USE**

Non-nucleoside reverse transcriptase inhibitor:
- HIV infection in combination with other antiretroviral drugs

**DOSE IN NORMAL RENAL FUNCTION**

600 mg once daily (tablets and capsules should be taken on an empty stomach to minimise side effects)
Oral solution: 720 mg once daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>315.7</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>99.5–99.75</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>2–4</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>40–55 (multiple dosing); 52–76 (single dosing)/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
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</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Antidepressants: concentration reduced by St John's wort – avoid concomitant use; concentration of sertraline reduced
- Antifungals: itraconazole and voriconazole concentration reduced; voriconazole increases efavirenz concentration – reduce dose of efavirenz by 50% and increase dose of voriconazole to 400 mg twice daily; possibly reduces caspofungin concentration – may possibly need to increase caspofungin dose
- Antipsychotics: possibly increased risk of ventricular arrhythmias with pimozone and sertindole – avoid concomitant use; possibly reduces aripiprazole concentration – increase aripiprazole dose
- Anxiolytics and hypnotics: risk of prolonged sedation with midazolam – avoid concomitant use
- Antivirals: saquinavir concentration significantly reduced; concentration of amprenavir, darunavir, lopinavir and atazanavir reduced – increase atazanavir dose; concentration reduced by nevirapine; monitor LFTs when used in combination with ritonavir
- Ciclosporin: concentration of ciclosporin possibly reduced
- Ergot alkaloids: risk of ergotism – avoid concomitant use
- Grapefruit juice: concentration possibly increased

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**

- Induces its own metabolism
- Metabolised by CYP450 3A4 and 2B6 systems
- Monitor cholesterol levels as increases of 10–20% in total cholesterol have been reported
- Half-life of 10 hours in haemodialysis patients has been reported
- Bioavailability of oral solution is less than that for capsules or tablets – therefore not interchangeable
Eletriptan

**CLINICAL USE**
Acute relief of migraine

**DOSE IN NORMAL RENAL FUNCTION**
40–80 mg repeated after 2 hours if migraine recurs (do not take 2nd dose for the same attack)
Maximum 80 mg in 24 hours

**PHARMACOKINETICS**
- Molecular weight: 463.4 (as hydrobromide)
- % Protein binding: 85
- % Excreted unchanged in urine: 9
- Volume of distribution (L/kg): 2–2.5

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>20 mg; maximum daily dose 40 mg</td>
</tr>
<tr>
<td>10–30</td>
<td>20 mg; maximum daily dose 40 mg, use with caution</td>
</tr>
<tr>
<td>&lt;10</td>
<td>20 mg; maximum daily dose 40 mg, use with caution</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–30 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Antibacterials: concentration increased by clarithromycin and erythromycin – avoid concomitant use
- Antidepressants: possibly increased serotonergic effects with duloxetine; increased serotonergic effects with St John’s wort – avoid concomitant use
- Antifungals: concentration increased by itraconazole and ketoconazole – avoid concomitant use
- Antivirals: concentration increased by indinavir, nelfinavir and ritonavir – avoid concomitant use
- Ergot alkaloids: increased risk of vasospasm

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  -

**OTHER INFORMATION**
- Non-renal clearance accounts for about 90% of the total clearance
- Manufacturer advises to avoid in severe renal impairment due to enhanced hypertensive effect
Emtricitabine

**CLINICAL USE**
Nucleoside reverse transcriptase inhibitor:
- Treatment of HIV-1 in combination with other antiretroviral agents

**DOSE IN NORMAL RENAL FUNCTION**
200 mg once daily (if weight >33 kg)
Oral solution: 240 mg once daily, (6 mg/kg if weight <33 kg)

**PHARMACOKINETICS**
- Molecular weight: 247.2 daltons
- % Protein binding: <4
- % Excreted unchanged in urine: 86
- Volume of distribution (L/kg): 1.1–1.7
- Half-life – normal/ESRF (hrs): 10/Increased

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 30–50: 200 mg every 48 hours
  - 15–30: 200 mg every 72 hours
  - <15: 200 mg every 96 hours

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR<15 mL/min
- HD: Dialysed. Dose as in GFR<15 mL/min
- HDF/High flux: Dialysed. Dose as in GFR<15 mL/min
- CAV/VVHD: Dialysed. Dose as in GFR=15–30 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antivirals: avoid concomitant use with lamivudine

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - COMMENTS

**OTHER INFORMATION**
- Haemodialysis should be started at least 12 hours after the last dose of emtricitabine
- 200 mg of the hard capsules is equivalent to 240 mg of the oral solution
- Dose may be reduced instead of increasing dosage interval
- Up to 30% of dose is removed by a 3 hour haemodialysis session
Enalapril maleate

CLINICAL USE
Angiotensin converting enzyme inhibitor:
- Hypertension
- Heart failure

DOSE IN NORMAL RENAL FUNCTION
2.5–40 mg daily

PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>492.5</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>50–60</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>20</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.17</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>11/34–60</td>
</tr>
</tbody>
</table>

DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Start with 2.5 mg per day and increase according to response</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Start with 2.5 mg per day and increase according to response</td>
</tr>
</tbody>
</table>

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

- CAPD: Dialysed. Dose as in GFR<10 mL/min
- HD: Dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Dialysed. Dose as in GFR=10–20 mL/min

IMPORTANT DRUG INTERACTIONS

- Diuretics: enhanced hypotensive effect; hyperkalaemia with potassium-sparing diuretics
- Epoetin: increased risk of hyperkalaemia; antagonism of hypotensive effect
- Lithium: reduced excretion, possibility of enhanced lithium toxicity
- Potassium salts: increased risk of hyperkalaemia
- Tacrolimus: increased risk of hyperkalaemia and nephrotoxicity

ADMINISTRATION

RECONSTITUTION
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - COMMENTS

OTHER INFORMATION

- Side effects (e.g. hyperkalaemia, metabolic acidosis) are more common in patients with impaired renal function
- Close monitoring of renal function during therapy is necessary in those with renal insufficiency
- Renal failure has been reported in association with ACE inhibitors in patients with renal artery stenosis, post renal transplant, and in those with severe congestive heart failure
- High incidence of anaphylactoid reactions has been reported in patients dialysed with high-flux polyacrylonitrile membranes and treated concomitantly with an ACE inhibitor – this combination should therefore be avoided
- ACE inhibitor cough may be helped by sodium cromoglycate inhalers
- Enalapril maleate is a prodrug that requires hepatic conversion to enalaprilat
- Enalaprilat injection available on a named patient basis

References:
Enfuvirtide

**CLINICAL USE**
Treatment of HIV-1 in combination with other antiretroviral agents

**DOSE IN NORMAL RENAL FUNCTION**
90 mg twice daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 4491.9
- % Protein binding: 92
- % Excreted unchanged in urine: No data
- Volume of distribution (L/kg): 4.4–6.6 litres
- Half-life – normal/ESRF (hrs): 3.2–4.4/Probably unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min): 35–50 Dose as in normal renal function
- 10–35 Dose as in normal renal function
- <10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HD: 13% dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: GFR=10–35 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- 1.1 mL water for injection

**ROUTE**
- SC

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- Do not shake vial or turn it upside down as this causes foaming
- The powder may take up to 45 minutes to dissolve
- Use within 24 hours if kept in refrigerator. Allow to reach room temperature before injecting

**OTHER INFORMATION**
- Renal calculi have been reported with enfuvirtide therapy
- \( C_{\text{max}} \) and AUC are increased in CKD 5 patients.

References:
Enoxaparin sodium (LMWH)

**CLINICAL USE**
- Prophylaxis of thromboembolic disorders of venous origin
- Treatment of deep vein thrombosis and pulmonary embolism
- Anticoagulation of the extracorporeal circulation during haemodialysis
- Acute coronary syndrome

**DOSE IN NORMAL RENAL FUNCTION**
- Prophylaxis DVT:
  - Moderate risk surgery: 20 mg once daily
  - High risk surgery/medical prophylaxis: 40 mg once daily
- Treatment DVT and PE: 1.5 mg/kg every 24 hours
- Anticoagulation of extracorporeal circuits – see ‘Other Information’
- Acute coronary syndrome: 1 mg/kg every 12 hours

**PHARMACOKINETICS**
- Molecular weight (daltons): Mean = 4500
- % Protein binding: No data
- % Excreted unchanged in urine: 10
- Volume of distribution (L/kg): 5 litres

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>DOSE IN RENAL IMPAIRMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>50–80</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>30–50</td>
<td>Dose as in normal renal function. Monitor carefully</td>
</tr>
<tr>
<td>&lt;30</td>
<td>Treatment: 1 mg/kg daily. Prophylaxis: 20 mg daily. See ‘Other Information’</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Analgesics: increased risk of bleeding with NSAIDs – avoid concomitant use with IV diclofenac; increased risk of haemorrhage with ketorolac – avoid concomitant use
  - Nitrates: anticoagulant effect reduced by infusions of glyceryl trinitrate
  - Drotrecogin alfa: manufacturer advises to avoid use of high doses of heparin with drotrecogin alfa
  - Use with care in patients receiving oral anticoagulants, platelet aggregation inhibitors, aspirin or dextran

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - SC
  - OTHER INFORMATION
  - In extracorporeal circulation during haemodialysis, 1 mg/kg enoxaparin is introduced into the arterial line of the
circuit at the beginning of the session. The effect of this dose is usually sufficient for a 4 hour session:

- If fibrin rings are found, a further dose of 0.5–1 mg/kg may be given.
- For patients with a high risk of haemorrhage, the dose should be reduced to 0.5 mg/kg for double vascular access or 0.75 mg/kg for single vascular access.
- The dose of protamine to neutralise the effect of enoxaparin should equal the dose of enoxaparin: 50 anti-heparin units of protamine should neutralise the antifactor-Xa activity generated by 1 mg of enoxaparin. If prothrombin time is still raised 2–4 hours later give 0.5 mg/kg infusion of protamine. (Hovanessian H. Letter. Annals of emergency medicine. 2006; 36(3): 278.)
- Rhone-Poulenc Rorer advise monitoring of the antifactor-Xa activity, whatever the severity of the renal impairment, when treatment doses are being employed. They also advise monitoring patients if given prolonged treatment with prophylactic doses.
- Low molecular weight heparins are renally excreted and hence accumulate in severe renal impairment. While the doses recommended for prophylaxis against DVT and prevention of thrombus formation in extracorporeal circuits are well tolerated in patients with ESRF, the doses recommended for treatment of DVT and PE have been associated with severe, sometimes fatal, bleeding episodes in such patients. Hence the use of unfractionated heparin would be preferable in these instances.
- Additional doses may be required if using LMWHs for anticoagulation in HDF.
- Information on doses in severe renal failure from New Zealand data sheet. [www.medsafe.govt.nz](http://www.medsafe.govt.nz)
Entecavir

CLINICAL USE
Treatment of chronic hepatitis B infection

DOSE IN NORMAL RENAL FUNCTION
500 mcg daily; 1000 mcg daily in lamivudine-refractory patients

PHARMACOKINETICS
Molecular weight 295.3 (daltons)
% Protein binding 13
% Excreted unchanged in urine 75
Volume of distribution (L/kg) Large
Half-life – normal/ESRF (hrs) 128–149

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
30–50 250 mcg daily; 500 mcg daily in lamivudine-refractory patients
10–30 150 mcg daily; 300 mcg daily in lamivudine-refractory patients
<10 50 mcg daily; 100 mcg daily in lamivudine-refractory patients

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD 0.3% dialysed. Dose as in GFR<10 mL/min
HD 13% dialysed. Dose as in GFR<10 mL/min
HDF/High flux Dialysed. Dose as in GFR<10 mL/min
CAV/ VVHD Likely to be dialysed. Dose as in GFR=10–30 mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● None known

ADMINISTRATION
RECONSTITUTION –
ROUTE ● Oral
RATE OF ADMINISTRATION –
COMMENTS –
Epirubicin hydrochloride

CLINICAL USE
Antineoplastic agent:
- Leukaemias
- Malignant lymphomas
- Multiple myeloma
- Various solid tumours

DOSE IN NORMAL RENAL FUNCTION
60–90 mg/m² every 3 weeks
High dose: 100–135 mg/m² every 3–4 weeks, or 45 mg/m² on days 1, 2, and 3, every 3 weeks
Or according to local protocol

DOSE IN RENAL IMPAIRMENT
GFR (mL/Min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function, but use lower dose

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unlikely to be dialysed. Dose as in normal renal function
HD Unlikely to be dialysed. Dose as in normal renal function
HDF/High flux Unknown dialysability. Dose as in normal renal function
CAV/VVHD Unknown dialysability. Dose as in normal renal function

PHARMACOKINETICS
Molecular weight (daltons) 580
% Protein binding 77
% Excreted unchanged in urine 9–10
Volume of distribution (L/kg) 14–38
Half-life – normal/ESRF (hrs) 30–40/Unchanged

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Antipsychotics: avoid concomitant use with clozapine – increased risk of agranulocytosis
- Ciclosporin: increased risk of neurotoxicity
- Ulcer-healing drugs: concentration reduced by cimetidine

ADMINISTRATION

RECONSTITUTION
Reconstitute with water for injection or sodium chloride 0.9% (rapid dissolution only)

ROUTE
- IV, intravesical (bladder instillation), intrathecal

RATE OF ADMINISTRATION
- IV: give via the tubing of a fast running intravenous infusion of sodium chloride 0.9% or glucose 5%, taking 3–5 minutes over the injection
- IV infusion: 30 minutes

COMMENTS
- For bladder instillation: concentration of epirubicin in bladder should be 50–80 mg per 50 mL once a week. To avoid undue dilution in urine, the patient should be instructed not to drink any fluid in the 12 hours prior to instillation
- In the case of local toxicity dose is reduced to 30 mg per 50 mL

OTHER INFORMATION
- A cumulative dose of 900–1000 mg/m² should only be exceeded with extreme caution. Above this level, the risk of irreversible congestive cardiac failure increases greatly
- Mainly metabolised in the liver; 27–40% eliminated by biliary excretion. Slow elimination through the liver is due to extensive tissue distribution. Urinary excretion accounts for approximately 10% of the dose in 48 hrs
- Patients with impaired hepatic function have prolonged and elevated plasma concentrations of epirubicin – dose reduction is required
- Epirubicin may make the urine red for 1–2 days after administration

RETURN TO CONTENTS
Eplerenone

**CLINICAL USE**

Aldosterone antagonist:
- Left ventricular dysfunction and heart failure

**DOSE IN NORMAL RENAL FUNCTION**

25–50 mg daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>414.5</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>50</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>43–57 litres</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>3–6</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function¹</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function¹</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function¹</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Dialysis Modality</th>
<th>Dose</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>10% dialysed.¹ Dose as in GFR&lt;10 mL/min</td>
<td></td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
<td></td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>GFR=10-20 mL/min</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- ACE inhibitors or AT-II antagonists: enhanced hypotensive effect; risk of severe hyperkalaemia
- Anti-arrhythmics: concentration increased by amiodarone – reduce eplerenone dose
- Antibacterials: concentration increased by clarithromycin and telithromycin – avoid concomitant use; concentration increased by erythromycin – reduce eplerenone dose; concentration reduced by rifampcin – avoid concomitant use; avoid concomitant use with lymecycline; increased risk of hyperkalaemia with trimethoprim
- Antidepressants: concentration reduced by St John’s wort – avoid concomitant use; increased risk of postural hypotension with tricyclics; enhanced hypotensive effect with MAOIs
- Anti-epileptics: concentration reduced by carbamazepine, phenytoin and phenobarbital – avoid concomitant use
- Antifungals: concentration increased by itraconazole and ketoconazole – avoid concomitant use; concentration increased by fluconazole – reduce eplerenone dose
- Antihypertensives: enhanced hypotensive effect, increased risk of first dose hypotensive effect with post-synaptic alpha-blockers
- Antivirals: concentration increased by nelfinavir and ritonavir – avoid concomitant use; concentration increased by saquinavir – reduce eplerenone dose
- Ciclosporin: increased risk of hyperkalaemia and nephrotoxicity
- NSAIDs: increased risk of hyperkalaemia (especially with indometacin); increased risk of nephrotoxicity; antagonism of diuretic effect
- Potassium salts: increased risk of hyperkalaemia
- Lithium: reduced lithium excretion – avoid concomitant use
- Tacrolimus: increased risk of hyperkalaemia and nephrotoxicity
- CYP3A4 inhibitors: Do not exceed a dose of 25 mg daily for eplerenone
- CYP3A4 inducers: reduced eplerenone concentration – avoid concomitant use
OTHER INFORMATION

- Monitor potassium levels regularly in people with renal impairment

References:

Epoetin alfa (Eprex)

**CLINICAL USE**
- Anaemia associated with renal impairment in pre-dialysis and dialysis patients, and in patients receiving cancer chemotherapy
- Increased yield of autologous blood

**DOSE IN NORMAL RENAL FUNCTION**
- Renal:
  - CORRECTION PHASE: (To raise haemoglobin to target level) 50 u/kg 2–3 times weekly; increase, according to response, by 25 u/kg 3 times weekly at intervals of 4 weeks. Rise in haemoglobin should not exceed 2 g/100 mL/month (optimum rise in haemoglobin up to 1 g/100 mL/month to avoid hypertension)
  - Target haemoglobin usually 10–12 g/100 mL
  - MAINTENANCE PHASE: Adjust dose to maintain required haemoglobin level; usual dose needed is 75–300 u/kg weekly in 1–3 divided doses
- Cancer: Initially 150 u/kg 3 times a week and adjust according to response
- Autologous blood harvest: 600 u/kg IV once or twice a week for 3 weeks prior to surgery

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Not dialysed. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Hyperkalaemia with ACE inhibitors and angiotensin-II antagonists

**ADMINISTRATION**
- ROUTE
  - IV/SC (maximum 1 mL per injection site)
- DOSAGE
  - 1–5 minutes
- COMMENTS
  - When given IV, higher doses normally needed to produce required response

**PHARMACOKINETICS**
- Molecular weight (daltons): 30,400
- % Protein binding: No data
- % Excreted unchanged in urine: No data
- Volume of distribution (L/kg): 0.03–0.05

**DOSE IN RENAIIMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**OTHER INFORMATION**
- Reported association of pure red cell aplasia (PRCA) with epoetin therapy. This is a very rare condition; due to failed production of red blood cell precursors in the bone marrow, resulting in profound anaemia. Possibly due to an immune response to the protein backbone of R-HuEPO. Resulting antibodies render the patient unresponsive to the therapeutic effects of all epoetins and darbepoetin
- Pre-treatment checks and appropriate correction/ treatment needed for iron, folate and B12 deficiency, infection, inflammation or aluminium toxicity, to produce optimum response to therapy
- Concomitant iron therapy (200–300 mg elemental oral iron) needed daily. IV iron may be needed for patients with very low serum ferritin (<100 nanograms/mL)
- May increase heparin requirement during HD
Epoetin beta (Neorecormon)

### CLINICAL USE
Anaemia associated with renal impairment in pre-dialysis and dialysis patients, and in patients receiving cancer chemotherapy

### DOSE IN NORMAL RENAL FUNCTION
- **Renal:**
  - **CORRECTION PHASE:** (To raise haemoglobin to target level) 60 u/kg SC or 40 u/kg IV 3 times weekly for 4 weeks; increase, according to response, in steps of 20 u/kg 3 times weekly at monthly intervals. Maximum dose 720 u/kg weekly. Target haemoglobin usually 10–12 g/100mL.
  - **MAINTENANCE DOSE:** (To maintain haemoglobin at target level) Half correction phase dose, then adjust according to response at intervals of 1–2 weeks
- **Cancer:** Initially 450 u/kg weekly in 3–7 divided doses and adjust according to response

### PHARMACOKINETICS
- **Molecular weight** (daltons) 30 400
- **% Protein binding** No data
- **% Excreted unchanged in urine** No data
- **Volume of distribution** (L/kg) 0.03–0.05

### DOSE IN RENAL IMPAIRMENT
- **GFR (mL/Min)**
  - 20–50 Dose as in normal renal function
  - 10–20 Dose as in normal renal function
  - <10 Dose as in normal renal function

### DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- **CAPD** Not dialysed. Dose as in normal renal function
- **HD** Not dialysed. Dose as in normal renal function
- **HDF/High flux** Not dialysed. Dose as in normal renal function
- **CAV/VVHD** Not dialysed. Dose as in normal renal function

### IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Risk of hyperkalaemia with ACE inhibitors and angiotensin-II antagonists

### ADMINISTRATION
- **RECONSTITUTION**
  - Reconstitute using diluent provided only for multidose vial and penfill cartridges
- **ROUTE**
  - SC, IV
- **RATE OF ADMINISTRATION**
  - 2 minutes
- **COMMENTS**
  - May also be given IV, but higher doses are needed to produce required response

### OTHER INFORMATION
- Pre-treatment checks and appropriate correction/treatment needed for iron, folate and B12 deficiencies, infection, inflammation or aluminium toxicity to produce optimum response to therapy
- Concomitant iron therapy (200–300 mg elemental oral iron) needed daily. IV iron may be needed for patients with very low serum ferritin (<100 nanograms/mL)
- May increase heparin requirement during HD
- Reported association of pure red cell aplasia (PRCA) with epoetin therapy. This is a very rare condition; due to failed production of red blood cell precursors in the bone marrow, resulting in profound anaemia. Possibly due to an immune response to the protein backbone of R-HuEPO. Resulting antibodies render the patient unresponsive to the therapeutic effects of all epoetins and darbepoetin
Epoprostenol (prostacyclin)

**CLINICAL USE**
- Vasodilation and inhibition of platelet aggregation without prolonging bleeding time
- Alternative to heparin in haemodialysis
- Treatment of peripheral vascular disease and pulmonary hypertension

**DOSE IN NORMAL RENAL FUNCTION**
- 2–50 ng/kg/minute, adjusted according to response
- Dialysis anticoagulation: 4 ng/kg/minute starting 10–15 minutes before and continuing during dialysis via the arterial line, adjusted according to response (range: 0.5–12 ng/kg/minute)

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>352.5</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>No data</td>
</tr>
<tr>
<td>% Excreted (as drug + metabolites)</td>
<td>40–90</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.357–1.015</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>2–6 minutes/–</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability.</td>
</tr>
<tr>
<td>HD</td>
<td>Unknown dialysability.</td>
</tr>
<tr>
<td>HDF/High Flux</td>
<td>Unknown dialysability.</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability.</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
- Increased hypotensive effect with ‘acetate’ dialysis

**ADMINISTRATION**

**RECONSTITUTION**
- 500 microgram vial with diluent provided gives solution of 10 micrograms/mL. Can be diluted further

**ROUTE**
- IV or into blood supplying dialyser

**RATE OF ADMINISTRATION**
- Via CRIP

**COMMENTS**
- Complicated dosing schedule – check calculations carefully
- Infusion rate may be calculated by the following formula:
  \[
  \text{Dose rate (mL/hr)} = \frac{\text{Dosage (ng/kg/min)} \times \text{body wt (kg)} \times 60}{\text{Concentration of infusion (ng/mL)}}
  \]
  (usually 10 000 ng/mL)

**OTHER INFORMATION**
- Monitor BP and heart rate. Reduce dose if patient becomes hypotensive. Cardiovascular effects cease 30 minutes after stopping the infusion
- Some patients may exhibit allergic reaction to buffer solution used to reconstitute epoprostenol
- Solution retains 90% potency for 12 hours after dilution
- The concentrated solution should be filtered using the filter provided in the pack

**RETURN TO CONTENTS**
Eprosartan

**CLINICAL USE**
Angiotensin-II antagonist:
- Hypertension

**DOSE IN NORMAL RENAL FUNCTION**
300–800 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 520.6 (as mesilate)
- % Protein binding: 98
- % Excreted unchanged in urine: <2 (as metabolites)
- Volume of distribution (L/kg): 13 litres
- Half-life – normal/ESRF (hrs): 5–9/unchanged

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function
  - Initially 300 mg daily and increase according to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Not dialysed. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Analgesics: antagonism of hypotensive effect and increased risk of renal impairment with NSAIDs; hyperkalaemia with ketorolac and other NSAIDs
- Ciclosporin: increased risk of hyperkalaemia and nephrotoxicity
- Diuretics: enhanced hypotensive effect; hyperkalaemia with potassium-sparing diuretics
- Epoetin: increased risk of hyperkalaemia; antagonism of hypotensive effect
- Lithium: increased risk of hyperkalaemia; antagonism of hypotensive effect
- Potassium salts: increased risk of hyperkalaemia
- Tacrolimus: increased risk of hyperkalaemia and nephrotoxicity

**ADMINISTRATION**
- RECONSTITUTION
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
- COMMENTS
- OTHER INFORMATION
  - Side effects (e.g. hyperkalaemia, metabolic acidosis) are more common in patients with impaired renal function
  - Close monitoring of renal function during therapy is necessary in those with renal insufficiency
  - Renal failure has been reported in association with AT-II antagonists in patients with renal artery stenosis, post renal transplant, and in those with severe congestive heart failure
Eptifibatide

**CLINICAL USE**

Antiplatelet agent:
- Prevention of early myocardial infarction in patients with unstable angina or non-ST segment-elevation myocardial infarction and with last episode of chest pain within 24 hours

**DOSE IN NORMAL RENAL FUNCTION**

IV bolus of 180 mcg/kg then by IV infusion at a rate of 2 mcg/kg/minute for up to 72–96 hours

**PHARMACOKINETICS**

- Molecular weight (daltons): 832
- % Protein binding: 25
- % Excreted unchanged in urine: 50
- Volume of distribution (L/kg): 0.185–0.26
- Half-life – normal/ESRF (hrs): 2.5/Increased

**DOSE IN RENAL IMPAIRMENT**

- **GFR (mL/MIN)**
  - 30–50: Reduce infusion to 1 mcg/kg/minute and use with caution due to limited experience
  - 10–30: Reduce infusion to 1 mcg/kg/minute and use with caution due to limited experience
  - <10: Reduce infusion to 1 mcg/kg/minute and use with caution due to limited experience

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Unknown dialysability. Dose as in GFR<10 mL/min
- HD: Dialysed. Dose as in GFR<10 mL/ min
- HDF/High flux: Dialysed. Dose as in GFR<10 mL/ min
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–30 mL/min

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Iloprost: increased risk of bleeding

**ADMINISTRATION**

- **RECONSTITUTION**
  -
- **ROUTE**
  - IV bolus, IV infusion
- **RATE OF ADMINISTRATION**
  - 1–2 mcg/kg/minute depending on renal function
- **COMMENTS**
  -

**OTHER INFORMATION**

- Antiplatelet effect lasts for about 4 hours after stopping infusion
- Main side effect is bleeding
- In patients with a GFR<50 mL/min, clearance is halved and plasma concentration doubled

RETURN TO CONTENTS
**Erlotinib**

**CLINICAL USE**
Antineoplastic agent:
- Treatment of locally advanced or metastatic non-small cell lung cancer after failure of at least 1 other regime

**DOSE IN NORMAL RENAL FUNCTION**
150 mg daily at least 1 hour before or 2 hours after food
Or see local protocol

**PHARMACOKINETICS**
- Molecular weight: 429.9 (as hydrochloride)
- % Protein binding: 93–95%
- % Excreted unchanged in urine: 9 (<2% as unchanged drug)
- Volume of distribution (L/kg): 232 litres
- Half-life – normal/ESRF (hrs): 36

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
<th>Dose as in normal renal function</th>
<th>Use with caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
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<tr>
<td>15–20</td>
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<td></td>
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<tr>
<td>&lt;15</td>
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</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose as in GFR&lt;15 mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;15 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;15 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;15 mL/min</td>
</tr>
<tr>
<td>CAV/ VVHD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: increased risk of bleeding with NSAIDs
- Anticoagulants: increased risk of bleeding with coumarins
- Antipsychotics: avoid concomitant use with clozapine, increased risk of agranulocytosis

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- Has not been tried in patients with a GFR<15 mL/min; therefore use with caution, but drug has limited renal excretion
- Major side effects are rash and diarrhoea
- Can cause interstitial lung disease and abnormal liver function tests
- Smoking may reduce erlotinib concentration by increasing clearance
Ertapenem

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
1 g daily

**PHARMACOKINETICS**
- Molecular weight: 497.5 (as sodium)
- % Protein binding: 85–95
- % Excreted unchanged in urine: 38
- Volume of distribution: 0.1 (L/kg)

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 30–50: Dose as in normal renal function
  - 10–30: Use 50–100% of dose
  - <10: Use 50% of dose, or 1 g 3 times a week. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Dialysed. Dose as in GFR<10 mL/min
- HD: Dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Dialysed. Dose as in GFR=10–30 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- 10 mL water for injection or sodium chloride 0.9%

**ROUTE**
- IV, (IM – not licensed)

**RATE OF ADMINISTRATION**
- IV Infusion: 30 minutes

**COMMENTS**
- Dilute in sodium chloride 0.9% only
- Incompatible with glucose
- Dilute solutions are stable for 6 hours at room temperature or 24 hours in a refrigerator. Use within 4 hours of removal from refrigerator

**OTHER INFORMATION**
- Approximately 30% of dose is dialysed after a 4 hour haemodialysis session
- Another on-line reference source says that 100% of the dose can be used in people with a GFR of 10–50 mL/min
- Anecdotally ertapenem has been used at a dose of 1 g 3 times a week
- Give at least 6 hours before haemodialysis session if unable to give post dialysis
Erythromycin

CLINICAL USE
Antibacterial agent

DOSE IN NORMAL RENAL FUNCTION
IV: 25–50 mg/kg/day
Oral: 250–500 mg every 6 hours or 0.5–1 g every 12 hours
Maximum 4 g daily

PHARMACOKINETICS
Molecular weight (daltons) 733.9
% Protein binding 70–95
% Excreted unchanged in urine 2–15
Volume of distribution (L/kg) 0.6–1.2 (increased in CKD 5)
Half-life – normal/ESRF (hrs) 1.5–2/4–7

DOSE IN RENAL IMPAIRMENT
GFR (mL/MIN)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 50–75 % of normal dose; maximum 2 g daily

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Not dialysed. Dose as in GFR<10 mL/min
HD Not dialysed. Dose as in GFR<10 mL/min
HDF/High flux Unknown dialysability. Dose as in GFR<10 mL/min
CAV/ VVHD Unknown dialysability. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Avoid concomitant use with reboxetine and cilostazol
- Anti-arrhythmics: increased risk of ventricular arrhythmias with parenteral erythromycin and amiodarone – avoid concomitant use; increased toxicity with disopyramide
- Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin and parenteral erythromycin avoid
- Anticoagulants: enhanced effect of coumarins
- Anti-epileptics: increased carbamazepine concentration and possibly valproate
- Antihistamines: possibly increases loratadine concentration; inhibits mizolastine metabolism – avoid concomitant use
- Antimalarials: avoid concomitant administration with artemether/ lumefantrine
- Antimuscarinics: avoid concomitant use with tolterodine
- Antipsychotics: increased risk of ventricular arrhythmias with amisulpride and parenteral erythromycin avoid concomitant use; possibly increases clozapine concentration and possibly increased risk of convulsions; possibly increased risk of ventricular arrhythmias with pimozide and sertindole – avoid concomitant use; possibly increased quetiapine concentration
- Antivirals: concentration of both drugs increased with amprenavir; concentration increased by ritonavir
- Antidepressants and antidepressants: inhibits midazolam and zopiclone metabolism; increases buspirone concentration
- Atomoxetine: increased risk of ventricular arrhythmias with parenteral erythromycin
- Calcium-channel blockers: possibly inhibit metabolism of felodipine and verapamil; avoid concomitant use with lercanidipine
- Ciclosporin: markedly elevated ciclosporin blood levels – decreased levels on withdrawing drug. Monitor blood levels of ciclosporin carefully and adjust dose promptly as necessary
- Colchicine: increased risk of colchicine toxicity
- Cytotoxics: possible interaction with docetaxol; increases vinblastine toxicity – avoid concomitant use
- Diuretics: increased eplerenone concentration – reduce eplerenone dose
- Ergot alkaloids: increase risk of ergotism – avoid concomitant use
- 5HT1 agonists: increased eletriptan concentration – avoid concomitant use
- Ivabradine: increased risk of ventricular arrhythmias – avoid concomitant use
- Lipid-lowering drugs: increased risk of myopathy; concentration of rosuvastatin reduced
- Pentamidine: increased risk of ventricular arrhythmias with pentamidine
- Sirolimus: concentration of both drugs increased
- Tacrolimus: markedly elevated tacrolimus blood levels – decreased levels on withdrawing drug. Monitor blood levels of tacrolimus carefully and adjust dose promptly as necessary
- Theophylline: inhibits theophylline metabolism; if erythromycin given orally decreased erythromycin concentration

**ADMINISTRATION**

**RECONSTITUTION**
- 1 g with 20 mL water for injection, then dilute resultant solution further to 1–5 mg/mL

**ROUTE**
- IV, oral

**RATE OF ADMINISTRATION**
- 20–60 minutes using constant rate infusion pump

**COMMENTS**
- Use central line if concentration greater than 5 mg/mL; if >10 mg/mL monitor carefully (some units use 1 g in 100 mL of sodium chloride 0.9%). (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006)

**OTHER INFORMATION**
- May also give one third of daily dose by infusion over 8 hours peripherally at concentration of 1 g/250 mL (4 mg/mL). Repeat 8 hourly, i.e. continuously
- Increased risk of ototoxicity in renal impairment
- Avoid peaks produced by oral twice-daily dosing, i.e. dose 4 times daily
- Monitor closely for thrombophlebitic reactions at site of infusion
Escitalopram

**CLINICAL USE**

SSRI antidepressant:
- Depressive illness
- Panic and social anxiety disorder

**DOSE IN NORMAL RENAL FUNCTION**

Antidepressant: 10–20 mg daily  
Panic and social anxiety disorder: 5–20 mg

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight</td>
<td>414.4 (as Oxalate)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>&lt;80</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>8</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>12–26</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>22–32/slightly increased</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in normal renal function</th>
<th>Dose in normal renal function. Start with a low dose and titrate slowly</th>
<th>Dose in normal renal function. Start with a low dose and titrate slowly</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>Dose as in normal renal function</td>
<td>Dose as in normal renal function. Start with a low dose and titrate slowly</td>
<td>Dose as in normal renal function. Start with a low dose and titrate slowly</td>
</tr>
<tr>
<td>10–30</td>
<td>Dose as in normal renal function</td>
<td>Dose as in normal renal function. Start with a low dose and titrate slowly</td>
<td>Dose as in normal renal function. Start with a low dose and titrate slowly</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
<td>Dose as in normal renal function. Start with a low dose and titrate slowly</td>
<td>Dose as in normal renal function. Start with a low dose and titrate slowly</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Modality</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>GFR=10–30 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs

- Analgesics: increased risk of bleeding with aspirin and NSAIDs; risk of CNS toxicity increased with tramadol
- Anticoagulants: effect of coumarins possibly enhanced
- Antidepressants: avoid concomitant use with MAOI, increased risk of toxicity; increased risk of CNS toxicity with moclobemide – avoid concomitant use; avoid concomitant use with St John’s wort; possibly enhanced serotonergic effects with duloxetine; can increase concentration of tricyclics; increased agitation and nausea with tryptophan
- Anti-epileptics: convulsive threshold lowered
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antivirals: plasma concentration possibly increased by ritonavir
- Dopaminergics: use selegiline with caution; increased risk of CNS toxicity with rasagiline
- 5HT1 agonist: increased risk of CNS toxicity with sumatriptan; possibly increased risk of serotonergic effects with frovatriptan
- Linezolid: use with care, possibly increased risk of side effects
- Lithium: increased risk of CNS effects
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**
  - Oral drops: 20 drops = 10 mg

**OTHER INFORMATION**

- Escitalopram is an isomer of citalopram
Esmolol hydrochloride

** Clinical Use **
- Beta-adrenoceptor blocker:
  - Short-term treatment of supraventricular arrhythmias (including AF, atrial flutter, sinus tachycardia)
  - Tachycardia and hypertension in the perioperative period

** Pharmacokinetics **
- Molecular weight: 331.8 (daltons)
- % Protein binding: 55
- % Excreted unchanged in urine: <2
- Volume of distribution: 1.9 (L/kg)
- Half-life – normal/ESRF (hrs): 9 minutes/unchanged

** Dose in Normal Renal Function **
- 50–300 micrograms/kg/minute; see product literature for titration schedule

** Important Drug Interactions **
- Antidepressants: enhanced hypotensive effect with MAOIs
- Antimalarials: increased risk of bradycardia with mefloquine
- Antipsychotics: enhanced hypotensive effect with phenothiazines
- Calcium-channel blockers: increased risk of bradycardia and AV block with diltiazem; severe hypotension and heart failure occasionally with nifedipine and possibly other dihydropyridines; asystole, severe hypotension and heart failure with verapamil – avoid concomitant verapamil use
- Antihypertensives: enhanced hypotensive effect; increased risk of withdrawal hypertension with clonidine; increased risk of first dose hypotensive effect with post-synaptic alpha-blockers
- Diuretics: enhanced hypotensive effect
- Moxisylyte: possible severe postural hypotension
- Sympathomimetics: severe hypertension with adrenaline and noradrenaline and possibly dobutamine
- Tropisetron: increased risk of ventricular arrhythmias – use with caution

** Administration **

** Reconstitution **

** Route **
- IV infusion

** Rate of Administration **
- 50–300 mcg/kg/minute

** Comments **
- Incompatible with sodium bicarbonate solutions
- Dilute to a concentration of 10 mg/mL with sodium chloride 0.9% or glucose 5%
- Local irritation has occurred with infusions of 20 mg/mL

** Other Information **
- Has an active renally-excreted metabolite
- Hyperkalaemia can occur in CKD 5
- Titrate dose according to blood pressure response
**Esomeprazole**

**CLINICAL USE**
Gastric acid suppression

**DOSE IN NORMAL RENAL FUNCTION**
20–40 mg daily
Zollinger-Ellison syndrome: 80–160 mg daily
(doses >80 mg given in divided doses)

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>345.4</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>97</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.22</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1.3/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed.</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unlikely to be dialysed.</td>
</tr>
<tr>
<td>CAV/VVHVD</td>
<td>Unlikely to be dialysed.</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: effect of coumarins possibly enhanced
- Anti-epileptics: effects of phenytoin enhanced
- Antivirals: reduced atazanavir concentration – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
5 mL sodium chloride 0.9%

**ROUTE**
- Oral, IV

**RATE OF ADMINISTRATION**
- Bolus: over 3 minutes
- Infusion: 10–30 minutes

**COMMENTS**
- Dilute with up to 100 mL sodium chloride 0.9%

**OTHER INFORMATION**
- Can be dispersed in half a glass of non-carbonated water. Stir well until it disintegrates; the liquid with pellets should be drunk immediately or within 30 minutes of preparation. The glass should then be rinsed with water which should also be drunk
- Do not crush or chew
Estramustine phosphate

**CLINICAL USE**
Alkylating agent:
- Prostate cancer

**DOSE IN NORMAL RENAL FUNCTION**
0.14–1.4 g daily in divided doses (usual initial dose 560–840 mg daily)

**PHARMACOKINETICS**
- Molecular weight: 564.3 (as sodium phosphate)
- % Protein binding: No data
- % Excreted unchanged in urine: 22–36
- Volume of distribution (L/kg): 0.43
- Half-life – normal/ESRF (hrs): 10 (estromustine: 20)

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function, use with caution</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Technique</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
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</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**
  - Don't give less than 1 hour before or 2 hours after meals

**OTHER INFORMATION**
- Can cause fluid retention so use with caution in renal impairment
- Estramustine phosphate sodium is rapidly dephosphorylated in the intestine and prostate to estramustine and estromustine, which accumulate in the prostatic tissue. The plasma half-lives of these metabolites are 10–20 hours. Estramustine and estromustine are further metabolised before excretion

References:
Etamsylate

**CLINICAL USE**
- Short-term treatment of blood loss in menorrhagia
- Prophylaxis of surgical bleeding (unlicensed)

**DOSE IN NORMAL RENAL FUNCTION**
- Menorrhagia: 500 mg 4 times a day during menstruation
- Surgical bleeding: 1–1.5 g daily or 250–500 mg every 4–6 hours

**PHARMACOKINETICS**
- Molecular weight (daltons): 263.3
- % Protein binding: >90
- % Excreted unchanged in urine: 72–80
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 3.7–8

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/Min)**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/HD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - None known

**ADMINISTRATION**
- **RECONSTITUTION**
  - 
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - 
- **COMMENTS**
  - 

*It is not licensed for use by anyone else.*
Ethambutol hydrochloride

**CLINICAL USE**
Antibacterial agent:
- Tuberculosis

**DOSE IN NORMAL RENAL FUNCTION**
15 mg/kg/day or 30 mg/kg 3 times a week (supervised dosing)

**PHARMACOKINETICS**
- Molecular weight: 277.2 daltons
- % Protein binding: 20–30
- % Excreted unchanged in urine: 50
- Volume of distribution: 1.6–3.2 L/kg

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>15 mg/kg every 24–36 hours, or 7.5–15 mg/kg/day</td>
</tr>
<tr>
<td>&lt;10</td>
<td>15 mg/kg every 48 hours, or 5–7.5 mg/kg/day</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Type</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR &lt; 10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR &lt; 10 mL/min, or on dialysis days only give 25 mg/kg post-dialysis</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR &lt; 10 mL/min, or on dialysis days only give 25 mg/kg post-dialysis</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose as in GFR = 10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - COMMENTS

**OTHER INFORMATION**
- Monitor plasma levels. Dosages should be individually determined and adjusted according to measured levels and renal replacement therapy
- Peak levels are taken 2–2.5 hours post dose (2–6 mg/L or 7–22 micromol/L); trough is taken pre dose (<1 mg/L or <4 micromol/L)
- Baseline visual acuity tests should be performed prior to initiating ethambutol
- Daily dosing is preferred by some specialists to aid compliance and ensure maximum therapeutic effect
Ethosuximide

**CLINICAL USE**

Epilepsy

**DOSE IN NORMAL RENAL FUNCTION**

500 mg – 2 g daily in divided doses

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>141.2</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>0%</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>12–20</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.6–0.9</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>40–60/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs

- Antibacterials: concentration increased by isoniazid
- Antidepressants: lower convulsive threshold
- Anti-epileptics: concentration possibly reduced by carbamazepine, phenytoin and primidone; concentration of phenytoin possibly increased; concentration increased by valproate
- Antimalarials: possibly increased risk of convulsions with chloroquine and hydroxychloroquine; anticonvulsant effect antagonised by mefloquine
- Antipsychotics: lower convulsive threshold

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**

- **COMMENTS**
  -

**OTHER INFORMATION**

References:


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Etodolac

**CLINICAL USE**
NSAID and analgesic

**DOSE IN NORMAL RENAL FUNCTION**
600 mg daily in 1–2 divided doses

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>287.4</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>&gt;99</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>1</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.4</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>6–7.4/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function, but avoid if possible</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function, but avoid if possible</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function, but only use if on dialysis</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Method</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in normal renal function See ‘Other Information’</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function See ‘Other Information’</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function See ‘Other Information’</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be dialysed. Use lowest possible dose</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs

- ACE inhibitors and angiotensin-II antagonists: antagonism of hypotensive effect, increased risk of nephrotoxicity and hyperkalaemia
- Analgesics: avoid concomitant use of 2 or more NSAIDs, including aspirin (increased side effects); avoid with ketorolac, increased risk of side effects and haemorrhage
- Antibacterials: possibly increased risk of convulsions with quinolones
- Anticoagulants: effects of coumarins enhanced; possibly increased risk of bleeding with heparins and coumarins
- Antidepressants: increased risk of bleeding with SSIs and venlafaxine
- Antidiabetic agents: effects of sulphonylureas enhanced
- Anti-epileptics: possibly increased phenytoin concentration
- Antivirals: increased risk of haematological toxicity with zidovudine; concentration possibly increased by ritonavir
- Ciclosporin: may potentiate nephrotoxicity
- Cytotoxic agents: reduced excretion of methotrexate; increased risk of bleeding with erlotinib
- Diuretics: increased risk of nephrotoxicity; antagonism of diuretic effect; hyperkalaemia with potassium-sparing diuretics
- Lithium: excretion decreased
- Pentoxifylline: increased risk of bleeding
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - 
- **COMMENTS**
  - Take with or after food
Inhibition of renal prostaglandin synthesis by NSAIDs may interfere with renal function, especially in the presence of existing renal disease – avoid if possible; if not, check serum creatinine 48–72 hours after starting NSAID – if increased, discontinue therapy.

In patients with renal, cardiac or hepatic impairment, especially those taking diuretics, caution is required since the use of NSAIDs may result in deterioration of renal function. The dose should be kept as low as possible and renal function should be monitored.

Use normal doses in patients with ERF on dialysis if they do not pass any urine.

Use with caution in renal transplant recipients – can reduce intrarenal autocoid synthesis.

Accumulation of etodolac is unlikely in ARF, CKD or dialysis patients as it is metabolised in the liver.
Etomidate

**CLINICAL USE**
Induction of anaesthesia

**DOSE IN NORMAL RENAL FUNCTION**
150–300 mcg/kg

**PHARMACOKINETICS**
- Molecular weight (daltons): 244.3
- % Protein binding: 76
- % Excreted unchanged in urine: 2
- Volume of distribution (L/kg): 2–4.5

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**: Unknown dialysability. Dose as in normal renal function
- **HD**: Unknown dialysability. Dose as in normal renal function
- **HDF/High flux**: Unknown dialysability. Dose as in normal renal function
- **CAV/VVHD**: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Adrenergic neurone blockers: enhanced hypotensive effect
- Antihypertensives: enhanced hypotensive effect
- Antidepressants: avoid MAOIs for 2 weeks before surgery; increased risk of arrhythmias and hypotension with tricyclics
- Antipsychotics: enhanced hypotensive effect

**ADMINISTRATION**

**RECONSTITUTION**

**ROUTE**
- Intravenous injection only

**RATE OF ADMINISTRATION**

**COMMENTS**

**OTHER INFORMATION**

- In cases of adrenocortical gland dysfunction and during very long surgical procedures, a prophylactic cortisol supplement may be required (e.g. 50–100 mg hydrocortisone)
Etoposide

CLINICAL USE
Antineoplastic agent

DOSE IN NORMAL RENAL FUNCTION
IV: 60–120 mg/m² daily according to local protocol
Oral: Twice the relevant IV dose should be given daily according to local protocol

PHARMACOKINETICS
Molecular weight (daltons) 588.6
% Protein binding 74–94
% Excreted unchanged in urine 29
Volume of distribution (L/kg) 0.17–0.5
Half-life – normal/ESRF (hrs) 4–11/19

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)

<table>
<thead>
<tr>
<th>GFR</th>
<th>% of dose</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;60</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>45–60</td>
<td>80%</td>
<td>see 'Other Information'</td>
</tr>
<tr>
<td>30–45</td>
<td>75%</td>
<td>see 'Other Information'</td>
</tr>
<tr>
<td>&lt;30</td>
<td>50%</td>
<td>based on clinical response and see 'Other Information'</td>
</tr>
</tbody>
</table>

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;30 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;30 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose as in GFR&lt;30 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR&lt;30 mL/min</td>
</tr>
</tbody>
</table>

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Anticoagulants: possibly enhanced anticoagulant effect with coumarins
- Antipsychotics: avoid concomitant use with clozapine, increased risk of agranulocytosis
- Ciclosporin: 50% reduction in etoposide clearance

ADMINISTRATION

RECONSTITUTION
- 5–10 mL of infusion fluid or water for injection

ROUTE
- Oral, IV

RATE OF ADMINISTRATION
- IV infusion: 5 minutes – 3.5 hours

COMMENTS
- Dilute with sodium chloride 0.9% or glucose 5% to give a solution concentration as low as 100 mcg/mL of etoposide

OTHER INFORMATION
- Avoid skin contact
- Liver metabolised, yielding inactive metabolites. Approximately 45% of an administered dose is excreted in the urine, 29% being excreted unchanged in 72 hrs. Up to 16% is recovered in the faeces
- One study suggested that patients with serum creatinine >130 µmol/L require a 30% dose reduction. (Joel S, Clark P, Slevin M. Renal function and etoposide pharmacokinetics: is dose modification necessary? *Am Soc Clin Oncol*. 1991; 10: 103) This dose adjustment was calculated to result in equivalent total dose exposure in patients with reduced renal function.
- Patients with a raised bilirubin and/or decreased albumin may have an increase in free etoposide and hence greater myelosuppression
- Reaches high concentration in kidney: possible accumulation in renal impairment
- Plasma clearance is reduced and volume of distribution increased in renal impairment
- Has been used without any problems in a haemodialysis patient, using a dose

- Bristol-Myers Squibb advise giving 75% of dose if GFR is 15–50 mL/min.
**Etoricoxib**

**CLINICAL USE**
Cox-2 inhibitor and analgesic

**DOSE IN NORMAL RENAL FUNCTION**
- RA: 90 mg once daily
- OA and other indications: 60 mg once daily
- Acute gout: 120 mg once daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 358.8
- % Protein binding: 92
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): 120 litres
- Half-life – normal/ESRF (hrs): 22/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function, but avoid if possible</th>
<th>Dose as in normal renal function, but avoid if possible</th>
<th>Dose as in normal renal function, but only use if on dialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapies</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Not Dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unknown dialysability. Use lowest possible dose</td>
</tr>
<tr>
<td>VVHD</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- ACE inhibitors and angiotensin-II antagonists: antagonism of hypotensive effect; increased risk of nephrotoxicity and hyperkalaemia
- Analgesics: avoid concomitant use of 2 or more NSAIDs, including aspirin (increased side effects); avoid with ketorolac, increased risk of side effects and haemorrhage
- Antibacterials: possibly increased risk of convulsions with quinolones; concentration reduced by rifampicin
- Anticoagulants: effects of coumarins enhanced; possibly increased risk of bleeding with heparins and coumarins
- Antidepressants: increased risk of bleeding with SSRIs and venlafaxine
- Antidiabetic agents: effects of sulphonylureas enhanced
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- Lithium: excretion decreased
- Pentoxifylline: increased risk of bleeding
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
  - Take with or without food but onset of action is faster without food
OTHER INFORMATION

- Clinical trials have shown renal effects similar to those observed with comparative NSAIDs. Monitor patient for deterioration in renal function and fluid retention.
- Inhibition of renal prostaglandin synthesis by NSAIDs may interfere with renal function, especially in the presence of existing renal disease – avoid if possible; if not, check serum creatinine 48–72 hours after starting NSAID – if raised, discontinue NSAID therapy.
- Use normal doses in patients with ERF on dialysis if they do not pass any urine.
- Use with caution in renal transplant recipients – can reduce intrarenal autacoid synthesis.
- Etoricoxib should be used with caution in uraemic patients predisposed to gastrointestinal bleeding or uraemic coagulopathies.
Everolimus (unlicensed product)

**CLINICAL USE**
Prophylaxis of acute rejection in allogenic renal and cardiac transplants, in combination with ciclosporin and prednisolone

**DOSE IN NORMAL RENAL FUNCTION**
0.75 mg twice daily
(Titrated according to levels – see ‘Other Information’)

**PHARMACOKINETICS**
Molecular weight (daltons) 958.2
% Protein binding 74
% Excreted unchanged in urine <5
Volume of distribution (L/kg) 235–449 litres
Half-life – normal/ESRF (hrs) 18–35/Unchanged

**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
CAPD Unknown dialysability. Dose as in normal renal function
HD Unknown dialysability. Dose as in normal renal function
HDF/High flux Unknown dialysability. Dose as in normal renal function
CAV/VVHD Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Ciclosporin: increases everolimus AUC by 168% and C\textsubscript{max} by 82%
- Rifampicin: decreases everolimus levels by factor of 3. Increase dose ×3 and monitor levels
- Antifungals: fluconazole, ketoconazole, itraconazole increase everolimus blood levels
- Antibacterials: erythromycin, clarithromycin increase everolimus levels. Rifabutin, rifampicin decrease everolimus levels
- Anticonvulsants: carbamazepine, phenobarbital, phenytoin decrease everolimus levels
- St John’s wort: decreases everolimus levels
- Grapefruit juice: increases everolimus levels

**ADMINISTRATION**

**RECONSTITUTION**

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**

**COMMENTS**

**OTHER INFORMATION**
- None of the metabolites contributes significantly to the immunosuppressive activity of everolimus
- C\textsubscript{max} and AUC are reduced by 60% and 16% respectively when everolimus is taken with a high fat meal. Take doses consistently either with or without food to achieve consistent blood levels
- Patients achieving whole-blood trough levels of ≥3.0 ng/mL have been found to have a lower incidence of biopsy-proven acute rejection
Exenatide

**CLINICAL USE**

Adjunctive therapy in type 2 diabetes mellitus

**DOSE IN NORMAL RENAL FUNCTION**

5–10 mcg twice daily within 60 minutes before the morning and evening meal

**PHARMACOKINETICS**

- Molecular weight: 4186.6 daltons
- % Protein binding: No data
- % Excreted unchanged in urine: Majority
- Volume of distribution (L/kg): 28 litres
- Half-life – normal/ESRF (hrs): 2.4/5.95\(^1\)

**DOSE IN RENAL IMPAIRMENT**

- GFR (mL/min)
  - 30–50: Increase dose to 10 mcg with caution
  - 10–30: Avoid. See 'Other Information'
  - <10: Avoid. See 'Other Information'

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Unknown dialysability. Dose as in GFR<10 mL/min
- HD: Unknown dialysability. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–30 mL/min

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Anticoagulants: possibly enhances anticoagulant effect of warfarin
- Other nephrotoxins: avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - SC
- **RATE OF ADMINISTRATION**
  - **COMMENTS**
  -

**OTHER INFORMATION**

- Clearance is reduced by 84% in patients with established renal failure
- Increased gastrointestinal side effects in patients with severe renal impairment and on dialysis
- May cause renal failure including proteinuria. Avoid in patients with pre-existing renal impairment

References:
Ezetimibe

**CLINICAL USE**
Hypercholesterolaemia either in combination with a statin or as monotherapy

**DOSE IN NORMAL RENAL FUNCTION**
10 mg daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>409.4</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>99.7</td>
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<tr>
<td>% Excreted unchanged in urine</td>
<td>11</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>No data</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>22/–</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

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<thead>
<tr>
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</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapies</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
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<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Ciclosporin: concentration of both drugs possibly increased
- Fibrates: avoid concomitant administration

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
  -

**OTHER INFORMATION**
- When used with a statin LFTs should be monitored before initiation of therapy and then at regular intervals
- If GFR<30 mL/min there is a 1.5 increase in the AUC of ezetimibe but no dose adjustment is required
- Very rarely, cases of rhabdomyolysis have occurred – discontinue if myopathy is suspected
Famciclovir

CLINICAL USE
Antiviral agent

DOSE IN NORMAL RENAL FUNCTION

- Zoster: 250 mg 3 times a day or 750 mg once daily (Immunocompromised: 500 mg 3 times daily)
- First genital herpes infection: 250 mg 3 times a day
- Acute recurrent genital herpes: 125 mg twice a day (Immunocompromised: 500 mg twice a day)
- Suppression: 250 mg twice daily (HIV patients: 500 mg twice daily)

PHARMACOKINETICS

Molecular weight (daltons) 321.3
% Protein binding <20 as penciclovir
% Excreted unchanged in urine 0
Volume of distribution (L/kg) 0.91–1.25
Half-life – normal/ESRF (hrs) 2
(penciclovir)/3.2–23.6
(3.8–25: penciclovir)

DOSE IN RENAL IMPAIRMENT

For immunocompromised patients, see 'Other Information'

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;40</td>
<td>500 mg 3×/day</td>
</tr>
<tr>
<td>30–39</td>
<td>250 mg 3×/day</td>
</tr>
<tr>
<td>10–29</td>
<td>125 mg 3×/day</td>
</tr>
<tr>
<td>&lt;10</td>
<td>250 mg 3 times a week</td>
</tr>
</tbody>
</table>

IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs
- Probenecid: decreased excretion of famciclovir
- Increased famciclovir levels reported with mycophenolate mofetil

ADMINISTRATION

RECONSTITUTION
- ROUTE
  - Oral
RATE OF ADMINISTRATION
- COMMENTS

OTHER INFORMATION

- Treatment of herpes infections in immunocompromised patients:
<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zoster</td>
<td>Simplex</td>
</tr>
<tr>
<td>&gt;40</td>
<td>500 mg 3×/day</td>
</tr>
<tr>
<td>30–39</td>
<td>250 mg 3×/day</td>
</tr>
<tr>
<td>10–29</td>
<td>125 mg 3×/day</td>
</tr>
</tbody>
</table>
- Well absorbed after oral administration; deacetylated and oxidised rapidly to form the potent and selective antiviral compound penciclovir
- Four hours' haemodialysis results in approximately 75% reduction in plasma concentration of penciclovir
Famotidine

**CLINICAL USE**

H₂-blocker:
- Conditions associated with hyperacidity

**DOSE IN NORMAL RENAL FUNCTION**

20–80 mg daily

Zollinger-Ellison syndrome: 80–800 mg daily in divided doses

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>337.4</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>15–20</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>25–30</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1.1–1.4</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>3/&gt;20</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>50% of normal dose</td>
</tr>
<tr>
<td>&lt;10</td>
<td>20 mg at night (maximum)</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Not dialysed. Dose as in GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Antifungals: absorption of itraconazole and ketoconazole reduced
- Ciclosporin: possibly increased ciclosporin levels
- Cytotoxics: possibly reduced dasatinib concentration

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**

- **COMMENTS**
  -
Felodipine

**CLINICAL USE**
Calcium-channel blocker:
- Hypertension
- Angina

**DOSE IN NORMAL RENAL FUNCTION**
Hypertension: 5–20 mg once daily
Angina: 5–10 mg daily

**PHARMACOKINETICS**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight</td>
<td>384.3</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>99</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>10</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>24/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapies</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/ VVHD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Antibacterials: metabolism possibly inhibited by erythromycin
- Anti-epileptics: effect reduced by carbamazepine, barbiturates, phenytoin and primidone
- Antifungals: metabolism inhibited by itraconazole and ketoconazole
- Antihypertensives: enhanced hypotensive effect, increased risk of first dose hypotensive effect of post-synaptic alpha-blockers
- Antivirals: concentration possibly increased by ritonavir
- Grapefruit juice: concentration increased – avoid concomitant use
- Tacrolimus: possibly increased tacrolimus concentration
- Theophylline: possibly increased theophylline concentration

**ADMINISTRATION**

**RECONSTITUTION**

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**

**COMMENTS**
-
Fenofibrate

**CLINICAL USE**
Treatment of hyperlipidaemias types IIa, IIb, III, IV and V

**DOSE IN NORMAL RENAL FUNCTION**
Depends on preparation

**PHARMACOKINETICS**
- Molecular weight (daltons): 360.8
- % Protein binding: 99
- % Excreted unchanged in urine: 0
- Volume of distribution (L/kg): 0.89
- Half-life – normal/ESRF (hrs): 20/140–360

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–60: 134 mg daily
  - 10–20: 67 mg daily
  - <10: Avoid

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Avoid
- HD: Not dialysed. Avoid
- HDF/High flux: Unlikely to be dialysed. Avoid
- CAV/VVHD: Unlikely to be dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: increased risk of myopathy with daptomycin – try to avoid concomitant use
- Anticoagulants: enhances effect of coumarins and phenindione; dose of anticoagulant should be reduced by up to 50% and readjusted by monitoring INR
- Antidiabetics: may improve glucose tolerance and have an additive effect with insulin or sulphonylureas
- Ciclosporin: ciclosporin levels appear to be unaffected; however, it is recommended that concomitant therapy should be avoided because of the possibility of elevated serum creatinine levels
- Lipid-regulating drugs: increased risk of myopathy in combination with statins and ezetimibe; increased risk of cholelithiasis and gall bladder disease with ezetimibe – avoid with ezetimibe

**ADMINISTRATION**

**RECONSTITUTION**
- route

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**
- A few studies have noted that use of second-generation fibrates in transplant recipients is hampered by frequent rises in serum creatinine
- Avoid use in patients with GFR<10 mL/min due to increased risk of rhabdomyolysis
Fenoprofen

**CLINICAL USE**
NSAID and analgesic

**DOSE IN NORMAL RENAL FUNCTION**
300–600 mg 3–4 times a day; maximum 3 g daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 558.6 (as calcium salt)
- % Protein binding: >99
- % Excreted unchanged in urine: 2–5
- Volume of distribution (L/kg): 0.1

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Start with low dose, but avoid if possible</td>
</tr>
<tr>
<td>10–20</td>
<td>Start with low dose, but avoid if possible</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Start with low dose, but only use if on dialysis</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Start with low doses and increase according to response. See ‘Other Information’</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Start with low doses and increase according to response. See ‘Other Information’</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Start with low doses and increase according to response. See ‘Other Information’</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- ACE Inhibitors and angiotensin-II antagonists: increased risk of hyperkalaemia and nephrotoxicity; reduced hypotensive effect
- Analgesics: avoid concomitant use with other NSAIDs or aspirin; avoid concomitant use with ketorolac (increased side effects and haemorrhage)
- Antibacterials: possibly increased risk of convulsions with quinolones
- Anticoagulants: effects of coumarins enhanced; possibly increased risk of bleeding with heparins and coumarins
- Antidepressants: increased risk of bleeding with SSRIs or venlafaxine
- Antidiabetic agents: effects of sulphonylureas enhanced
- Anti-epileptics: possibly enhanced effect of phenytoin
- Antivirals: concentration possibly increased by ritonavir; increased risk of haematological toxicity with zidovudine
- Ciclosporin: may potentiate nephrotoxicity
- Cytotoxic agents: reduced excretion of methotrexate; increased risk of bleeding with erlotinib
- Lithium: excretion reduced
- Diuretics: increased risk of nephrotoxicity; antagonism of diuretic effect; hyperkalaemia with potassium-sparing diuretics
- Pentoxifylline: increased risk of bleeding
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**

RECONSTITUTION -
ROUTE - Oral
RATE OF ADMINISTRATION -
COMMENTS -

RETURN TO CONTENTS
OTHER INFORMATION

- Contraindicated in patients with history of significantly impaired renal function
- Inhibition of renal prostaglandin synthesis by NSAIDs may interfere with renal function, especially in the presence of existing renal disease – avoid use if possible; if not, check serum creatinine 48–72 hours after starting NSAID – if it has increased, discontinue therapy
- Possibility of decreased platelet aggregation
- Can use normal doses in patients with ERF on dialysis
- Use with caution in renal transplant recipients – can reduce intrarenal autocoid synthesis
- Associated with nephrotic syndrome, interstitial nephritis, hyperkalaemia, sodium retention
Fentanyl

**CLINICAL USE**
Opioid analgesic:
- Short surgical procedures
- Ventilated patients
- Chronic intractable pain

**DOSE IN NORMAL RENAL FUNCTION**
- IV injection:
  - with spontaneous respiration: 50–200 mcg, then 50 mcg as required
  - with assisted ventilation: 0.3–3.5 mg, then 100–200 mcg as required
- IV infusion:
  - with spontaneous respiration: 50–80 nanograms/kg/minute adjusted according to response
  - with assisted ventilation: 10 mcg/kg over 10 minutes, then 0.1–3 mcg/kg/minute
- Topical (chronic pain): 12–300 mcg/hour, patches changed every 72 hours
- Lozenges: 200–800 mcg over 15 minutes, repeated after 15 minutes if required; maximum 2 doses per pain episode and 4 doses daily

**PHARMACOKINETICS**
- Molecular weight (daltons) 336.5
- % Protein binding 80–85
- % Excreted unchanged in urine <7
- Volume of distribution (L/kg) 4
- Half-life – normal/ESRF (hrs) 2–7/Possibly increased

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50 Dose as in normal renal function Titrate according to response
- 10–20 75% of normal dose. Titrate according to response
- <10 50% of normal dose. Titrate according to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Not dialysed. Dose as in GFR<10mL/min
- HD Not dialysed. Dose as in GFR<10mL/min
- HDF/High flux Not dialysed. Dose as in GFR<10mL/min
- CAV/VVHD Not dialysed. Dose as in GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antidepressants: possible CNS excitation or depression (hypertension or hypotension) in patients also receiving MAOIs (including moclobemide) – avoid concomitant use; possibly increased sedative effects with tricyclics
- Antivirals: concentration increased by ritonavir
- Sodium oxybate: enhanced effect of sodium oxybate – avoid concomitant use

**ADMINISTRATION**
- RECONSTITUTION
  - ROUTE
    - IV, IM, topically, oral
  - RATE OF ADMINISTRATION
  - COMMENTS
    - Compatible with sodium chloride 0.9% and glucose 5%

**OTHER INFORMATION**
- For short surgical procedures the degree of renal impairment is irrelevant
- For other indications, renal impairment may have a moderate effect on the elimination of the drug; however, as fentanyl is titrated to response the usual dose and method of administration remains valid
Ferrous gluconate

**CLINICAL USE**
Iron deficiency anaemia

**DOSE IN NORMAL RENAL FUNCTION**
Prophylaxis: 2 tablets daily
Therapeutic: 4–6 tablets daily in divided doses

**PHARMACOKINETICS**
Molecular weight 482.2 (daltons)
% Protein binding –
% Excreted – unchanged in urine
Volume of distribution – (L/kg)
Half-life – normal/ESRF (hrs) –

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**: Not dialysed. Dose as in normal renal function
- **HD**: Not dialysed. Dose as in normal renal function
- **HDF/High flux**: Not dialysed. Dose as in normal renal function
- **CAV/VVHD**: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: reduced absorption of 4-quinolones and tetracyclines
- Dimercaprol: avoid concomitant use
- Mycophenolate: may significantly reduce absorption of mycophenolate

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**

- **COMMENTS**

**OTHER INFORMATION**

- One 300 mg ferrous gluconate tablet contains 35 mg elemental iron
- Best taken before food to aid absorption
- Phosphate binding agents, e.g. calcium carbonate or magnesium carbonate, reduce absorption of iron from the gut
- Monitor serum iron, transferrin saturation and ferritin levels (in line with local policy)

**ONE 300 mg ferrous gluconate tablet contains 35 mg elemental iron**

**RETURN TO CONTENTS**
Ferrous sulphate

**CLINICAL USE**
Iron deficiency anaemia

**DOSE IN NORMAL RENAL FUNCTION**
Prophylaxis: 200 mg daily
Therapeutic: 200 mg 2–3 times daily
M/R: 1–2 tablets daily

**PHARMACOKINETICS**
- Molecular weight: 278 (daltons)
- % Protein binding: –
- % Excreted unchanged in urine: –
- Volume of distribution: – (L/kg)
- Half-life: – (normal/ESRF (hrs))

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Not dialysed. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: reduced absorption of 4-quinolones and tetracyclines
- Dimercaprol: avoid concomitant use
- Mycophenolate: may significantly reduce absorption of mycophenolate

**ADMINISTRATION**
**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  -
- **COMMENTS**
  -

**OTHER INFORMATION**
- One 200 mg ferrous sulphate tablet contains 65 mg elemental iron
- Absorption of iron may be enhanced with concurrent administration of ascorbic acid
- Phosphate binding agents, e.g. calcium carbonate or magnesium carbonate, reduce absorption of iron from the gut
- Monitor: serum iron, transferrin saturation and ferritin levels (in line with local policy)
Fexofenadine hydrochloride

**CLINICAL USE**
Antihistamine:
● Symptomatic relief of rhinitis and urticaria

**DOSE IN NORMAL RENAL FUNCTION**
120–180 mg daily depending on condition

**PHARMACOKINETICS**
- Molecular weight (daltons) 538.1
- % Protein binding 60–70
- % Excreted unchanged in urine 10
- Volume of distribution (L/kg) 5–6
- Half-life – normal/ESRF (hrs) 11–15/19–25

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50 Dose as in normal renal function.
  - Use with care
  - 10–20 Initial dose 60 mg once or twice daily. ‘See Other Information’
  - <10 Initial dose 60 mg once daily. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAP Unlikely dialysability. Dose as in GFR<10 mL/min
- HD Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/ VVHD Unlikely to be dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Aluminium/magnesium containing antacids: reduced absorption – avoid for 2 hours

**ADMINISTRATION**
- **RECONSTITUTION**
  - **ROUTE**
    - Oral
  - **RATE OF ADMINISTRATION**
  - **COMMENTS**
    - Take before food

**OTHER INFORMATION**
- Less than 1.5% of a dose is metabolised via the CP450 3A4 system
- Larger doses may be used in patients with renal impairment, but increase carefully as can result in increased sedation

RETURN TO CONTENTS
Filgrastim

**CLINICAL USE**
Recombinant human granulocyte-colony stimulating factor (rhG-CSF):
- Treatment of neutropenia

**DOSE IN NORMAL RENAL FUNCTION**
0.5–1.2 MU/kg/day according to indication and patient response

**PHARMACOKINETICS**
<table>
<thead>
<tr>
<th>Molecular weight (daltons)</th>
<th>18 800</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Protein binding</td>
<td>Very high</td>
</tr>
<tr>
<td>% Excreted</td>
<td>0</td>
</tr>
<tr>
<td>unchanged in urine</td>
<td></td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.15</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>3.5/-</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>DOSE</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function and titrate dose to response</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function and titrate dose to response</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function and titrate dose to response</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Type</th>
<th>Dose Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - IV, SC
- **RATE OF ADMINISTRATION**
  - IV: Over 30 minutes or continuous IV infusion over 24 hours
  - SC: Can give as continuous SC infusion over 24 hours

**COMMENTS**
- IV: Dilute with glucose 5% ONLY; minimum concentration 0.2 MU per mL – add Human Serum Albumin if concentration is less than 1.5 MU per mL
- SC: Continuous infusion – dilute with 20mL of glucose 5%
- Dilute Neupogen may be adsorbed to glass and plastic materials – follow recommendations for dilution

**OTHER INFORMATION**
- One very small study (2–3 patients) concluded that body clearance of filgrastim was not affected by any degree of renal impairment
Finasteride

**CLINICAL USE**
- Benign prostatic hypertrophy
- Male pattern baldness

**DOSE IN NORMAL RENAL FUNCTION**
- BPH: 5 mg daily
- Male pattern baldness: 1 mg daily

**PHARMACOKINETICS**
- Molecular weight: 372.5 daltons
- % Protein binding: ≈93%
- % Excreted unchanged in urine: <0.05
- Volume of distribution: 1.07 L/kg

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs:
  - None known

**ADMINISTRATION**
- RECONSTITUTION
  -
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
  -
- COMMENTS
  -

**OTHER INFORMATION**
- Data sheet states that no dosage adjustment is required in renally impaired patients whose creatinine clearance is as low as 9 mL/min. No studies have been done in patients with creatinine clearance of less than 9 mL/min
Flecainide acetate

**CLINICAL USE**
Class Ic anti-arrhythmic agent:
- Ventricular arrhythmias and tachycardias

**DOSE IN NORMAL RENAL FUNCTION**
- Supraventricular arrhythmias: 100–300 mg daily in 2 divided doses
- Ventricular arrhythmias: 200–400 mg daily in 2 divided doses
- IV bolus: 2 mg/kg over 10–30 minutes (maximum 150 mg), then IV infusion of 1.5 mg/kg/hour for 1 hour, subsequently 0.1–0.25 mg/kg/hour; maximum 600 mg in 24 hours

**PHARMACOKINETICS**
- Molecular weight (daltons): 474.4
- % Protein binding: 32–58
- % Excreted unchanged in urine: 42
- Volume of distribution (L/kg): 8.31

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in GFR&lt;10 mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>See ‘Other Information’</td>
</tr>
<tr>
<td>10–20</td>
<td>See ‘Other Information’</td>
</tr>
<tr>
<td>&lt;10</td>
<td>See ‘Other Information’</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>CAPD</th>
<th>Dose as in GFR&lt;10 mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD</td>
<td>Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dose as in GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anti-arrhythmics: concentration increased by amiodarone – halve dose of flecainide; increased myocardial depression with other anti-arrhythmics
- Antidepressants: concentration increased by fluoxetine; increased risk of ventricular arrhythmias with tricyclics
- Antihistamines: increased risk of ventricular arrhythmias with mizolastine
- Antihypertensives: increased myocardial depression and bradycardia with beta-blockers; increased myocardial depression and asystole with verapamil
- Antimalarials: concentration increased by quinine; avoid concomitant use with artemether/lumefantrine
- Antipsychotics: increased risk of ventricular arrhythmias with antipsychotics that prolong the QT interval and phenothiazines; increased risk of arrhythmias with clozapine
- Antivirals: concentration increased by ritonavir and possibly amprenavir; increased risk of ventricular arrhythmias – avoid concomitant use
- Diuretics: increased cardiac toxicity if hypokalaemia occurs
- 5HT₂ antagonists: increased risk of ventricular arrhythmias with dolasetron – avoid concomitant use; use tropisetron with caution

**ADMINISTRATION**

**RECONSTITUTION**

**ROUTE**
- Oral, IV bolus, IV infusion

**RATE OF ADMINISTRATION**
- See ‘Other Information’

**COMMENTS**
- Infusion: Dilute with 5% glucose infusion; if chloride containing solutions are used the injection should be added to a volume of not less than 500 mL, otherwise a precipitate will form
- Plasma levels of 200–1000 nanograms/mL may be needed to obtain the maximum therapeutic effect. Plasma levels above...
700–1000 nanograms/mL are associated with increased likelihood of adverse events.

**OTHER INFORMATION**

- Product information recommendation: patients with severe renal impairment (defined as being a creatinine clearance <35 mL/minute), reduce each dose recommended for IV infusion by half.
- Product information recommendation: patients with severe renal impairment as defined above, that the maximum initial oral dosage should be 100 mg daily (or 50 mg twice daily) with frequent plasma level monitoring strongly recommended.
- Electrolyte disturbances should be corrected before using flecainide.
- Plasma levels quoted in product information are trough levels. Sample prior to dose.

**References:**

Flucloxacillin

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: 250–500 mg every 6 hours
- IV: 250 mg – 2 g every 6 hours
- IM: 250–500 mg every 6 hours
- Endocarditis: maximum 2 g every 4 hours if > 85 kg
- Osteomyelitis: maximum 8 g daily in divided doses

**PHARMACOKINETICS**
- Molecular weight (daltons) 453.9
- % Protein binding 95
- % Excreted unchanged in urine 66–76
- Volume of distribution (L/kg) 0.13
- Half-life – normal/ESRF (hrs) 53–60 minutes/135–173 minutes

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>As in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>As in normal renal function</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>As in normal renal function up to a total daily dose of 4 g</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Not dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Reduces excretion of methotrexate

**ADMINISTRATION**

**RECONSTITUTION**
- IV: 250 mg and 500 mg in 5–10 mL water for injection; 1 g in 15–20 mL water for injection
- IM: 250 mg in 1.5 mL water for injection; 500 mg in 2 mL water for injection

**ROUTE**
- IV, IM, oral

**RATE OF ADMINISTRATION**
- Bolus: 3–4 minutes
- Infusion: 30–60 minutes

**COMMENTS**
- Compatible with various infusion fluids

**OTHER INFORMATION**
- Monitor urine for protein at high doses
- Sodium content of injection: 2.26 mmol/g
- Monitor liver function tests in hypoalbuminaemic patients receiving high doses of flucloxacillin (e.g. CAPD patients)
Fluconazole

**CLINICAL USE**
Antifungal agent

**DOSE IN NORMAL RENAL FUNCTION**
50–400 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons) 306.3
- % Protein binding 11–12
- % Excreted unchanged in urine 80
- Volume of distribution (L/kg) 0.65–0.7
- Half-life – normal/ESRF (hrs) 30/98

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Dose as in normal renal function</th>
<th>&lt;10</th>
<th>50% of normal dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

| CAPD | Dialysed. Dose as in GFR<10mL/min |
| HD   | Dialysed. 50% of normal dose daily, or 100% of normal dose 3 times a week after dialysis |
| HDF/High flux | Dialysed. 50% of normal dose daily, or 100% of normal dose 3 times a week after dialysis |
| CAV/ VVHD | Dialysed. Dose as in normal renal function |
| CVVHD/HDF | Dialysed. 400–800 mg every 24 hours¹ |

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous drug interactions with other drugs
- Analgesics: increases concentration of celecoxib – halve celecoxib dose; increases concentration of parecoxib – reduce parecoxib dose; inhibits metabolism of alfentanil
- Antibacterials: increases rifabutin levels – reduce dose; metabolism accelerated by rifampicin
- Anticoagulants: potentiates effect of coumarins
- Antidepressants: avoid concomitant use with reboxetine
- Antidiabetics: possibly enhances hypoglycaemic effect of nateglinide; increases concentration of sulphonylureas
- Anti-epileptics: increases phenytin levels; possibly increased carbamazepine concentration
- Antimalarials: avoid concomitant administration with artemether/ lumefantrine
- Antipsychotics: increased risk of ventricular arrhythmias with pimozide and sertindole – avoid concomitant use; possibly increase quetiapine levels – reduce dose of quetiapine
- Antivirals: increases nevirapine, ritonavir, tipranavir and zidovudine levels, and possibly saquinavir
- Anxiolytics and hypnotics: increases midazolam levels
- Bosentan: increased bosentan levels – avoid concomitant use
- Calcium-channel blockers: avoid with nisoldipine
- Ciclosporin: increases blood/serum ciclosporin levels
- Diuretics: increased eplerenone levels – avoid concomitant use; concentration of fluconazole increased by hydrochlorothiazide
- Ergot alkaloids: increased risk of ergotism – avoid concomitant use
- Ivabradine: increased ivabradine levels – reduce initial dose
- Lipid-lowering drugs: possibly increased risk of myopathy with atorvastatin or simvastatin
- Sirolimus: may increase sirolimus concentration
- Tacrolimus: increases blood/serum tacrolimus levels
- Theophylline: possibly increases theophylline levels

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral, IV

**RATE OF ADMINISTRATION**
- IV: 5–10 mL/minute peripherally

**COMMENTS**
- Oral = IV dose. Very high bioavailability

¹ Return to contents
OTHER INFORMATION

- Oral bioavailability is 90%
- Approximately 50% is removed during a 3 hour haemodialysis session
- Has been used as adjunct to IV amphotericin and IP flucytosine in CAPD peritonitis
- No dose adjustment is required for single dose therapy
- Recurrent yeast peritonitis: flucytosine 2000mg orally stat, then 1000mg daily in addition to fluconazole 150mg IP or 200mg orally on alternate days. Remove Tenckhoff after 4–7 days if no response
- Dose of 800mg is appropriate as long as dialysate flow rate is 2L/hour and treating a relatively resistant organism.1

References:
Flucytosine

**CLINICAL USE**
Antifungal agent

**DOSE IN NORMAL RENAL FUNCTION**
100–200 mg/kg per day in 4 divided doses

**PHARMACOKINETICS**
- Molecular weight (daltons): 129.1
- % Protein binding: 2–4%
- % Excreted unchanged in urine: 90%
- Volume of distribution (L/kg): 0.65–0.91

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–40</td>
<td>50 mg/kg 12 hourly</td>
</tr>
<tr>
<td>10–20</td>
<td>50 mg/kg 24 hourly</td>
</tr>
<tr>
<td>&lt;10</td>
<td>50 mg/kg then dose according to levels. Dose of 0.5–1 g daily is usually adequate</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**
  - Dialysed. Give 50 mg/kg daily in 4 divided doses. Monitor levels
- **HD**
  - Dialysed. Dose as in GFR<10 mL/min, given post dialysis. Monitor trough level pre dialysis, and reduce post-dialysis dose accordingly
- **HDF/High flux**
  - Dialysed. Dose as in GFR<10 mL/min, given post dialysis. Monitor trough level pre dialysis, and reduce post-dialysis dose accordingly
- **CAV/VVHD**
  - Dialysed. Give dose as in GFR=10–20 mL/min and monitor blood levels, pre dose

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Cytarabine: concentration of flucytosine possibly reduced

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - IV peripherally through a blood filter
  - RATE
  - 20–40 minutes

**OTHER INFORMATION**
- Monitor blood levels 24 hours after therapy commences. Pre-dose level 25–50 mg/L is usually adequate. Do not exceed 80 mg/L
- 250 mL intravenous flucytosine infusion contains 34.5 mmol sodium
- Bone marrow suppression more common in patients with renal impairment
- Tablets available on named patient basis only
- Can be given IP at a dose of 50 mg/L
# Fludarabine phosphate

## CLINICAL USE
B-cell chronic lymphocytic leukaemia

## DOSE IN NORMAL RENAL FUNCTION
- **IV:** 25 mg/m² daily for 5 days, repeated every 28 days
- **Oral:** 40 mg/m² for 5 days every 28 days

## PHARMACOKINETICS
- Molecular weight: 365.2
- % Protein binding: 19–29
- % Excreted unchanged in urine: 40–60
- Volume of distribution (L/kg): 0.8–4
- Half-life – normal/ESRF (hrs): 20/24

## DOSE IN RENAL IMPAIRMENT
- GFR (mL/min): 30–70: 50–75% of normal dose
- 10–30: 50–75% of normal dose. Use with care
- <10: 50% of normal dose. Use with care

## DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- **CAPD:** Unknown dialysability. Dose as in GFR<10 mL/min
- **HD:** Unknown dialysability. Dose as in GFR<10 mL/min
- **HDF/High flux:** Unknown dialysability. Dose as in GFR<10 mL/min
- **CAV/VVHD:** Unknown dialysability. Dose as in GFR=10–30 mL/min

## IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs:
- Antipsychotics: avoid concomitant use with clozapine, increased risk of agranulocytosis
- Cytotoxics: increased pulmonary toxicity with pentostatin (unacceptably high incidence of fatalities); increases intracellular concentration of cytarabine

## ADMINISTRATION
**RECONSTITUTION**
- Reconstitute each vial with 2 mL of water to give a concentration of 25 mg/mL

**ROUTE**
- IV, oral

**RATE OF ADMINISTRATION**
- Infusion should be administered over 30 minutes

**COMMENTS**
- IV bolus in 10 mL of sodium chloride 0.9%
- IV infusion in 100 mL of sodium chloride 0.9%

## OTHER INFORMATION
- Rapidly dephosphorylated in plasma to (2-F-9-ß-D-arabinofuranosyladenine) 2-F-ara-ATP, which is necessary for cellular uptake
- Approximately 60% of an administered dose is excreted in the urine within 24 hrs
- Administer up to achievement of clinical response (usually 6 cycles) then discontinue
- Patients with renal failure (GFR=17–41 mL/min/m²) receiving 20% of dose had a similar AUC as patients with normal renal function receiving the full dose

**RETURN TO CONTENTS**
## FLUDROCORTISONE ACETATE

**FLUDROCORTISONE ACETATE**

It is not licensed for use by anyone else.

### CLINICAL USE
Replacement therapy in adrenal insufficiency

### DOSE IN NORMAL RENAL FUNCTION
50–300 micrograms daily

### PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>422.5</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>70–80</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>80% (as metabolites)</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>Widely distributed</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>3.5 (Biological half-life 18–36 hours)</td>
</tr>
</tbody>
</table>

### DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

### DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVH</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

### IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs

- Antibacterials: metabolism accelerated by rifamycins; metabolism possibly inhibited by erythromycin
- Anticoagulants: efficacy of coumarins may be altered
- Anti-epileptics: metabolism accelerated by carbamazepine, barbiturates, phenytoin and primidone
- Antifungals: increased risk of hypokalaemia with amphotericin – avoid concomitant use; metabolism possibly inhibited by itraconazole and ketoconazole
- Antivirals: concentration possibly increased by ritonavir
- Cytotoxics: increased risk of haematological toxicity with methotrexate
- Vaccines: high dose corticosteroids can impair immune response to vaccines – avoid concomitant use with live vaccines

### ADMINISTRATION

**RECONSTITUTION**

- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - COMMENTS
  - Use for as short a time and as low a dose as possible

RETURN TO CONTENTS
Flumazenil

CLINICAL USE

Reversal of sedative effects of benzodiazepines in anaesthetic, intensive care, and diagnostic procedures.

DOSE IN NORMAL RENAL FUNCTION

- Initially 200 micrograms over 15 seconds, then 100 micrograms at 60 second intervals if required; usual dose range 300–600 micrograms; maximum dose 1 mg, or 2 mg in intensive care situations.
- If drowsiness recurs, an IV infusion of 100–400 micrograms per hour may be given.

PHARMACOKINETICS

- Molecular weight (daltons): 303.3
- % Protein binding: 50
- % Excreted unchanged in urine: <0.1
- Volume of distribution (L/kg): 0.6–1.1
- Half-life – normal/ESRF (hrs): 0.7–1.3/Unchanged

DOSE IN RENAL IMPAIRMENT

- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Unknown dialysability. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS

- Potentially hazardous interactions with other drugs: None known

ADMINISTRATION

RECONSTITUTION

- ROUTE
  - IV injection, IV infusion

RATE OF ADMINISTRATION

- See ‘Dose in normal renal function’

COMMENTS

- Infusion: suitable diluents include sodium chloride 0.9%, sodium chloride 0.45% and glucose 5%

OTHER INFORMATION

- The half-life of flumazenil is shorter than those of diazepam and midazolam – patients should be closely monitored to avoid the risk of them becoming re-sedated.
Fluorouracil

**CLINICAL USE**
Antineoplastic agent

**DOSE IN NORMAL RENAL FUNCTION**
- IV infusion: 15 mg/kg/day to a total dose of 12–15 g
- IV bolus: 12 mg/kg/day for 3 days, then 6 mg/kg on alternate days or 15 mg/kg once a week
- Maintenance: 5–15 mg/kg once a week
- Intra-arterial infusion: 5–7.5 mg/kg by continuous 24-hour infusion
- Oral: 15 mg/kg weekly; maximum 1 g in a day
- Or consult relevant local chemotherapy protocol

**PHARMACOKINETICS**
- Molecular weight (daltons) 130.1
- % Protein binding 10
- % Excreted unchanged in urine 15
- Volume of distribution (L/kg) 0.25–0.5
- Half-life – normal/ESRF (hrs) 16 minutes/Unchanged

**DOSE IN RENAL IMPAIRMENT GFR (mL/min)**
- 20–50 Dose as in normal renal function
- 10–20 Dose as in normal renal function
- <10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Some removal likely. Dose as in normal renal function
- HD Dialysed. Dose as in normal renal function
- HDF/High flux Dialysed. Dose as in normal renal function
- CAV/VVHD Dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: possibly enhances effect of coumarins
- Antipsychotics: avoid concomitant use with clozapine, increased risk of agranulocytosis
- Metronidazole and cimetidine inhibit metabolism (increased toxicity)
- Temoporfin: increased skin photosensitivity with topical fluorouracil

**ADMINISTRATION**
**RECONSTITUTION**
- Consult relevant local protocol
**ROUTE**
- IV infusion intermittent or continuous, IV injection, intra-arterial, oral, topical
**RATE OF ADMINISTRATION**
- 30–60 minutes, 4 hours or as a continuous infusion over 24 hours or consult relevant local protocol

**OTHER INFORMATION**
- Use ideal body weight in patients showing obesity, ascites, and oedema
- Roche recommends decreasing the initial dose by one-third to one-half in patients with impaired hepatic or renal function
- Distributed throughout the body water, activated in target cells, most of dose (80%) is metabolised by the liver, 60–80% is excreted as respiratory CO₂ and 2–3% by the biliary system
- Following a single IV dose, approximately 15% is excreted unchanged in the urine
Fluoxetine

**CLINICAL USE**

SSRI antidepressant:
- Depressive illness
- Bulimia nervosa
- Obsessive compulsive disorder

**DOSE IN NORMAL RENAL FUNCTION**

20–60 mg daily depending on indication

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>345.8 (as hydrochloride)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>94.5</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>20–40</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>Acute dosing: 24–72/Unchanged</td>
</tr>
<tr>
<td></td>
<td>Chronic dosing: 4–6 days/Increased</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

GFR (mL/min)

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in normal renal function</th>
<th>20–50</th>
<th>Dose as in normal renal function</th>
<th>10–20</th>
<th>Use low dose, or on alternate days and increase according to response</th>
<th>&lt;10</th>
</tr>
</thead>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose in GFR &lt; 10 mL/min</th>
<th>Dose in GFR &lt; 10 mL/min</th>
<th>Dose in GFR &lt; 10 mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in</td>
<td>Not dialysed. Dose as in</td>
<td>Not dialysed. Dose as in</td>
</tr>
<tr>
<td>HD</td>
<td>GFR &lt; 10 mL/min</td>
<td>GFR &lt; 10 mL/min</td>
<td>GFR &lt; 10 mL/min</td>
</tr>
<tr>
<td>HDF/High</td>
<td>Not dialysed. Dose as in</td>
<td>Not dialysed. Dose as in</td>
<td>Not dialysed. Dose as in</td>
</tr>
<tr>
<td>flux</td>
<td>GFR &lt; 10 mL/min</td>
<td>GFR &lt; 10 mL/min</td>
<td>GFR &lt; 10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in</td>
<td>Not dialysed. Dose as in</td>
<td>Not dialysed. Dose as in</td>
</tr>
<tr>
<td></td>
<td>GFR &lt; 10 mL/min</td>
<td>GFR &lt; 10 mL/min</td>
<td>GFR = 10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs

- Analgesics: increased risk of bleeding with aspirin and NSAIDs; risk of CNS toxicity increased with tramadol
- Anti-arrhythmics: increased flecainide concentration
- Anticoagulants: effect of coumarins possibly enhanced
- Antidepressants: avoid concomitant use with MAOIs and moclobemide, increased risk of toxicity; avoid concomitant use with St John’s wort; possibly enhanced serotonergic effects with duloxetine; can increase tricyclic antidepressant concentration; increased agitation and nausea with tryptophan
- Anti-epileptics: antagonism (lowered convulsive threshold); concentration of carbamazepine and phenytoin increased
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: concentration of haloperidol, clozapine, risperidone, sertraline and zotepine increased; possibly inhibit aripiprazole metabolism – reduce aripiprazole dose
- Antivirals: concentration possibly increased by ritonavir
- Ciclosporin: may increase ciclosporin concentration
- Dopaminergics: increased risk of hypertension and CNS excitation with selegiline – avoid concomitant use; increased risk of CNS toxicity with rasagiline – avoid concomitant use
- 5HT1 agonist: increased risk of CNS toxicity with sumatriptan; possibly increased risk of serotonergic effects with frovatriptan
- Lithium: increased risk of CNS effects (lithium toxicity reported)
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**

- **COMMENTS**

RETURN TO CONTENTS
Accumulation may occur in patients with severe renal failure during chronic treatment (metabolites are excreted renally).

Choong-Ki L., Var T., Blaine T. W. Fluoxetine in depressed patients with renal failure and in depressed patients with normal kidney function *General Hosp. Psychiatry*. 1996; 18(1): 8–13, studied 7 patients undergoing haemodialysis and concluded that the process of HD does not alter the pharmacokinetics of fluoxetine or its major metabolite. All patients received fluoxetine 20 mg per day for 8 weeks.
Flupentixol

**CLINICAL USE**

Antipsychotic:
- Schizophrenia and other psychoses
- Depression

**DOSE IN NORMAL RENAL FUNCTION**

- Psychosis:
  - Oral: 3–9 mg twice daily
  - Deep IM: 50 mg 4 weekly – 300 mg 2 weekly; maximum dose 400 mg weekly; 20–40 mg every 2–4 weeks may be adequate in some patients
- Depression: 0.5–3 mg daily (doses above 2 mg should be in 2 divided doses, and 2nd dose should not be after 4 pm)

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>434.5 (588.8 as decanoate)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>&gt;95</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>Negligible</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>12–14</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>22–36 (IM: 3–8 days)/Increased</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Start with quarter to half of the dose and titrate slowly</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
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</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Modality</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Alcohol: enhanced effects
- Anaesthetics: enhanced hypotensive effects
- Analgesics: increased risk of convulsions with tramadol; enhanced hypotensive and sedative effects with opioids
- Antidepressants: increased plasma level of tricyclics
- Anti-epileptics: anticonvulsant effect antagonised
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: avoid concomitant use of clozapine with depot preparations in case of neutropenia
- Antivirals: concentration possibly increased with ritonavir
- Anxiolytics and hypnotics: increased sedative effects
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use
- Avoid concomitant use with drugs that prolong the QT interval

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral, IM

**COMMENTS**

- May cause hypotension and sedation in renal impairment
- Increased CNS sensitivity in renally impaired patients – start with small doses as can accumulate
- For IM injection a 20 mg test dose should first be given
- Oral bioavailability is 40–55%
- Peak levels occur 7 days after IM injection and 4 hours after oral administration

**OTHER INFORMATION**

- Oral, IM

**RETURN TO CONTENTS**
Fluphenazine

**CLINICAL USE**

Antipsychotic:
- Mania, schizophrenia and other psychoses
- Short-term use for anxiety, psychomotor agitation, excitement and violent or dangerously impulsive behaviour

**DOSE IN NORMAL RENAL FUNCTION**

**Oral:**
- Mania, schizophrenia and other psychoses: 2–20 mg daily in 2–3 divided doses
- Short-term use for anxiety, psychomotor agitation, excitement and violent or dangerously impulsive behaviour: 1–2 mg twice daily

**Deep IM:**
- Schizophrenia and other psychoses: 12.5–100 mg every 14–35 days

**PHARMACOKINETICS**

- Molecular weight: 437.5, 510.4 (as hydrochloride), 591.8 (as decanoate)
- % Protein binding: >90
- % Excreted unchanged in urine: 20
- Volume of distribution (L/kg): 10
- Half-life – normal/ESRF (hrs): 14.7 (6–9 days after IM)

**DOSE IN RENAL IMPAIRMENT**

- **GFR (mL/min):**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Start with a low dose and titrate slowly

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD:** Not dialysed. Dose as in GFR<10 mL/min
- **HD:** Not dialysed. Dose as in GFR<10 mL/min
- **HDF/High flux:** Unknown dialysability. Dose as in GFR<10 mL/min
- **CAV/VVHD:** Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Anaesthetics: enhanced hypotensive effect
- Analgesics: increased risk of convulsions with tramadol; enhanced hypotensive and sedative effects with opioids
- Anti-arrhythmics: increased risk of ventricular arrhythmias with anti-arrhythmics that prolong the QT interval; avoid concomitant use with amiodarone
- Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin – avoid concomitant use
- Antidepressants: increased plasma level of tricyclics; possibly increased risk of ventricular arrhythmias and antimuscarinic side effects
- Anticonvulsant: antagonises anticonvulsant effect
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: increased risk of ventricular arrhythmias with pimozide – avoid concomitant use; avoid concomitant use of depot formulations with clozapine (cannot be withdrawn quickly if neutropenia occurs)
- Antivirals: concentration possibly increased with ritonavir
- Anxiolytics and hypnotics: increased sedative effects
- Beta-blockers: enhanced hypotensive effect; increased risk of ventricular arrhythmias with sotalol
- Diuretics: enhanced hypotensive effect
- Lithium: increased risk of extrapyramidal side effects and possibly neurotoxicity
- Pentamidine: increased risk of ventricular arrhythmias
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use
- Avoid concomitant use with drugs that prolong the QT interval

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral, IM
- **RATE OF ADMINISTRATION**
  - **COMMENTS**

**RETURN TO CONTENTS**
Flurbiprofen

**CLINICAL USE**

NSAID and analgesic

**DOSE IN NORMAL RENAL FUNCTION**

150–200 mg daily in divided doses, increased in acute conditions to 300 mg daily

Dysmenorrhoea: 50–100 mg every 4–6 hours; maximum 300 mg daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>244.3</td>
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<tr>
<td>% Protein binding</td>
<td>99</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;3</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.1–0.2</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>3–6/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function, but avoid if possible</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function, but avoid if possible</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function, but only if on dialysis</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Removal very unlikely. Dose as in GFR&lt;10 mL/min. See ‘Other Information’</td>
</tr>
<tr>
<td>HD</td>
<td>Removal very unlikely. Dose as in GFR&lt;10 mL/min. See ‘Other Information’</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min. See ‘Other Information’</td>
</tr>
<tr>
<td>CAV/</td>
<td>Removal very unlikely. Dose as in GFR=10–20 mL/min</td>
</tr>
<tr>
<td>VVHD</td>
<td>Removal very unlikely. Dose as in GFR&lt;10 mL/min. See ‘Other Information’</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs

- ACE inhibitors and angiotensin-II antagonists: antagonism of hypotensive effect; increased risk of nephrotoxicity and hyperkalaemia
- Analgesics: avoid concomitant use with other NSAIDs or aspirin; avoid concomitant use with ketorolac (increased side effects and haemorrhage)
- Antibacterials: possibly increased risk of convulsions with quinolones
- Anticoagulants: effects of coumarins enhanced; possibly increased risk of bleeding with heparins and coumarins
- Antidepressants: increased risk of bleeding with SSRIs or venlafaxine
- Antidiabetic agents: effects of sulphonylureas enhanced
- Anti-epileptics: possibly enhanced effect of phenytoin
- Antivirals: concentration possibly increased by ritonavir; increased risk of haematological toxicity with zidovudine
- Ciclosporin: may potentiate nephrotoxicity
- Cytotoxic agents: reduced excretion of methotrexate; increased risk of bleeding with erlotinib
- Lithium: excretion reduced (risk of lithium toxicity)
- Diuretics: increased risk of nephrotoxicity; antagonism of diuretic effect; hyperkalaemia with potassium-sparing diuretics
- Pentoxifylline: increased risk of bleeding
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**

- 

**ROUTE**

- Oral

**RATE OF ADMINISTRATION**

- COMMENTS

-
OTHER INFORMATION

- NSAIDs have been reported to cause nephrotoxicity in various forms; interstitial nephritis, nephrotic syndrome and renal failure. In patients with renal, cardiac or hepatic impairment, caution is required since the use of NSAIDs may result in deterioration of renal function.

- Inhibition of renal prostaglandin synthesis by NSAIDs may interfere with renal function, especially in the presence of existing renal disease – avoid if possible; if not, check serum creatinine 48–72 hours after starting NSAID – if creatinine has increased, discontinue therapy.

- Use normal doses in patients with ERF on dialysis if they do not pass any urine.

- Use with caution in renal transplant recipients – can reduce intrarenal autocoid synthesis.
Flutamide

CLINICAL USE
Treatment of advanced prostate cancer

DOSE IN NORMAL RENAL FUNCTION
250 mg every 8 hours; start 3 days before LHRH agonist

PHARMACOKINETICS
Molecular weight 276.2 (daltons)
% Protein binding >90
% Excreted unchanged in urine 45
Volume of distribution No data
Half-life – normal/ESRF (hrs) 6/Slightly increased (active metabolite)

DOSE IN RENAL IMPAIRMENT
GFR (mL/MIN)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Not dialysed. Dose as in normal renal function
HD Not dialysed. Dose as in normal renal function
HDF/High flux Not dialysed. Dose as in normal renal function
CAV/ VVHD Not dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
-Anticoagulants: effects of coumarins enhanced

ADMINISTRATION
RECONSTITUTION
- ROUTE Oral
- RATE OF ADMINISTRATION
- COMMENTS
-
Fluvastatin

**CLINICAL USE**

HMG CoA reductase inhibitor:
- Primary hypercholesterolaemia
- Slowing progression of atherosclerosis
- Secondary prevention of coronary events after percutaneous coronary intervention

**DOSE IN NORMAL RENAL FUNCTION**

20–80 mg daily in the evening
XL: 80 mg daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
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</thead>
<tbody>
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<td>Molecular weight (daltons)</td>
<td>433.4 (as sodium salt)</td>
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<tr>
<td>% Protein binding</td>
<td>&gt;98</td>
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<tr>
<td>% Excreted</td>
<td>6</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.35</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1.4–3.2/–</td>
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</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
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</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Removal unlikely.</td>
</tr>
<tr>
<td>HD</td>
<td>Removal unlikely.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Removal unlikely.</td>
</tr>
<tr>
<td>CAV/</td>
<td>Removal unlikely.</td>
</tr>
<tr>
<td>VVHD</td>
<td>Removal unlikely.</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Antibacterials: rifampicin increases metabolism; increased risk of myopathy with daptomycin
- Anticoagulants: anticoagulant effect enhanced
- Ciclosporin: concomitant treatment with ciclosporin may lead to risk of muscle toxicity
- Colchicine: isolated cases of myopathy have been reported
- Lipid-lowering drugs: increased risk of myopathy with gemfibrozil, fibrates and nicotinic acid – avoid concomitant use with gemfibrozil

**ADMINISTRATION**

RECONSTITUTION
- ROUTE
  - Oral
RATE OF ADMINISTRATION
- COMMENTS
- OTHER INFORMATION

- The Committee on Safety of Medicines has advised that rhabdomyolysis associated with lipid-lowering drugs, such as the fibrates and statins, appears to be rare (approx. 1 case in every 100,000 treatment years), but may be increased in those with renal impairment and possibly in those with hypothyroidism
- Manufacturer’s literature indicates fluvastatin is contraindicated in patients with severe renal impairment (creatinine greater than or equal to 160 µmol/L)
Fluvoxamine maleate

**CLINICAL USE**
SSRI antidepressant:
- Depression
- Obsessive compulsive disorder

**DOSE IN NORMAL RENAL FUNCTION**
- 50–300 mg daily (doses over 150 mg in divided doses)
- Depression: usual maintenance dose 100 mg daily
- Obsessive compulsive disorder: usual maintenance dose 100–300 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 434.4
- % Protein binding: 80
- % Excreted unchanged in urine: 2
- Volume of distribution (L/kg): 25

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/MIN)
  - 30–50: Dose as in normal renal function
  - 10–30: Dose as in normal renal function
  - <10: Dose as in normal renal function but titrate slowly

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Not dialysed. Dose as in GFR<10 mL/min
- CAV/ VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs:
  - Analgesics: increased risk of bleeding with aspirin and NSAIDs; possibly increased concentration of methadone; increased risk of CNS toxicity with tramadol
  - Anti-arrhythmics: increased risk of toxicity with mexiletine
  - Anticoagulants: effect of coumarins possibly enhanced
  - Antidepressants: avoid concomitant use with reboxetine, MAOIs, moclobemide and St John’s wort; possibly enhanced serotonergic effects with duloxetine, fluvoxamine inhibits metabolism of duloxetine – avoid concomitant use; can increase tricyclics concentration; increased agitation and nausea with tryptophan
  - Anti-epileptics: antagonise anticonvulsant threshold; concentration of carbamazepine and phenytoin increased
  - Antimalarials: avoid concomitant use with artemether/lumefantrine
  - Antipsychotics: plasma concentration of clozapine and olanzapine increased
  - Antivirals: plasma concentration possibly increased by ritonavir
  - Ciclosporin: may increase ciclosporin concentration
  - Dopaminergics: increased risk of CNS toxicity with rasagiline; hypertension and CNS excitation with selegiline – avoid concomitant use
  - 5HT1 agonist: risk of CNS toxicity increased with sumatriptan; possibly increased risk of serotonergic effects with frovatriptan; inhibits metabolism of frovatriptan; possibly inhibits metabolism of zolmitriptan – reduce zolmitriptan dose
  - Linezolid: use with care, possibly increased risk of side effects
  - Lithium: increased risk of CNS effects – monitor levels
  - Sibutramine: increased risk of CNS toxicity – avoid concomitant use
  - Theophylline: increased theophylline concentrations – avoid concomitant use; if not possible, halve theophylline dose and monitor levels

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  -
Folic acid

CLINICAL USE

- Folate-deficient megaloblastic anaemia
- Supplement in HD patients

DOSE IN NORMAL RENAL FUNCTION

5 mg daily for 4 months, then weekly according to response
Maintenance: 5 mg every 1–7 days

PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>441.4</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>70</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>Varies with daily dose</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>No data</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>2.5/–</td>
</tr>
</tbody>
</table>

DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
</tbody>
</table>

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Dialysed. Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose as in normal renal function</td>
<td></td>
</tr>
</tbody>
</table>

IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs
- Anti-epileptics: reduces phenytoin, primidone and phenobarbital levels

ADMINISTRATION

RECONSTITUTION

- ROUTE
  - Oral
RATE OF ADMINISTRATION

COMMENTS

OTHER INFORMATION

- If seriously folate deficient, give 10 mg/day for 1 month, then 5 mg/day
- Doses up to 15 mg daily have been used in cases of malabsorption
- Most nutritionists recommend 0.5–1 mg folic acid daily for patients on HD or CAPD; may accumulate in uraemic patients
- Dosage used by dialysis units varies from 5 mg daily to 5 mg once weekly
Folinic acid (calcium folinate)

CLINICAL USE
- Folinic acid rescue
- Enhancement of 5-fluorouracil cytotoxicity in advanced colorectal cancer
- Folate deficiency

DOSE IN NORMAL RENAL FUNCTION
Varies according to indication

PHARMACOKINETICS
- Molecular weight (daltons) 511.5
- % Protein binding 54
- % Excreted unchanged in urine 80–90 (as inactive metabolites)
- Volume of distribution (L/kg) 17.5
- Half-life – normal/ESRF (hrs) 32–35 minutes/

DOSE IN RENAL IMPAIRMENT

GFR (mL/Min)
- 20–50 Dose as in normal renal function
- 10–20 Dose as in normal renal function
- <10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD Some removal likely. Dose as in normal renal function
- HD Some removal likely. Dose as in normal renal function
- HDF/High flux Dialysed. Dose as in normal renal function
- CAV/HHF Some removal likely. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Should not be administered simultaneously with a folic acid antagonist as this may nullify the effect of the antagonist

ADMINISTRATION

RECONSTITUTION
- For IV infusion, compatible with: sodium chloride 0.9%, glucose 5%, sodium lactate injection

ROUTE
- IM, IV injection, IV infusion, oral

RATE OF ADMINISTRATION
- Because of the calcium content of leucovorin solutions, no more than 160 mg/minute should be injected IV

COMMENTS

RETURN TO CONTENTS
Fondaparinux sodium

**CLINICAL USE**
- Prophylaxis of deep vein thrombosis
- Treatment of deep vein thrombosis, pulmonary embolism, unstable angina and after a myocardial infarction

**DOSE IN NORMAL RENAL FUNCTION**
- Prophylaxis DVT:
  - Surgical: 2.5 mg 6 hours after surgery, then 2.5 mg daily
  - Medical: 2.5 mg daily
- Treatment DVT and PE:
  - <50 kg: 5 mg daily
  - 50–100 kg: 7.5 mg daily
  - >100 kg: 10 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 1728
- % Protein binding: 97–98.6 (to antithrombin)
- % Excreted unchanged in urine: 64–77
- Volume of distribution (L/kg): 0.1–0.12
- Half-life – normal/ESRF (hrs): 17–21/72

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min):
  - 20–50: Prophylactic dose: 1.5 mg daily. See ‘Other Information’
  - 10–20: Reduce dose. See ‘Other Information’
  - <10: Reduce dose. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HD: Dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10 mL/min
- CAV/ VVHD: Unknown dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
- Increased risk of bleeding in combination with any other drugs that affect coagulation

**ADMINISTRATION**
- RECONSTITUTION
- ROUTE
  - SC
- RATE OF ADMINISTRATION
- COMMENTS

**OTHER INFORMATION**
- In patients with a GFR of 30–50 mL/min and weight >100 kg, give an initial dose of 10 mg then reduce to 7.5 mg daily for treatment of a DVT; use with caution
- Manufacturer advises to avoid in severe renal impairment due to increased risk of bleeding
- Clearance of fondaparinux increases by up to 20% during haemodialysis
- Has been used successfully at a dose of 2.5 mg instilled into the dialysis circuit for anticoagulation during dialysis. (Haase M, Bellomo R, Rocktaesche J, et al. Use of fondaparinux (arixtra) in a dialysis patient with symptomatic heparin-induced thrombocytopenia type II. *Nephrol Dial Transplant*. 2005 Feb; 20(2): 444–6)

*Fondaparinux sodium is not licensed for use by anyone else.*
Formoterol fumarate (efomoterol)

**CLINICAL USE**
Long acting selective beta-2 agonist

**DOSE IN NORMAL RENAL FUNCTION**
1–2 puffs twice daily
Turbohaler: 4.5–18 mcg 1–2 times daily; maximum 54 mcg daily, maximum 36 mcg daily in COPD

**PHARMACOKINETICS**
Molecular weight (daltons) 804.9
% Protein binding 61–64
% Excreted unchanged in urine 6.4–8
Volume of distribution (L/kg) No data
Half-life – normal/ESRF (hrs) 8/

**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
CAPD Not dialysed. Dose as in normal renal function
HD Unlikely to be dialysed. Dose as in normal renal function
HDF/High flux Unlikely to be dialysed. Dose as in normal renal function
CAV/VVHD Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
● None known

**ADMINISTRATION**
RECONSTITUTION –
ROUTE ● Inhaled
RATE OF ADMINISTRATION –
COMMENTS –
Fosamprenavir

**CLINICAL USE**
Protease inhibitor:
- For HIV infection, in combination with other antiretroviral drugs

**DOSE IN NORMAL RENAL FUNCTION**
700 mg twice daily with ritonavir 100 mg twice daily

**PHARMACOKINETICS**
- Molecular weight: 625.7 (as calcium salt) (daltons)
- % Protein binding: 90 (amprenavir)
- % Excreted unchanged in urine: <1 (amprenavir)
- Volume of distribution: 6 (amprenavir) (L/kg)
- Half-life – normal/ESRF (hrs): 7.7/Unchanged (amprenavir)

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux: Unlikely to be dialysed. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs:
- Anti-arrhythmics: possibly increased concentration of amiodarone, flecainide, lidocaine and propafenone (increased risk of ventricular arrhythmias) – avoid concomitant use
- Antibacterials: concentration of both drugs increased with erythromycin; increases concentration of rifabutin – reduce rifabutin dose; concentration significantly reduced by rifampicin – avoid concomitant use; possibly increases dapson concentration; avoid concomitant use with telithromycin in severe renal and hepatic impairment
- Antidepressants: concentration reduced by St John’s wort – avoid concomitant use; possibly increases side effects of tricyclics; possibly reduces paroxetine concentration
- Antimalarials: avoid concomitant administration with arteether/lumefantrine
- Antipsychotics: possibly inhibits aripiprazole metabolism – reduce aripiprazole dose; possibly increases clozapine concentration; possibly increases pimozone and sertindole concentration (increased risk of ventricular arrhythmias) – avoid concomitant use
- Antivirals: concentration reduced by efavirenz, lopinavir and tipranavir; concentration possibly reduced by nevirapine; concentration increased by ritonavir
- Anxiolytics and hypnotics: increased risk of prolonged sedation and respiratory depression with alprazolam, clonazepam, diazepam, flurazepam and midazolam
- Cilostazol: possibly increases cilostazol concentration – avoid concomitant use
- Ergot alkaloids: increased risk of ergotism – avoid concomitant use
- Immunosuppressants: monitor ciclosporin, tacrolimus and sirolimus levels
- Statins: possibly increased risk of myopathy with atorvastatin; possibly increased myopathy with simvastatin – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- Prodrug of amprenavir, 700 mg of fosamprenavir is equivalent to 600 mg amprenavir
Foscarnet sodium

**CLINICAL USE**

Antiviral agent:
- Treatment and maintenance therapy of cytomegalovirus retinitis (CMV)
- Mucocutaneous herpes simplex infection (HSV)

**DOSE IN NORMAL RENAL FUNCTION**

- CMV: 60 mg/kg every 8 hours induction dose for 2–3 weeks, then 60 mg/kg daily, increase to 90–120 mg/kg if tolerated
- Mucocutaneous herpes simplex infection: 40 mg/kg every 8 hours

**PHARMACOKINETICS**

- Molecular weight (daltons) 300
- % Protein binding 14–17
- % Excreted unchanged in urine 85
- Volume of distribution (L/kg) 0.4–0.6
- Half-life – normal/ESRF (hrs) 2–4/>100

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>CMV Dose</th>
<th>HSV Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>28 mg/kg every 8 hours</td>
<td>15 mg/kg every 8 hours</td>
</tr>
<tr>
<td>10–20</td>
<td>15 mg/kg every 8 hours</td>
<td>6 mg/kg every 8 hours</td>
</tr>
<tr>
<td>&lt;10</td>
<td>6 mg/kg every 8 hours</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

| CAPD         | Dialysed. Dose as in GFR<10mL/min. See ‘Other Information’ |
| HD           | Dialysed. Dose as in GFR<10mL/min. See ‘Other Information’ |
| HDF/High flux| Dialysed. Dose as in GFR<10mL/min. See ‘Other Information’ |
| CAV/VVH      | Dialysed. Dose as in GFR=10–20mL/min. See ‘Other Information’ |

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Antivirals: avoid with lamivudine
- Ciclosporin: may cause acute renal failure in combination

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Centrally (undiluted); peripherally (diluted)

**RATE OF ADMINISTRATION**

- Continuous infusion over 24 hours, or intermittent infusion over at least 60 minutes

**COMMENTS**

- If given peripherally dilute with glucose 5% or sodium chloride 0.9% to a concentration of 12 mg/mL or less
- Alternatively, piggy-back the undiluted foscarnet dose to 1 litre of a glucose 5% or sodium chloride 0.9% infusion
- If given centrally, can be administered undiluted but additional fluids should be given to reduce the risk of nephrotoxicity

**OTHER INFORMATION**

Some renal units dose by creatinine clearance/weight as follows:

<table>
<thead>
<tr>
<th>Clearance mL/min/kg</th>
<th>CMV Dose mg/kg 8 hourly</th>
<th>HSV Dose mg/kg 8 hourly</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.6</td>
<td>1.4</td>
<td>55</td>
</tr>
<tr>
<td>1.4</td>
<td>1.2</td>
<td>49</td>
</tr>
<tr>
<td>1.2</td>
<td>1.1</td>
<td>42</td>
</tr>
<tr>
<td>1</td>
<td>0.8</td>
<td>35</td>
</tr>
<tr>
<td>0.8</td>
<td>0.6</td>
<td>28</td>
</tr>
<tr>
<td>0.6</td>
<td>0.4</td>
<td>21</td>
</tr>
<tr>
<td>0.4</td>
<td>0.2</td>
<td>14</td>
</tr>
<tr>
<td>0.2</td>
<td>0.1</td>
<td>10</td>
</tr>
</tbody>
</table>

**Maintenance therapy doses for CMV**

<table>
<thead>
<tr>
<th>Clearance mL/min/kg</th>
<th>Dose mg/kg daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.6</td>
<td>1.4</td>
</tr>
<tr>
<td>1.4</td>
<td>1.2</td>
</tr>
<tr>
<td>1.2</td>
<td>1.1</td>
</tr>
<tr>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>0.8</td>
<td>0.6</td>
</tr>
<tr>
<td>0.6</td>
<td>0.4</td>
</tr>
<tr>
<td>0.4</td>
<td>0.2</td>
</tr>
<tr>
<td>0.2</td>
<td>0.1</td>
</tr>
</tbody>
</table>

- Maintain adequate hydration to prevent renal toxicity
- Monitor serum calcium and magnesium
- Some units use full-dose ganciclovir and half-dose foscarnet concomitantly for treatment of resistant CMV disease

RETURN TO CONTENTS
Fosinopril sodium

**CLINICAL USE**
Angiotensin-converting enzyme inhibitor:
- Hypertension
- Heart failure

**DOSE IN NORMAL RENAL FUNCTION**
10–40 mg once daily

**PHARMACOKINETICS**
- Molecular weight (daltons) 585.6
- % Protein binding 95
- % Excreted unchanged in urine <1
- Volume of distribution (L/kg) 0.15
- Half-life – normal/ESRF (hrs) 11.5–14–14–32

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/min)**
  - 20–50 Dose as in normal renal function
  - 10–20 Dose as in normal renal function. Start with low dose
  - <10 Dose as in normal renal function. Start with low dose

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD** Not dialysed. Dose as in GFR<10mL/min
- **HD** Not dialysed. Dose as in GFR<10mL/min
- **HDF/High flux** Unlikely to be dialysed. Dose as in GFR<10mL/min
- **CAV/VVHD** Unlikely to be dialysed. Dose as in GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Analgesics: antagonism of hypotensive effect and increased risk of renal impairment with NSAIDs; hyperkalaemia with ketorolac and other NSAIDs
- Ciclosporin: increased risk of hyperkalaemia and nephrotoxicity
- Diuretics: enhanced hypotensive effect; hyperkalaemia with potassium-sparing diuretics
- Epoetin: increased risk of hyperkalaemia; antagonism of hypotensive effect
- Lithium: reduced excretion, possibility of enhanced lithium toxicity
- Potassium salts: increased risk of hyperkalaemia
- Tacrolimus: increased risk of hyperkalaemia and nephrotoxicity

**ADMINISTRATION**
**RECONSTITUTION** –
**ROUTE**
- Oral
**RATE OF ADMINISTRATION** –
**COMMENTS** –

**OTHER INFORMATION**
- Hepatobiliary elimination compensates for diminished renal excretion
- Hyperkalaemia and other side effects more common in patients with impaired renal function
- Close monitoring of renal function during therapy necessary in those with renal insufficiency
- Renal failure has been reported in association with ACE inhibitors in patients with renal artery stenosis, post renal transplant, and those with congestive heart failure
- High incidence of anaphylactoid reactions has been reported in patients dialysed with high-flux polyacrylonitrile membranes and treated concomitantly with an ACE inhibitor – this combination should therefore be avoided
Fosphenytoin sodium

**CLINICAL USE**
- Control of status epilepticus
- Seizures associated with neurosurgery or head injury when oral phenytoin is not possible

**DOSE IN NORMAL RENAL FUNCTION**
- Status epilepticus:
  - Treatment: 20 mg PE/kg (loading dose) by IV infusion
  - Maintenance: 4–5 mg PE/kg daily in 1–2 divided doses
- Prophylaxis or treatment of seizures: 10–15 mg PE/kg by IV infusion; then convert to phenytoin or 4–5 mg PE/kg daily in 1–2 divided doses

**PHARMACOKINETICS**
- Molecular weight (daltons): 406.2
- % Protein binding: 95–99
- % Excreted unchanged in urine: 1–5
- Volume of distribution (L/kg): 4.3–10.8 litres
- Half-life – normal/ESRF (hrs): 18.9 (IV), 41.2 (IM)/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Reduce dose or rate by 10–25% and monitor carefully (except for status epilepticus)
  - 10–20: Reduce dose or rate by 10–25% and monitor carefully (except for status epilepticus)
  - <10: Reduce dose or rate by 10–25% and monitor carefully (except for status epilepticus)

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as for GFR<10 mL/min
- HD: Not dialysed. Dose as for GFR<10 mL/min
- HDF/High flux: Unlikely to be dialysed. Dose as for GFR<10 mL/min
- CAV/VVHD: Not dialysed. Dose as for GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: enhanced effect with NSAIDs; metabolism of methadone accelerated
- Anti-arrhythmics: increased concentration with amiodarone; concentration of disopyramide and mexiletine reduced
- Antibacterials: level increased by clarithromycin, chloramphenicol, isoniazid, metronidazole, co-trimoxazole and trimethoprim (+ antifolate effect); concentration increased or decreased by ciprofloxacin; concentration of doxycycline and telithromycin reduced; concentration reduced by rifampicin
- Anticoagulants: increased metabolism of coumarins (reduced effect but also reports of enhancement)
- Antidepressants: MAOIs, SSRIs and tricyclics antagonise anticonvulsant effect, concentration increased by fluoxetine and fluvoxamine; reduced concentration of mianserin, mirtazapine, paroxetine and possibly tricyclics; concentration reduced by St John’s wort – avoid
- Anti-epileptics: concentration of both drugs reduced with carbamazepine; concentration may also be increased by carbamazepine, ethosuximide, oxicarbazepine and topiramate; possibly reduced concentration of ethosuximide, active oxicarbazepine metabolite, primidone (but active metabolite increased), topiramate and valproate; reduced concentration of lamotrigine, tiagabine and zonisamide; concentration reduced by vigabatrin
- Antifungals: reduced concentration of ketoconazole, itraconazole, posaconazole, voriconazole and possibly caspofungin – avoid with itraconazole, increase voriconazole dose and possibly caspofungin; levels increased by fluconazole, miconazole and voriconazole
- Antimalarials: antagonise anticonvulsant effect; increased antifolate effect with pyrimethamine
- Antipsychotics: antagonise anticonvulsant effect; aripiprazole concentration possibly reduced – increase aripiprazole dose
metabolism of clozapine, quetiapine and sertindole increased

- Calcium-channel blockers: levels increased by diltiazem; reduced concentration of diltiazem, felodipine, isradipine, nisoldipine and verapamil and possibly dihydropyridines, nicardipine and nifedipine
- Ciclosporin: reduced ciclosporin levels
- Corticosteroids: metabolism accelerated (effect reduced)
- Cytotoxics: metabolism inhibited by fluorouracil; increased antifolate effect with methotrexate; reduced phenytoin absorption; reduced concentration of busulfan, etoposide and imatinib – avoid with imatinib
- Disulfiram: levels of phenytoin increased
- Diuretics: concentration of eplerenone reduced – avoid concomitant use; increased risk of osteomalacia with carbonic anhydrase inhibitors; antagonises effect of furosemide
- Oestrogens and progestogens: metabolism increased (reduced contraceptive effect)
- Sulfinpyrazone: concentration increased by sulfinpyrazone
- Tacrolimus: reduced tacrolimus levels
- Theophylline: concentration of both drugs reduced
- Ulcer-healing drugs: metabolism inhibited by cimetidine; absorption reduced by sucralfate; enhanced effect with esomeprazole and omeprazole

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - IV, IM

**RATE OF ADMINISTRATION**

- Status epilepticus: 100–150 mg PE/min
- Treatment and prophylaxis of seizures: 50–100 mg PE/min

**COMMENTS**

- Dilute further when using for IV infusion with sodium chloride 0.9% or glucose 5% to 1.5–25 mg PE/mL

**OTHER INFORMATION**

- 75 mg of fosphenytoin sodium is equivalent to 50 mg of phenytoin
- 0.037 mmol of phosphate/mg of fosphenytoin
- Decreased protein binding in renal failure
- Monitor ECG, BP and respiratory function during infusion
- When substituting IV, IM use same dose and frequency as for oral phenytoin, administer at a rate of 50–100 mg PE/min
- May increase blood glucose in diabetic patients
- Some is dialysed out, as not all PE is protein-bound
- Half-life of fosphenytoin to phenytoin is 15 minutes; more rapid in renal failure due to reduced protein binding
Frovatriptan

CLINICAL USE
Acute relief of migraine

DOSE IN NORMAL RENAL FUNCTION
2.5 mg; a second dose can be taken if required after at least 2 hours
Maximum daily dose is 5 mg

PHARMACOKINETICS
Molecular weight 243.3 (daltons)
% Protein binding 15
% Excreted unchanged in urine 10–32
Volume of distribution 3–4.2 (L/kg)
Half-life – normal/ESRF (hrs) 26/ Unchanged

DOSE IN RENAL IMPAIRMENT
GFR (mL/MIN)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Likely dialysability. Dose as in normal renal function
HD Likely dialysability. Dose as in normal renal function
HDF/High flux Likely dialysability. Dose as in normal renal function
CAV/HD Likely dialysability. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● Antidepressants: blood levels of frovatriptan increased 27–49% by fluvoxamine – avoid concomitant use; possibly increased serotonergic effects with duloxetine and SSRIs; increased serotonergic effects with St John’s wort – avoid concomitant use
● Ergot alkaloids: increased risk of vasospasm

ADMINISTRATION
RECONSTITUTION
–
ROUTE
● Oral
RATE OF ADMINISTRATION
–
COMMENTS
–
Fulvestrant

**CLINICAL USE**
Treatment of post-menopausal women with oestrogen-receptor-positive, locally advanced or metastatic breast cancer

**DOSE IN NORMAL RENAL FUNCTION**
250 mg monthly

**PHARMACOKINETICS**
- Molecular weight: 606.8 daltons
- % Protein binding: 99%
- % Excreted unchanged in urine: <1%
- Volume of distribution: 3–5 L/kg
- Half-life – normal/ESRF: 40 days/unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>As in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>As in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>As in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux: Unlikely to be dialysed. Dose as in normal renal function
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**
- RECONSTITUTION
- ROUTE
  - IM
- RATE OF ADMINISTRATION
- COMMENTS

**OTHER INFORMATION**
As it is an intramuscular injection, use with caution in patients who are heparinised.
Furosemide (frusemide)

**CLINICAL USE**
Loop diuretic

**DOSE IN NORMAL RENAL FUNCTION**
oral: 20 mg – 1 g daily
IV: 20 mg – 1.5 g daily
Doses titrated to response

**PHARMACOKINETICS**
Molecular weight (daltons) 330.7
% Protein binding 91–99
% Excreted unchanged in urine 80–90
Volume of distribution (L/kg) 0.07–0.2
Half-life – normal/ESRF (hrs) 0.5–2/9.7

**DOSE IN RENAL IMPAIRMENT**
GFR (mL/min)
20–50 Dose as in normal renal function
10–20 increased doses may be required
<10 Dose as in normal renal function; increased doses may be required

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
CAPD Not dialysed. Dose as in GFR<10mL/min
HD Not dialysed. Dose as in GFR<10mL/min
HDF/High flux Not dialysed. Dose as in GFR<10mL/min
CAV/VVHD Not dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs

- Analgesics: increased risk of nephrotoxicity with NSAIDs; antagonism of diuretic effect with NSAIDs
- Anti-arrhythmics: risk of cardiac toxicity with anti-arrhythmics if hypokalaemia occurs; effects of lidocaine and mexiletine antagonised
- Antibacterials: increased risk of ototoxicity with aminoglycosides, polymyxins and vancomycin; avoid concomitant use with lymecycline
- Antidepressants: increased risk of hypokalaemia with reboxetine; enhanced hypotensive effect with MAOIs; increased risk of postural hypotension with tricyclics
- Anti-epileptics: increased risk of hyponatraemia with carbamazepine
- Antifungals: increased risk of hypokalaemia with amphotericin
- Antihypertensives: enhanced hypotensive effect; increased risk of first dose hypotensive effect with alpha-blockers; increased risk of ventricular arrhythmias with sotalol if hypokalaemia occurs
- Antipsychotics: increased risk of ventricular arrhythmias with amisulpiride, sertindole or pimozide (avoid with pimozide) if hypokalaemia occurs; enhanced hypotensive effect with phenothiazines
- Atomoxetine: hypokalaemia increases risk of ventricular arrhythmias
- Cardiac glycosides: increased toxicity if hypokalaemia occurs
- Ciclosporin: variable reports of increased nephrotoxicity, ototoxicity and hepatotoxicity
- Lithium: risk of toxicity

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - IV peripherally or centrally, 1M, oral
- **RATE OF ADMINISTRATION**
  - 1 hour; not greater than 4 mg/minute
- **COMMENTS**
  - 250 mg to 50mL sodium chloride 0.9% or undiluted via CRIP
  - Increased danger of ototoxicity and nephrotoxicity if infused at faster rate than approximately 4 mg/minute
  - Protect from light

RETURN TO CONTENTS
OTHER INFORMATION

- 500 mg orally = 250 mg IV
- Excreted by tubular secretion, therefore in severe renal impairment (GFR 5-10 mL/min) higher doses may be required due to a reduction in the number of functioning nephrons
- Furosemide acts within 1 hour of oral administration, (after IV peak effect within 30 minutes) diuresis complete within 6 hours
Gabapentin

**CLINICAL USE**

Anti-epileptic:
- Adjunctive treatment of partial seizures with or without secondary generalisation
- Neuropathic pain
- Trigeminal neuralgia (unlicensed)

**DOSE IN NORMAL RENAL FUNCTION**

- 300 mg on day 1; 300 mg twice daily on day 2; 300 mg 3 times daily on day 3; then increased according to response to 1.2 g daily (in 3 divided doses)
- If necessary may be further increased in steps of 300 mg daily to a maximum 3.6 g daily
- Usual range 0.9–3.6 g daily in 3 divided doses

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>171.2</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>&lt;3</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>≈100</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.7</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>5–7/52</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

- **GFR (mL/min)**
  - 30–60 Start at low dose and increase dose according to response
  - 15–30 Start at low dose and increase dose according to response
  - <15 300 mg on alternate days or 100 mg at night initially, increase according to tolerability

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Probably dialysed. Dose as in GFR&lt;15 mL/min. See ‘Other Information’</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Loading dose of 300–400 mg in patients who have never received gabapentin. Maintenance dose of 100–300 mg after each HD session and increase according to tolerability. See ‘Other Information’</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Antacids: reduce absorption
- Antidepressants: antagonism of anticonvulsive effect (convulsive threshold lowered)
- Antimalarials: possibly increased risk of convulsions with chloroquine and hydroxychloroquine; anticonvulsant effect antagonised by mefloquine

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**

- **COMMENTS**
  -

**OTHER INFORMATION**

- For neuropathic pain in renal patients do not give loading dose
- Can cause false positive readings with some urinary protein tests
- For neuropathic pain or restless legs in patients with moderate to severe renal impairment, start with 100 mg daily and increase according to response
Galantamine

**CLINICAL USE**
Mild to moderate dementia in Alzheimer's disease

**DOSE IN NORMAL RENAL FUNCTION**
4–12 mg twice daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 368.3 (as hydrobromide)
- % Protein binding: 18
- % Excreted unchanged in urine: 18–22
- Volume of distribution (L/kg): 175 litres
- Half-life – normal/ESRF (hrs): 7–8 (XL: 8–10)/Increased

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function but start with lower doses

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Dialysed. Dose as in GFR<10 mL/min
- HD: Dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: erythromycin increases plasma concentration of galantamine

**ADMINISTRATION**
- **RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
- **COMMENTS**

RETURN TO CONTENTS
Ganciclovir

CLINICAL USE
Antiviral agent:
- Treatment of life- or sight-threatening cytomegalovirus (CMV) in immunocompromised people
- CMV prophylaxis in immunosuppressed patients secondary to organ transplantation

DOSE IN NORMAL RENAL FUNCTION
- Induction/treatment of active CMV disease: 5 mg/kg 12-hourly for 14–21 days
- Maintenance for CMV retinitis: 6 mg/kg daily per day for 5 days per week or 5 mg/kg daily until recovery of adequate immunity

PHARMACOKINETICS
- Molecular weight (daltons) 255.2
- % Protein binding <2
- % Excreted unchanged in urine 84.6–94.6
- Volume of distribution (L/kg) 0.54–0.87
- Half-life – normal/ESRF (hrs) 2.9/28.5

DOSE IN RENAL IMPAIRMENT
GFR (mL/Min)
- 20–50 See ‘Other Information’
- 10–20 See ‘Other Information’
- <10 See ‘Other Information’

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD Dialysed. 1.25 mg/kg every day
- HD Dialysed. 1.25 mg/kg every day, given post dialysis on dialysis days
- HDF/High flux Dialysed. 1.25 mg/kg every day, given post dialysis on dialysis days
- CAV/ VVHD Dialysed. 2.5 mg/kg per day

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Antibacterials: increased risk of convulsions with imipenem-cilastatin
- Antivirals: possibly increased didanosine concentration; avoid with lamivudine; profound myelosuppression with zidovudine – avoid if possible
- Increased risk of myelosuppression with other myelosuppressive drugs
- Mycophenolate: concomitant treatment with ganciclovir and mycophenolate increase plasma levels of both drugs

ADMINISTRATION
RECONSTITUTION
- Reconstitute 1 vial (500 mg) with 10 mL water for injection (50 mg/mL), then transfer dose to 100 mL sodium chloride 0.9%

ROUTE
- IV peripherally in fast-flowing vein or centrally – see below

RATE OF ADMINISTRATION
- Over 1 hour

COMMENTS
- May give 50% dose over 15 minutes after HD in washback (unlicensed)

OTHER INFORMATION
From SPC:
Creatinine Clearance Dose
(mL/min) (mg/kg/hours)
>70 5 mg/kg 12 hourly
50 69 2.5 mg/kg 12 hourly
25 49 2.5 mg/kg 24 hourly
10 24 1.25 mg/kg 24 hourly
<10 1.25 mg/kg 24 hourly, given after haemodialysis on dialysis days

Alternative regimen used by some units:
Creatinine Clearance Dose
(mL/min) (mg/kg/hours)
>50 5 mg/kg 12 hourly
25 50 2.5 mg/kg 12 hourly
10 25 2.5 mg/kg 24 hourly
<10 1.25 mg/kg 24 hourly

- Monitor patient for myelosuppression, particularly in patients receiving prophylactic co-trimoxazole therapy
- Pre-dialysis therapeutic blood levels in range 5–12 mg/L
- Not to be infused in concentrations over 10 mg/mL peripherally
Gemcitabine

**CLINICAL USE**
- Palliative treatment, or first-line treatment with cisplatin, of locally advanced or metastatic non-small cell lung cancer
- Pancreatic and breast cancer
- Bladder cancer in combination with cisplatin

**DOSE IN NORMAL RENAL FUNCTION**
1–1.25 g/m², frequency dependent on chemotherapy regimen; dose reduced according to toxicity

**PHARMACOKINETICS**
- Molecular weight (daltons): 299.7 (as hydrochloride)
- % Protein binding: Negligible
- % Excreted unchanged in urine: <10
- Volume of distribution (L/kg): 12.4 litres/m² (women); 17.5 litres/m² (men)
- Half-life – normal/ESRF (hrs): 42–94 minutes

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Use with caution See ‘Other Information’</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td>Use with caution See ‘Other Information’</td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in GFR</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Likely dialysability. Dose as in GFR &lt;10 mL/min</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR &lt;10 mL/min. Dose after dialysis, and give next dialysis after 48 hours</td>
<td></td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR &lt;10 mL/min. Dose after dialysis, and give next dialysis after 48 hours</td>
<td></td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose as in GFR=10–20 mL/min</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - None known

**ADMINISTRATION**

**RECONSTITUTION**
- Reconstitute with sodium chloride 0.9%, 5 mL to 200 mg vial and 25 mL to 1 g vial
- Can be further diluted in sodium chloride 0.9% if required

**ROUTE**
- IV

**RATE OF ADMINISTRATION**
- 30 minutes

**OTHER INFORMATION**
- Rapidly metabolised by cytidine deaminase in the liver, kidney, blood and other tissues. The active intracellular metabolites have not been detected in plasma or urine. Urinary excretion of parent drug and inactive metabolite (dFdU) accounts for 99%
- Terminal T½ is ~1 hour; this increases if the drug is administered over a longer period
- Causes reversible haematuria with or without proteinuria in about 50% of patients; no evidence for cumulative renal toxicity with repeated dosing of gemcitabine
- Haemolytic uraemic syndrome (HUS) has been reported with a crude incidence rate of 0.015%
- A study looking at the use of gemcitabine 500–1000 mg/m² administered IV on days 1, 8, and 15 every 28 days in patients with renal dysfunction, concluded that this regimen was well tolerated in patients with a GFR as low as 30 mL/min. (Data on file from Eli Lilly)
- Another study in patients with serum creatinine in the range 130–420 µmol/L, at doses of 650 mg/m² – 800 mg/m² weekly for 3 weeks out of a 4 week cycle, found dose limiting toxicities, including neutropenia, fever, raised transaminases and increased serum creatinine. It was concluded that a reduced dose of gemcitabine may be appropriate in patients with established renal impairment. (Egorin MJ, Venook MP, Rosner G, et al. Phase 1 study of gemcitabine (G) in patients with organ dysfunction. Proc Annu Meet Am Soc Clin Oncol. 1998; 17: A719)
Gemfibrozil

**CLINICAL USE**

Hyperlipidaemias of types IIa, IIb, III, IV and V

**DOSE IN NORMAL RENAL FUNCTION**

1.2 g daily, usually in 2 divided doses; range 0.9–1.2 g daily

**PHARMACOKINETICS**

- Molecular weight (daltons): 250.3
- % Protein binding: >97
- % Excreted unchanged in urine: <6
- Volume of distribution (L/kg): 9–13 litres

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Initial dose</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Initially 900 mg daily</td>
<td>Carefully</td>
</tr>
<tr>
<td>10–20</td>
<td>Initially 900 mg daily</td>
<td>Monitor carefully</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Initially 900 mg daily</td>
<td>Monitor carefully</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Not dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Not dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**

- Potentially hazardous drug interactions with other drugs
  - Antibacterials: increased risk of myopathy with daptomycin – try to avoid concomitant use
  - Anticoagulants: enhances effect of coumarins and phenindione; dose of anticoagulant should be reduced by up to 50% and adjusted by monitoring INR
  - Antidiabetics: may improve glucose tolerance and have an additive effect with insulin or sulphonylureas; rosiglitazone concentration increased – possibly reduce rosiglitazone dose; possibly enhanced effect with nateglinide; increased risk of severe hypoglycaemia with repaglinide – avoid concomitant use
  - Ciclosporin: Parke-Davis have one report on file of an interaction with ciclosporin where serum ciclosporin levels were decreased. No effects on muscle were noted
  - Cytotoxics: bexarotene concentration increased – avoid concomitant use
  - Lipid-regulating drugs: increased risk of myopathy in combination with statins and ezetimibe – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**

- Adverse effects have not been reported in patients with renal disease, but such patients should start treatment at 900 mg daily, which may be increased after careful assessment of response and renal function
- Cases of rhabdomyolysis may be increased in those with renal impairment
- Approximately 60–70% is excreted in the urine as both conjugated and unconjugated drug
- Gemfibrozil alone has caused myalgia and myositis, but the effects appear to occur much more frequently and are more severe when a statin is also used. The combination is therefore not recommended
Gentamicin

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
- Once daily dose: 5–7 mg/kg, dose is then adjusted according to levels
- Endocarditis: 1 mg/kg every 8 hours
- Intrathecal: 1–5 mg daily
- PD peritonitis: see local policy

**PHARMACOKINETICS**
- Molecular weight (daltons): 477.6
- % Protein binding: 0–30
- % Excreted unchanged in urine: 90
- Volume of distribution (L/kg): 0.3

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Monitor levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–70</td>
<td>3–5 mg/kg daily</td>
<td>and monitor levels</td>
</tr>
<tr>
<td>10–30</td>
<td>2–3 mg/kg daily</td>
<td>and monitor levels</td>
</tr>
<tr>
<td>5–10</td>
<td>2 mg/kg every 48–72 hours</td>
<td>according to levels</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
<th>Monitor levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Dialysed. CAPD clearance is about 3 mL/min. Dose in GFR=5–10 mL/min. Monitor levels</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR=5–10 mL/min. Give after dialysis</td>
<td></td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR=5–10 mL/min. Give after dialysis</td>
<td></td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose in GFR= 30–70 mL/min according to severity of infection, and measure levels</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Botulinum toxin: neuromuscular block enhanced – risk of toxicity
- Ciclosporin: increased risk of nephrotoxicity
- Cytotoxics: increased risk of nephrotoxicity and possibly of ototoxicity with platinum compounds
- Diuretics: increased risk of ototoxicity with loop diuretics
- Muscle relaxants: effects of non-depolarising muscle relaxants and suxamethonium enhanced
- Parasympathomimetics: antagonism of effect of neostigmine and pyridostigmine
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - IV, IM, IP, intrathecal
- **RATE OF ADMINISTRATION**
  - Bolus IV: over not less than 3 minutes
  - Short infusion: 20–30 minutes
  - Once daily large infusions over 30–60 minutes
- **COMMENTS**
  - Can be added to sodium chloride or glucose 5%

**OTHER INFORMATION**
- Concurrent penicillins may result in subtherapeutic blood levels
- Monitor blood levels. 1 hour post-dose peak levels must not exceed 10 mg/L. Pre-dose trough levels should be less than 2 mg/L
- IP therapy commonly used for PD peritonitis. Dose varies according to local protocol and whether CAPD or APD dialysis. Monitoring of blood levels is advisable, as absorption is increased by inflamed peritoneum
- Potential nephrotoxicity of the drug may worsen residual renal function
- Long-term concurrent use of gentamicin with teicoplanin causes additive ototoxicity
**Glibenclamide**

**CLINICAL USE**
Non-insulin dependent diabetes mellitus

**DOSE IN NORMAL RENAL FUNCTION**
Initially 5 mg daily (elderly patients – 2.5 mg) adjusted according to response; maximum 15 mg daily

**PHARMACOKINETICS**
- Molecular weight: 494 daltons
- % Protein binding: 97%
- % Excreted unchanged in urine: <5
- Volume of distribution (L/kg): 0.125
- Half-life – normal/ESRF (hrs): 2.1–10/

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Initial dose of 1.25–2.5 mg once a day. Monitor closely</td>
</tr>
<tr>
<td>10–20</td>
<td>Initial dose of 1.25–2.5 mg once a day. Monitor closely</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Initial dose of 1.25–2.5 mg once a day. Use cautiously, with continuous monitoring</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapies</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Low dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: effects enhanced by NSAIDs
- Antibacterials: effects enhanced by chloramphenicol, sulphonamides, and trimethoprim; effects possibly enhanced by ciprofloxacin and norfloxacin; effect reduced by rifamycins
- Anticoagulants: effect possibly enhanced by coumarins; also possibly changes to INR
- Antifungals: concentration increased by fluconazole and miconazole and possibly voriconazole
- Bosentan: increased risk of hepatotoxicity – avoid concomitant use
- Ciclosporin: may increase ciclosporin levels
- Sulfinpyrazone: enhanced effect of sulphonylureas

**ADMINISTRATION**

<table>
<thead>
<tr>
<th>RECONSTITUTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>–</td>
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</table>

<table>
<thead>
<tr>
<th>ROUTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>RATE OF ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>–</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Take with breakfast</td>
</tr>
</tbody>
</table>

**OTHER INFORMATION**
- Metabolites of glibenclamide are only weakly hypoglycaemic; this is not clinically relevant where renal and hepatic functions are normal. If creatinine clearance <10 mL/min, accumulation of metabolite and unchanged drug in plasma may cause prolonged hypoglycaemia
- Company information states that use is contraindicated in severe renal impairment
- Compensatory excretion via bile in faeces occurs in renal impairment

RETURN TO CONTENTS
Gliclazide

**CLINICAL USE**
Non-insulin dependent diabetes mellitus

**DOSE IN NORMAL RENAL FUNCTION**
Initially: 40–80mg daily, with breakfast, adjusted according to response up to 160mg as a single dose; higher doses should be divided; maximum 320mg daily

**PHARMACOKINETICS**
Molecular weight (daltons) 323.4
% Protein binding Approx 95%
% Excreted unchanged in urine <5%
Volume of distribution (L/kg) 0.24
Half-life – normal/ESRF (hrs) 10–12 (MR: 12–20)/Prolonged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Initial Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Initially 20–40mg daily. Use with caution and monitor</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Initially 20–40mg daily. Use with caution and monitor</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Initially 20–40mg daily. Use with caution and monitor closely</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Method</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be dialysed. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: effects enhanced by NSAIDs
- Antibacterials: effects enhanced by chloramphenicol, sulphonamides, and trimethoprim; effect reduced by rifamycins
- Anticoagulants: effect possibly enhanced by coumarins; also possibly changes to INR
- Antifungals: concentration increased by fluconazole and miconazole and possibly voriconazole – avoid with miconazole
- Sulfinpyrazone: enhanced effect of sulphonylureas

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- Prolonged

**COMMENTS**
- 

**OTHER INFORMATION**
- Care should be exercised in patients with hepatic and/or renal impairment, and a small starting dose should be used with careful patient monitoring
- Company contraindicates prescribing of Diamicron in severe renal impairment, which they define as creatinine clearance below 40mL/min

**RETURN TO CONTENTS**
**Glimepiride**

**CLINICAL USE**
Non-insulin dependent diabetes mellitus

**DOSE IN NORMAL RENAL FUNCTION**
1–4 mg daily; maximum 6 mg daily taken shortly before or with first main meal

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>490.6</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>&gt;99</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>0 (58–60% as metabolites)</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.113</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>5–9/Prolonged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Start with a low dose and monitor closely</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Renal Replacement Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD/High Flux</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be dialysed. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Analgesics: effects enhanced by NSAIDs
- Antibacterials: effects enhanced by chloramphenicol, sulphonamides, and trimethoprin; effect reduced by rifamycins
- Anticoagulants: effect possibly enhanced by coumarins; also possibly changes to INR
- Antifungals: concentration increased by fluconazole and miconazole and possibly voriconazole
- Sulfinpyrazone: enhanced effect of sulphonylureas

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
-
Glipizide

**CLINICAL USE**
Non-insulin dependent diabetes mellitus

**DOSE IN NORMAL RENAL FUNCTION**
Initially 2.5–5 mg daily, adjusted according to response; maximum 20 mg daily; up to 15 mg may be given as a single dose before breakfast; higher doses divided

**PHARMACOKINETICS**
- Molecular weight: 445.5 (daltons)
- % Protein binding: 98–99%
- % Excreted unchanged in urine: <10
- Volume of distribution (L/kg): 0.13–0.16

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Initially 2.5 mg daily. Titrate according to response</td>
</tr>
<tr>
<td>10–20</td>
<td>Initially 2.5 mg daily. Titrate according to response</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Initially 2.5 mg daily. Titrate according to response</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unlikely to be dialysed. Dose as in GFR=10–20 mL/min</td>
</tr>
<tr>
<td>VVHD</td>
<td>GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: effects enhanced by NSAIDs
- Antibacterials: effects enhanced by chloramphenicol, sulphonamides, and trimethoprim; effect reduced by rifamycins
- Anticoagulants: effect possibly enhanced by coumarins; also possibly changes to INR
- Antifungals: concentration increased by fluconazole, posaconazole and miconazole and possibly voriconazole – avoid with miconazole
- Ciclosporin: may increase ciclosporin levels
- Sulfinpyrazone: enhanced effect of sulphonylureas

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- RATE OF ADMINISTRATION
- COMMENTS

**OTHER INFORMATION**
- Company does not recommend the use of Glibenese in patients with renal insufficiency
- Renal or hepatic insufficiency may cause elevated blood levels of glipizide (increased risk of serious hypoglycaemic reactions)
Glyceryl trinitrate

**CLINICAL USE**

Vasodilator:
- Treatment and prophylaxis of angina, left ventricular failure, hypertension during surgery
- Anal fissures

**DOSE IN NORMAL RENAL FUNCTION**

- S/L tablets: 0.3–1 mg as required
- Buccal: 2–10 mg 3 times daily or when required
- Oral dose depends on preparation used
- Patches: 5–15 mg every 24 hours
- IV infusion: 10–200 mcg/minute; up to 400 mcg/min may be required during surgery
- Anal fissures: 0.2–0.8% ointment every 12 hours

**PHARMACOKINETICS**

- Molecular weight (daltons): 227,1
- % Protein binding: 30–60
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): 2–3
- Half-life – normal/ESRF (hrs): 1–4 minutes/unchanged

**DOSE IN RENAL IMPAIRMENT**

- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Anticoagulants: infusion of GTN reduces anticoagulant effect of heparins
- Antidepressants: tricyclics may reduce effect of sublingual tablets due to dry mouth
- Antimuscarinics: may reduce effect of sublingual tablets due to dry mouth
- Sildenafil: hypotensive effect significantly enhanced – avoid concomitant use
- Tadalafil: hypotensive effect significantly enhanced – avoid concomitant use
- Vardenafil: hypotensive effect significantly enhanced – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**

- –

**ROUTE**

- IV, buccal, S/L, oral, topical

**RATE OF ADMINISTRATION**

- 10–400 mcg/minute (depends on response)

**COMMENTS**

- Compatible with sodium chloride 0.9% and glucose 5%
- Incompatible with polyvinylchloride bags

**OTHER INFORMATION**

- Tolerance may develop; may be minimised by having nitrate-‘free’ periods
- IV infusions contain propylene glycol which can cause lactic acidosis – restrict to using for no more than 3 consecutive days
Granisetron

**CLINICAL USE**
Prevention or treatment of nausea and vomiting induced by cytotoxic chemotherapy, radiotherapy, or postoperative nausea and vomiting (PONV)

**DOSE IN NORMAL RENAL FUNCTION**
- Cytotoxic chemotherapy or radiotherapy:
  - PO: 1–2 mg within 1 hour before start of treatment, then 2 mg daily in 1–2 divided doses during treatment
  - IV: 3 mg before start of cytotoxic therapy; up to 2 additional 3 mg doses can be given within 24 hours no less than 10 minutes apart
  - IV Infusion: 40 mcg/kg (max 3 mg) before treatment; repeated once more if required
- PONV: 1 mg IV before induction of anaesthesia; then 1 mg as required (maximum 2 mg in one day)

**PHARMACOKINETICS**
- Molecular weight (daltons): 312.4 (348.9 as hydrochloride)
- % Protein binding: ≤65
- % Excreted unchanged in urine: <20
- Volume of distribution (L/kg): 3

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/MIN)**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Unknown dialysability. Dose as in normal renal function.
  - Company recommends timing HD for greater than 2 hours after granisetron dose
- HDF/High flux: Unknown dialysability. Dose as in normal renal function.
  - Company recommends timing HD for greater than 2 hours after granisetron dose
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function.

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - None known

**ADMINISTRATION**
- **RECONSTITUTION**
  - **ROUTE**
    - Oral, IV bolus, IV infusion
  - **RATE OF ADMINISTRATION**
    - IV bolus: diluted in 5 mL sodium chloride 0.9% over not less than 30 seconds
    - IV infusion: 20–50 mL over 5 minutes
  - **COMMENTS**
    - Compatible with sodium chloride 0.9%, sodium chloride 0.18% and glucose 4% solution, glucose 5%, Hartmann’s solution, sodium lactate injection, 10% mannitol
    - Maximum administered dose over 24 hours should not exceed 9 mg

**OTHER INFORMATION**
- No special dosing adjustments necessary in patients with renal or hepatic failure
Griseofulvin

**CLINICAL USE**
Antifungal agent:
- Dermatophyte infections of the skin, scalp, hair and nails

**DOSE IN NORMAL RENAL FUNCTION**
500 mg daily, in divided doses or as a single dose, in severe infection dose may be doubled

**PHARMACOKINETICS**
- Molecular weight (daltons): 352.8
- % Protein binding: 84
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): 1.2–1.41

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Not dialysed. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs:
- Anticoagulants: metabolism of coumarins accelerated (reduced anticoagulant effect)
- Ciclosporin: griseofulvin possibly reduces ciclosporin concentration (two reports of such an interaction in literature)
- Oestrogens and progestogens: metabolism of oral contraceptives accelerated (reduced contraceptive effect)

**ADMINISTRATION**
- **RECONSTITUTION**
  - **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**

**OTHER INFORMATION**
- Use with extreme caution in patients with SLE
Guanethidine monosulphate

**CLINICAL USE**
Treatment of hypertensive crisis

**DOSE IN NORMAL RENAL FUNCTION**
10–20 mg, repeated after 3 hours if required

**PHARMACOKINETICS**
- Molecular weight: 296.4 daltons
- % Protein binding: <5
- % Excreted unchanged in urine: 25–60%
- Volume of distribution (L/kg): Large
- Half-life – normal/ESRF (hrs): 120–240/increased

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Give every 24 hours</td>
</tr>
<tr>
<td>10–20</td>
<td>Give every 24 hours</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Give every 24–36 hours; use with caution</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Likely dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Sympathomimetics: hypotensive effect antagonised by ephedrine, isometheptene, metaraminol, methylphenidate, noradrenaline, oxymetazoline, phenylephrine, phenylpropanolamine, pseudoephedrine and xylometazoline

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - IM

**RATE OF ADMINISTRATION**
- **COMMENTS**
- **OTHER INFORMATION**
  - Blood pressure should fall within 30 minutes of dose
Haloperidol

**CLINICAL USE**
- Sedative in severe anxiety
- Intractable hiccup
- Motor tics
- Nausea and vomiting
- Schizophrenia and other psychoses

**DOSE IN NORMAL RENAL FUNCTION**
- Anxiety: 0.5 mg twice daily
- Hiccup: 1.5 mg 3 times daily
- Nausea and vomiting: maximum 10 mg/day in divided doses; SC infusion: 2.5–10 mg daily
- Schizophrenia: Oral: 1.5–5 mg 2–3 times daily, up to 30 mg daily in resistant cases
- IM/IV: 2–10 mg initially then every 4–8 hours; maximum 18 mg daily
- Deep IM: 50–300 mg every 4 weeks; higher doses may sometimes be required
- Motor tics: 0.5–1.5 mg 3 times daily, increased according to response

**PHARMACOKINETICS**
- Molecular weight (daltons) 375.9
- % Protein binding 92
- % Excreted unchanged in urine 1
- Volume of distribution (L/kg) 14–21
- Half-life – normal/ESRF (hrs) 12–38/–

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Dose as in normal renal function</th>
<th>Start with lower doses. For single doses use 100% of normal dose. Accumulation with repeated dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
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<tr>
<td>10–20</td>
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<tr>
<td>&lt;10</td>
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</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapies</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effects
- Analgesics: increased risk of convulsions with tramadol; enhanced hypotensive and sedative effects with opioids; possibly severe drowsiness with indomethacin
- Anti-arrhythmics: increased risk of ventricular arrhythmias with anti-arrhythmics that prolong the QT interval; increased risk of ventricular arrhythmias with amiodarone – avoid concomitant use
- Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin – avoid concomitant use; concentration reduced by rifampicin
- Antidepressants: concentration increased by fluoxetine and venlafaxine; concentration of tricyclics increased
- Anti-epileptics: metabolism increased by carbamazepine, primidone and phenobarbital; lowered seizure threshold
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: avoid concomitant use of depot formulations with clozapine (cannot be withdrawn quickly if neutropenia occurs)
- Antivirals: concentration possibly increased with ritonavir
- Anxiolytics and hypnotics: increased sedative effects; concentration increased by buspirone
- Atomoxetine: increased risk of ventricular arrhythmias
- Lithium: increased risk of extrapyramidal side effects and possibly neurotoxicity
- Pentamidine: increased risk of ventricular arrhythmias
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral, IM or IV (slow bolus)
- **RATE OF ADMINISTRATION**
  - **COMMENTS**
  -


OTHER INFORMATION

- May cause hypotension and excessive sedation
- Increased CNS sensitivity in renally impaired patients – start with small doses; metabolites may accumulate
- Equivalent IV/IM dose = 40% of oral dose
Heparin

**CLINICAL USE**
Anticoagulant

**DOSE IN NORMAL RENAL FUNCTION**
- Treatment of deep vein thrombosis and pulmonary embolism:
  - IV: Loading dose: 5000–10 000 units then a continuous intravenous infusion of 18 units/kg/hour
- Treatment of deep vein thrombosis:
  - SC: 15 000 units every 12 hours, dose is adjusted according to laboratory monitoring
- Prophylaxis: 5000 units every 8–12 hours or according to local protocols

**PHARMACOKINETICS**
- Molecular weight (daltons): 3000–40 000
- % Protein binding: >90
- % Excreted unchanged in urine: 0 (up to 50% after large doses)
- Volume of distribution (L/kg): 0.06–0.1
- Half-life – normal/ESRF (hrs): 1–6/Slightly prolonged (half-life increases with dose)

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Not dialysed. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: increased risk of bleeding with NSAIDs – avoid concomitant use with IV diclofenac; increased risk of haemorrhage with ketorolac – avoid concomitant use
- Nitrates: anticoagulant effect reduced by infusions of glyceryl trinitrate
- Drotrecogin alfa: manufacturer advises to avoid use of high doses of heparin with drotrecogin alfa
- Use with care in patients receiving oral anticoagulants, platelet aggregation inhibitors, aspirin or dextran

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - IV infusion or bolus, SC
- **RATE OF ADMINISTRATION**
  - 18 units/kg/hour, or according to local protocol

**COMMENTS**
- HD
  - Half-life is slightly prolonged in haemodialysis patients after intravenous administration
  - Also used for the maintenance of extracorporeal circuits in cardiopulmonary bypass and haemodialysis
  - 1 mg protamine is required to neutralise 100 IU heparin; give slowly over 10 minutes, and do not exceed a total dose of 50 mg
  - To reduce or prevent fibrin formation in patients on PD, heparin may be added to PD fluid at a concentration of 1000 IU/L

**RETURN TO CONTENTS**
Hydralazine hydrochloride

**CLINICAL USE**
Vasodilator antihypertensive agent

**DOSE IN NORMAL RENAL FUNCTION**
- Oral:
  - Hypertension: 25–50 mg twice daily; maximum daily dose 100 mg in women and slow acetylators, 200 mg in fast acetylators
  - Heart failure: 25–75 mg 3–4 times daily
- IV: slow IV injection: 5–10 mg over 20 minutes; repeat after 20–30 minutes if necessary
- Infusion: 200–300 micrograms/minute initially, reducing to 50–150 micrograms/minute

**PHARMACOKINETICS**
- Molecular weight (daltons): 196.6
- % Protein binding: 87
- % Excreted unchanged in urine: 2–14
- Volume of distribution (L/kg): 0.5–0.9
- Half-life – normal/ESRF (hrs): 2–4/16

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Start at low dose and adjust in accordance with response
  - 10–20: Start at low dose and adjust in accordance with response
  - <10: Start at low dose and adjust in accordance with response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Not dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Not dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: increased hypotensive effects

**ADMINISTRATION**
- RECONSTITUTION
  - 20 mg with 1 mL water for injection then dilute with 10 mL sodium chloride 0.9% for IV injection or 500 mL sodium chloride 0.9% for IV infusion
- ROUTE
  - Oral, IV peripherally
- RATE OF ADMINISTRATION
  - As above
- COMMENTS
  - Minimum volume of 60 mg in 60 mL. (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006)

**OTHER INFORMATION**
- Avoid long-term use in severe renal insufficiency and dialysis patients, due to accumulation of metabolites
Hydrocortisone acetate

**CLINICAL USE**
Corticosteroid:
- Local inflammation of joints and soft tissue

**DOSE IN NORMAL RENAL FUNCTION**
5–50 mg according to joint size

**PHARMACOKINETICS**
- Molecular weight: 404.5 daltons
- % Protein binding: >90
- % Excreted unchanged in urine: Minimal
- Volume of distribution: 0.4–0.7 L/kg
- Half-life – normal/ESRF (hrs): Approx 100 minutes/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
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<tr>
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<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapies</th>
<th>Dose as in normal renal function</th>
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<tbody>
<tr>
<td>CAPD</td>
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</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: metabolism accelerated by rifampicin; metabolism possibly inhibited by erythromycin
- Anticoagulants: efficacy of coumarins may be altered
- Anti-epileptics: metabolism accelerated by carbamazepine, barbiturates, phenytoin and primidone
- Antifungals: increased risk of hypokalaemia with amphotericin – avoid concomitant use; metabolism possibly inhibited by itraconazole and ketoconazole
- Antivirals: concentration possibly increased by ritonavir
- Ciclosporin: rare reports of convulsions in patients on ciclosporin and high-dose corticosteroids
- Cytotoxics: increased risk of haematological toxicity with methotrexate
- Diuretics: enhanced hypokalaemic effects of acetazolamide, loop diuretics and thiazide diuretics
- Vaccines: high dose corticosteroids can impair immune response to vaccines – avoid concomitant use with live vaccines

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Intra-articular, periarticular

**RATE OF ADMINISTRATION**
- COMMENTS
  - OTHER INFORMATION

- Used for its local effects. Systemic absorption occurs slowly
Hydrocortisone sodium succinate

**CLINICAL USE**
Corticosteroid:
- Anti-inflammatory agent in respiratory, GI, endocrine disorders, and allergic states
- Shock

**DOSE IN NORMAL RENAL FUNCTION**
**Oral**: 20–30 mg in divided doses for replacement
**IV/IM**: 100–500 mg, 3–4 times in 24 hours, or as required

**PHARMACOKINETICS**
- Molecular weight: 484.5 (486.4 as sodium phosphate)
- % Protein binding: >90
- % Excreted: Minimal
- Volume of distribution: 0.4–0.7 (L/kg)
- Half-life – normal/ESRF (hrs): Approx 100 minutes/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/ MIN)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
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<tr>
<td>10–20</td>
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<tr>
<td>&lt;10</td>
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</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>CAPD</th>
<th>Unlikely to be dialysed. Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High Flux</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
- Antibacterials: metabolism accelerated by rifampicin; metabolism possibly inhibited by erythromycin
- Anticoagulants: efficacy of coumarins may be altered
- Anti-epileptics: metabolism accelerated by carbamazepine, barbiturates, phenytoin and primidone
- Antifungals: increased risk of hypokalaemia with amphotericin – avoid concomitant use; metabolism possibly inhibited by itraconazole and ketoconazole
- Antivirals: concentration possibly increased by ritonavir
- Ciclosporin: rare reports of convulsions in patients on ciclosporin and high-dose corticosteroids
- Cytotoxics: increased risk of haematological toxicity with methotrexate
- Diuretics: enhanced hypokalaemic effects of acetazolamide, loop diuretics and thiazide diuretics
- Vaccines: high dose corticosteroids can impair immune response to vaccines – avoid concomitant use with live vaccines

**ADMINISTRATION**

**RECONSTITUTION**
- IV injection, IM injection: add 2 mL of sterile water for injection
- IV infusion: add not more than 2 mL water for injection, then add to 100–1000 mL (not less than 100 mL) glucose 5% or sodium chloride 0.9%

**ROUTE**
- IV injection, IV infusion, IM

**RATE OF ADMINISTRATION**
- IV bolus: 2–3 minutes

**COMMENTS**
- Minimum volume 100 mg in 50 mL. (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006)

**OTHER INFORMATION**
- Non-plasma protein bound hydrocortisone is removed by HD
- One study has shown that plasma clearance rates of hydrocortisone during haemodialysis were 30–63% higher than after dialysis. No recommendations exist to indicate dosing should be altered to take account of this
Hydromorphone hydrochloride

**CLINICAL USE**
Relief of severe cancer pain

**DOSE IN NORMAL RENAL FUNCTION**
1.3 mg 4 hourly, increasing dose as required
SR: 4 mg 12 hourly, increasing dose as required

**PHARMACOKINETICS**
- Molecular weight (daltons): 321.8
- % Protein binding: 7.1
- % Excreted unchanged in urine: 6
- Volume of distribution (L/kg): 24.4 litres
- Half-life – normal/ESRF (hrs): 2.5/--

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/min)**
  - 20–50: Dose as in normal renal function
  - 10–20: Reduce dose – start with lowest dose and titrate according to response
  - <10: Reduce dose – start with lowest dose and titrate according to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**
  - Unknown dialysability. Dose as in GFR<10mL/min
- **HD**
  - Unknown dialysability. Dose as in GFR<10mL/min
- **HDF/High flux**
  - Unknown dialysability. Dose as in GFR<10mL/min
- **CAV/VVHD**
  - Unknown dialysability. Dose as in GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Alcohol: can cause dose dumping with sustained release preparations
- Antidepressants: possible CNS excitation or depression with MAOIs – avoid concomitant use and for 2 weeks after stopping MAOI; possible CNS excitation or depression with moclobemide; increased sedative effects with tricyclics
- Antivirals: concentration possibly increased by ritonavir
- Sodium oxybate: enhanced effect of sodium oxybate – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
- --

**OTHER INFORMATION**
- 1.3 mg of hydromorphone is equivalent to 10 mg oral morphine
- Metabolised to mainly hydromorphone-3-glucuronide and some hydromorphone-6-glucuronide, which also have opioid activity, and which accumulate in renal failure. May cause neuroexcitation and cognitive impairment

RETURN TO CONTENTS
Hydroxycarbamide (hydroxyurea)

**CLINICAL USE**
Antineoplastic agent

**DOSE IN NORMAL RENAL FUNCTION**
15–40 mg/kg daily
Consult local protocol

**PHARMACOKINETICS**
Molecular weight (daltons) 76.05
% Protein binding 75–80
% Excreted unchanged in urine 9–95
Volume of distribution (L/kg) 0.5
Half-life – normal/ESRF (hrs) 2–6/

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as a % of normal dose and titrate to response</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 60</td>
<td>85%</td>
</tr>
<tr>
<td>45–60</td>
<td>80%</td>
</tr>
<tr>
<td>30–45</td>
<td>75%</td>
</tr>
<tr>
<td>10–30</td>
<td>50%</td>
</tr>
<tr>
<td>&lt; 10</td>
<td>20%</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**
  Likely dialysability. Dose as in GFR<10 mL/min
- **HD**
  Likely dialysability. Dose as in GFR<10 mL/min
- **HDF/High flux**
  Likely dialysability. Dose as in GFR<10 mL/min
- **CAV/VVHD**
  Likely dialysability. Dose as in GFR=10–30 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antipsychotics: avoid concomitant use with clozapine, increased risk of agranulocytosis
- Antivirals: increased toxicity with didanosine and stavudine – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
-

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
-

**COMMENTS**
-

**OTHER INFORMATION**
- Full blood count, renal and hepatic function should be monitored repeatedly during treatment
- Dosage should be based on the patient’s actual or ideal weight, whichever is less
- Hydroxyurea has been associated with impairment of renal tubular function and accompanied by elevation in serum uric acid, BUN, and creatinine levels
- The following formula can be used to determine the fraction of normal dose used for renally impaired patients:
  \[ \text{Fraction of normal dose} = \left( \frac{f}{k_f - 1} \right) + 1 \]
  \(f = \text{fraction of the original dose excreted as active or toxic moiety} (f = 0.35 \text{ for hydroxyurea})\)
  \(k_f = \text{patient's creatinine clearance (mL/min)} \div 120 \text{ mL/minute} \)
- Administer with caution to patients with marked renal dysfunction; such patients may rapidly develop visual and auditory hallucinations and significant haematologic toxicity
- After oral administration, hydroxyurea is readily absorbed from the GI tract and peak plasma concentrations are reached within 2 hrs. 50% is hepatically metabolised; 50% of a dose recovered in urine within 12 hours, mainly as intact drug; remainder excreted as carbon dioxide via the lungs or via the urine as urea

References:
Hydroxychloroquine sulphate

**CLINICAL USE**
- Rheumatoid arthritis
- Systemic lupus erythematosus
- Dermatological conditions caused or aggravated by sunlight
- Malaria (unlicensed in UK)

**DOSE IN NORMAL RENAL FUNCTION**
200–400 mg daily in divided doses; maximum of 6.5 mg/kg/day
Prophylaxis of malaria: 400 mg weekly

**PHARMACOKINETICS**
- Molecular weight 434
daltons
- % Protein binding 30–40%
- % Excreted unchanged in urine 3
- Volume of distribution (L/kg) Large
- Half-life – normal/ESRF (hrs) 5.9–504/

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>Maximum 75% of dose</td>
</tr>
<tr>
<td>10–30</td>
<td>25–50% of dose (equivalent of 150 mg daily)</td>
</tr>
<tr>
<td>&lt;10</td>
<td>25–50% of dose (equivalent of 50–100 mg daily) – use with caution</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10mL/min
- HD: Not dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10mL/min
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–30 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anti-arrhythmics: increased risk of ventricular arrhythmias with amiodarone – avoid concomitant use
- Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin – avoid concomitant use
- Anti-epileptics: antagonism of anticonvulsant effect
- Antimalarials: increased risk of convulsions with mefloquine; avoid concomitant use with artemether/lumefantrine
- Ciclosporin: increased ciclosporin concentration (increased risk of toxicity)
- Digoxin: possibly increased concentration of digoxin
- Lanthanum: absorption possibly reduced by lanthanum – give at least 2 hours apart

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- Take with a meal or a glass of milk
- Excretory patterns are not well characterised, but hydroxychloroquine and its metabolites are slowly excreted via the kidneys
- Attempt to avoid prolonged use in renal failure
- In renal insufficiency, need more than annual eye examinations
- Doses from Seyffart, probably not actually practical to give reduced dose so try giving longer dose intervals

RETURN TO CONTENTS
Hydroxyzine hydrochloride

**CLINICAL USE**

Antihistamine:
- Pruritus
- Anxiety (short term)

**DOSE IN NORMAL RENAL FUNCTION**

- Pruritus: 25 mg at night increasing as necessary to 3–4 times a day
- Anxiety: 50–100 mg 4 times daily

**PHARMACOKINETICS**

Molecular weight (daltons) 447.8
% Protein binding No data
% Excreted unchanged in urine 0
Volume of distribution (L/kg) 19.5
Half-life – normal/ESRF (hrs) 20/–

**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**

- 20–50 Dose as in normal renal function
- 10–20 Start with small dose, e.g. 25 mg at night and increase to 2–3 times a day if necessary
- <10 Start with small dose, e.g. 25 mg at night and increase to 2–3 times a day if necessary

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD Not dialysed. Dose as in GFR<10 mL/min
- HD Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux Not dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD Not dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- COMMENTS
- 

**OTHER INFORMATION**

- Increased possibility of side effects, particularly drowsiness
**Hyoscine butylbromide**

**CLINICAL USE**
Symptomatic relief of gastrointestinal or genitourinary disorders due to smooth muscle spasm

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: 20 mg 4 times a day
- Irritable bowel syndrome: 10 mg 3 times a day, increasing to 20 mg 4 times a day if required
- IV/IM: 20 mg repeated after 30 minutes if required; maximum 100 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 440.4
- % Protein binding: 10
- % Excreted unchanged in urine: 1–2
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 8

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Dialysed. Dose as in normal renal function
- HD: Dialysed. Dose as in normal renal function
- HDF/High flux: Dialysed. Dose as in normal renal function
- CAV/VVHD: Not Dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
- Oral, IV, IM

**RATE OF ADMINISTRATION**
- COMMENTS
- 

**OTHER INFORMATION**
- Only 2–8% of oral dose is absorbed
Hyoscine hydrobromide

**CLINICAL USE**
- Motion sickness
- Premedication
- Palliative care

**DOSE IN NORMAL RENAL FUNCTION**
- Motion sickness:
  - Oral: 300 mcg 30 minutes before start of journey then 300 mcg every 6 hours if required; maximum 3 doses in 24 hours
  - Topical: 1 patch 5–6 hours before journey, replace after 72 hours
- Premedication (SC/IM): 200–600 mcg 30–60 minutes before anaesthesia
- SC Infusions: Excessive secretions (patch can also be used for this indication): 0.6–2.4 mg over 24 hours
- Bowel colic: 20–60 mg over 24 hours

**PHARMACOKINETICS**
- Molecular weight (daltons) 438.3
- % Protein binding 10
- % Excreted unchanged in urine 2 (1 – oral, 34 – transdermal)
- Volume of distribution (L/kg) No data
- Half-life – normal/ESRF (hrs) 8

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Dialysed. Dose as in normal renal function
- HD Dialysed. Dose as in normal renal function
- HDF/High flux Dialysed. Dose as in normal renal function
- CAV/ VVHD Not Dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral, topical, SC, IM

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- Only 2–8% of oral dose is absorbed
Ibandronic acid

**CLINICAL USE**
- Reduction of bone damage in bone metastases in breast cancer
- Hypercalcaemia of malignancy
- Post-menopausal osteoporosis

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: 50 mg daily
- IV: 6 mg every 3–4 weeks
- Hypercalcaemia of malignancy: 2–4 mg as a single dose, repeated according to serum calcium level
- Post-menopausal osteoporosis: 150 mg monthly (oral), 3 mg every 3 months (IV bolus)

**PHARMACOKINETICS**
- Molecular weight 319.2 (Ibandronate Na 359.2)
- % Protein binding 87
- % Excreted unchanged in urine 50–60
- Volume of distribution 90 litres
- Half-life – normal/ESRF (hrs) 10–72/Insignificantly increased

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 30–50: Dose as in normal renal function. See ‘Other Information’
  - 10–30: Oral: 50 mg weekly, IV infusion: 2 mg every 3–4 weeks. See ‘Other Information’
  - <10: Oral: 50 mg weekly, IV infusion: 2 mg every 3–4 weeks. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR<10 mL/min
- HD: Dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–30 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral, IV infusion, IV bolus

**RATE OF ADMINISTRATION**
- Infusion: over 15 minutes – 2 hours (depends on indication and renal function)
- IV bolus: over 15–30 seconds

**COMMENTS**
- Add dose to 100–500 mL glucose 5% or sodium chloride 0.9% (depends on indication and renal function)

**OTHER INFORMATION**
- Oral bioavailability <1%
- Swallow tablets whole with a glass of water on an empty stomach, at least 30 minutes before breakfast and any other oral medication
- The patient should stand or sit upright for at least 60 minutes after taking tablets
- Don’t give infusion over 15 minutes if creatinine clearance <50 mL/min; give in 500 mL over 1 hour
- Bolus dose is contraindicated if GFR<30 mL/min due to lack of studies
- One study used a dose of 6 mg over 30 minutes in various degrees of renal impairment with no deterioration in renal function.\(^1\)
- Clearance is reduced in severe renal impairment
- Due to the high bone-binding effect with ibandronic acid a dose of 2 mg monthly in haemodialysis patients is equivalent to a dose of 4–5 mg in patients with normal renal function.\(^2\)
- May cause osteonecrosis of the jaw similar to other bisphosphonates

References:
IBANDRONIC ACID


Ibuprofen

**CLINICAL USE**
NSAID and analgesic

**DOSE IN NORMAL RENAL FUNCTION**
Initially: 1.2–1.8 g daily in 3–4 divided doses, after food. Maximum 2.4 g daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 206.3
- % Protein binding: 90–99
- % Excreted unchanged in urine: 1
- Volume of distribution (L/kg): 0.14
- Half-life – normal/ESRF (hrs): 2/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function, but avoid if possible</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**: Not dialysed. Dose as in normal renal function. See ‘Other Information’
- **HD**: Not dialysed. Dose as in normal renal function. See ‘Other Information’
- **HDF/High flux**: Not dialysed. Dose as in normal renal function. See ‘Other Information’
- **CAV/VVHD**: Not dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs

- ACE inhibitors and angiotensin-II antagonists: antagonism of hypotensive effect; increased risk of nephrotoxicity and hyperkalaemia
- Analgesics: avoid concomitant use of 2 or more NSAIDs, including aspirin (increased side effects); avoid with ketorolac (increased risk of side effects and haemorrhage); possibly reduced antiplatelet effect with aspirin

<table>
<thead>
<tr>
<th>NSAID and analgesic</th>
<th>Antiplatelet agents: possibly reduced antiplatelet effect with aspirin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticoagulants: effects of coumarins enhanced; possibly increased risk of bleeding with heparins and coumarins</td>
<td></td>
</tr>
<tr>
<td>Antidepressants: increased risk of bleeding with SSRIs and venlafaxine</td>
<td></td>
</tr>
<tr>
<td>Anti-diabetic agents: effects of sulphonylureas enhanced</td>
<td></td>
</tr>
<tr>
<td>Anti-epileptics: possibly increased phenytoin concentration</td>
<td></td>
</tr>
<tr>
<td>Antivirals: increased risk of haematological toxicity with zidovudine; concentration possibly increased by ritonavir</td>
<td></td>
</tr>
<tr>
<td>Ciclosporin: may potentiate nephrotoxicity; hyperkalaemia with potassium-sparing diuretics</td>
<td></td>
</tr>
<tr>
<td>Diuretics: increased risk of nephrotoxicity; antagonism of diuretic effect; hyperkalaemia with potassium-sparing diuretics</td>
<td></td>
</tr>
<tr>
<td>Lithium: excretion decreased</td>
<td></td>
</tr>
<tr>
<td>Pentoxifylline: increased risk of bleeding</td>
<td></td>
</tr>
<tr>
<td>Tacrolimus: increased risk of nephrotoxicity</td>
<td></td>
</tr>
</tbody>
</table>

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**

- Inhibition of renal prostaglandin synthesis by NSAIDs may interfere with renal function, especially in the presence of existing renal disease – avoid if possible; if not, check serum creatinine 48–72 hours after starting NSAID – if raised, discontinue NSAID therapy
- Use normal doses in patients with ERF on dialysis if they do not pass any urine
- Use with caution in renal transplant recipients – can reduce intrarenal autacoid synthesis
Idarubicin hydrochloride

**CLINICAL USE**

Antineoplastic agent:
- Acute non-lymphoblastic leukaemia (ANLL)
- 2nd line for acute lymphoblastic leukaemia (ALL), breast cancer
- With other cytotoxic agents in combination chemotherapy regimens

**DOSE IN NORMAL RENAL FUNCTION**

- **IV:**
  - ANLL: 12 mg/m² daily for 3 days in combination with cytarabine, or 8 mg/m² daily for 5 days with or without combination therapy
  - ALL: 12 mg/m² daily for 3 days
- **Oral:**
  - ANLL: 30 mg/m² daily for 3 days as a single agent, or 15–30 mg/m² daily for 3 days in combination with other anti-leukaemic agents
- Breast cancer: 45 mg/m² given either as a single dose or divided over 3 consecutive days every 3–4 weeks
- Maximum cumulative dose is 400 mg/m² daily
- Or see local protocol

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAP**
  - Not dialysed. Dose as in GFR<10 mL/min
- **HD**
  - Not dialysed. Dose as in GFR<10 mL/min
- **HDF/High flux**
  - Unknown dialysability. Dose as in GFR<10 mL/min
- **CAV/VVHD**
  - GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Other myelosuppressant medication and radiotherapy: increased risk of myelosuppression

**ADMINISTRATION**

**RECONSTITUTION**
- 5 mL water for injection per 5 mg

**ROUTE**
- IV, oral, intravesical

**RATE OF ADMINISTRATION**
- Give via the tubing of a fast running intravenous infusion of sodium chloride 0.9% or glucose 5%, over 5–10 minutes

**COMMENTS**
- Incompatible with alkaline solutions and heparin
- Reconstituted solution is physically and chemically stable for 7 days at 2–8°C and 72 hours at room temperature
- Does not contain any antibacterial preservative so maximum recommended stability is 24 hours

**OTHER INFORMATION**
- May cause the urine to become red for 1–2 days after administration
- Metabolised to an active metabolite, idarubicinol, which has a half-life of 33–60 hours (oral), 41–69 (IV). It is eliminated by renal and hepatobiliary excretion
Oral bioavailability is 18–39%, 29–58% for idarubicinol
17% (IV)/8% (oral) is recovered in the faeces over 5 days and 16% (IV)/5% (oral) is recovered in the urine over 4 days
A phase II study instilled 6.25–12.5 mg of idarubicin diluted in 45 mL of sodium chloride 0.9% (0.125–0.25 mg/mL) into the bladder of patients with resected recurrent bladder cancer although it may not be any more effective than doxorubicin or epirubicin and toxicity may limit its use. (Boccardo F, Cannata D, Cussotto M, et al. Intravesical idarubicin: a dose-finding study. Cancer Chemother Pharmacol. 1996; 38(1): 102-5)
Ifosfamide

CLINICAL USE
Antineoplastic agent:
- Treatment of solid tumours, lymphomas and soft tissue sarcoma

DOSE IN NORMAL RENAL FUNCTION
- Usual total dose for each course is either 8–12 g/m², equally divided as single daily doses over 3–5 days, or 5–6 g/m² (maximum 10 g) given as a 24 hour infusion
- Or according to local protocol

PHARMACOKINETICS
Molecular weight (daltons) 261.1
% Protein binding 0
% Excreted unchanged in urine 12–18
Volume of distribution (L/kg) 0.4–0.64
Half-life – normal/ESRF (hrs) 4–8/

DOSE IN RENAL IMPAIRMENT
GFR (mL/Min)
>60 80% of normal dose
30–60 80% of normal dose
15–30 80% of normal dose
<15 60% of normal dose

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Dialysed. Dose as in GFR<15 mL/ min. Following dose, do not perform CAPD exchange for 12 hours
HD Dialysed. Dose as in GFR<15 mL/ min. Dose at minimum of 12 hours before next HD session
HDF/High flux Dialysed. Dose as in GFR<15 mL/ min. Dose at minimum of 12 hours before next HDF session
CAV/VVHD Dialysed. Dose as in GFR=15–30 mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Anticoagulants: possibly enhanced effect of coumarins
- Antipsychotics: avoid concomitant use with clozapine (increased risk of agranulocytosis)

ADMINISTRATION

RECONSTITUTION
- Reconstitute 1 g vial with 12.5 mL water for injection. Reconstitute 2 g vial with 25 mL water for injection. The resultant solution of 8% ifosfamide should NOT be injected directly into the vein

ROUTE
- IV injection: dilute to less than a 4% solution
- IV infusion: dilute as detailed below

RATE OF ADMINISTRATION
- IV infusion:
  - Infuse in glucose 5% or sodium chloride 0.9% over 30–120 minutes, or
  - Inject directly into a fast running infusion, or
  - Made up in 3 L of glucose 5% or sodium chloride 0.9%; each litre should be given over 8 hours

COMMENTS
- Nephrotoxicity may occur with oliguria, raised uric acid, increased BUN and serum creatinine, and decreased creatinine clearance
- Ifosfamide is known to be more nephrotoxic than cyclophosphamide; hence greater caution is advised
- SPC contraindicates the use of ifosfamide if serum creatinine >120 µmol/L
- If patient is anuric and on dialysis, neither the ifosfamide nor its metabolites nor mesna should appear in the urinary tract. The use of mesna may therefore be unnecessary, although this would be a clinical decision
- If the patient is passing urine, mesna should be given to prevent urothelial toxicity
- Ifosfamide is a prodrug – converted by hepatic microsomal enzymes to alkylating metabolites. Excretion is primarily renal. Approximately 80% of dose is excreted as parent compound

RETURN TO CONTENTS
Doses from Kintzel PE, Dorr RT.

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 60</td>
<td>80% of dose</td>
</tr>
<tr>
<td>45–60</td>
<td>75% of dose</td>
</tr>
<tr>
<td>30–45</td>
<td>70% of dose</td>
</tr>
</tbody>
</table>

References:
Iloprost

**CLINICAL USE**
Prostacyclin analogue:
- Treatment of pulmonary hypertension
- Relief of pain, promotion of ulcer-healing and limb salvage in patients with severe peripheral arterial ischaemia (unlicensed product)

**DOSE IN NORMAL RENAL FUNCTION**
- Pulmonary hypertension:
  - Nebulised: 2.5–5 mcg per inhalation session 6 to 9 times per day
  - IV: Usually 1–8 ng/kg/min, but can use higher doses (up to 25 ng/kg/min) according to response
- Severe peripheral arterial ischaemia:
  - Dose is adjusted according to individual tolerability within the range of 0.5–2 ng/kg/min over 6 hours daily

**PHARMACOKINETICS**
- Molecular weight (daltons) 360.5
- % Protein binding ≈60
- % Excreted unchanged in urine <5
- Volume of distribution (L/kg) 0.6–0.8
- Half-life – normal/ESRF (hrs) 0.3–0.5/Unchanged

**DOSE IN RENAL IMPAIRMENT**
GFR (mL/MIN)
- 20–50  Dose as in normal renal function
- 10–20  Dose as in normal renal function
- <10   Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD  Unknown dialysability. Dose as in normal renal function
- HD  Unknown dialysability. Dose as in normal renal function
- HDF/High flux  Unknown dialysability. Dose as in normal renal function
- CAV/ VVHD  Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: enhanced anticoagulant effect and increased risk of bleeding with heparin, coumarins and phenindione, as iloprost inhibits platelet aggregation
- Increased risk of bleeding with NSAIDs, aspirin, clopidogrel, eptifibatide and tirofiban

**ADMINISTRATION**

**RECONSTITUTION**
- Dilute 0.1 mg with 500 mL sodium chloride 0.9% or glucose 5%. Final concentration = 0.2 micrograms iloprost/mL

**ROUTE**
- Nebulised, IV infusion via peripheral vein or central venous catheter

**RATE OF ADMINISTRATION**
- Infuse 0.1 mg over 6 hours daily (see below)

**COMMENTS**
- Treatment should be started at an infusion rate of 10 mL/hour for 30 minutes, which corresponds to a dose of 0.5 nanograms/kg/minute for a patient of 65 kg
- Then increase dose in steps of 10 mL/hour every 30 minutes up to a rate of 40 mL/hour (50 mL/hour if patient's body weight is more than 75 kg)
- If side effects occur (e.g. headache, nausea, or an undesired drop in BP), infusion rate should be reduced until the tolerable dose is found; if side effects are severe, infusion should be interrupted
- For rest of the treatment period, continue with dose found to be tolerated in the first 2–3 days

**OTHER INFORMATION**
- BP and heart rate must be measured at the start of the infusion and after every increase in dose
- Duration of treatment is up to 4 weeks. Shorter treatment periods (3–5 days) are often sufficient in Raynaud’s phenomenon
- Iloprost infusions can also be used to control blood pressure during a scleroderma hypertensive crisis
- For fluid-restricted patients, dilute 0.1 mg iloprost with 50 mL sodium chloride 0.9%, and run at a rate of 1–4 mL/hour
- Toxic by inhalation, contact with skin, and if swallowed
Imatinib

**CLINICAL USE**
Antineoplastic agent

**DOSE IN NORMAL RENAL FUNCTION**
400–600 mg daily, increasing to a maximum of 400 mg twice daily

**PHARMACOKINETICS**
- Molecular weight: 589.7 (as mesilate)
- % Protein binding: 95
- % Excreted unchanged in urine: 5
- Volume of distribution: No data
- Half-life – normal/ESRF (hrs): 18/Unknown

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/MIN)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function. See ‘Other Information’
  - <10: Dose as in normal renal function. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in GFR<10mL/min
- HD: Unlikely to be dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Unlikely to be dialysed. Dose as in GFR<10mL/min
- CAV/VVHD: GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: concentration reduced by rifampicin – avoid concomitant use
- Anticoagulants: enhanced anticoagulant effect of warfarin

- Antidepressants: concentration reduced by St Johnswort
- Anti-epileptics: concentration reduced by phenytoin – avoid concomitant use; absorption of phenytoin possibly reduced
- Antipsychotics: avoid concomitant use with clozapine, (increased risk of agranulocytosis)
- Ciclosporin: may increase ciclosporin levels
- Tacrolimus: may increase tacrolimus levels

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**
- Associated with oedema and superficial fluid retention in 50–70% cases. Probability is increased in patients receiving higher doses, age >65 years, and those with a prior history of cardiac disease. Severe fluid retention (e.g. pleural effusion, pericardial effusion, pulmonary oedema and ascites) has been reported in up to 16% of patients. Can be managed by diuretic therapy, and dose reduction or interruption of imatinib therapy
- Severe elevation of serum creatinine has been observed in approximately 1% of patients
- Oral bioavailability is 98%
- Main circulating metabolite is N-demethylated piperazine derivative, and has similar potency to the parent compound. Catalysed by cytochrome P450 CYP3A4. Mainly hepatically metabolised with 68% excreted in faeces and 13% in urine in 7 days. Half-life is 40 hours in normal renal function
Imidapril hydrochloride

**CLINICAL USE**
Angiotensin-converting enzyme inhibitor:
- Hypertension

**DOSE IN NORMAL RENAL FUNCTION**
2.5–20 mg once daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 441.9
- % Protein binding: 85
- % Excreted unchanged in urine: 9 (as imidaprilat)
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 2/Increased (>24 hours as imidaprilat)

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Initially 2.5 mg daily and adjust according to response</td>
</tr>
<tr>
<td>10–20</td>
<td>Initially 2.5 mg daily and adjust according to response</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Initially 2.5 mg daily and adjust according to response</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Probably dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Probably dialysed. Dose as in GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs

- Anaesthetics: enhanced hypotensive effect
- Analgesics: antagonism of hypotensive effect and increased risk of renal impairment with NSAIDs; hyperkalaemia with ketorolac and other NSAIDs
- Ciclosporin: increased risk of hyperkalaemia and nephrotoxicity
- Diuretics: enhanced hypotensive effect; hyperkalaemia with potassium-sparing diuretics
- Epoetin: increased risk of hyperkalaemia; antagonism of hypotensive effect
- Lithium: reduced excretion, possibility of enhanced lithium toxicity
- Potassium salts: increased risk of hyperkalaemia
- Tacrolimus: increased risk of hyperkalaemia and nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**

- Imidapril is a prodrug, rapidly converted to the active imidaprilat
- Hyperkalaemia and other side effects are more common in patients with impaired renal function
- Close monitoring of renal function during therapy is necessary in those with renal insufficiency
- Renal failure has been reported in association with ACE inhibitors with renal artery stenosis, post renal transplant or congestive heart failure
- High incidence of anaphylactoid reactions have been reported in patients dialysed with high-flux polyacrylonitrile membranes and treated concomitantly with an ACE inhibitor – combination should therefore be avoided
Imipramine hydrochloride

CLINICAL USE
Tricyclic antidepressant

DOSE IN NORMAL RENAL FUNCTION
25 mg up to 3 times daily increasing up to 150–200 mg daily; maximum 300 mg in hospital patients

PHARMACOKINETICS
Molecular weight (daltons) 316.9
% Protein binding 95
% Excreted unchanged in urine 5
Volume of distribution (L/kg) 31
Half-life – normal/ESRF (hrs) 9–28/–

DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Not dialysed. Dose as in normal renal function
HD Not dialysed. Dose as in normal renal function
HDF/High flux Not dialysed. Dose as in normal renal function
CAV/VVHD Not dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Alcohol: increased sedative effect
- Analgesics: increased risk of CNS toxicity with tramadol; possibly increased risk of side effects with nefopam; possibly increased sedative effects with opioids
- Anti-arrhythmics: increased risk of ventricular arrhythmias with amiodarone – avoid concomitant use; increased risk of ventricular arrhythmias with drugs that prolong the QT interval; increased risk of arrhythmias with propafenone
- Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin – avoid concomitant use; concentration reduced by rifampicin
- Anticoagulants: may alter anticoagulant effect of coumarins
- Antidepressants: enhanced CNS excitation and hypertension with MAOIs and moclobemide – avoid concomitant use; concentration possibly increased with SSRIs
- Anti-epileptics: convulsive threshold lowered; concentration reduced by carbamazepine, primidone, barbiturates and possibly phenytoin
- Antimalaria: avoid concomitant use with artemether/lumeferantrine
- Antipsychotics: increased risk of ventricular arrhythmias especially with pimozide; increased antimuscarinic effects with clozapine and phenothiazines; concentration increased by antipsychotics
- Anti-arrhythmics: convulsive threshold lowered; concentration reduced by carbamazepine, primidone, barbiturates and possibly phenytoin
- Antihypertensives: hypertensive effect; increased risk of hypertension on clonidine withdrawal
- Atomoxetine: increased risk of ventricular arrhythmias and possibly convulsions
- Beta-blockers: increased risk of ventricular arrhythmias with sotalol; concentration increased by labetalol and propranolol
- Clonidine: tricyclics antagonise hypotensive effect; increased risk of hypertension on clonidine withdrawal
- Dopaminergics: avoid use with entacapone; CNS toxicity reported with selegiline and rasagiline
- Pentamidine: increased risk of ventricular arrhythmias
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use
- Sympathomimetics: increased risk of hypertension and arrhythmias with adrenaline and noradrenaline; metabolism possibly inhibited by methylphenidate
It is not licensed for use by anyone else.

**ADMINISTRATION**

RECONSTITUTION

- ROUTE
  - Oral

RATE OF ADMINISTRATION

- COMMENTS

**OTHER INFORMATION**

- Imipramine metabolised to active metabolite desipramine, which has <1% urinary excretion
Indapamide

**CLINICAL USE**
Thiazide-like diuretic:
- Essential hypertension

**DOSE IN NORMAL RENAL FUNCTION**
2.5 daily in the morning
Modified release: 1.5 mg daily in the morning

**PHARMACOKINETICS**
- Molecular weight (daltons) 365.8
- % Protein binding 79
- % Excreted unchanged in urine 5–7
- Volume of distribution (L/kg) 0.3–1.3
- Half-life – normal/ESRF (hrs) 14–24/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50 Dose as in normal renal function
  - 10–20 Dose as in normal renal function
  - <10 Dose as in normal renal function. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Not dialysed. Dose as in GFR<10 mL/min
- HD Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux Not dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Analgesics: increased risk of nephrotoxicity with NSAIDs; antagonism of diuretic effect
  - Anti-arrhythmics: hypokalaemia leads to increased cardiac toxicity; effects of lidocaine and mexiletine antagonised
  - Antibacterials: avoid administration with lymecycline
  - Antidepressants: increased risk of hypokalaemia with reboxetine; enhanced hypotensive effect with MAOIs; increased risk of postural hypotension with tricyclics
  - Anti-epileptics: increased risk of hyponatraemia with carbamazepine
  - Antifungals: increased risk of hypokalaemia with amphotericin
  - Antihypertensives: enhanced hypotensive effect; increased risk of first dose hypotension with post-synaptic alpha-blockers like prazosin; hypokalaemia increases risk of ventricular arrhythmias with sotalol
  - Antipsychotics: hypokalaemia increases risk of ventricular arrhythmias with amisulpride or sertindole; enhanced hypotensive effect with phenothiazines; hypokalaemia increases risk of ventricular arrhythmias with pimozide – avoid concomitant use
  - Atomoxetine: hypokalaemia increases risk of ventricular arrhythmias.
  - Cardiac glycosides: increased toxicity if hypokalaemia occurs
  - Ciclosporin: increased risk of nephrotoxicity and possibly hypomagnesaemia
  - Lithium excretion reduced (increased toxicity)

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**
- If pre-existing renal insufficiency is aggravated – stop indapamide
- Doses greater than 2.5 mg daily are not recommended
- Caution if hypokalaemia develops
- Ineffective in ERF
- One-month studies of functionally anephric patients undergoing chronic haemodialysis have not shown evidence of drug accumulation, despite the fact that indapamide is not dialysable

RETURN TO CONTENTS
INDINAVIR

**CLINICAL USE**
Protease inhibitor:
- Treatment of HIV infection, in combination with a nucleoside reverse transcriptase inhibitor

**DOSE IN NORMAL RENAL FUNCTION**
800 mg every 8 hours

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>711.9 (as sulphate)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>60</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>10.4</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>14</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1.8/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in normal renal function</th>
<th>Monitor closely</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be dialysed. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Anti-arrhythmics: possibly increased amiodarone concentration – avoid concomitant use
- Antibacterials: rifampicin increases metabolism – avoid concomitant use; increased rifabutin concentration and rifabutin reduces indinavir concentration – reduce dose of rifabutin by 50% and increase dose of indinavir; avoid with telithromycin in severe renal and hepatic failure
- Antidepressants: plasma concentration reduced by St John's wort – avoid concomitant use
- Anti-epileptics: concentration possibly reduced by carbamazepine, phenytoin, primidone and barbiturates
- Antifungals: ketoconazole inhibits metabolism – reduce dose of indinavir to 600 mg every 8 hours; concentration increased byitraconazole – consider reducing indinavir
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: possibly increased risk of ventricular arrhythmias with pimozide and sertindole – avoid concomitant use; possibly inhibits aripiprazole metabolism – reduce aripiprazole dose
- Antivirals: avoid with atazanavir; concentration reduced by efavirenz and nevirapine; with nelfinavir and darunavir, concentration of both drugs increased; concentration increased by ritonavir; saquinavir concentration increased
- Anxiolytics and hypnotics: increased risk of prolonged sedation with alprazolam and midazolam – avoid concomitant use
- Cilostazol: concentration of cilostazol possibly increased – avoid concomitant use
- Ergot alkaloids: risk of ergotism – avoid concomitant use
- Lipid-regulating drugs: increased risk of myopathy with simvastatin – avoid concomitant use; and possibly with atorvastatin
- 5HT1 agonists: concentration of eletriptan increased – avoid concomitant use
- Sildenafil: concentration of sildenafil increased – reduce initial sildenafil dose
- Vardenafil: concentration of vardenafil increased – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
  - Drink 1.5 litres of water in 24 hours
Give 1 hour before, or 2 hours after food, or with a low fat meal with water

Mild renal insufficiency is usually due to crystalluria, but a case of interstitial nephritis has been reported

If nephrolithiasis with flank pain occurs (with or without haematuria), temporarily stop therapy (e.g. for 1–3 days)

If giving with didanosine, leave 1 hour between each drug

OTHER INFORMATION
Indometacin

**CLINICAL USE**

NSAID:
- Pain and inflammation in rheumatic disease and other musculoskeletal disorders
- Acute gout
- Dysmenorrhoea
- Closure of ductus arteriosus

**DOSE IN NORMAL RENAL FUNCTION**

- Oral: 50–200 mg daily in divided doses, after food
- PR: 100 mg twice daily if required
- Gout: 150–200 mg daily in divided doses
- Dysmenorrhoea: up to 75 mg daily
- Maximum combined oral and PR: 150–200 mg daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>357.8</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>90–99</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>5–20 (60% as metabolites)</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.34–1.57</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1–16/unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function, but avoid if possible</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function, but avoid if possible</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function, but avoid if possible</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function, but only use if CKD 5 and on dialysis</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function See ‘Other Information’</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unlikely to be dialysed</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- ACE inhibitors and angiotensin-II antagonists: antagonism of hypotensive effect; increased risk of nephrotoxicity and hyperkalaemia
- Analgesics: avoid concomitant use of 2 or more NSAIDs, including aspirin (increased side effects); avoid with ketorolac (increased risk of side effects and haemorrhage)
- Antibacterials: possibly increased risk of convulsions with quinolones
- Anticoagulants: effects of coumarins and phenindione enhanced; possibly increased risk of bleeding with heparins
- Antidepressants: increased risk of bleeding with SSRIs and venlafaxine
- Antidiabetic agents: effects of sulphonylureas enhanced
- Anti-epileptic agents: effects of phenytoin enhanced
- Antipsychotics: possible severe drowsiness with haloperidol
- Antivirals: increased risk of haematological toxicity with zidovudine; concentration possibly increased by ritonavir
- Ciclosporin: increased risk of nephrotoxicity
- Cytotoxic agents: reduced excretion of methotrexate
- Diuretics: increased risk of nephrotoxicity, hyperkalaemia with potassium-sparing diuretics; antagonism of diuretic effect
- Lithium: lithium excretion reduced
- Pentoxifylline: possibly increased risk of bleeding
- Probenecid: excretion of indometacin reduced
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral, PR, IV

- **RATE OF ADMINISTRATION**
  - 20–30 minutes

- **COMMENTS**
  -
OTHER INFORMATION

- Inhibition of renal prostaglandin synthesis by NSAIDs may interfere with renal function, especially in the presence of existing renal disease – avoid if possible; if not, check serum creatinine 48–72 hours after starting NSAID – if raised, discontinue NSAID therapy

- Use normal doses in patients with ERF on dialysis if they do not pass any urine
- Use with caution in renal transplant recipients – can reduce intrarenal autocoid synthesis
Indoramin

**CLINICAL USE**
Alpha-adrenoceptor blocker:
- Hypertension
- Benign prostatic hyperplasia (BPH)

**DOSE IN NORMAL RENAL FUNCTION**
- Hypertension: 25 mg twice daily initially, increasing to a maximum of 200 mg daily in 2–3 divided doses
- Benign prostatic hyperplasia: 20 mg twice daily increasing to a maximum of 100 mg daily in divided doses

**PHARMACOKINETICS**
- Molecular weight (daltons): 383.9 (as hydrochloride)
- % Protein binding: >90
- % Excreted unchanged in urine: <2
- Volume of distribution (L/kg): 7.4
- Half-life – normal/ESRF (hrs): 5/Increased by 50% (reduced by 40% in HD patients)

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- NSAIDs: antagonism of hypotensive effect
- Antidepressants: enhanced hypotensive effect, especially with MAOIs and linezolid – avoid concomitant use
- Beta-blockers: enhanced hypotensive effect; increased risk of first dose hypotensive effect
- Calcium-channel blockers: enhanced hypotensive effect; increased risk of first dose hypotensive effect
- Diuretics: enhanced hypotensive effect; increased risk of first dose hypotensive effect
- Moxisylyte: possibly severe postural hypotension when used in combination
- Vardenafil, sildenafil and tadalafil: enhanced hypotensive effect – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**
- For BPH, 20 mg at night may be adequate in the elderly
- In the elderly the half-life can be prolonged to 6.6–32.8 hours with a mean of 14.7 hours due to reduced clearance
- Seyffart recommends a maximum dose of 50 mg daily for patients with severe renal impairment if not on dialysis. Dialysis patients should receive a maximum of 100 mg daily on dialysis days, but 50 mg on non-dialysis days
Inositol nicotinate

**CLINICAL USE**
Peripheral vascular disease

**DOSE IN NORMAL RENAL FUNCTION**
3 g daily in 2–3 divided doses, maximum 4 g daily

**PHARMACOKINETICS**
- Molecular weight: 810.7 daltons
- % Protein binding: High
- % Excreted unchanged in urine: No data
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 24

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td></td>
</tr>
<tr>
<td>10–30</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Unknown dialysability. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**
- **RECONSTITUTION**
  - **ROUTE**
    - Oral
  - **RATE OF ADMINISTRATION**
    - **COMMENTS**
      - Unknown

**OTHER INFORMATION**
- Slowly hydrolysed to nicotinic acid
Insulin – soluble (Actrapid or Humulin S)

**CLINICAL USE**
- Hyperglycaemia, control of diabetes mellitus
- Emergency management of hyperkalaemia

**DOSE IN NORMAL RENAL FUNCTION**
Variable

**PHARMACOKINETICS**
- Molecular weight (daltons) 5808
- % Protein binding 5%
- % Excreted unchanged in urine 0%
- Volume of distribution (L/kg) 0.15
- Half-life – normal/ESRF (hrs) 2–5/13

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Variable</td>
</tr>
<tr>
<td>10–20</td>
<td>Variable</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Variable</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose according to clinical response</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose according to clinical response</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose according to clinical response</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose according to clinical response</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Fibrates: may improve glucose tolerance; additive effect with insulin

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - IV via CRIP

**RATE OF ADMINISTRATION**
- Over 30 minutes or as required

**COMMENTS**
- Add 15–25 IU insulin to 50 mL 50% glucose
- For maintenance infusion or sliding scale infusion, add 50 IU insulin to 500 mL 10% glucose and adjust rate according to blood glucose levels
- Continue infusing insulin/glucose solution at rate of 10 mL/hour according to serum potassium

**OTHER INFORMATION**
- Monitor blood glucose
- Prior to insulin/glucose infusion for hyperkalaemia, give IV 20 mL 10% calcium gluconate to protect myocardium and 50–100 mL 8.4% sodium bicarbonate to correct acidosis
- Commence calcium resonium 15 g 4 times per day orally
- Insulin is metabolised renally; therefore, requirements may be reduced in ERF
Interferon alfa-2a (Roferon-A)

**CLINICAL USE**
1. Hairy cell leukaemia
2. AIDS related Kaposi’s sarcoma
3. Chronic myelogenous leukaemia
4. Cutaneous T-cell lymphoma
5. Chronic hepatitis B
6. Chronic hepatitis C
7. Follicular non-Hodgkin’s lymphoma
8. Advanced renal cell carcinoma
9. Malignant melanoma

**DOSE IN NORMAL RENAL FUNCTION**
1. Hairy cell leukaemia: 1.5–3 million IU daily or 3 times per week
2. AIDS related Kaposi’s sarcoma: 3–36 million IU daily or 3 times per week
3. Chronic myelogenous leukaemia: 3–9 million IU daily or 3 times per week
4. Cutaneous T-cell lymphoma: 3–18 million IU daily or 3 times per week
5. Chronic hepatitis B: 2.5–5 million IU/m² 3 times per week
6. Chronic hepatitis C: 3–6 million IU 3 times per week
7. Follicular non-Hodgkin’s lymphoma: 6 million IU/m² on days 22–26 of each 28 day cycle
8. Advanced renal cell carcinoma: 9–18 million IU 3 times per week
9. Malignant melanoma: 1.5–3 million IU 3 times a week

**PHARMACOKINETICS**
- Molecular weight (daltons): 19 000
- % Protein binding: 0
- % Excreted unchanged in urine: Negligible
- Volume of distribution (L/kg): 0.4
- Half-life – normal/ESRF (hrs): 3.7–8.5/–

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/min)**
  - 20–50: Dose as in normal renal function
  - Monitor renal function closely
  - 10–20: Dose as in normal renal function
  - Monitor renal function closely
  - <10: Use with great caution. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**: Not dialysed. Dose as in GFR < 10 mL/min
- **HD**: Not dialysed. Dose as in GFR < 10 mL/min
- **HDF/High flux**: Dialysed. Dose as in GFR < 10 mL/min
- **CAV/VVHD**: Not dialysed. Dose as in GFR = 10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Immunosuppressants, e.g. ciclosporin, tacrolimus, sirolimus may have an antagonistic effect

**ADMINISTRATION**

**RECONSTITUTION**
- –

**ROUTE**
- SC, IM

**RATE OF ADMINISTRATION**
- –

**COMMENTS**
- –

**OTHER INFORMATION**
- Interferon up-regulates the cell surface presentation of class II histocompatibility antigens, which raises the possibility of drug-induced allograft rejection. There are numerous clinical reports of allograft rejection, acute renal failure and graft loss after interferon therapy. Hence extreme care should be exercised in the use of interferon after renal transplantation.
- Interferon is metabolised primarily in the kidney. It is excreted in the urine, but is reabsorbed by the tubules where it undergoes lysosomal degradation. In patients undergoing haemodialysis, the interferon molecule may accumulate as it is too large to be dialysed and will not undergo renal degradation. Hence, the dose may need to be adjusted.
Interferon alfa-2b

**CLINICAL USE**

Intron A:
- Chronic hepatitis B
- Chronic hepatitis C
- Hairy cell leukaemia
- Multiple myeloma
- Carcinoid tumour
- Chronic myelogenous leukaemia
- Follicular lymphoma
- Malignant melanoma

**DOSE IN NORMAL RENAL FUNCTION**

- Chronic hepatitis B: 5–10 million IU 3 times a week
- Chronic hepatitis C: 3 million IU 3 times a week
- Hairy cell leukaemia: 2 million IU/m² 3 times a week
- Multiple myeloma: 3 million IU/m² 3 times a week
- Carcinoid tumour: 3–9 million IU/m² 3 times a week
- Chronic myelogenous leukaemia: 4–5 million IU/m² daily
- Follicular lymphoma: 5 million IU 3 times a week
- Malignant melanoma: 20 million IU/m² (IV infusion) daily for 5 days, decreasing to 10 million IU/m² (SC) 3 times a week

**PHARMACOKINETICS**

- Molecular weight (daltons): 15000–21000
- % Protein binding: Negligible
- % Excreted unchanged in urine: 0
- Volume of distribution (L/kg): 0.4
- Half-life – normal/ESRF (hrs): 2–7

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Monitor renal function closely</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
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<tr>
<td>10–20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Use with great caution. See ‘Other Information’</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapies</th>
<th>Dose as in GFR=10–20 mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAH/VVHD</td>
<td>Not dialysed</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Immunosuppressants, e.g. cyclosporin, tacrolimus, sirolimus may have an antagonistic effect
- Administration of interferon in combination with other chemotherapeutic agents, e.g. cytarabine, cyclophosphamide, doxorubicin, teniposide may lead to increased risk of severe toxicity

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - IM, SC, IV
- **RATE OF ADMINISTRATION**
  - 20 minutes
- **COMMENTS**
  - Add to sodium chloride 0.9%

**OTHER INFORMATION**

- Interferon up-regulates the cell surface presentation of class II histocompatibility antigens, which raises the possibility of drug-induced allograft rejection. There are numerous clinical reports of allograft rejection, acute renal failure and graft loss after interferon therapy. Hence extreme care should be exercised in the use of interferon after renal transplantation
- Interferon is metabolised primarily in the kidney. It is excreted in the urine, but is reabsorbed by the tubules where it undergoes lysosomal degradation. In patients undergoing haemodialysis, the interferon molecule may accumulate as it is too large to be dialysed and will not undergo renal degradation. Hence, the dose may need to be adjusted
Several small controlled trials have examined the efficacy of low-dose interferon therapy (3 MU 3 times a week given after dialysis) for chronic hepatitis C in patients on haemodialysis. Treatment appears to have been remarkably effective, possibly because reduced renal clearance of interferon results in higher and more sustained levels of the drug. (Huraib S, Tanimu D, Romeh SA, et al. Interferon-α in chronic hepatitis C infection in dialysis patients. *Am J Kidney Dis*. 1999; 34(1): 55–60)
Interferon beta

CLINICAL USE
Treatment of relapsing, remitting multiple sclerosis

DOSE IN NORMAL RENAL FUNCTION
Interferon beta-1a:
- Avonex: 6 million IU (30 micrograms) once a week
- Rebif: 22–44 micrograms 3 times a week
Interferon beta-1b:
- Betaferon: 8 million IU every second day

PHARMACOKINETICS
Molecular weight (daltons) 18 500–22 500
% Protein binding No data
% Excreted unchanged in urine Negligible. See ‘Other Information’
Volume of distribution (L/kg) 3
Half-life – normal/ESRF (hrs) 5–10

DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>DOSE</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function Monitor renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function Monitor renal function</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Use with caution due to risk of accumulation, and monitor renal function</td>
<td></td>
</tr>
</tbody>
</table>

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>THERAPY</th>
<th>DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Ciclosporin and tacrolimus: interferon reported to reduce the activity of hepatic cytochrome P450 enzymes

ADMINISTRATION
RECONSTITUTION
- With diluent provided
ROUTE
- IM (Avonex), SC (Rebif, Betaferon)
RATE OF ADMINISTRATION
- COMMENTS
- Stable for 6 hours at 2–8°C once reconstituted

OTHER INFORMATION
- Pre-treatment with paracetamol is recommended to reduce incidence of flu-like symptoms
- Vary the site of injection each week
- Rare cases of lupus erythematosus syndrome have occurred
- Transient increases in creatinine, potassium, urea, nitrogen and urinary calcium may occur
- Interferon up-regulates the cell surface presentation of class II histocompatibility antigens, which raises the possibility of drug-induced allograft rejection. There are numerous clinical reports of allograft rejection, acute renal failure and graft loss after interferon therapy. Hence extreme care should be exercised in the use of interferon after renal transplantation
- Interferon is metabolised primarily in the kidney. It is excreted in the urine, but is reabsorbed by the tubules where it undergoes lysosomal degradation. In patients undergoing haemodialysis, the interferon molecule may accumulate as it is too large to be dialysed and will not undergo renal degradation. Hence, the dose may need to be adjusted
Interferon gamma-1b (Immukin)

**CLINICAL USE**
Adjunct to antibiotics to reduce the frequency of serious infections in patients with chronic granulomatous disease.

**DOSE IN NORMAL RENAL FUNCTION**
50 mcg/m² 3 times a week or 1.5 mcg/kg 3 times a week if surface area <0.5 m².

**PHARMACOKINETICS**
- Molecular weight: 15 000–21 000 daltons
- % Protein binding: No data
- % Excreted: Negligible
- Unchanged in urine
- Volume of distribution (L/kg): 0.2–0.6
- Half-life – normal/ESRF (hrs): 5.9

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as for normal renal function closely if dose adjustment is needed</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>No data on use in renal impairment. Dose as for normal renal function and monitor renal function closely</td>
</tr>
<tr>
<td>10–20</td>
<td>No data on use in renal impairment. Dose as for normal renal function and monitor renal function closely</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Use with caution due to risk of accumulation. Monitor renal function closely</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Modality</th>
<th>Dose considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely dialysability. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs:
- Avoid with vaccines

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - SC

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**
- Pre-treatment with paracetamol is recommended to reduce incidence of flu-like symptoms
- Interferon up-regulates the cell surface presentation of class II histocompatibility antigens, which raises the possibility of drug-induced allograft rejection. There are numerous clinical reports of allograft rejection, acute renal failure and graft loss after interferon therapy. Hence extreme care should be exercised in the use of interferon after renal transplantation.
- Interferon is metabolised primarily in the kidney. It is excreted in the urine, but is reabsorbed by the tubules where it undergoes lysosomal degradation. In patients undergoing haemodialysis, the interferon molecule may accumulate as it is too large to be dialysed and will not undergo renal degradation. Hence, the dose may need to be adjusted.

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**RETURN TO CONTENTS**
Ipratropium bromide

### Clinical Use
Anticholinergic bronchodilator:
- Reversible airways obstruction, particularly in COPD

### Dose in Normal Renal Function
- Nebuliser solution: 250–500 micrograms 3–4 times daily
- Inhaler: 20–80 micrograms 3–4 times daily

### Pharmacokinetics
- Molecular weight: 430.4 daltons
- % Protein binding: <20
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): 4.6
- Half-life – normal/ESRF (hrs): 1.6

### Dose in Renal Impairment

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

### Dose in Patients Undergoing Renal Replacement Therapies
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Not dialysed. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as normal renal function

### Important Drug Interactions
Potentially hazardous interactions with other drugs
- None known

### Administration
**Reconstitution**
- **Route**
  - Inhaled

**Rate of Administration**
- Nebuliser: according to nebuliser
- The dose of nebuliser solution may need to be diluted in order to obtain a final volume suitable for the nebuliser
- Sterile sodium chloride 0.9% should be used if dilution is required

### Other Information
- Following inhalation, only a small amount of ipratropium reaches the systemic circulation. Any swallowed drug is poorly absorbed from the GI tract
Irbesartan

CLINICAL USE
Angiotensin-II receptor antagonist:
- Hypertension
- Diabetic nephropathy

DOSE IN NORMAL RENAL FUNCTION
75–300 mg daily

PHARMACOKINETICS
Molecular weight (daltons) 428.5
% Protein binding 96
% Excreted unchanged in urine <2
Volume of distribution (L/kg) 53–93 litres
Half-life – normal/ESRF (hrs) 11–15/Unchanged

DOSE IN RENAL IMPAIRMENT
GFR (mL/Min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Not dialysed. Initial dose 75 mg daily and gradually increase
HD Not dialysed. Initial dose 75 mg daily and gradually increase
HDF/High flux Unknown dialysability. Initial dose 75 mg daily and gradually increase
CAV/VVHD Unknown dialysability. Initial dose 75 mg daily and gradually increase

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Analgesics: antagonism of hypotensive effect and increased risk of renal impairment with NSAIDs; hyperkalaemia with ketorolac and other NSAIDs
- Ciclosporin: increased risk of hyperkalaemia and nephrotoxicity
- Diuretics: enhanced hypotensive effect; hyperkalaemia with potassium-sparing diuretics
- Epoetin: increased risk of hyperkalaemia; antagonism of hypotensive effect
- Lithium: reduced excretion (possibility of enhanced lithium toxicity)
- Potassium salts: increased risk of hyperkalaemia
- Tacrolimus: increased risk of hyperkalaemia and nephrotoxicity

ADMINISTRATION

RECONSTITUTION
- ROUTE
- Oral

RATE OF ADMINISTRATION
- COMMENTS

OTHER INFORMATION
- Hyperkalaemia and other side effects are more common in patients with impaired renal function
- Renal failure has been reported in association with angiotensin-II antagonists in patients with renal artery stenosis, post renal transplant, and in those with congestive heart failure
- Close monitoring of renal function during therapy is necessary in those with renal insufficiency
Irinotecan hydrochloride

**CLINICAL USE**
Treatment of metastatic colorectal cancer resistant to fluorouracil, or in conjunction with fluorouracil

**DOSE IN NORMAL RENAL FUNCTION**
Without 5-FU: 350 mg/m² every 3 weeks
With 5-FU: 180 mg/m² every 2 weeks

**PHARMACOKINETICS**
Molecular weight 677.2 daltons
% Protein binding 65
% Excreted unchanged in urine 20
Volume of distribution 110–234 litres/m²
Half-life – normal/ESRF (hrs) 14

**DOSE IN RENAL IMPAIRMENT**
GFR (mL/min)
20–50 Dose as in normal renal function and monitor closely
10–20 Dose as in normal renal function and monitor closely
<10 Reduce dose (50–80 mg/m²) and monitor closely. Increase as tolerated

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
CAPD Unlikely to be dialysed. Dose as in GFR<10 mL/min
HD Unlikely to be dialysed. Dose as in GFR<10 mL/min
HDF/High flux Unlikely to be dialysed. Dose as in GFR<10 mL/min
CAV/VVHD Unlikely to be dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antipsychotics: avoid concomitant use with clozapine (increased risk of agranulocytosis)
- Antivirals: metabolism possibly inhibited by atazanavir (increased risk of toxicity)

**ADMINISTRATION**
RECONSTITUTION
- ROUTE
  - IV infusion
RATE OF ADMINISTRATION
- Over 30–90 minutes
COMMENTS
- Dilute in 250 mL sodium chloride 0.9% or glucose 5%

**OTHER INFORMATION**
- Manufacturer advises avoiding use in renal impairment due to lack of data
- Metabolism is primarily hepatic: where irinotecan is rapidly converted to active metabolite SN-38 by hepatic carboxylesterase enzymes
- Excretion is predominantly biliary: 64% excreted in faeces. The mean 24 hr urinary excretion of irinotecan and SN-38 (its active metabolite) was 19.9% and 0.25% respectively
- Infrequent reports of renal insufficiency due to inadequate hydration
- Transient, mild to moderate increase in serum creatinine reported in 7.3% patients

RETURN TO CONTENTS
Iron dextran 5% solution

**CLINICAL USE**

- Prophylaxis of iron deficiency anaemia (when oral treatment is ineffective or contraindicated)
- Treatment of iron deficiency during epoetin therapy especially if serum ferritin is very low (<50 nanograms/mL)

**DOSE IN NORMAL RENAL FUNCTION**

- Total iron infusion: Dose of iron dextran (mg) = weight (kg) × [Target Hb (g/L) – Actual Hb (g/L)] × 0.24 + 500 mg iron for iron stores (if body weight >35 kg)
- Target haemoglobin level (110 g/L for renal patients as a guide)

  or

  100–200 mg 2 or 3 times a week depending on haemoglobin

- A test dose is essential. Give 0.5 mL or 25 mg iron over 15 minutes and observe for 60 minutes (15 minutes if using low dose bolus) for anaphylaxis. Have resuscitative equipment and drugs at hand (adrenaline, chlorphenamine and hydrocortisone)

**PHARMACOKINETICS**

- Molecular weight (daltons) 165 000
- % Protein binding 0
- % Excreted in urine <0.2
- Volume of distribution (L/kg) 0.031–0.055
- Half-life – normal/ESRF (hrs) 5–20/–

**DOSE IN RENAL IMPAIRMENT**

- GFR (mL/Min)
  - 20–50 Dose as in normal renal function
  - 10–20 Dose as in normal renal function
  - <10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD Not dialysed. Dose as in normal renal function
- HD Not dialysed. Dose as in normal renal function
- HDF/High flux Not dialysed. Dose as in normal renal function
- CAV/VVHD Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

- Potentially hazardous interactions with other drugs
  - Dimercaprol: avoid concomitant use
  - Oral iron: reduced absorption of oral iron

**ADMINISTRATION**

- ROUTE
  - IV, IM
- RATE OF ADMINISTRATION
  - Infusion: 100 mL over 30 minutes
  - Bolus: 10 mg/minute
  - Total dose infusion: over 4–6 hours; increase rate of infusion to 45–60 drops per minute
- COMMENTS
  - Infusion: 100–200 mg in 100 mL sodium chloride or glucose 5%
  - Bolus: add to 10–20 mL sodium chloride or glucose 5%
  - Total dose infusion: add to 500 mL sodium chloride 0.9% or glucose 5%
  - Keep under strict supervision during and for 1 hour after infusion

**OTHER INFORMATION**

- Do not give to patients with history of asthma
- If patients with a history of allergy are prescribed iron dextran, give adequate antihistamine cover prior to administration
- The dose of iron dextran varies widely from 100 mg per dialysis session for 6–10 sessions, to single doses of 500 mg to 1 g
- The incidence of anaphylaxis with the Cosmofer brand of iron dextran is significantly lower than with the old Imferon brand, since the iron is complexed to a much shorter dextran chain than was used previously
Iron sucrose

**CLINICAL USE**
- Prophylaxis of iron deficiency anaemia (when oral treatment is ineffective or contraindicated)
- Treatment of iron deficiency during epoetin therapy especially if serum ferritin is very low (<50 nanograms/mL)

**DOSE IN NORMAL RENAL FUNCTION**
According to local protocol. See ‘Other Information’

**PHARMACOKINETICS**
- Molecular weight: 34,000–60,000 daltons
- % Protein binding: No data
- % Excreted: <5 unchanged in urine
- Volume of distribution: 8 litres (L/kg)
- Half-life – normal/ESRF (hrs): 6

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
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<tr>
<td>10–20</td>
<td></td>
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<tr>
<td>&lt;10</td>
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</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed.</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Dimercaprol: avoid concomitant use
- Do not administer with oral iron

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - IV

**RATE OF ADMINISTRATION**
- Bolus: 1 mL/minute
- Infusion: in sodium chloride 0.9% at a concentration of 1 mg/mL over 20–30 minutes per 100 mg

**COMMENTS**
- A test dose is required before administration
- Doses can be administered via the venous limb of the dialysis machine
- Stable for 24 hours at room temperature

**OTHER INFORMATION**
- Some regimes are:
  - 50–300 mg weekly
  - 100 mg once or twice monthly
  - 20–40 mg with each dialysis
- Oral iron can be restarted 5 days after completion of the course of IV iron
Isoniazid

**CLINICAL USE**
Antibacterial agent:
- Treatment and prophylaxis of tuberculosis in ‘at risk’ immunocompromised patients

**DOSE IN NORMAL RENAL FUNCTION**
- IM/IV: 200–300 mg daily
- Oral: 5 mg/kg to a maximum of 300 mg in single or divided doses
- Intermittent regimes: 15 mg/kg twice weekly or 10 mg 3 times weekly
- Prophylaxis: 100–200 mg daily
- Intrapeural: 50–250 mg
- Intrathecal: 25–50 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons) 137.1
- % Protein binding 0
- % Excreted unchanged in urine 4–32
- Volume of distribution (L/kg) 0.75
- Half-life – normal/ESRF (hrs) 1.2–3.5/1–17 (depends on acetylator status)

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: 200–300 mg daily

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Dialysed. Dose as in GFR<10 mL/min
- HD: Dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Probably dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anti-epileptics: metabolism of carbamazepine, ethosuximide and phenytoin inhibited (enhanced effect); also with carbamazepine, isoniazid hepatotoxicity possibly increased

**ADMINISTRATION**
- RECONSTITUTION
  - Dilute with water for injection if required
- ROUTE
  - Oral, IM, IV, intrapleural, intrathecal
- RATE OF ADMINISTRATION
  - Not critical. Give by slow IV bolus
- COMMENTS
  -

**OTHER INFORMATION**
- Adjust dose accordingly if hepatic illness, slow/fast acetylator status identified
- Pyridoxine 10 mg daily has been recommended for prophylaxis of peripheral neuritis
Isosorbide dinitrate

**CLINICAL USE**

Vasodilator:
- Prophylaxis and treatment of angina
- Left ventricular failure

**DOSE IN NORMAL RENAL FUNCTION**

- Oral:
  - Angina: 30–120 mg daily in divided doses;
  - LVF: 40–240 mg daily
- IV: 2–20 mg/hour depending on response

**PHARMACOKINETICS**

- Molecular weight (daltons): 236.1
- % Protein binding: <1
- % Excreted unchanged in urine: 10–20
- Volume of distribution (L/kg): 2–4
- Half-life – normal/ESRF (hrs): 0.5–1/

**DOSE IN RENAL IMPAIRMENT**

- GFR (mL/Min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Sildenafil: hypotensive effect significantly enhanced – avoid concomitant use
- Tadalafil: hypotensive effect significantly enhanced – avoid concomitant use
- Vardenafil: hypotensive effect significantly enhanced – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**

- ROUTE:
  - Oral, IV infusion
- RATE OF ADMINISTRATION:
  - 1 mg/10 mL; 60 mL/hour = 6 mg/hour
  - 2 mg/10 mL; 30 mL/hour = 6 mg/hour
- COMMENTS:
  - Dilute using sodium chloride 0.9% or glucose 5% to 1 mg/10 mL or 2 mg/10 mL; final volume 500 mL
  - Use of PVC giving sets and containers should be avoided since significant losses of the active ingredient by absorption can occur

**OTHER INFORMATION**

- Isosorbide dinitrate undergoes extensive first pass metabolism, mainly in the liver; major metabolites are isosorbide-2-mononitrate and isosorbide-5-mononitrate
- Both metabolites possess vasodilatory activity and may contribute to the activity of the parent compound
- Both metabolites have longer half-lives than the parent compound
Isosorbide mononitrate

**CLINICAL USE**

Vasodilator:
- Treatment and prophylaxis of angina
- Adjunct in congestive heart failure

**DOSE IN NORMAL RENAL FUNCTION**

20–120 mg/day in divided doses

**PHARMACOKINETICS**

- Molecular weight (daltons) 191.1
- % Protein binding <4
- % Excreted unchanged in urine 2
- Volume of distribution (L/kg) 0.6
- Half-life – normal/ESRF (hrs) 1.5–5/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Probably dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Sildenafil: hypotensive effect significantly enhanced – avoid concomitant use
- Tadalafil: hypotensive effect significantly enhanced – avoid concomitant use
- Vardenafil: hypotensive effect significantly enhanced – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- –

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- –

**OTHER INFORMATION**
- Tolerance may develop. This may be minimised by having nitrate-‘free’ periods
Isotretinoin

**CLINICAL USE**

Treatment of nodulo-cystic and conglobate acne, and severe acne which has failed to respond to an adequate course of systemic antibiotics.

**DOSE IN NORMAL RENAL FUNCTION**

0.5–1 mg/kg daily in 1–2 divided doses initially. Maximum cumulative dose: 150 mg/kg per course.

Topically: 1–2 times daily.

**PHARMACOKINETICS**

- Molecular weight: 300.4 daltons
- % Protein binding: 99.9%
- % Excreted: As metabolites
- Volume of distribution: No data
- Half-life: 10–20 hours

**DOSE IN RENAL IMPAIRMENT**

- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Initial dose 10 mg daily and slowly increase as tolerated up to 1 mg/kg daily. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Not dialysed. Dose as in GFR < 10 mL/min
- HD: Not dialysed. Dose as in GFR < 10 mL/min
- HDF/High flux: Unlikely to be dialysed. Dose as in GFR < 10 mL/min
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Antibacterials: possible increased risk of benign intracranial hypertension with tetracyclines – avoid concomitant use

**ADMINISTRATION**

- RECONSTITUTION
  - ROUTE
    - Oral, topical (0.05% gel)
  - COMMENTS

**OTHER INFORMATION**

- Since the drug is highly protein bound, it is not expected to be significantly removed by dialysis
- Watch for signs of vitamin A toxicity

RETURN TO CONTENTS
Ispaghula husk

CLINICAL USE
Bulk-forming laxative

DOSE IN NORMAL RENAL FUNCTION
- Fibrelief: 1–6 sachets daily in water in 1–3 divided doses
- Fybogel: One sachet (3.5 g) in water twice daily
- Isogel: 2 teaspoonfuls in water 1–2 times daily (constipation), 3 times daily (diarrhoea)
- Regulan: 1 sachet in water 1–3 times daily

PHARMACOKINETICS
Molecular weight (daltons) –
% Protein binding 0
% Excreted unchanged in urine 0
Volume of distribution (L/kg) Not absorbed
Half-life – normal/ESRF (hrs) Not absorbed

DOSE IN RENAL IMPAIRMENT

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<th>GFR (mL/Min)</th>
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DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

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<td>Not dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- None known

ADMINISTRATION

RECONSTITUTION
- –
ROUTE
- Oral
RATE OF ADMINISTRATION
- –
COMMENTS
- Fybogel and regulan should be stirred into 150 mL water and taken as quickly as possible, preferably after meals
- Additional fluid intake should be maintained

OTHER INFORMATION
- Fybogel is low in sodium and potassium, containing approximately 0.4 mmol sodium and 0.7 mmol potassium per sachet. It is sugar and gluten free and contains aspartame (contributes to the phenylalanine intake and may affect control of phenylketonuria)
- Orange and lemon/lime flavours of regulan contain: 3.4 g ispaghula husk BP, 0.23 mmol sodium, <1 mmol potassium per sachet and are gluten and sugar free. They also contain aspartame
- Fybogel contains aspartame
- Fluid restrictions in dialysis patients can render these treatments inappropriate
Isradipine

**CLINICAL USE**
Calcium-channel blocker:
- Essential hypertension

**DOSE IN NORMAL RENAL FUNCTION**
Initially 2.5 mg twice daily, increased if necessary to 10 mg twice daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 371.4
- % Protein binding: 95%
- % Excreted unchanged in urine: 0%
- Volume of distribution (L/kg): 3–4

**DOSE IN RENAL IMPAIRMENT**

<table>
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<tr>
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**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

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**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Antibacterials: metabolism accelerated by rifampicin
- Anti-epileptics: effect reduced by carbamazepine, barbiturates, phenytoin and primidone
- Antifungals: metabolism possibly inhibited by itraconazole and ketoconazole
- Antihypertensives: enhanced hypotensive effect; increased risk of first dose hypotensive effect of post-synaptic alpha-blockers
- Antivirals: concentration possibly increased by ritonavir
- Grapefruit juice: concentration increased – avoid concomitant use
- Theophylline: possibly increased theophylline concentration

**ADMINISTRATION**

**RECONSTITUTION**
- –

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- –

**COMMENTS**
- –

**OTHER INFORMATION**
- In elderly patients, or where hepatic or renal function is impaired, initial dose should be 1.25 mg twice daily. Dose should be increased according to the requirements of the individual patient
Itraconazole

**CLINICAL USE**
Antifungal agent

**DOSE IN NORMAL RENAL FUNCTION**
100–200 mg every 12–24 hours according to indication

**PHARMACOKINETICS**
- Molecular weight (daltons): 705.6
- % Protein binding: 99.8
- % Excreted unchanged in urine: <0.03
- Volume of distribution (L/kg): 10

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Not dialysed. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: possibly inhibits alfentanil metabolism
- Antibacterials: metabolism accelerated by rifabutin and rifampicin – avoid with rifabutin; possibly increased rifabutin concentration – reduce rifabutin dose; clarithromycin can increase itraconazole concentration
- Anticoagulants: effect of coumarins enhanced
- Antidepressants: avoid concomitant use with reboxetine
- Antidiabetics: can enhance effects of repaglinide
- Anti-epileptics: concentration reduced by carbamazepine, barbiturates and phenytoin – avoid with phenytoin
- Antihistamines: inhibits mizolastine metabolism – avoid concomitant use
- Antimalarials: avoid concomitant use with artremether/luemfantrine
- Antipsychotics: possibly inhibits metabolism of aripiprazole – reduce aripiprazole dose; increased risk of ventricular arrhythmias with pimozide and sertindole – avoid concomitant use; possibly increased quetiapine concentration – reduce quetiapine dose
- Antivirals: concentration possibly increased by amprenavir; concentration of indinavir increased – may need to reduce indinavir dose; with ritonavir concentration of both drugs may be increased; concentration of saquinavir possibly increased; concentration reduced by efavirenz
- Anxiolytics and hypnotics: concentration of buspirone, midazolam and alprazolam increased – reduce buspirone dose
- Bosentan: possibly increased bosentan concentration
- Calcium-channel blockers: negative inotropic effect possibly increased; metabolism of felodipine and possibly dihydropyridines inhibited; avoid concomitant use with lercanidipine and nisoldipine
- Cardiac glycosides: concentration of digoxin increased
- Ciclosporin: metabolism of ciclosporin inhibited (increased plasma ciclosporin levels)
- Cytotoxics: metabolism of busulfan inhibited, increased risk of toxicity; possibly inhibits metabolism of vincristine, increased risk of neurotoxicity; possibly increased side effects with cyclophosphamide
- Diuretics: increased eplerenone levels – avoid concomitant use
- Ergot alkaloids: increased risk of ergotism – avoid concomitant use
- 5HT₁ agonists: increased eletriptan concentration – avoid concomitant use
- Ivabradine: possibly increased ivabradine levels – reduce initial dose
- Lipid-lowering drugs: increased risk of myopathy with atorvastatin and...
simvastatin – avoid concomitant use with simvastatin, and maximum atorvastatin dose 40 mg.¹

- Sirolimus: concentration increased by itraconazole
- Tacrolimus: possibly increased tacrolimus levels
- Ulcer-healing drugs: absorption reduced by histamine H₂ antagonists and proton pump inhibitors
- Vardenafil: possibly increased vardenafil concentration – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral, IV infusion

**RATE OF ADMINISTRATION**
- Over 60 minutes

**COMMENTS**
- Add 250 mg vial to 50 mL sodium chloride 0.9%, administer 60 mL (increased volume due to large displacement value)

**OTHER INFORMATION**

- Preparations absorbed at different rates: liquid is absorbed within 2.5 hours, capsules within 2–5 hours
- Oral bioavailability of itraconazole may be lower in some patients with renal insufficiency, e.g. those receiving CAPD
- Janssen-Cilag advise no dose alterations required in renal impairment as drug is extensively metabolised in the liver, and pharmacokinetics are unchanged in patients with ERF compared to normal

References:
Ivabradine hydrochloride

**CLINICAL USE**
Symptomatic treatment of chronic stable angina pectoris in patients with sinus rhythm, if beta-blockers are contraindicated

**DOSE IN NORMAL RENAL FUNCTION**
2.5–7.5 mg twice daily (dose is reduced if heart rate is consistently below 50 beats per minute)

**PHARMACOKINETICS**
- Molecular weight: 504.5 (daltons)
- % Protein binding: 70
- % Excreted unchanged in urine: 4
- Volume of distribution (L/kg): 100 litres
- Half-life – normal/ESRF (hrs): 2/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 15–20: Dose as in normal renal function
  - <15: Dose as in normal renal function. Use with caution

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in GFR<15 mL/min
- HD: Unlikely to be dialysed. Dose as in GFR<15 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<15 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anti-arrhythmics: increased risk of ventricular arrhythmias with amiodarone and disopyramide
- Antibacterials: concentration possibly increased by clarithromycin and telithromycin – avoid concomitant use; increased risk of ventricular arrhythmias with erythromycin – avoid concomitant use
- Antifungals: concentration increased by ketoconazole – avoid concomitant use; concentration increased by fluconazole – reduce initial ivabradine dose; concentration possibly increased by itraconazole – avoid concomitant use
- Antimalarials: increased risk of ventricular arrhythmias with mefloquine
- Antipsychotics: increased risk of ventricular arrhythmias with pimozide or sertindole
- Antivirals: concentration possibly increased by nelfinavir and ritonavir – avoid concomitant use
- Beta-blockers: increased risk of ventricular arrhythmias with sotalol
- Calcium-channel blockers: concentration increased by diltiazem and verapamil – avoid concomitant use
- Grapefruit juice: ivabradine concentration increased
- Pentamidine: increased risk of ventricular arrhythmias
- St John’s wort: ivabradine concentration reduced – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

RETURN TO CONTENTS
Ketamine

**CLINICAL USE**
Anaesthetic agent, analgesic

**DOSE IN NORMAL RENAL FUNCTION**
- All doses are expressed as the base:
  1.15 mg ketamine hydrochloride = 1 mg of base
- Anaesthesia: IM
  - Short procedures: initially 6.5–13 mg/kg (10 mg/kg usually gives 12–25 minutes of surgical anaesthesia)
  - Painful diagnostic manoeuvres: initially 4 mg/kg
- IV Injection:
  - Initially 1–4.5 mg/kg over at least 60 seconds (2 mg/kg usually gives 5–10 minutes of surgical anaesthesia)
  - IV Infusion: Induction total dose of 0.5–2 mg/kg; maintenance 10–45 mcg/kg/min; adjust rate according to response if infusion required
- Analgesia:
  - IM: 1.5–2 mg/kg
  - IV Infusion: 2–3 mg/kg or infusion rate 5–10 mg/hour of a solution of 5 mg/mL

**PHARMACOKINETICS**
- Molecular weight 274.2 (as hydrochloride)
- % Protein binding 20–50
- % Excreted unchanged in urine 2 (88% as metabolites)
- Volume of distribution (L/kg) 4
- Half-life – normal/ESRF (hrs) 2–4/ Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50 Dose as in normal renal function
  - 10–20 Dose as in normal renal function
  - <10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Unlikely dialysability. Dose as in normal renal function
- HD Not Dialysed. Dose as in normal renal function
- HDF/High flux Unknown dialysability. Dose as in normal renal function
- CAV/ Not Dialysed. Dose as in normal renal function
- VVHD Not Dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Adrenergic-neurone blockers: enhanced hypotensive effect
- Antihypertensives: enhanced hypotensive effect
- Antidepressants: stop MAOIs 2 weeks before surgery; increased risk of arrhythmias and hypotension with tricyclics
- Antipsychotics: enhanced hypotensive effect
- Memantine: increased risk of CNS toxicity, avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - IV bolus, IV Infusion, IM
  - Injection: over at least 60 seconds
  - Infusion: Depends on clinical indication

**COMMENTS**
- For infusion add to glucose 5% or sodium chloride 0.9%, dilute to 1 mg/mL. In the USA can dilute to 2 mg/mL in fluid restricted patients (Dollery)
- Incompatible with diazepam and barbiturates
- Use infusion solutions within 24 hours
- 100 mg/mL strength must be diluted with an equal volume of water for injection, sodium chloride 0.9% or glucose 5% before use
- Minimum volume 50 mg/mL (undiluted).

**OTHER INFORMATION**
- Contraindicated in patients with severe hypertension; 1–2 mg/kg can increase arterial systolic blood pressure by approximately 20–40 mmHg
- Avoid in those prone to hallucinations or psychotic disorders
- 4–10% can be removed by haemodialysis

RETURN TO CONTENTS
Ketoconazole

**CLINICAL USE**
Antifungal agent

**DOSE IN NORMAL RENAL FUNCTION**
200–400 mg once daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>531.4</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>&gt;90</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>13</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.36</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>2/3.3</td>
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**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

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<td>HD</td>
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<tr>
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</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Analgesics: inhibits buprenorphine metabolism – reduce buprenorphine dose
- Anti-arrhythmics: increased risk of ventricular arrhythmias with disopyramide – avoid concomitant use
- Antibacterials: metabolism increased by rifampicin; may reduce rifampicin concentration; concentration possibly reduced by isoniazid; avoid concomitant use with telithromycin in severe renal and hepatic impairment
- Anticoagulants: anticoagulant effect of coumarins enhanced
- Antidepressants: avoid concomitant use with reboxetine; ketoconazole increases concentration of mirtazapine
- Anti-epileptics: concentration of ketoconazole reduced by phenytoin; concentration of carbamazepine possibly increased
- Antihistamines: concentration of loratidine possibly increased; avoid concomitant use with mizolastine
- Antimalarials: manufacturer advises avoid artemether and lumefantrine with ketoconazole
- Antipsychotics: increased risk of ventricular arrhythmias with pimozide – avoid concomitant use; possibly increased concentration of quetiapine – reduce quetiapine dose; increased risk of ventricular arrhythmias with sertindole – avoid concomitant use; inhibits aripiprazole metabolism – reduce aripiprazole dose
- Antivirals: concentration of both drugs increased with darunavir; inhibits metabolism of indinavir; concentration reduced by nevirapine – avoid concomitant use; ketoconazole and ritonavir can increase concentration of each other; concentration of saquinavir increased; concentration increased by amprenavir
- Anxiolytics and hypnotics: concentration of alprazolam and midazolam increased (risk of prolonged sedation)
- Calcium-channel blockers: increased concentration of felodipine; avoid with lercanidipine and nisoldipine; possibly inhibits metabolism of dihydropyridines
- Ciclosporin: increased ciclosporin concentration
- Cilostazol: possibly increased concentration of cilostazol, avoid concomitant use
- Cinacalcet: increased cinacalcet concentration
- Diuretics: increased eplerenone concentration – avoid concomitant use
- Domperidone: possibly increased risk of arrhythmias
- Ergot alkaloids: increased risk of ergotism with ergotamine and methysergide – avoid concomitant use
- 5HT_1 agonists: increased concentration of eletriptan – avoid concomitant use; increased almotriptan concentration (increased toxicity)
Ivabradine: concentration of ivabradine increased – avoid concomitant use
Lanthanum: reduces absorption of ketoconazole – give at least 2 hours apart
Sirolimus: concentration increased by ketoconazole – avoid concomitant use
Statins: possibly increased risk of myopathy with atorvastatin and simvastatin – avoid concomitant use with simvastatin
Tacrolimus: increased tacrolimus concentration
Theophylline; possibly increased concentration of theophylline
Vardenafil: increased concentration of vardenafil, avoid concomitant use

ADMINISTRATION
RECONSTITUTION
 ROUTE
  Oral, topical

OTHER INFORMATION
  Monitor LFTs especially if on long-term treatment
Ketoprofen

**CLINICAL USE**
NSAID and analgesic

**DOSE IN NORMAL RENAL FUNCTION**
Oral: 100–200 mg daily in 2–4 divided doses
Dysmenorrhoea: 50 mg every 8 hours
PR: 100 mg at night
IM: 50–100 mg every 4 hours, maximum 200 mg daily

**PHARMACOKINETICS**
Molecular weight (daltons) 254.3
% Protein binding 99
% Excreted unchanged in urine <1
Volume of distribution (L/kg) 0.1
Half-life – normal/ESRF (hrs) 1.5–8/5–9

**DOSE IN RENAL IMPAIRMENT**
GFR (mL/min)

<table>
<thead>
<tr>
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<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function, but avoid if possible</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function, but avoid if possible</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function, but only use if on dialysis</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Type</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function. See ‘Other Information’</td>
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<td>HD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function. See ‘Other Information’</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function. See ‘Other Information’</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be dialysed. Dose as in GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- ACE inhibitors and angiotensin-II antagonists: antagonism of hypotensive effect, increased risk of nephrotoxicity and hyperkalaemia
- Analgesics: avoid concomitant use of 2 or more NSAIDs, including aspirin (increased side effects); avoid with ketorolac (increased risk of side effects and haemorrhage)
- Antibacterials: possibly increased risk of convulsions with quinolones
- Anticoagulants: effects of coumarins enhanced; possibly increased risk of bleeding with heparins and coumarins
- Antidepressants: increased risk of bleeding with SSRIs and venlafaxine
- Antidiabetic agents: effects of sulphonylureas enhanced
- Anti-epileptics: possibly increased phenytoin concentration
- Antivirals: increased risk of haematological toxicity with zidovudine; concentration possibly increased by ritonavir
- Ciclosporin: may potentiate nephrotoxicity
- Cytotoxic agents: reduced excretion of methotrexate; increased risk of bleeding with erlotinib
- Diuretics: increased risk of nephrotoxicity; antagonism of diuretic effect, hyperkalaemia with potassium-sparing diuretics
- Lithium: excretion decreased
- Pentoxifylline: increased risk of bleeding
- Probenecid: excretion reduced by probenecid
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**

**ROUTE**
- Oral, IM, rectal. The injection must not be given by the IV route

**RATE OF ADMINISTRATION**

**COMMENTS**
- Administer by deep IM injection into the upper, outer quadrant of the buttock

**OTHER INFORMATION**
- Combined oral and rectal treatment, maximum total daily dose 200 mg
- Inhibition of renal prostaglandin synthesis by NSAIDs may interfere with renal function, especially in the presence of existing renal disease – avoid if possible; if not, check serum creatinine 48–72 hours after starting NSAID – if raised, discontinue NSAID therapy
Use normal doses in patients with ERF on dialysis if they do not pass any urine
Use with caution in renal transplant recipients – can reduce intrarenal autocoid synthesis
NSAIDs decrease platelet aggregation

Associated with nephrotic syndrome, interstitial nephritis, hyperkalaemia and sodium retention
Ketorolac trometamol

**CLINICAL USE**
Short-term management of moderate to severe acute postoperative pain

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: 10 mg every 4–6 hours (elderly every 6–8 hours); maximum 40 mg daily; maximum duration 7 days
- IM/IV: initially 10 mg, then 10–30 mg when required every 4–6 hours (every 2 hours in initial postoperative period); maximum 90 mg daily (elderly and patients less than 50 kg: maximum 60 mg daily); maximum duration 2 days

**PHARMACOKINETICS**
- Molecular weight (daltons): 376.4
- % Protein binding: >99
- % Excreted unchanged in urine: Approx 60
- Volume of distribution (L/kg): 0.15
- Half-life – normal/ESRF (hrs): IM dose: 3.5–9.2/5.9–19.2

**DOSE IN RENAL IMPAIRMENT**
<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Maximum 60 mg daily</td>
</tr>
<tr>
<td>10–20</td>
<td>Avoid if possible. Use small doses and monitor closely</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Avoid if possible. Use small doses and monitor closely</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in GFR<10mL/min
- HD: Unlikely to be dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10mL/min
- CAV/ VVHD: Unknown dialysability. Dose as in GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- ACE inhibitors and angiotensin-II antagonists: antagonism of hypotensive effect; increased risk of nephrotoxicity and hyperkalaemia
- Analgesics: avoid concomitant use of 2 or more NSAIDs, including aspirin (increased risk of side effects and haemorrhage)
- Antibacterials: possibly increased risk of convulsions with quinolones
- Anticoagulants increased risk of bleeding with heparins, phenindione and coumarins – avoid concomitant use; increased risk of haemorrhage with parenteral ketorolac and heparin – avoid concomitant use
- Antidepressants: increased risk of bleeding with SSRIs and venlafaxine
- Antidiabetics: effects of sulphonylureas possibly enhanced
- Anti-epileptics: effect of phenytoin possibly enhanced
- Antivirals: increased risk of haematological toxicity with zidovudine: concentration possibly increased by ritonavir
- Ciclosporin: increased risk of nephrotoxicity
- Cytotoxics: excretion of methotrexate reduced; increased risk of bleeding with erlotinib
- Diuretics: increased risk of nephrotoxicity; antagonism of diuretic effect; hyperkalaemia with potassium-sparing diuretics
- Lithium: excretion of lithium reduced – avoid concomitant use
- Pentoxifylline: risk of ketorolac associated bleeding increased – avoid concomitant use
- Probenecid: delays excretion of ketorolac – avoid concomitant use
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - IM, IV, oral
- **RATE OF ADMINISTRATION**
  - IV bolus over no less than 15 seconds
- **COMMENTS**
  - Compatible with sodium chloride 0.9%, glucose 5%, Ringers, lactated Ringers or plasmalyte solutions
Drugs that inhibit prostaglandin biosynthesis (including NSAIDs) have been reported to cause nephrotoxicity, including, but not limited to, glomerular nephritis, interstitial nephritis, renal papillary necrosis, nephrotic syndrome and acute renal failure. In patients with renal, cardiac or hepatic impairment, caution is required since the use of NSAIDs may result in deterioration of renal function. Ketorolac and its metabolites are excreted primarily by the kidney. Reported renal side effects include increased urinary frequency, oliguria, acute renal failure, hyponatraemia, hyperkalaemia, haemolytic uraemic syndrome, flank pain (with or without haematuria), raised serum urea and creatinine.
Klean-Prep

**CLINICAL USE**
Colonic lavage prior to diagnostic examination or surgical procedures requiring a clean colon

**DOSE IN NORMAL RENAL FUNCTION**
4 sachets, each reconstituted in 1 litre of water, at a rate of 250 mL every 10–15 minutes

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>3350 (Macrogol)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>N/A</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>N/A</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>N/A</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not absorbed. Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>Not absorbed. Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>HDF/HiIFlux</td>
<td>Not absorbed. Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not absorbed. Dose as in normal renal function</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
● None known

**ADMINISTRATION**

**RECONSTITUTION**
● Each sachet in 1 litre of water
**ROUTE**
● Oral
**RATE OF ADMINISTRATION**
● 250 mL every 15–30 minutes
● If given via NG tube, rate is 20–30 mL/minute

**COMMENTS**
● Klean-Prep is formulated to be hyperosmotic and draw water into the bowel.

None is absorbed systemically

**OTHER INFORMATION**

Each sachet of Klean-Prep contains:
— Polyethylene glycol 3350 – 59.0 g
— Anhydrous sodium sulphate – 5.685 g
— Sodium bicarbonate – 1.685 g
— Sodium chloride – 1.465 g
— Potassium chloride – 0.7425 g
● The electrolyte content of 1 sachet when made up in 1 litre of water is:
— Sodium – 125 mmol
— Sulphate – 40 mmol
— Chloride – 35 mmol
— Bicarbonate – 20 mmol
— Potassium – 10 mmol

RETURN TO CONTENTS
LABETALOL HYDROCHLORIDE

**CLINICAL USE**
Beta-adrenoceptor blocker:
- Hypertensive crisis, hypertension

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: 50–800 mg twice daily (in 3–4 divided doses in high doses); maximum 2.4 g daily
- IV infusion: 2 mg/minute until satisfactory response; usual total dose 50–200 mg
- IV bolus: 50 mg over 1 minute, repeated at 5 minute intervals to a total dose of 200 mg
- Pregnancy: 20–160 mg/hour
- Hypertension after an MI: 15–120 mg/hour

**PHARMACOKINETICS**
- Molecular weight (daltons) 364.9
- % Protein binding 50
- % Excreted unchanged in urine 5
- Volume of distribution (L/kg) 5.6
- Half-life – normal/ESRF (hrs) 4–8/Unchanged

**DOSE IN RENAL IMPAIRMENT**
<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/ VVHD: Probably not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Analgesics: NSAIDs antagonise hypotensive effect
- Anti-arrhythmics: increased risk of myocardial depression and bradycardia;

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
- Oral, IV

**RATE OF ADMINISTRATION**
- 2 mg/minute initially then titrate according to response or to indication

**COMMENTS**
- 200 mg labetalol (40 mL) to 200 mL glucose 5%
- Can be used undiluted. (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006)

**OTHER INFORMATION**
- No adverse effects on renal function
- No accumulation in renal impairment
- Hypoglycaemia can occur in dialysis patients
- Tachyphylaxis can occur with prolonged use
Lacidipine

**CLINICAL USE**
Calcium-channel blocker:
- Hypertension

**DOSE IN NORMAL RENAL FUNCTION**
2–6 mg once daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 455.5
- % Protein binding: 95%
- % Excreted unchanged in urine: 0%
- Volume of distribution (L/kg): 0.9–2.3
- Half-life – normal/ESRF (hrs): 13–19/

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Unknown dialysability. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs:
- Anaesthetics: enhanced hypotensive effect
- Anti-epileptics: effect possibly reduced by carbamazepine, barbiturates, phenytoin and primidone
- Antifungals: metabolism possibly inhibited by itraconazole and ketoconazole
- Antihypertensives: enhanced hypotensive effect, increased risk of first dose hypotensive effect of post-synaptic alpha-blockers
- Antivirals: concentration possibly increased by ritonavir
- Ciclosporin: 10 kidney transplant patients on ciclosporin, prednisone and azathioprine were given 4 mg lacidipine daily. A very small increase in the trough serum levels (+6%) and AUC (+14%) of the ciclosporin occurred
- Grapefruit juice: concentration increased – avoid concomitant use
- Theophylline: possibly increased theophylline concentration

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**
  -

RETURN TO CONTENTS
Lactulose

CLINICAL USE
- Constipation
- Hepatic encephalopathy

DOSE IN NORMAL RENAL FUNCTION
- Constipation: initially 15 mL twice daily; adjust according to requirements
- Hepatic encephalopathy: 30–50 mL 3 times daily adjusted to produce 2–3 soft stools daily

PHARMACOKINETICS
Molecular weight 342.3 (daltons)
% Protein binding No data
% Excreted unchanged in urine <3
Volume of distribution N/A – not absorbed (L/kg)
Half-life – normal/ESRF (hrs) No data

DOSE IN RENAL IMPAIRMENT
GFR (mL/Min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Not dialysed. Dose as in normal renal function
HD Not dialysed. Dose as in normal renal function
HDF/High flux Not dialysed. Dose as in normal renal function
CAV/ VVHD Not dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- None known

ADMINISTRATION
RECONSTITUTION
–
ROUTE
- Oral
RATE OF ADMINISTRATION
–
COMMENTS
–

OTHER INFORMATION
- May take up to 72 hours to work
- Not significantly absorbed from GIT
- Safe for diabetics (lactulose is converted to lactic, formic and acetic acid in the bowel)
- Osmotic and bulking effect
Lamivudine

**CLINICAL USE**
Nucleoside reverse transcriptase inhibitor:
- Treatment of HIV in combination with other antiretroviral drugs
- Treatment of chronic hepatitis B in adults

**DOSE IN NORMAL RENAL FUNCTION**
HIV: 150 mg twice daily or 300 mg daily
Hepatitis B: 100 mg daily

**PHARMACOKINETICS**
- Molecular weight: 229.3 daltons
- % Protein binding: <36
- % Excreted unchanged in urine: 70
- Volume of distribution (L/kg): 1.3

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>HIV: 150 mg daily.</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>Hepatitis B: 100 mg stat then 50 mg daily</td>
</tr>
<tr>
<td>15–30</td>
<td>Hepatitis B: 100 mg stat then 25 mg daily</td>
</tr>
<tr>
<td>5–15</td>
<td>Hepatitis B: 35 mg stat then 15 mg daily</td>
</tr>
<tr>
<td>&lt;5</td>
<td>Hepatitis B: 35 mg stat then 10 mg daily</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapies</th>
<th>Dosing Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;5 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;5 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;5 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR=5–15 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Trimethoprim: inhibits excretion of lamivudine – avoid concomitant use of high dose co-trimoxazole
- Antivirals: avoid concomitant use with foscarnet, emtricitabine and IV ganciclovir

**ADMINISTRATION**

**RECONSTITUTION**
- Route: Oral
- Rate of Administration: –
- Comments: Administer with or without food

**OTHER INFORMATION**
- 15 mL of oral suspension contains 3 g of sucrose
- Dosage from Bennett (4th edition):
  - GFR>50 mL/min: 100% of dose
  - GFR=10–50 mL/min: 150 mg loading dose then 50–150 mg daily
  - GFR<10 mL/min: 50 mg loading dose then 25–50 mg daily

References:
Lamotrigine

CLINICAL USE
- Monotherapy and adjunctive treatment of partial seizures, and primary and secondary generalised tonic-clonic seizures
- Trigeminal neuralgia (unlicensed)

DOSE IN NORMAL RENAL FUNCTION
25–200 mg daily in 1–2 divided doses, according to clinical indication. Maximum 500 mg daily; 700 mg with enzyme-inducing drugs

PHARMACOKINETICS
- Molecular weight (daltons) 256.1
- % Protein binding 55
- % Excreted unchanged in urine <10
- Volume of distribution (L/kg) 0.92–1.22
- Half-life – normal/ESRF (hrs) 24–35/Unchanged

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
- 20–50 Caution. Start with low doses and monitor closely
- 10–20 Caution. Start with low doses and monitor closely
- <10 Caution. Start with low doses and monitor closely

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD Unlikely dialysability. Dose as in GFR<10 mL/min.
- HD Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD Unknown dialysability. Dose as in GFR=10–20 mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Antibacterials: concentration reduced by rifampicin
- Antidepressants: antagonism of anticonvulsant effect
- Antimalarials: mefloquine antagonises anticonvulsant effect; chloroquine and hydroxychloroquine occasionally reduce seizure threshold
- Oestrogens and progestogens: concentration of lamotrigine reduced and the dose may need to be increased by as much as 2-fold

ADMINISTRATION
- RECONSTITUTION
  - ROUTE
    - Oral
  - RATE OF ADMINISTRATION
    - COMMENTS

OTHER INFORMATION
- There is no experience of treatment with lamotrigine in patients with renal failure. Pharmacokinetic studies using single doses in subjects with renal failure indicate that lamotrigine pharmacokinetics are little affected, but plasma concentrations of the major glucuronide metabolite increase almost 8-fold due to reduced renal clearance
- The 2-N-glucuronide is inactive and accounts for 75–90% of the metabolised drug present in the urine. Although the metabolite is inactive the consequences of accumulation are unknown; hence the company advise caution with the use of lamotrigine in renal impairment
- The half-life of lamotrigine is affected by other drugs; reduced to 14 hours when given with enzyme-inducing drugs, e.g. carbamazepine and phenytoin, and is increased to approximately 70 hours when co-administered with sodium valproate alone
Lansoprazole

**CLINICAL USE**
Gastric acid suppression

**DOSE IN NORMAL RENAL FUNCTION**
- 15–30 mg daily in the morning; duration dependent on indication
- Zollinger-Ellison syndrome: initially 60 mg daily; adjust according to response (if >120 mg, give in 2 divided doses)

**PHARMACOKINETICS**
- Molecular weight: 369.4 daltons
- % Protein binding: 97%
- % Excreted unchanged in urine: 0 (% 15–30 as metabolites)
- Volume of distribution: 25–33 litres

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**: Unlikely to be dialysed. Dose as in normal renal function
- **HD**: Not dialysed. Dose as in normal renal function
- **HDF/High flux**: Unknown dialysability. Dose as in normal renal function
- **CAV/VVHD**: Unknown dialysability, probably not removed. Dose as in normal renal function.

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antivirals: concentration of atazanavir possibly reduced
- Ciclosporin: theoretical, interaction unlikely – little information available
- Cilostazol: possibly increased cilostazol concentration – avoid concomitant use
- Tacrolimus: may increase tacrolimus concentration

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- Lansoprazole is metabolised substantially by the liver; no dose adjustment is necessary in renal impairment
Lanthanum carbonate

**CLINICAL USE**
Phosphate binder in patients with CKD 5

**DOSE IN NORMAL RENAL FUNCTION**
Usually 750 mg – 1.5 g 3 times a day with meals

**PHARMACOKINETICS**
- Molecular weight: 457.8 daltons
- % Protein binding: >99.7%
- % Excreted unchanged in urine: Negligible
- Volume of distribution (L/kg): Not absorbed
- Half-life – normal/ESRF (hrs): 36

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Renal Replacement Therapy</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>VVHD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antifungals: absorption of ketoconazole reduced – give at least 2 hours apart
- Antimalarials: absorption of chloroquine and hydroxychloroquine possibly reduced – give at least 2 hours apart

**ADMINISTRATION**

- **ROUTE**
  - Oral

- **RATE OF ADMINISTRATION**
  - Must be chewed WITH food; do not take before meals

**OTHER INFORMATION**
- Following ingestion, lanthanum carbonate is converted in the GI tract to the insoluble lanthanum phosphate, which is not readily absorbed into the blood
- Bioavailability of drugs administered concomitantly may be reduced due to binding by lanthanum carbonate
- Very little is absorbed
- If not taken with meals, may result in vomiting
**Leflunomide**

**CLINICAL USE**
Disease modifying agent:
- Active rheumatoid arthritis
- Psoriatic arthritis

**DOSE IN NORMAL RENAL FUNCTION**
- Rheumatoid arthritis: 100 mg daily for 3 days then 10–20 mg daily
- Psoriatic arthritis: 100 mg daily for 3 days then 20 mg daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>270.2</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>&gt;99</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>0</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>11 litres</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>2 weeks (metabolite)/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Use with caution</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Use with caution</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Use with caution</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Use with caution</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Hepatotoxic or haemotoxic drugs: increased risk of toxicity
- Lipid-lowering agents: effect significantly reduced by colestyramine
- Live vaccines: avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- Administer with food

**OTHER INFORMATION**

- Contraindicated by manufacturer due to insufficient evidence
- US licence says it can be used in renal impairment with caution
- Protein binding is variable in CKD
- In haemodialysis and PD the free fraction of the active metabolite in plasma is doubled
Lenalidomide

**CLINICAL USE**

Treatment of multiple myeloma in combination with dexamethasone

**DOSE IN NORMAL RENAL FUNCTION**

25 mg daily on days 1–21 of a 28 day cycle; reduce dose if patient has neutropenia or thrombocytopenia; see data sheet

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>259.3</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>22.7–29.2</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>65–85</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>86 litres</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>3.5/&gt;9</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>10 mg daily, increasing to 15 mg after 2 cycles if patient is not responding</td>
</tr>
<tr>
<td>&lt;30</td>
<td>15 mg every 48 hours</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>15 mg 2–3 times a week</td>
</tr>
<tr>
<td>HD</td>
<td>15 mg 3 times a week post dialysis</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>15 mg 3 times a week post dialysis</td>
</tr>
<tr>
<td>CAV/</td>
<td>Probably dialysed. Dose as in GFR=30–50 mL/min</td>
</tr>
<tr>
<td>VVHD</td>
<td>15 mg 3 times a week post dialysis</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs

- Cardiac glycosides: possibly increases concentration of digoxin

**ADMINISTRATION**

<table>
<thead>
<tr>
<th>RECONSTITUTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>–</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ROUTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>– Oral</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>RATE OF ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>–</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>–</td>
</tr>
</tbody>
</table>

**OTHER INFORMATION**

- May cause acute renal failure – monitor renal function during treatment. Patients with renal impairment are more likely to develop side effects
Lenograstim

CLINICAL USE
Recombinant human granulocyte-colony stimulating factor (rHuG-CSF):
- Reduction of duration of neutropenia

DOSE IN NORMAL RENAL FUNCTION
- Cytotoxic neutropenia: 150 mcg/m² (19.2 MIU/m²) daily SC
- Mobilisation of peripheral blood progenitor cells: 10 mcg/kg (1.28 MIU/kg) daily
- Bone marrow transplant: 150 mcg/m² (19.2 MIU/m²) daily as an IV infusion

PHARMACOKINETICS
Molecular weight (daltons) 20 000
% Protein binding No data
% Excreted <1 unchanged in urine
Volume of distribution 1 (L/kg)
Half-life – normal/ESRF (hrs) 3–4

DOSE IN RENAL IMPAIRMENT
GFR (mL/MIN)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Not dialysed. Dose as in normal renal function
HD Not dialysed. Dose as in normal renal function
HDF/High flux Unlikely to be dialysed. Dose as in normal renal function
CAV/VVHD Not dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- None known

ADMINISTRATION
RECONSTITUTION
- Water for injection (1 mL)
ROUTE
- SC, IV
RATE OF ADMINISTRATION
- 30 minutes
COMMENTS
- Dilute lenograstim-13.4 in up to 50 mL sodium chloride 0.9%
- Dilute lenograstim-33.6 in up to 100 mL sodium chloride 0.9%
Lepirudin

**CLINICAL USE**

Anticoagulant:
- Patients with heparin associated thrombocytopenia

**DOSE IN NORMAL RENAL FUNCTION**

0.4 mg/kg bolus, followed by 0.15 mg/kg/hr (max 16.5 mg/hour) infusion adjusted according to APTT, usually for 2–10 days (maximum body weight 110 kg)

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>6979.4</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>No data</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>35</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>12.2 litres</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>10 minutes (initial half-life) 1.3 (terminal)/48</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

**GFR (mL/min)**

- **45–60** Reduce bolus to 0.2 mg/kg and infusion rate by 50%
- **30–44** Reduce bolus to 0.2 mg/kg and infusion rate to 30% of normal
- **15–29** Reduce bolus to 0.2 mg/kg and infusion rate to 15% of normal
- **<15** Avoid, or if APTT is below lower therapeutic limit then 0.1 mg/kg on alternate days as an IV bolus

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Modality</th>
<th>Dose and Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as for GFR&lt;15 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as for GFR&lt;15 mL/min. See ‘Other Information’</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as for GFR&lt;15 mL/min. See ‘Other Information’</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as for GFR =15–29 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Thrombolytics: may increase risk of bleeding complications; enhance effect of lepirudin
- Antiplatelets and anticoagulants: increased risk of bleeding complications

**ADMINISTRATION**

**RECONSTITUTION**

- 1 mL water for injection or sodium chloride 0.9%

**ROUTE**

- IV

**RATE OF ADMINISTRATION**

- 0.15 mg/kg/hour

**COMMENTS**

- Further dilute with sodium chloride 0.9% or glucose 5% if for infusion
- Bolus concentration should be 5 mg/mL and infusion 2 mg/mL
- Change syringe at least every 12 hours after start of infusion

**OTHER INFORMATION**

- Lepirudin may also be used for the prevention of clotting in the extracorporeal circulation during haemodialysis and haemofiltration (non-licensed indication)
- Dose for dialysis anticoagulation if <4.5 hr session is 0.141– 0.152 mg/kg as an IV bolus pre-dialysis.
- Alternative is 0.01 mg/kg IV bolus, followed by a continuous infusion of 0.01 mg/kg/hour, adjusted to APTT 1.5–2 normal (0.005 mg/kg/hr was adequate). (Schneider T, Heuer B, Deller A, et al. Continuous haemofiltration with r-hirudin (lepirudin) as anticoagulant in a patient with heparin induced thrombocytopenia. *Wien Klin Wochenschr*. 2000, Jun; 112(12): 552–5.)
- Recent reports of 7 cases of severe anaphylactic reactions resulting in 5 fatalities and at least 6 of the cases were after re-exposure. In some cases it was used outside its therapeutic indication

**RETURN TO CONTENTS**
Use with great caution, as it cannot be reversed.

Results from studies in pigs have found that Von Willebrand factor 66 IU/kg can reduce bleeding time.

References:

- Significant accumulation with long-term use in renal impairment.
Lercanidipine hydrochloride

**CLINICAL USE**
Calcium-channel antagonist:
- Mild to moderate hypertension

**DOSE IN NORMAL RENAL FUNCTION**
10–20 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 648.2
- % Protein binding: >98
- % Excreted unchanged in urine: 50 (as metabolites)
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 8–10/Increased

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Use small doses and titrate to response
  - 10–20: Use small doses and titrate to response
  - <10: Use small doses and titrate to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Unlikely to be dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Antibacterials: avoid concomitant use with erythromycin
- Anti-epileptics: effect reduced by carbamazepine, barbiturates, phenytoin and primidone
- Antifungals: metabolism possibly inhibited by itraconazole and ketoconazole – avoid concomitant use
- Antihypertensives: enhanced hypotensive effect, increased risk of first dose hypotensive effect of post-synaptic alpha-blockers
- Antivirals: concentration increased by ritonavir – avoid concomitant use
- Cardiac glycosides: digoxin concentration increased
- Ciclosporin: concentration of both drugs may be increased – avoid concomitant use
- Grapefruit juice: concentration increased – avoid concomitant use
- Theophylline: possibly increased theophylline concentration

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - COMMENTS
  - Take before food

**OTHER INFORMATION**
- Causes less peripheral oedema than other calcium-channel blockers
## Letrozole

### CLINICAL USE
Treatment of advanced breast cancer

### DOSE IN NORMAL RENAL FUNCTION
2.5 mg daily

### PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>285.3</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>60</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>6</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1.87</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>48/Unchanged</td>
</tr>
</tbody>
</table>

### DOSE IN RENAL IMPAIRMENT GFR (mL/Min)

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

### DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Probably dialysed. Use with caution</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Use with caution</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Use with caution</td>
</tr>
<tr>
<td>CAV/ VVHD</td>
<td>Probably dialysed. Use with caution</td>
</tr>
</tbody>
</table>

### IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- None known

### ADMINISTRATION

#### RECONSTITUTION
-

#### ROUTE
- Oral

#### RATE OF ADMINISTRATION
-

#### COMMENTS
-

---

RETURN TO CONTENTS
Leuprorelin acetate

CLINICAL USE
Treatment of advanced prostate cancer and endometriosis

DOSE IN NORMAL RENAL FUNCTION
- 11.25 mg every 3 months (SC depot injection, prostate cancer only)
- Or 3.75 mg every 4 weeks
- Endometriosis: 3.75 mg every month or 11.25 mg every 3 months for maximum 6 months (not to be repeated)

PHARMACOKINETICS
- Molecular weight (daltons) 1269.5
- % Protein binding 43–49
- % Excreted unchanged in urine <5 (+ metabolites)
- Volume of distribution (L/kg) 27 litres
- Half-life – normal/ESRF (hrs) 3/increased

DOSE IN RENAL IMPAIRMENT
GFR (mL/Min)
- 20–50 Dose as in normal renal function
- 10–20 Dose as in normal renal function
- <10 Dose as in normal renal function

Monitor closely

DOSE IN RENAL REPLACEMENT THERAPIES
- CAP Unlikely to be dialysed. Dose as in normal renal function
- HD Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux Unknown dialysability. Dose as in normal renal function
- CAV/VVHD Unlikely to be dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- None known

ADMINISTRATION
- RECONSTITUTION
  - With diluent provided
- ROUTE
  - IM, SC depot
- RATE OF ADMINISTRATION
  - COMMENTS
  -

OTHER INFORMATION
- Women on dialysis may be at greater risk of ovarian hyperstimulation, possibly because dialysis affects circulating leuprorelin concentration so endogenous gonadotrophins were still excreted. Alternatively, haemodialysis patients may have increased responsiveness to endogenous gonadotrophins

RETURN TO CONTENTS
Levamisole (unlicensed product)

### CLINICAL USE
Treatment of roundworm (*Ascaris lumbricoides*)

### DOSE IN NORMAL RENAL FUNCTION
120–150 mg as a single dose

### PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>204.3</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>19–26</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>5</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>100–120 litres</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>3–4 (16 for metabolites)</td>
</tr>
</tbody>
</table>

### DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

### DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Modalities</th>
<th>Dialysability</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Unknown. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

### IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Alcohol: may produce a disulfiram-like reaction
- Phenytoin: increased levels of phenytoin have been reported
- Warfarin: enhanced INR

### ADMINISTRATION

#### RECONSTITUTION
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - COMMENTS
  -

### OTHER INFORMATION

- Available on a named patient basis from IDIS
- Avoid in patients with pre-existing blood disorders
- Has also been used in haemodialysis patients to enhance response to Hepatitis B vaccine. (Kayatas M. Levamisole treatment enhances protective antibody response to hepatitis B vaccine in hemodialysis patients. *Artif Organs*. 2002 Jun; 26(6): 492–6)
Levetiracetam

**CLINICAL USE**
Anti-epileptic agent

**DOSE IN NORMAL RENAL FUNCTION**
250 mg – 1.5 g twice daily

**PHARMACOKINETICS**
- Molecular weight (daltons) 170.2
- % Protein binding <10
- % Excreted unchanged in urine 66 (95% drug + metabolite)
- Volume of distribution (L/kg) 0.5–0.7
- Half-life – normal/ESRF (hrs) 6–8/25

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 50–79 500–1000 mg twice daily
- 30–49 250–750 mg twice daily
- <30 250–500 mg twice daily

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Likely dialysability. 750 mg loading dose then 500–1000 mg daily
- HD Dialysed. 750 mg loading dose then 500–1000 mg once daily
- HDF/High flux Dialysed. 750 mg loading dose then 500–1000 mg once daily
- CAV/ VVHD GFR=30–49 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antidepressants: antagonism of anticonvulsant effect (convulsive threshold lowered)
- Antimalarials: mefloquine antago
izes anticonvulsant effect; chloroquine and hydroxychloroquine occasionally reduce seizure threshold

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral, IV

**RATE OF ADMINISTRATION**
- 15 minutes

**COMMENTS**
- Dilute in 100 mL sodium chloride or glucose 5%

**OTHER INFORMATION**
- 51% of the dose is removed with 4 hours of haemodialysis
- The inactive metabolite (ucb L057) accumulates in renal failure

References:
Levocetirizine hydrochloride

**CLINICAL USE**
Antihistamine:
● Symptomatic relief of allergy such as hay fever, urticaria

**DOSE IN NORMAL RENAL FUNCTION**
5 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons) 461.8
- % Protein binding 90
- % Excreted unchanged in urine 85.4 (includes metabolites)
- Volume of distribution (L/kg) 0.4
- Half-life – normal/ESRF (hrs) 6–9.8/Increased

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>5 mg every 48 hours. See ‘Other Information’</td>
</tr>
<tr>
<td>10–30</td>
<td>5 mg every 72 hours. See ‘Other Information’</td>
</tr>
<tr>
<td>&lt;10</td>
<td>5 mg every 72 hours. See ‘Other Information’</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely dialysability. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Unlikely dialysability. Dose as in GFR=10–30 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
● None known

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  ● Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**
  -

**OTHER INFORMATION**
● Data sheet recommends avoid, but anecdotally it has been used at normal dose in haemodialysis patients
● Less than 10% is removed during a 4 hour haemodialysis session
Levofloxacin

CLINICAL USE
Antibacterial agent

DOSE IN NORMAL RENAL FUNCTION
250–500 mg once or twice a day (varies depending on indication)

PHARMACOKINETICS
Molecular weight (daltons) 361.4
% Protein binding 30–40
% Excreted unchanged in urine >85
Volume of distribution (L/kg) 1.1–1.5
Half-life – normal/ESRF (hrs) 6–8/35

DOSE IN RENAL IMPAIRMENT
GFR (mL/MIN)

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Initial dose</th>
<th>Dose adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>250–500 mg</td>
<td>Then reduce dose by 50%</td>
</tr>
<tr>
<td>10–20</td>
<td>250–500 mg</td>
<td>Then 125 mg 12–24 hourly</td>
</tr>
<tr>
<td>&lt;10</td>
<td>250–500 mg</td>
<td>Then 125 mg 24–48 hourly</td>
</tr>
</tbody>
</table>

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Renal Replacement Therapy</th>
<th>Dose and Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Not dialysed. Loading dose: 500 mg then 250 mg every 24 hours.</td>
</tr>
<tr>
<td>VVHD</td>
<td></td>
</tr>
</tbody>
</table>

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Analgesics: possibly increased risk of convulsions with NSAIDs
- Anticoagulants: anticoagulant effect of coumarins and phenindione enhanced
- Antimalarials: manufacturer advises avoid concomitant use with artemether and lumefantrine
- Ciclosporin: half-life of ciclosporin increased by 33%; increased risk of nephrotoxicity
- Tacrolimus: may increase tacrolimus concentration
- Theophylline: possibly increased risk of convulsions

ADMINISTRATION

RECONSTITUTION
- ROUTE
  - Oral, IV
- RATE OF ADMINISTRATION
  - 30 minutes per 250 mg
- COMMENTS
  -

OTHER INFORMATION
- Dose and frequency depend on indication

References:
Levomepromazine (methotrimeprazine)

CLINICAL USE
- Treatment of schizophrenia
- Adjunctive treatment in palliative care
- Nausea and vomiting

DOSE IN NORMAL RENAL FUNCTION
- Schizophrenia: Oral, initially 25–50 mg daily, increasing to 100–200 mg in 3 divided doses; maximum dose 1 g daily
- Palliative care:
  - Oral: 12.5–50 mg every 4–8 hours
  - IM/IV: 12.5–50 mg every 6–8 hours
  - SC Infusion: 5–200 mg daily

PHARMACOKINETICS
- Molecular weight (daltons): 328.5
- % Protein binding: No data
- % Excreted unchanged in urine: 1
- Volume of distribution (L/kg): 23–42
- Half-life – normal/ESRF (hrs): 30/–

DOSE IN RENAL IMPAIRMENT
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Start with small dose and increase as necessary

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD: Unknown dialysability. Dose as in GFR<10mL/min
- HD: Unknown dialysability. Dose as in GFR<10mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10mL/min
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Analgesics: increased risk of convulsions with tramadol; increased hypotension and sedation with opioid analgesics
- Anti-arrhythmics: increased risk of ventricular arrhythmias due to prolongation of QT interval; increased risk of ventricular arrhythmias with amiodarone – avoid concomitant administration
- Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin – avoid concomitant administration
- Antidepressants: possibly increased plasma level of tricyclics, increased antimuscarinic effects and ventricular arrhythmias; avoid concomitant administration with MAOIs (2 fatalities have been reported)
- Anticonvulsant: lowers anticonvulsant threshold
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: increased risk of ventricular arrhythmias with pimozide – avoid concomitant use
- Antivirals: plasma concentration possibly increased by ritonavir
- Antihypertensives: enhanced hypotensive effect; increased risk of ventricular arrhythmias with sotalol
- Anxiolytics and hypnotics: increased sedation
- Dihydropyridines: enhanced hypotensive effect
- Lithium: increased risk of extrapyramidal effects and neurotoxicity
- Pentamidine: increased risk of ventricular arrhythmias – avoid concomitant use
- Selgicline: increased risk of CNS toxicity – avoid concomitant use
ADMINISTRATION

RECONSTITUTION

ROUTE
○ Oral, IV, IM, SC

RATE OF ADMINISTRATION

COMMENTS
○ For a subcutaneous infusion dilute in sodium chloride 0.9% and give via a syringe driver

Compatible with diamorphine
○ For IV injection, dilute with an equal volume of sodium chloride 0.9%

OTHER INFORMATION

○ In renal disease there is an increased risk of cerebral sensitivity
Levothyroxine sodium (thyroxine)

**CLINICAL USE**
Hypothyroidism

**DOSE IN NORMAL RENAL FUNCTION**
25–300 micrograms daily depending on thyroid hormone levels

**PHARMACOKINETICS**
- Molecular weight (daltons) 798.9
- % Protein binding 99.97
- % Excreted unchanged in urine 30–55
- Volume of distribution (L/kg) 8.7–9.7
- Half-life – normal/ESRF (hrs) 6–7 days/ Unchanged

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50 Dose as in normal renal function
- 10–20 Dose as in normal renal function
- <10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Not dialysed. Dose as in normal renal function
- HD Not dialysed. Dose as in normal renal function
- HDF/High flux Not dialysed. Dose as in normal renal function
- CAV/ VVHD Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: effect of coumarins and phenindione enhanced

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  -

**OTHER INFORMATION**
- Uraemic toxins may result in inhibition of the enzyme associated with conversion of L-thyroxine to liothyronine
Lidocaine hydrochloride

CLINICAL USE

- Local anaesthetic
- Ventricular arrhythmias

DOSE IN NORMAL RENAL FUNCTION

- Local anaesthetic: usually 1 or 2% solutions used, according to patient’s weight and procedure
- Ventricular arrhythmias: 100 mg as a bolus in patients without gross circulatory impairment (50 mg in lighter patients or in severely impaired circulation), followed by an infusion of 4 mg/min for 30 minutes, 2 mg/min for 2 hours, then 1 mg/min or according to local policy

PHARMACOKINETICS

- Molecular weight (daltons) 288.8
- % Protein binding 66
- % Excreted unchanged in urine <10
- Volume of distribution (L/kg) 1.3
- Half-life – normal/ESRF (hrs) 1–2/1.3–3

DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)

- 20–50 Dose as in normal renal function
- 10–20 Dose as in normal renal function
- <10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

- CAPD Unlikely to be dialysed. Dose as in normal renal function
- HD Not dialysed. Dose as in normal renal function
- HDF/High flux Unknown dialysability. Dose as in normal renal function
- CAV/VVHD Not dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs

- Anti-arrhythmics: increased risk of myocardial depression
- Antibacterials: increased risk of ventricular arrhythmias with quinupristin/dalfopristin
- Antipsychotics: increased risk of ventricular arrhythmias with antipsychotics that prolong the QT interval
- Antivirals: concentration possibly increased by ampranavir, atazanavir, darunavir and lopinavir – avoid concomitant use with amprenavir and darunavir
- Beta-blockers: increased risk of myocardial depression; increased risk of lidocaine toxicity with propranolol
- Diuretics: effects antagonised by hypokalaemia
- Dolasetron and tropisetron: increased risk of ventricular arrhythmias – avoid concomitant use
- Ulcer-healing drugs: concentration increased by cimetidine, increased toxicity

ADMINISTRATION

- RECONSTITUTION
- ROUTE
  - IV, SC, topical
- RATE OF ADMINISTRATION
  - According to dose
- COMMENTS
  - Usually 1–2 mg/mL in glucose 5%
  - Minimum volume 8–20 mg/mL but watch for extravasation. (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006

OTHER INFORMATION

- IV injection lasts for only 15–20 minutes
Linezolid

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
600 mg twice daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 337.3
- % Protein binding: 31
- % Excreted unchanged in urine: 30
- Volume of distribution (L/kg): 0.6
- Half-life – normal/ESRF (hrs): 5–7/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Dose as in normal renal function, but monitor closely. See ‘Other Information’</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**: Likely to be dialysed. Dose as in GFR<10mL/min
- **HD**: Dialysed. Dose as in GFR<10mL/min
- **HDF/High flux**: Dialysed. Dose as in GFR<10mL/min
- **CAV/VVHD**: Dialysed. Dose as in normal renal function
- **CVVHDF**: Dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antidepressants: increased risk of serotonergic syndrome with SSRIs and tricyclics; avoid concomitant use with MAOIs, moclobemide
- Selegiline: avoid concomitant use
- Sympathomimetics: enhanced hypertensive effect with adrenaline, noradrenaline, dopamine, dobutamine, phenylpropanolamine and pseudoephedrine – use with caution

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral, IV
  - **RATE OF ADMINISTRATION**
    - Over 30–120 minutes
  - **COMMENTS**

**OTHER INFORMATION**

- 30% of dose is removed by a 3 hour haemodialysis session
- In patients with GFR<10mL/min, if platelet count drops on a dose of 600 mg twice daily, consider reducing dose to 600 mg once daily
- Two metabolites accumulate in renal failure which have MAOI activity but no antibacterial activity – monitor patients closely
- There is 5 mmol sodium per 300 mL infusion
- Linezolid is a weak, reversible non-selective inhibitor of MAO therefore can be used with drugs not normally given with MAOIs (e.g. SSRIs) but monitor closely
- In patients who have been on linezolid for longer than 28 days, there have been reports of peripheral neuropathy and/or optic neuropathy occasionally leading to loss of vision, anaemia requiring transfusions, and lactic acidosis – visual function should be monitored in these patients
- After oral or IV administration, adequate drug concentrations can be found in PF fluid to treat VRE peritonitis. (Salzer W. Antimicrobial-resistant gram-positive bacteria in PD peritonitis. *Perit Dial Int*. 2005; **25**: 313–19.)

References:
Liothyronine sodium (tri-iodothyronine)

**CLINICAL USE**

Hypothyroidism

**DOSE IN NORMAL RENAL FUNCTION**

- Oral: 10–20 micrograms daily, increased to 60 micrograms in 2–3 divided doses
- IV: 5–20 micrograms every 4–12 hours, or 50 micrograms initially then 25 micrograms every 8 hours, reducing to 25 micrograms twice a day

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>673</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>&lt;99</td>
</tr>
<tr>
<td>% Excreted</td>
<td>2.5</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.1–0.2</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>24–48/–</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Not dialysed. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Anticoagulants: effect of coumarins and phenindione enhanced

**ADMINISTRATION**

**RECONSTITUTION**

- Dissolve with 1–2 mL water for injection

**RATE OF ADMINISTRATION**

- IV, oral

**COMMENTS**

- Alkaline solution – may cause irritation if given IM

**OTHER INFORMATION**

- 20mcg of liothyronine is equivalent to 100mcg of levotyroxine
- Protein-losing states, such as nephrotic syndrome, will result in a decrease in total T3 and T4
- Thyroxine (T4) is the drug of choice in hypothyroidism, but T3 can be useful due to its rapid onset of action
- Elderly patients should receive smaller initial doses
Lisinopril

**CLINICAL USE**

Angiotensin-converting enzyme inhibitor:
- Hypertension, heart failure, following myocardial infarction in haemodynamically stable patients
- Diabetic nephropathy

**DOSE IN NORMAL RENAL FUNCTION**

2.5–80 mg daily
After a myocardial infarction: 2.5–10 mg daily

**PHARMACOKINETICS**

- Molecular weight (daltons) 441.5
- % Protein binding 0
- % Excreted unchanged in urine 80–90
- Volume of distribution (L/kg) 0.44–0.51
- Half-life – normal/ESRF (hrs) 12/40–50

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Initial dose</th>
<th>Titrate according to response</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>2.5 mg daily</td>
<td>daily and titrate</td>
</tr>
<tr>
<td>10–20</td>
<td>2.5 mg daily</td>
<td>daily and titrate</td>
</tr>
<tr>
<td>&lt;10</td>
<td>2.5 mg daily</td>
<td>daily and titrate</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>MODality</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/ VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Anaesthetics: enhanced hypotensive effect
- Analgesics: antagonism of hypotensive effect and increased risk of renal impairment with NSAIDs; hyperkalaemia with ketorolac and other NSAIDs
- Ciclosporin: increased risk of hyperkalaemia and nephrotoxicity
- Diuretics: enhanced hypotensive effect; hyperkalaemia with potassium-sparing diuretics
- Epoetin: increased risk of hyperkalaemia; antagonism of hypotensive effect
- Lithium: reduced risk of hyperkalaemia; antagonism of hypotensive effect
- Potassium salts: increased risk of hyperkalaemia
- Tacrolimus: increased risk of hyperkalaemia and nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**

- **COMMENTS**

**OTHER INFORMATION**

- Close monitoring of renal function during therapy is necessary in those with renal insufficiency
- Renal failure has been reported in association with ACE inhibitors and has been mainly in patients with severe congestive heart failure, renal artery stenosis, and post renal transplant
- High incidence of anaphylactoid reactions has been reported in patients dialysed with high-flux polyacrylonitrile membranes and treated concomitantly with an ACE inhibitor – this combination should therefore be avoided
- Hyperkalaemia and other side effects are more common in patients with impaired renal function
Lithium carbonate

**CLINICAL USE**
- Treatment and prophylaxis of mania, manic depressive illness, and recurrent depression
- Aggressive or self-mutilating behaviour

**DOSE IN NORMAL RENAL FUNCTION**
See individual preparations. Adjust according to lithium plasma concentration

**PHARMACOKINETICS**
- Molecular weight: 73.9 (daltons)
- % Protein binding: 0
- % Excreted unchanged in urine: 95
- Volume of distribution: 0.5–0.9 L/kg

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Avoid if possible, or reduce dose and monitor plasma concentration carefully</td>
</tr>
<tr>
<td>10–20</td>
<td>Avoid if possible, or reduce dose and monitor plasma concentration carefully</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Avoid if possible, or reduce dose and monitor plasma concentration carefully</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose in intoxication. Dose as in GFR&lt;10mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Dialysed in lithium intoxication. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed in lithium intoxication. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed in lithium intoxication. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/ VVHD</td>
<td>Dialysed. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
- ACE inhibitors and angiotensin-II antagonists: lithium excretion reduced

- Analgesics: NSAIDs and ketorolac reduce excretion of lithium
- Anti-arrhythmics: increased risk of ventricular arrhythmias with amiodarone – avoid concomitant use
- Antidepressants: increased risk of CNS effects with SSRIs; risk of toxicity with tricyclics; possible increased serotonergic effects with venlafaxine
- Antipsychotics: increased risk of extrapyramidal side effects and possibly neurotoxicity with clozapine, haloperidol and phenothiazines; increased risk of ventricular arrhythmias with sertindole – avoid concomitant use; increased risk of extrapyramidal side effects with sulpiride
- Diuretics: lithium excretion reduced by loop diuretics, potassium-sparing diuretics, aldosterone antagonists and thiazides; lithium excretion increased by acetazolamide
- Methyldopa: neurotoxicity may occur without increased lithium levels

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
  - Different preparations vary widely in bioavailability; a change in the preparation used requires the same precautions as initiation of treatment

**OTHER INFORMATION**
- Doses are adjusted to achieve lithium plasma concentrations of 0.4–1.0 mmol/L (lower end of range for maintenance therapy in elderly patients) in samples taken 12 hours after the preceding dose. It takes 4–7 days to reach steady state
- Long-term treatment may result in permanent changes in kidney histology and impairment of renal function. High serum concentration of lithium, including episodes of acute lithium toxicity, may aggravate these changes. The minimum clinically effective dose of lithium should always be used
Bennett (4th ed.) suggests 25–50% of normal dose if GFR<10 mL/min, and 50–75% of normal dose if GFR between 10–50 mL/min – monitor lithium plasma concentrations closely.

- Lithium generally should not be used in patients with severe renal disease because of increased risk of toxicity.
- Dialysability: serum lithium concentrations rebound within 5–8 hours post haemodialysis because of redistribution of the drug, often necessitating repeated courses of haemodialysis. Peritoneal dialysis is less effective at removing lithium and is only used if haemodialysis is not possible.
- Up to one-third of patients on lithium may develop polyuria, usually due to lithium blocking the effect of ADH. This reaction is reversible on withdrawal of lithium therapy.
Lofepramine

CLINICAL USE
Tricyclic antidepressant

DOSE IN NORMAL RENAL FUNCTION
140–210 mg daily in 2–3 divided doses

PHARMACOKINETICS
Molecular weight (daltons) 455.4 (as hydrochloride)
% Protein binding 99
% Excreted unchanged in urine Mainly as metabolites
Volume of distribution (L/kg) Large
Half-life – normal/ESRF (hrs) 1.7–5/

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Start with a small dose and titrate slowly

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unknown dialysability. Dose as in GFR<10 mL/min
HD Unknown dialysability. Dose as in GFR<10 mL/min
HDF/High flux Unknown dialysability. Dose as in GFR<10 mL/min
CAV/ VVHD Unknown dialysability. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● Alcohol: increased sedative effect
● Analgesics: increased risk of CNS toxicity with tramadol; possibly increased risk of side effects with nefopam; possibly increased sedative effects with opioids
● Anti-arrhythmics: increased risk of ventricular arrhythmias with amiodarone – avoid concomitant use; increased risk of ventricular arrhythmias with drugs that prolong the QT interval; increased risk of arrhythmias with propafenone
● Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin – avoid concomitant use; concentration reduced by rifampicin
● Anticoagulants: may enhance or reduce anticoagulant effect of coumarins
● Antidepressants: enhanced CNS excitation and hypertension with MAOIs and moclobemide; concentration possibly increased with SSRIs
● Anti-epileptics: convulsive threshold lowered; some anti-epileptics may lower plasma concentration of some tricyclics
● Antimalarials: avoid concomitant use with artether/lumefantrine
● Antipsychotics: increased risk of ventricular arrhythmias and antimuscarinic effects; concentration increased by tricyclics
● Antivirals: increased tricyclic side effects with amprenavir; concentration possibly increased with ritonavir
● Atomoxetine: increased risk of ventricular arrhythmias; possibly increased risk of convulsions
● Beta-blockers: increased risk of ventricular arrhythmias with sotalol
● Clonidine: tricyclics antagonise hypotensive effect; increased risk of hypertension on clonidine withdrawal
● Dopaminergics: avoid use with entacapone; CNS toxicity reported with selegiline and rasagiline
● Pentamidine: increased risk of ventricular arrhythmias
● Sympathomimetics: increased risk of hypertension and arrhythmias with adrenaline and noradrenaline; metabolism possibly inhibited by methylphenidate
● Sibutramine: increased risk of CNS toxicity – avoid concomitant use

ADMINISTRATION
RECONSTITUTION –
ROUTE ● Oral
RATE OF ADMINISTRATION –
COMMENTS –
Lomustine

CLINICAL USE
Treatment of Hodgkin’s disease and certain solid tumours

DOSE IN NORMAL RENAL FUNCTION
120–130 mg/m² every 6–8 weeks if used alone; lower dose is used in combination treatment and compromised bone marrow function

PHARMACOKINETICS
- Molecular weight: 233.7 daltons
- % Protein binding: 60
- % Excreted: 50 (as metabolites) unchanged in urine
- Volume of distribution: No data

DOSE IN RENAL IMPAIRMENT
GFR (mL/Min)
- 45–60: 75% of dose
- 30–45: 50–70% of dose
- <30: Not recommended. See ‘Other Information’

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD: Unlikely to be dialysed. Avoid
- HD: Not dialysed. Avoid. See ‘Other Information’
- HDF/High flux: Unknown dialysability. Avoid. See ‘Other Information’
- CAV/VVHD: Unlikely to be dialysed. Avoid. See ‘Other Information’

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- None known

ADMINISTRATION

RECONSTITUTION
- ROUTE
- Oral
- RATE OF ADMINISTRATION
- COMMENTS
- OTHER INFORMATION
- Bone marrow toxicity is delayed
- Relatively rapid and complete oral absorption, followed by first pass metabolism. Part of lomustine metabolism is mediated through hepatic microsomal enzymes. Metabolites predominantly excreted by kidneys; 10% excreted as CO₂ and <5% in faeces
- Dosage from BC Cancer Agency:
  - GFR=12–48 mL/min, give 75% of previous dose
  - GFR<12 mL/min, give 25–50% of previous dose

RETURN TO CONTENTS
Loperamide hydrochloride

**CLINICAL USE**
Antidiarrhoeal agent

**DOSE IN NORMAL RENAL FUNCTION**
4 mg stat, then 2 mg after each loose stool; maximum 16 mg daily

**PHARMACOKINETICS**
- **Molecular weight (daltons)**: 513.5
- **% Protein binding**: 80
- **% Excreted unchanged in urine**: <10
- **Volume of distribution (L/kg)**: No data
- **Half-life – normal/ESRF (hrs)**: 9–14/–

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/Min)**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function. Maximum dose usually 12 mg daily depending on tolerability

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- **HD**: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- **HDF/High flux**: Unknown dialysability. Dose as in GFR<10 mL/min
- **CAV/VVHD**: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**
- **RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- In normal doses loperamide may cause excessive drowsiness in CKD 5
**Lopinavir**

**CLINICAL USE**

Protease inhibitor:
- Treatment of HIV infected patients, in combination with other antiretroviral agents

**DOSE IN NORMAL RENAL FUNCTION**

3 capsules twice daily (in combination with ritonavir, Kaletra), or 5 mL twice daily

**PHARMACOKINETICS**

| Molecular weight (daltons) | 628.8 |
| % Protein binding          | 98–99 |
| % Excreted unchanged in urine | 2.2 |
| Volume of distribution (L/kg) | 0.5 |
| Half-life – normal/ESRF (hrs) | 5–6/12–17 |

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function. Monitor closely</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**: Unlikely to be dialysed. Dose as in GFR<10mL/min
- **HD**: Unlikely to be dialysed. Dose as in GFR<10mL/min
- **HDF/High flux**: Unlikely to be dialysed. Dose as in GFR<10mL/min
- **CAV/VVHD**: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Antibacterials: concentration reduced by rifampicin – avoid concomitant use; avoid concomitant use with telithromycin in severe renal and hepatic impairment
- Antidepressants: concentration reduced by St John’s wort – avoid concomitant use
- Anti-epileptics: concentration possibly reduced by carbamazepine, phenytoin and primidone
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: possibly inhibits metabolism of aripiprazole – reduce dose of aripiprazole; increased concentration of sertrindole (increased risk of ventricular arrhythmias) – avoid concomitant use
- Antivirals: amprenavir concentration reduced, concentration reduced by efavirenz, tipranavir and nelfinavir; active metabolite of nelfinavir increased; concentration possibly reduced by nevirapine; concentration of saquinavir and tenofivir increased; concentration increased by darunavir and darunavir concentration reduced
- Barbiturates: concentration reduced by phenobarbital
- Ciclosporin: may increase concentration of ciclosporin
- Cilostazol: possibly increases concentration of cilostazol – avoid concomitant use
- Sirolimus: may increase concentration of sirolimus
- Statins: increased risk of myopathy with atorvastatin; possibly increased risk of myopathy with simvastatin – avoid concomitant use
- Tacrolimus: may increase concentration of tacrolimus

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - **Oral**

**RATE OF ADMINISTRATION**
- **COMMENTS**
  - Take with food

**OTHER INFORMATION**
- 3 capsules = 5 mL of oral solution
Loratadine

**CLINICAL USE**
Antihistamine:
- Symptomatic relief of allergy such as hay fever, urticaria

**DOSE IN NORMAL RENAL FUNCTION**
10 mg daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>382.9</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>97–99</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>40</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>No data</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>12–15/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**
  - Not dialysed. Dose as in normal renal function
- **HD**
  - Not dialysed. Dose as in normal renal function
- **HDF/High flux**
  - Unknown dialysability. Dose as in normal renal function
- **CAV/VVHD**
  - Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Antibacterials: concentration possibly increased by erythromycin
- Antifungals: concentration of loratadine possibly increased by ketoconazole – avoid concomitant use
- Antivirals: concentration possibly increased by amprenavir – avoid concomitant use; concentration possibly increased by ritonavir

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  -

**OTHER INFORMATION**

- Patients with renal impairment are at increased risk of sedation
Lorazepam

**CLINICAL USE**

Benzodiazepine:
- Short-term use in anxiety or insomnia
- Status epilepticus
- Perioperative

**DOSE IN NORMAL RENAL FUNCTION**

- Anxiety: 1–4 mg daily in divided doses
- Insomnia associated with anxiety: 1–2 mg at bedtime
- Acute panic attacks (IV/IM): 25–30 mcg/kg; repeat 6 hourly if required; usual range 1.5–2.5 mg
- Status epilepticus: 4 mg IV repeated once after 10 minutes

**PHARMACOKINETICS**

- Molecular weight (daltons) 321.2
- % Protein binding 85
- % Excreted unchanged in urine <1
- Volume of distribution (L/kg) 0.9–1.3
- Half-life – normal/ESRF (hrs) 10–20/32–70

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Unlikely dialysability. Dose as in normal renal function.
- HD: Not dialysed. Dose as in normal renal function.
- HDF/High flux: Unknown dialysability. Dose as in normal renal function.
- CAV/VVHD: Not dialysed. Dose as in normal renal function.

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Antibacterials: metabolism possibly increased by rifampicin
- Antipsychotics: increased sedative effects; increased risk of hypotension, bradycardia and respiratory depression when parenteral benzodiazepines are given with IM olanzapine
- Antivirals: concentration possibly increased by ritonavir
- Disulfiram: metabolism inhibited, increased sedative effects
- Sodium oxybate: enhanced effects of sodium oxybate – avoid
- Ulcer-healing drugs: metabolism inhibited by cimetidine

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral, IV, IM, sublingual
- **RATE OF ADMINISTRATION**
  - Slow IV bolus
- **COMMENTS**
  - Onset of effect after IM injection is similar to oral administration
  - IV route preferred over IM route
  - Dilute 1:1 with sodium chloride 0.9% or water for injection
  - Can be used undiluted. (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006)

**OTHER INFORMATION**

- Patients with impaired renal or hepatic function should be monitored frequently and have their dosage adjusted carefully according to response. Lower doses may be sufficient in these patients
- Lorazepam as intact drug is not removed by dialysis. The glucuronide metabolite is highly dialysable, but is pharmacologically inactive
- Increased CNS sensitivity in patients with renal impairment

RETURN TO CONTENTS
Lormetazepam

**CLINICAL USE**
Benzodiazepine:
- Insomnia (short-term use)

**DOSE IN NORMAL RENAL FUNCTION**
0.5–1.5 mg at night

**PHARMACOKINETICS**
- Molecular weight (daltons): 335.2
- % Protein binding: 85
- % Excreted unchanged in urine: <6 (86 as metabolites)
- Volume of distribution (L/kg): 4.6
- Half-life – normal/ESRF (hrs): 11–16/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min): 20–50
  - Dose as in normal renal function
- 10–20
  - Dose as in normal renal function. Start with small doses
- <10
  - Dose as in normal renal function. Start with small doses

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10mL/min
- HD: Not dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10mL/min
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: metabolism possibly increased by rifampicin
- Antipsychotics: increased sedative effects
- Antivirals: concentration possibly increased by ritonavir
- Disulfiram: metabolism inhibited, increased sedative effects
- Sodium oxybate: enhanced effect – avoid concomitant use

**ADMINISTRATION**
**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**
  -

**OTHER INFORMATION**
- Increased CNS sensitivity in renal impairment
- Long-term use may lead to dependence and withdrawal symptoms in certain patients
- The half-life of the glucuronide metabolite is increased in renal impairment
Losartan potassium

**CLINICAL USE**
Angiotensin-II receptor antagonist:
- Hypertension
- Type 2 diabetic nephropathy

**DOSE IN NORMAL RENAL FUNCTION**
25–100 mg daily

**PHARMACOKINETICS**
Molecular weight (daltons) 461
% Protein binding > 98
% Excreted unchanged in urine 4
Volume of distribution (L/kg) 0.4
Half-life – normal/ESRF (hrs) 1.5–2.5 (active metabolite 3–9)/4–6

**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Titration</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Initial dose 25 mg and titrate according to response</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Initial dose 25 mg and titrate according to response</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapies</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/ VVHD</td>
<td>Not dialysed. Dose as in GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs:
- Anaesthetics: enhanced hypotensive effect
- Analgesics: antagonism of hypotensive effect and increased risk of renal impairment with NSAIDs; hyperkalaemia with ketorolac and other NSAIDs
- Ciclosporin: increased risk of hyperkalaemia and nephrotoxicity
- Diuretics: enhanced hypotensive effect; hyperkalaemia with potassium-sparing diuretics
- Epoetin: increased risk of hyperkalaemia; antagonism of hypotensive effect
- Lithium: reduced excretion (possibility of enhanced lithium toxicity)
- Potassium salts: increased risk of hyperkalaemia
- Tacrolimus: increased risk of hyperkalaemia and nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- Adverse reactions, especially hyperkalaemia are more common in patients with renal impairment
- Renal failure has been reported in association with angiotensin-II antagonists in patients with renal artery stenosis, post renal transplant, and in those with congestive heart failure
- Close monitoring of renal function during therapy is necessary in those with renal insufficiency
Lymecycline

CLINICAL USE
Antibacterial agent:
● Also used for treatment of acne

DOSE IN NORMAL RENAL FUNCTION
● 408 mg (1 capsule) twice daily, increasing to 3–4 capsules daily in severe infections
● Acne: 408 mg daily for at least 8 weeks

PHARMACOKINETICS
Molecular weight (daltons) 602.6
% Protein binding Approx 25–60
% Excreted unchanged in urine 25
Volume of distribution (L/kg) Approx 1.3–1.7
Half-life – normal/ESRF (hrs) 10/Increased

DOSE IN RENAL IMPAIRMENT
GFR (mL/Min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Avoid. See ‘Other Information’

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Not dialysed. Dose as in GFR<10mL/min
HD Not dialysed. Dose as in GFR<10mL/min
HDF/High flux Unknown dialysability. Dose as in GFR<10mL/min
CAV/ VVHD Unlikely to be dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● Anticoagulants: possibly enhanced anticoagulant effect of coumarins and phenindione
● Oestrogens: possibly reduce contraceptive effects of oestrogens (risk probably small)
● Retinoids: possible increased risk of benign intracranial hypertension – avoid concomitant use

ADMINISTRATION
RECONSTITUTION –
ROUTE
● Oral
RATE OF ADMINISTRATION –
COMMENTS
● Do not take iron preparations, indigestion remedies or phosphate binders at the same time of day as lymecycline

OTHER INFORMATION
● Lymecycline is a tetracycline derivative
● 408 mg lymecycline ≡ 300 mg tetracycline
● Not recommended in severe renal impairment as lymecycline is mainly excreted by the kidneys
Mebendazole

**CLINICAL USE**
Treatment of threadworm, roundworm, whipworm, and hookworm infections

**DOSE IN NORMAL RENAL FUNCTION**
- Threadworm: 100 mg as a single dose; if re-infection occurs repeat after 2–3 weeks
- Whipworm, roundworm, hookworm: 100 mg twice daily for 3 days
- Echinococcosis: 40–50 mg/kg daily for at least 3–6 months

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>295.3</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>95</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>2</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1–1.2</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>0.93/–</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose in Normal Renal Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose in Normal Renal Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Cimetidine: possibly inhibits metabolism of mebendazole
- Phenytoin, carbamazepine and phenobarbital: lower mebendazole concentrations, only relevant when being used in high doses for echinococcosis

**ADMINISTRATION**

**RECONSTITUTION**
-)

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
-)

**COMMENTS**
-)

**OTHER INFORMATION**

- Contraindicated in pregnancy
- Undergoes first pass metabolism
- Poorly absorbed from the gastrointestinal tract (5–10%)
Medroxyprogesterone acetate

CLINICAL USE
Cachexia (unlicensed), contraception, epilepsy, male hypersexuality, malignant neoplasms, respiratory disorders, sickle-cell disease, dysfunctional uterine bleeding, endometriosis

DOSE IN NORMAL RENAL FUNCTION
- Cachexia (unlicensed): 500 mg twice daily
- Contraception: 150 mg (deep IM) within first 5 days of cycle or within first 5 days after parturition, repeated every 12 weeks
- Breast cancer: Oral: 400–800 mg daily; IM: Initially 500–1000 mg daily for 4 weeks then 500 mg twice weekly
- Other hormone sensitive malignancies: Oral: 100–600 mg daily, IM: 500 mg, frequency dependent on cancer
- Endometrial cancer: 200–400 mg daily
- Renal adenocarcinoma: 200–400 mg daily
- Dysfunctional uterine bleeding: 2.5–10 mg daily for 5–10 days beginning on day 16–21 of cycle, repeated for 2–3 cycles
- Endometriosis: 10 mg 3 times a day for 90 consecutive days, beginning on day 1 of cycle
- Progestogenic opposition of oestrogen HRT: 10 mg daily for the last 14 days of each 28 day oestrogen HRT cycle
- See product literature for more specific information

PHARMACOKINETICS
Molecular weight (daltons) 386.5
% Protein binding 94
% Excreted unchanged in urine <5
Volume of distribution (L/kg) >20 litres
Half-life – normal/ESRF (hrs) 24–48 (up to 50 days after IM administration)

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function. Monitor carefully

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Antibacterials: metabolism of progestogens accelerated by rifamycins (reduced contraceptive effect)
- Anticoagulants: progestogens antagonise anticoagulant effect of coumarins and phenindione
- Antidepressants: contraceptive effect reduced by St John's wort – avoid concomitant use
- Anti-epileptics: metabolism accelerated by carbamazepine, oxcarbazepine, phenytoin, primidone and topiramate and barbiturates (reduced contraceptive effect); concentration of lamotrigine reduced
- Antifungals: metabolism accelerated by griseofulvin (reduced contraceptive effect); occasional reports of breakthrough bleeding when used with terbinafine if used for contraception
- Antivirals: contraceptive effect reduced by nelfinavir; metabolism accelerated by nevirapine (reduced contraceptive effect); amprenavir concentration reduced and amprenavir increases medroxyprogesterone concentration
- Aprepitant: possible contraceptive failure
- Bosentan: possible contraceptive failure
- Ciclosporin: progestogens inhibit metabolism of ciclosporin (increased plasma concentration)
- Tacrolimus: contraceptive effect of progestogens possibly reduced by tacrolimus
<table>
<thead>
<tr>
<th>ADMINISTRATION</th>
<th>OTHER INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>RECONSTITUTION</td>
<td>⚫ Do not use in patients with porphyria</td>
</tr>
<tr>
<td>ROUTE</td>
<td>⚫ Mainly metabolised in the liver</td>
</tr>
<tr>
<td>● Oral, IM</td>
<td>References:</td>
</tr>
<tr>
<td>COMMENTS</td>
<td></td>
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<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Mefenamic acid

**CLINICAL USE**

NSAID:
- Mild to moderate rheumatic pain
- Dysmenorrhoea and menorrhagia

**DOSE IN NORMAL RENAL FUNCTION**

500 mg 3 times a day

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>241.3</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>99</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>6</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1.06</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>2–4/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in normal renal function, but avoid if possible</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
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<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Modality</th>
<th>Dose Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function. See 'Other Information'</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function. See 'Other Information'</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function. See 'Other Information'</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be dialysed. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- ACE inhibitors and angiotensin-II antagonists: antagonism of hypotensive effect; increased risk of nephrotoxicity and hyperkalaemia
- Analgesics: avoid concomitant use of 2 or more NSAIDs, including aspirin (increased side effects); avoid with ketorolac (increased risk of side effects and haemorrhage)
- Antibacterials: possibly increased risk of convulsions with quinolones
- Anticoagulants: effects of coumarins enhanced; possibly increased risk of bleeding with heparins and coumarins
- Antidepressants: increased risk of bleeding with SSRIs and venlafaxine
- Antidiabetic agents: effects of sulphonylureas enhanced
- Anti-epileptics: possibly increased phenytoin concentration
- Antivirals: increased risk of haematological toxicity with zidovudine; concentration possibly increased by ritonavir
- Ciclosporin: may potentiate nephrotoxicity
- Cytotoxic agents: reduced excretion of methotrexate; increased risk of bleeding with erlotinib
- Diuretics: increased risk of nephrotoxicity; antagonism of diuretic effect; hyperkalaemia with potassium-sparing diuretics
- Lithium: excretion decreased
- Pentoxifylline: increased risk of bleeding
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  -
- **COMMENTS**
  -
 OTHER INFORMATION

- As with other prostaglandin inhibitors, allergic glomerulonephritis has occurred occasionally. There have also been reports of acute interstitial nephritis with haematuria and proteinuria and occasionally nephrotic syndrome.
- Inhibition of renal prostaglandin synthesis by NSAIDs may interfere with renal function, especially in the presence of existing renal disease – avoid use if possible; if not, check serum creatinine 48–72 hours after starting NSAID – if raised, discontinue NSAID therapy.
- Use with caution in renal transplant recipients (can reduce intrarenal autacoid synthesis).
- Use normal doses in patients with CKD 5 on dialysis if they do not pass any urine.
Mefloquine

**CLINICAL USE**
Malaria prophylaxis and treatment

**DOSE IN NORMAL RENAL FUNCTION**
- **Prophylaxis:** 250 mg weekly
- **Treatment:**
  - Non-immune patients: 20–25 mg/kg in 2–3 divided doses; maximum 1.5 g
  - Partially-immune patients: 15 mg/kg in 2–3 divided doses

**PHARMACOKINETICS**
- **Molecular weight:** 414.8 (as hydrochloride)
- **% Protein binding:** 98
- **% Excreted unchanged in urine:** 9 (+4% metabolites)
- **Volume of distribution (L/kg):** 20
- **Half-life – normal/ESRF (hrs):** 21 days

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in normal renal function</th>
<th>Dose as in normal renal function</th>
<th>Use with caution Prophylaxis: Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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</tr>
<tr>
<td>&lt;10</td>
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<td></td>
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</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapies</th>
<th>Dose</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed</td>
<td>Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed</td>
<td>Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed</td>
<td>Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/ VVHD</td>
<td>Not dialysed</td>
<td>Dose as in GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- **Anti-arrhythmics:** increased risk of ventricular arrhythmias with amiodarone
  - Avoid concomitant use
- **Antibacterials:** increased risk of ventricular arrhythmias with moxifloxacin
  - Avoid concomitant use
- **Anti-epileptics:** antagonism of anticonvulsant effect
- **Antimalarials:** increased risk of convulsions with chloroquine, hydroxychloroquine and quinine; avoid concomitant use with artemether and lumefantrine
- **Antipsychotics:** increased risk of ventricular arrhythmias, avoid concomitant use with pimozide
- **Atomoxetine:** increased risk of ventricular arrhythmias
- **Ivabradine:** increased risk of ventricular arrhythmias

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**

**OTHER INFORMATION**
- **Start prophylaxis 1–3 weeks before arriving in malarial area and continue for 4 weeks after leaving the malarial area**
- **Increased risk of convulsions in patients with epilepsy**
Meloxicam

**CLINICAL USE**
Cox II inhibitor and analgesic

**DOSE IN NORMAL RENAL FUNCTION**
7.5–15 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 351.4
- % Protein binding: 99
- % Excreted unchanged in urine: 3
- Volume of distribution (L/kg): 11 litres
- Half-life – normal/ESRF (hrs): 20

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function, but avoid if possible</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function, but avoid if possible</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in normal renal function. See ‘Other Information’.</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function. See ‘Other Information’.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unlikely to be dialysed. Dose as in normal renal function. See ‘Other Information’.</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- ACE inhibitors and angiotensin-II antagonists: antagonism of hypotensive effect; increased risk of nephrotoxicity and hyperkalaemia
- Analgesics: avoid concomitant use of 2 or more NSAIDs, including aspirin (increased risk of side effects); avoid with ketorolac (increased risk of side effects and haemorrhage)
- Antibacterials: possibly increased risk of convulsions with quinolones
- Anticoagulants: effects of coumarins enhanced; possibly increased risk of bleeding with heparins and coumarins
- Antidepressants: increased risk of bleeding with SSRIs and venlafaxine
- Antidiabetic agents: effects of sulphonylureas enhanced
- Anti-epileptics: possibly increased phenytoin concentration
- Antivirals: increased risk of haematological toxicity with zidovudine; concentration possibly increased by ritonavir
- Ciclosporin: may potentiate nephrotoxicity
- Cytotoxic agents: reduced excretion of methotrexate; increased risk of bleeding with erlotinib
- Diuretics: increased risk of nephrotoxicity; antagonism of diuretic effect; hyperkalaemia with potassium-sparing diuretics
- Lithium: decreased excretion leading to increased lithium levels
- Pentoxifylline: possibly increased risk of bleeding
- Tacrolimus: possibly increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral, PR
- **RATE OF ADMINISTRATION**
  - **COMMENTS**

**OTHER INFORMATION**
- Clinical trials have shown renal effects similar to those observed with comparative NSAIDs. Monitor patient for deterioration in renal function and fluid retention
- Inhibition of renal prostaglandin synthesis by NSAIDs may interfere with renal function, especially in the presence of existing renal disease – avoid if possible; if not, check serum creatinine 48–72 hours after starting NSAID – if raised, discontinue NSAID therapy
Use with caution in renal transplant recipients (can reduce intrarenal autocoid synthesis)

Meloxicam should be used with caution in uraemic patients predisposed to gastrointestinal bleeding or uraemic coagulopathies

Use normal doses in patients with CKD 5 on dialysis if they do not pass any urine
Melphalan

**CLINICAL USE**

Alkylation agent:
- Myelomas
- Solid tumours
- Lymphomas
- Polycythaemia vera

**DOSE IN NORMAL RENAL FUNCTION**

- Orally: 150–200 micrograms/kg daily
- Polycythaemia vera: 6–10 mg daily, reduced after 5–7 days to 2–4 mg daily, then further reduced to 2–6 mg per week
- IV administration: 16–200 mg/m² according to indication and local protocol

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tr>
<td>Molecular weight (daltons)</td>
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<td>60–90</td>
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<tr>
<td>% Excreted unchanged in urine</td>
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<tr>
<td>Volume of distribution (L/kg)</td>
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</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>0.5–2.5/4–6</td>
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</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as per local protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>See ‘Other Information’</td>
</tr>
<tr>
<td>10–20</td>
<td>See ‘Other Information’</td>
</tr>
<tr>
<td>&lt;10</td>
<td>See ‘Other Information’</td>
</tr>
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</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose as per local protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Antipsychotics: avoid concomitant use with clozapine (increased risk of agranulocytosis)
- Ciclosporin: increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**

- 10 mL of provided diluent

**ROUTE**

- IV, oral

**RATE OF ADMINISTRATION**

- Inject slowly into a fast running infusion solution or via an infusion bag

**COMMENTS**

- Further dilution with sodium chloride 0.9%

**OTHER INFORMATION**

- Melphalan clearance, though variable, is decreased in renal impairment
- Incomplete and variable oral absorption – 25–89% post oral dose; AUC decreased by 39% when taken with food
- Spontaneous degradation rather than enzymatic metabolism; Percentage of dose excreted in the urine as active or toxic moiety ranges from 11–93%; 20–50% excreted in the faeces within 6 days
- Currently available pharmacokinetic data do not justify an absolute recommendation on dosage reduction when administering melphalan tablets to patients with renal impairment, but it may be prudent to use a reduced dosage initially until tolerance is established
- When melphalan injection is used at conventional IV dosage (8–40 mg/m² BSA) in patients with moderate to severe renal impairment, it is recommended that the initial dose should be reduced by 50% and subsequent dosage be determined by the degree of haematological suppression
- For high IV doses of melphalan (100–240 mg/m² BSA), the need for dose reduction depends upon the degree of renal impairment, whether autologous bone marrow stem cells are re-infused, and therapeutic need. High dose melphalan is not recommended in patients with more severe renal impairment (EDTA clearance less than 30 mL/minute)
- It should be borne in mind that dose reduction of melphalan in renal impairment is somewhat arbitrary. At moderate doses, where melphalan is used as part of a combined regimen, dosage reductions of up to 50% may be appropriate. However, at high doses, e.g. conditioning for bone marrow transplant, there is a risk of under-dosing the patient and not achieving the desired therapeutic effect.

RETURN TO CONTENTS
effect, so the dose should be reduced with caution in these instances

- Adequate hydration and forced diuresis may be necessary in patients with poor renal function

- In myeloma patients with renal damage, temporary but significant increases in blood urea levels have been observed during melphalan therapy
Mepacrine hydrochloride (unlicensed product)

<table>
<thead>
<tr>
<th>CLINICAL USE</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Giardiasis</td>
</tr>
<tr>
<td>● Discoid lupus erythematosus</td>
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<table>
<thead>
<tr>
<th>DOSE IN NORMAL RENAL FUNCTION</th>
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</thead>
<tbody>
<tr>
<td>100 mg every 8 hours for 5–7 days</td>
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</table>

<table>
<thead>
<tr>
<th>PHARMACOKINETICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
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<tr>
<td>% Protein binding</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
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<tr>
<td>Half-life – normal/ESRF (hrs)</td>
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<table>
<thead>
<tr>
<th>DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)</th>
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<tbody>
<tr>
<td>20–50</td>
</tr>
<tr>
<td>10–20</td>
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<tr>
<td>&lt;10</td>
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</table>

<table>
<thead>
<tr>
<th>IMPORTANT DRUG INTERACTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potentially hazardous interactions with other drugs</td>
</tr>
<tr>
<td>● Alcohol: can cause a mild disulfiram reaction</td>
</tr>
<tr>
<td>● Antimalarials: increased concentration of primaquine (increased risk of toxicity)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>RECONSTITUTION</td>
</tr>
<tr>
<td>–</td>
</tr>
<tr>
<td>ROUTE</td>
</tr>
<tr>
<td>● Oral</td>
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<table>
<thead>
<tr>
<th>RATE OF ADMINISTRATION</th>
</tr>
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<tbody>
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<table>
<thead>
<tr>
<th>COMMENTS</th>
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</table>

<table>
<thead>
<tr>
<th>OTHER INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Still detectable in the urine after 2 months</td>
</tr>
</tbody>
</table>
Meptazinol

**CLINICAL USE**
Opioid analgesic used for moderate to severe pain

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: 200 mg every 3–6 hours
- IM: 75–100 mg every 2–4 hours; obstetric analgesia: 100–150 mg depending on patient's weight (2 mg/kg)
- IV: 50–100 mg every 2–4 hours

**PHARMACOKINETICS**
- Molecular weight: 269.8 (as hydrochloride)
- % Protein binding: 27
- % Excreted unchanged in urine: <5
- Volume of distribution: 3.1 (L/kg)
- Half-life – normal/ESRF (hrs): 1.4–4

**DOSE IN RENAL IMPAIRMENT GFR (mL/min)**
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function. Start with low doses

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR<10 mL/min
- HD: Likely dialysability. Dose as in GFR<10 mL/min
- HDF/High flux: Likely dialysability. Dose as in GFR<10 mL/min
- CAV/CAVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antidepressants: possible CNS excitation or depression with MAOIs – avoid concomitant use; possible CNS excitation or depression with moclobemide; possibly increased sedative effects with tricyclics
- Sodium oxybate: enhanced effect of sodium oxybate – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral, IV, IM

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- Oral and IM peak analgesic effect occurs within 30–60 minutes and last for 3–4 hours
- IV works immediately and lasts for at least 1 hour

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Mercaptopurine

**CLINICAL USE**
Antineoplastic agent:
- Acute leukaemias
- Inflammatory bowel disease (unlicensed)

**DOSE IN NORMAL RENAL FUNCTION**
Usual dose is 2.5 mg/kg/day, but the dose and duration of administration depend on the nature and dosage of other cytotoxic agents given in conjunction.

**PHARMACOKINETICS**
- Molecular weight: 170.2 daltons
- % Protein binding: 20%
- % Excreted unchanged in urine: 7%
- Volume of distribution (L/kg): 0.1–1.7
- Half-life – normal/ESRF (hrs): 1–1.5/

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/MIN)**
  - 20–50: Caution – reduce dose. See ‘Other Information’
  - 10–20: Caution – reduce dose. See ‘Other Information’
  - <10: Caution – reduce dose. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**: Unknown dialysability. Dose as in GFR<10mL/min
- **HD**: Dialysed. Dose as in GFR<10mL/min
- **HDF/High flux**: Dialysed. Dose as in GFR<10mL/min
- **CAV/VVHD**: Unknown dialysability. Dose as in GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**
- Antibacterials: increased risk of haematological toxicity with co-trimoxazole and trimethoprim
- Anticoagulants: possibly reduced anticoagulant effect of coumarins
- Antipsychotics: avoid concomitant use with clozapine (increased risk of agranulocytosis)

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
  -

**OTHER INFORMATION**
- Absorption of an oral dose is incomplete, averaging ~50%. This is largely due to first pass metabolism in the liver (less when given with food). There is enormous interindividual variability in absorption, which can result in a 5-fold variations in AUC
- It is extensively metabolised (by intracellular activation). At conventional doses clearance is primarily hepatic. Renal clearance may become important at high doses
- The active metabolites have a longer half-life than the parent drug
- Wellcome UK recommend consideration be given to reducing the dose in patients with impaired hepatic or renal function, although no specific dosing guidelines are available
- With renal impairment, the following dosing intervals have been suggested: 24–36 hrs for CrCl of 50–80mL/min, and 48 hrs for CrCl of 10–50mL/min. (Summerhayes M, Daniels S (eds). *Practical Chemotherapy – A Multidisciplinary guide*. 1st ed. Abingdon: Radcliffe Medical Press Ltd. 2003. p. 384)
- A recent study on anti-cancer drug renal toxicity and elimination concluded that the dose of 6-mercaptopurine does not require modification in patients with decreased renal function (except in conjunction with allopurinol). This study also gives % excreted unchanged in urine as 21%. (Kintzel PE, Dorr RT. Anticancer drug renal toxicity and elimination: dosing guidelines for altered renal function. *Cancer Treat Rev*. 1995; 21: 33–64)
Meropenem

CLINICAL USE
Antibacterial agent

DOSE IN NORMAL RENAL FUNCTION
500 mg – 1 g every 8 hours
Higher doses used in cystic fibrosis and meningitis (up to 2 g every 8 hours)

PHARMACOKINETICS
Molecular weight 437.5 (daltons)
% Protein binding 2
% Excreted unchanged in urine 70
Volume of distribution (L/kg) 0.35
Half-life – normal/ESRF (hrs) 1/6–13.7

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
20–50 500 mg – 2 g every 12 hours
10–20 500 mg – 1 g every 12 hours or 500 mg every 8 hours
<10 500 mg – 1 g every 24 hours

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Dialysed. Dose as in GFR<10mL/min
HD Dialysed. Dose as in GFR<10mL/min or 1–2 g post dialysis
HDF/High flux Dialysed. Dose as in GFR<10mL/min
CAV/ VVHD Dialysed. 0.5–1 g every 8 hours
CVVHDF 1 g every 12 hours

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● Probencid: avoid concomitant use

ADMINISTRATION
RECONSTITUTION
● Add 5 mL water for injection to each 250 mg of meropenem

ROUTE
● IV

RATE OF ADMINISTRATION
● Bolus: 5 minutes
● IV Infusion: 15–30 minutes

COMMENTS
● Further dilute in 50–200 mL sodium chloride 0.9%, glucose 5% or glucose 10% if for infusion
● Stable for 24 hours once reconstituted
● Minimum volume 1 g in 10 mL. (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006)

OTHER INFORMATION
● Metabolite is inactive and renally excreted
● Each 1 g vial contains 3.9 mmol of sodium chloride
● Has less potential to induce seizures than imipenem
● Has been used intraperitoneally for peritoneal dialysis Pseudomonas peritonitis at concentration of 100 mg/L
● 50% is removed by CVVH; 13–53% by CVVHDF, 50% by intermittent HD.2
● Differences in renal replacement doses are due to the different flow rates used in the studies

References:
Mesalazine

**CLINICAL USE**
Induction and maintenance of remission in ulcerative colitis

**DOSE IN NORMAL RENAL FUNCTION**
Dose depends on preparation

**PHARMACOKINETICS**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
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<td>% Protein binding</td>
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<td>% Excreted unchanged in urine</td>
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<tr>
<td>Volume of distribution (L/kg)</td>
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<tr>
<td>Half-life – normal/ESRF (hrs)</td>
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</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Caution – use only if necessary. Start with low dose and increase according to response</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**
  - Unlikely to be dialysed. Dose as in GFR<10 mL/min

- **HD**
  - Unlikely to be dialysed. Dose as in GFR<10 mL/min

- **HDF/High flux**
  - Unknown dialysability. Dose as in GFR<10 mL/min

- **CAV/VVHD**
  - Unknown dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**

- Potentially hazardous interactions with other drugs
  - None known

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral, PR

**RATE OF ADMINISTRATION**

- **COMMENTS**

**OTHER INFORMATION**

- Mesalazine is excreted rapidly by the kidney, mainly as its metabolite N-acetyl-5-aminosalicylic acid
- Nephrotoxicity has been reported
- Mesalazine is best avoided in patients with established renal impairment, but if necessary should be used with caution, and the patient carefully monitored
Mesna

**CLINICAL USE**
Prophylaxis of urothelial toxicity in patients treated with ifosfamide or cyclophosphamide

**DOSE IN NORMAL RENAL FUNCTION**
Dose and timing depends on cytotoxic agent and on route of administration of mesna

**PHARMACOKINETICS**
- Molecular weight: 164.2 (daltons)
- % Protein binding: 70%
- % Excreted unchanged in urine: 32%
- Volume of distribution: 0.65 L/kg
- Half-life – normal/ESRF (hrs): 0.3/–

**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**
- 20–50: See ‘Other Information’
- 10–20: See ‘Other Information’
- <10: See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR<10 mL/min
- HD: Probably dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Probably dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**

**ROUTE**
- Oral, IV bolus, IV infusion

**RATE OF ADMINISTRATION**
- IV bolus: over 15–30 minutes
- IV infusion: over 12–24 hours

**COMMENTS**
- Compatible with sodium chloride 0.9% and glucose 5%
- Mesna injection can be administered orally in orange juice or cola to improve palatability

**OTHER INFORMATION**
- Urinary output should be maintained at 100 mL/hr (as required for oxazaphosphorine treatment)
- The dose of mesna is dependent on the dose of oxazaphosphorine, e.g. reduce dose of cyclophosphamide to 50% of normal if GFR <10 mL/min; hence, dose of mesna will consequently be reduced
- From what is known about the pharmacokinetics and mechanism of action of mesna, its availability in the urinary tract depends on renal function
- In the case of completely anuric patients (extremely rare) neither cyclophosphamide nor its metabolites should appear in the urinary tract: the use of mesna concomitantly may therefore be unnecessary in anuric patients. If there is any risk of cyclophosphamide or its metabolites entering the urinary tract, mesna should probably be given to prevent urothelial toxicity
- Limited kinetic information would suggest mesna would be eliminated by haemodialysis
Metformin hydrochloride

**CLINICAL USE**
- Non-insulin dependent diabetes mellitus
- Polycystic ovary syndrome

**DOSE IN NORMAL RENAL FUNCTION**
500 mg 3 times a day; maximum 2 g daily in divided doses
Polycystic ovary syndrome: 1.5–1.7 g daily in 2–3 divided doses

**PHARMACOKINETICS**
- Molecular weight: 165.6 (daltons)
- % Protein binding: Negligible
- % Excreted unchanged in urine: 100
- Volume of distribution (L/kg): 1–4

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min): 40–50 25–50% of dose
- 10–40 25% of dose. See ‘Other Information’
- <10 Avoid. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Avoid
- HD: Dialysed. Avoid
- HDF/High flux: Dialysed. Avoid
- CAV/VVHD: Probably dialysed. Avoid

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Alcohol: increased risk of lactic acidosis
- Cimetidine: Inhibits renal excretion of metformin

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral
  - RATE OF ADMINISTRATION
  - COMMENTS

**OTHER INFORMATION**
- Lactic acidosis is a rare but serious metabolic complication that can occur due to metformin accumulation. Reported cases have occurred primarily in diabetic patients with significant renal impairment
- As metformin is renally excreted eGFR values should be determined before initiating treatment and regularly thereafter:
  - at least annually in patients with normal renal function
  - at least 2–4 times a year in patients with an eGFR at the lower limit of normal and in elderly subjects
- Special caution should be exercised in the elderly in situations where renal function may become impaired, e.g. initiating therapy with antihypertensives, diuretics or NSAIDs
Methadone hydrochloride

**CLINICAL USE**
- Treatment of opioid drug addiction
- Analgesic for moderate to severe pain

**DOSE IN NORMAL RENAL FUNCTION**
- Opioid addiction: 10–40 mg per day, increasing by 10 mg per day until there are no signs of withdrawal or intoxication; reduce gradually
- Analgesia: 5–10 mg every 6–8 hours

**PHARMACOKINETICS**
- Molecular weight (daltons): 346.9
- % Protein binding: 60–90
- % Excreted unchanged in urine: 15–60
- Volume of distribution (L/kg): 3–6
- Half-life – normal/ESRF (hrs): 13–47/–

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: 50% of normal dose, and titrate according to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antidepressants: concentration possibly increased by fluvoxamine; possible CNS excitation or depression with MAOIs and moclobemide – avoid concomitant use; possibly increased sedative effects with tricyclics
- Anti-epileptics: concentration reduced by carbamazepine and phenytoin
- Antifungals: concentration increased by voriconazole – may need to reduce methadone dose
- Antivirals: methadone possibly increases concentration of zidovudine; concentration reduced by amprenavir, efavirenz, nelfinavir and ritonavir; concentration possibly reduced by abacavir and nevirapine
- Atomoxetine: increased risk of ventricular arrhythmias
- Sodium oxybate: enhanced effect of sodium oxybate – avoid concomitant use

**ADMINISTRATION**
- RECONSTITUTION
  - ROUTE
  - IM, SC, oral
- RATE OF ADMINISTRATION
  - COMMENTS
  - Methadone is probably not suitable to be used as an analgesic for patients with severe renal impairment

**OTHER INFORMATION**
- Overdosage with methadone can be reversed using naloxone
- Risk of QT interval prolongation especially with high doses and concomitant risk factors

---

It is not licensed for use by anyone else.
### Methenamine hippurate

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
1 g every 8–12 hours

**PHARMACOKINETICS**

<table>
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**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
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</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Avoid. See ‘Other Information’</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Avoid. See ‘Other Information’</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>Unknown dialysability. Avoid. See ‘Other Information’</td>
<td></td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Avoid. See ‘Other Information’</td>
<td></td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: increased risk of crystalluria with sulphonamides
- Diuretics: effects antagonised by acetazolamide

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- Avoid hippurate salt in renal impairment due to the risk of hippurate crystalluria
- Methenamine is not recommended in severe renal impairment as urinary concentrations are too low for it to be effective
- Contraindicated in metabolic acidosis, severe dehydration, renal parenchymal infections and hepatic failure
Methotrexate

CLINICAL USE
Antineoplastic agent:
- Severe rheumatoid arthritis
- Severe uncontrolled psoriasis
- Crohn's disease
- Neoplastic disease

DOSE IN NORMAL RENAL FUNCTION
- Rheumatoid arthritis: Oral, SC, IM, IV: 7.5–20 mg once a week
- Psoriasis: (Oral) 10–25 mg once weekly, adjusted to response
- Crohn's disease: 15–25 mg weekly
- Neoplastic disease: Dose by weight or surface area according to specific indication

PHARMACOKINETICS
Molecular weight (daltons) 454.4
% Protein binding 45–60
% Excreted unchanged in urine 80–90
Volume of distribution (L/kg) 0.4–0.8
Half-life – normal/ESRF (hrs) 2–17/Increased

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
- 20–50 50–100% of normal dose
- 10–20 50% of normal dose
- <10 Contraindicated

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Not dialysed. Contraindicated
HD Dialysed. Haemodialysis clearance is 38–40 mL/minute. 50% of normal dose at least 12 hours before next dialysis. Use with caution
HDF/High flux Dialysed. 50% of normal dose at least 12 hours before next dialysis. Use with caution
CAV/ VVHD Unknown dialysability. Dose as in GFR=10–20 mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Anaesthetics: antifolate effect increased by nitrous oxide – avoid concomitant use
- Analgesics: increased risk of toxicity with NSAIDs
- Antibacterials: absorption possibly reduced by neomycin; antifolate effect increased with co-trimoxazole and trimethoprim; penicillins and possibly ciprofloxacin reduce excretion of methotrexate (increased risk of toxicity); increased haematological toxicity with doxycycline and tetracycline
- Antimalarials: antifolate effect enhanced by pyrimethamine
- Antipsychotics: avoid concomitant use with clozapine (increased risk of agranulocytosis)
- Ciclosporin: methotrexate may inhibit the clearance of ciclosporin or its metabolites; ciclosporin may inhibit methotrexate elimination
- Corticosteroids: increased risk of haematological toxicity
- Cytotoxics: increased pulmonary toxicity with cisplatin
- Probencid: excretion of methotrexate reduced
- Retinoids: concentration increased by acitretin, also increased hepatotoxicity – avoid concomitant use

ADMINISTRATION
RECONSTITUTION
- Compatible with glucose 5%, sodium chloride 0.9%, compound sodium lactate, or Ringers solution
ROUTE
- Oral, IM, IV (bolus injection or infusion), intrathecal, intra-arterial, intraventricular
RATE OF ADMINISTRATION
- Slow IV injection
COMMENTS
- High-dose methotrexate may cause precipitation of methotrexate or its metabolites in renal tubules. A high fluid throughput and alkalinisation of urine, using sodium bicarbonate if necessary, is recommended

RETURN TO CONTENTS
OTHER INFORMATION

- The dose is well absorbed at doses <30 mg/m² – bioavailability is decreased by food and milk. Metabolism is via liver and intracellular metabolism to polyglutamated products.
- Excreted primarily by the kidneys (>90%), although small amounts via the bile. Clearance is higher in children than in adults.
- Calcium folinate (calcium leucovorin) is a potent agent for neutralising the immediate toxic effects of methotrexate on the haematopoietic system.
- Calcium folinate rescue may begin 24/32/36 hours post start of methotrexate therapy, according to local protocol. Doses of up to 120 mg may be given over 12–24 hours by IM or IV injection or infusion, followed by 12–15 mg IM, or 15 mg orally every 6 hours for the next 48 hours.
- Renal function should be closely monitored throughout treatment.
- An approximate correction for renal function may be made by reducing the dose in proportion to the reduction in creatinine clearance based on a normal creatinine clearance of 60 mL/minute/m².
- Alternative dosing regimen:

<table>
<thead>
<tr>
<th>CrCl (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;80</td>
<td>100%</td>
</tr>
<tr>
<td>60</td>
<td>65%</td>
</tr>
<tr>
<td>45</td>
<td>50%</td>
</tr>
<tr>
<td>&lt;30</td>
<td>Avoid</td>
</tr>
</tbody>
</table>

Methyldopa

**CLINICAL USE**
Hypertension

**DOSE IN NORMAL RENAL FUNCTION**
250 mg 2–3 times a day, increasing to a maximum dose of 3 g daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 238.2
- % Protein binding: <15
- % Excreted unchanged in urine: 25–40
- Volume of distribution (L/kg): 0.5
- Half-life – normal/ESRF (hrs): 1.6–2/6–16

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function and adjust according to response</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>10–20</td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dosage Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/Highf</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Probably dialysed. Dose as in</td>
</tr>
<tr>
<td>VVHD</td>
<td>GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Antidepressants: avoid concomitant use with MAOIs
- Lithium: neurotoxicity (without increased plasma-lithium concentrations)
- Salbutamol: acute hypotension reported with salbutamol infusions

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENT**
- 

**OTHER INFORMATION**
- Active metabolites with long half-life
- Interferes with serum creatinine measurement
- Orthostatic hypotension more common in renally impaired patients
Methylprednisolone

**CLINICAL USE**

Corticosteroid:
- Suppression of inflammatory and allergic disorder
- Immunosuppressant
- Rheumatic disease
- Cerebral oedema

**DOSE IN NORMAL RENAL FUNCTION**

Oral: 2–40 mg daily
IM/IV: 10–500 mg
Graft rejection: up to 1 g daily for up to 3 days. See ‘Other Information’

**PHARMACOKINETICS**

- Molecular weight (daltons): 375
- % Protein binding: 40–60
- % Excreted unchanged in urine: <10
- Volume of distribution (L/kg): 1.2–1.5
- Half-life – normal/ESRF (hrs): 2.4–3.5/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose as in normal renal function</th>
</tr>
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<tbody>
<tr>
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<td></td>
</tr>
<tr>
<td>&lt;10</td>
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</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Dialysed. Dose as in normal renal function
- HD: Dialysed. Dose as in normal renal function
- HDF/High flux: Dialysed. Dose as in normal renal function
- CAV/VVHD: Dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

- Potentially hazardous interactions with other drugs
  - Antibacterials: metabolism accelerated by rifampicin; metabolism possibly inhibited by erythromycin and clarithromycin
  - Anticoagulants: efficacy of coumarins may be altered
  - Anti-epileptics: metabolism accelerated by carbamazepine, barbiturates, phenytoin and primidone
  - Antifungals: increased risk of hypokalaemia with amphotericin – avoid concomitant use; metabolism possibly inhibited by itraconazole and ketoconazole
  - Antivirals: concentration possibly increased by ritonavir
  - Ciclosporin: rare reports of convulsions in patients on ciclosporin and high-dose corticosteroids; levels of ciclosporin increased with high dose methylprednisolone
  - Cytotoxics: increased risk of haematological toxicity with methotrexate
  - Diuretics: enhanced hypokalaemic effects of acetazolamide, loop diuretics and thiazide diuretics
  - Vaccines: high dose corticosteroids can impair immune response to vaccines; avoid concomitant use with live vaccines

**ADMINISTRATION**

**RECONSTITUTION**

- Use solvent supplied (Solu-medrone) or see manufacturer’s recommendations

**ROUTE**

- Oral, IM, IV peripherally or centrally

**RATE OF ADMINISTRATION**

- 30 minutes

**COMMENTS**

- NB: Rapid bolus injection may be associated with arrhythmias or cardiovascular collapse

**OTHER INFORMATION**

- A single dose of 500 mg – 1 g is often given at transplantation
- Three 500 mg – 1 g doses at 24 hour intervals are often used as first line for reversal of acute rejection episodes. (Some units use 300–500 mg daily for 3 days.)
- Anecdotally, possesses less mineralocorticoid activity than equipotent doses of prednisolone
Metoclopramide hydrochloride

**CLINICAL USE**
Nausea and vomiting

**DOSE IN NORMAL RENAL FUNCTION**
10 mg 3 times a day.
Use in patients under 20 years should be restricted

**PHARMACOKINETICS**
- Molecular weight (daltons) 354.3
- % Protein binding 13–22
- % Excreted unchanged in urine 20–30
- Volume of distribution (L/kg) 3.5
- Half-life – normal/ESRF (hrs) 4–6/15

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/MIN) 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Dialysed. Dose as in normal renal function
- HDF/High flux: Dialysed. Dose as in normal renal function
- CAV/VVHD: Dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Ciclosporin: increased ciclosporin blood levels

**ADMINISTRATION**
**RECONSTITUTION**
- **ROUTE**
  - Oral, IV, IM
- **RATE OF ADMINISTRATION**
  - 1–2 minutes
- **COMMENTS**

**OTHER INFORMATION**
- Increased risk of extrapyramidal reactions in severe renal impairment
- Can be used for hiccups at a dose of 10 mg 3 times a day

---

RETURN TO CONTENTS
Metolazone

**CLINICAL USE**
Thiazide diuretic, acts synergistically with loop diuretics:
- Oedema
- Hypertension

**DOSE IN NORMAL RENAL FUNCTION**
- Oedema: 5–10 mg, increased to 20 mg daily; maximum 80 mg daily
- Hypertension: 5 mg initially; maintenance: 5 mg on alternate days

**PHARMACOKINETICS**
- Molecular weight (daltons) 365.8
- % Protein binding 95
- % Excreted unchanged in urine 80–95
- Volume of distribution (L/kg) 1.6
- Half-life – normal/ESRF (hrs) 8–10/–

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50 Dose as in normal renal function
- 10–20 Dose as in normal renal function
- <10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Unlikely to be dialysed. Dose as in normal renal function
- HD Not dialysed. Dose as in normal renal function
- HDF/High flux Unknown dialysability. Dose as in normal renal function
- CAV/VHD Not Dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: increased risk of nephrotoxicity with NSAIDs; antagonism of diuretic effect
- Anti-arrhythmics: hypokalaemia leads to increased cardiac toxicity; effects of lidocaine and mexiletine antagonised
- Antibacterials: avoid administration with lymecycline
- Antidepressants: increased risk of hypokalaemia with reboxetine; enhanced hypotensive effect with MAOIs; increased risk of postural hypotension with tricyclics
- Anti-epileptics: increased risk of hyponatraemia with carbamazepine
- Antifungals: increased risk of hypokalaemia with amphotericin
- Antihypertensives: enhanced hypotensive effect; increased risk of first dose hypotension with post-synaptic alpha-blockers like prazosin; hypokalaemia increases risk of ventricular arrhythmias with sotalol
- Antipsychotics: hypokalaemia increases risk of ventricular arrhythmias with amisulpride or sertindole; enhanced hypotensive effect with phenothiazines; hypokalaemia increases risk of ventricular arrhythmias with pimozide – avoid concomitant use
- Atomoxetine: hypokalaemia increases risk of ventricular arrhythmias with amisulpride or sertindole; enhanced hypotensive effect with phenothiazines; hypokalaemia increases risk of ventricular arrhythmias with pimozide – avoid concomitant use
- Cardiac glycosides: increased toxicity if hypokalaemia occurs
- Ciclosporin: increased risk of nephrotoxicity and possibly hypomagnesaemia
- Lithium excretion reduced, increased toxicity

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  -

**OTHER INFORMATION**
- May result in profound diuresis. Monitor patient’s fluid balance carefully
- Monitor for hypokalaemia
- In patients with creatinine clearance less than 50 mL/minute there is no clinical evidence of accumulation
# Metoprolol tartrate

## CLINICAL USE

Beta-adrenoceptor blocker:
- Hypertension
- Angina
- Cardiac arrhythmias
- Migraine prophylaxis
- Hyperthyroidism

## DOSE IN NORMAL RENAL FUNCTION

**Oral:**
- Hypertension: 100–400 mg daily in divided doses
- Angina: 50–100 mg 2–3 times daily
- Arrhythmias: 100–300 mg in 2–3 divided doses
- Migraine: 100–200 mg daily in divided doses
- Hyperthyroidism: 50 mg 4 times daily

In surgery: 2–4 mg by slow IV injection then 2 mg as required to a maximum of 10 mg

## PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>684.8</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>10–12</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>5–10</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>5.6</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1–9 (av: 3.5)/Unchanged</td>
</tr>
</tbody>
</table>

## DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Start with small doses and titrate in accordance with response</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Start with small doses and titrate in accordance with response</td>
</tr>
</tbody>
</table>

## DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Probably dialysed. Dose as in GFR=10–20 mL/min</td>
</tr>
<tr>
<td>VVHD</td>
<td>GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

## IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs:
- Anaesthetics: enhanced hypotensive effect
- Analgesics: NSAIDs antagonise hypotensive effect
- Anti-arrhythmics: increased risk of myocardial depression and bradycardia; increased risk of bradycardia, myocardial depression and AV block with amiodarone; concentration increased by propafenone
- Antibacterials: concentration reduced by rifampicin
- Antidepressants: enhanced hypotensive effect with MAOIs; concentration increased by citalopram and escitalopram and possibly by paroxetine
- Antihypertensives: enhanced hypotensive effect; increased risk of withdrawal hypertension with clonidine; increased risk of first dose hypotensive effect with post-synaptic alpha-blockers such as prazosin
- Antimalarials: increased risk of bradycardia with mefloquine; avoid with artemether/lumefantrine
- Antipsychotics enhanced hypotensive effect with phenothiazines
- Calcium-channel blockers: increased risk of bradycardia and AV block with diltiazem; hypotension and heart failure possible with nifedipine and nisoldipine; asystole, severe hypotension and heart failure with verapamil
- Diuretics: enhanced hypotensive effect
- Moxisylyte: possible severe postural hypotension
- Sympathomimetics: severe hypertension with adrenaline and noradrenaline and possibly with dobutamine
Tropisetron: increased risk of ventricular arrhythmias – use with caution

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral, IV

**RATE OF ADMINISTRATION**

- For bolus injection, 1–2 mg/minute or by continuous infusion via CRIP

**COMMENTS**

- A total dose of 10–15 mg IV is usually sufficient

**OTHER INFORMATION**

- Can cause hypoglycaemia in dialysis patients
- Almost all the drug is excreted as inactive metabolites. Accumulation of the metabolites will occur in renal failure, but does not seem to cause any side effects
Metronidazole

**CLINICAL USE**

Antibiotic:
- Anaerobic and protozoal infections

**DOSE IN NORMAL RENAL FUNCTION**

- Oral: 200–500 mg every 8–12 hours
- IV: 500 mg every 8 hours
- PR: 1 g every 8–12 hours

**PHARMACOKINETICS**

- Molecular weight (daltons): 171.2
- % Protein binding: 10–20
- % Excreted unchanged in urine: 20
- Volume of distribution (L/kg): 0.7–1.5
- Half-life – normal/ESRF (hrs): 5.6–11.4/7–21

**DOSE IN RENAL IMPAIRMENT**

- **GFR (mL/MIN)**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Not dialysed. Dose as in normal renal function
- HD: Dialysed. Dose as in normal renal function
- HDF/High flux: Dialysed. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Alcohol: disulfiram-like reaction
- Anticoagulants: effects of coumarins enhanced
- Anti-epileptics: metabolism of phenytoin inhibited; concentration reduced by primidone and barbiturates
- Ciclosporin: raised blood level of ciclosporin
- Cytotoxics: busulfan concentration increased; metabolism of fluorouracil inhibited

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - IV, oral, PR
- **RATE OF ADMINISTRATION**
  - IV: 5 mL/minute, i.e. 500 mg over 20 minutes
- **COMMENTS**

**OTHER INFORMATION**

- Active metabolites have long half-life in renal impairment
- Increased incidence of GIT reactions and vestibular toxicity in renal failure
- Drug induced lupus is a rare adverse drug reaction
- Rectally: dose frequency reduced to 12 hours after 3 days
- 500 mg /100 mL infusion provides 14 mmol sodium

RETURN TO CONTENTS
Mexiletine hydrochloride

**CLINICAL USE**
Ventricular arrhythmias, especially after a myocardial infarction

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: 400 mg loading dose, followed by 200–250 mg 3–4 times daily commencing 2 hours after the loading dose
- IV injection: 100–250 mg at a rate of 25 mg/minute with ECG monitoring, followed by an infusion of 250 mg as a 0.1% solution over 1 hour, 125 mg/hour for 2 hours then 500 micrograms/minute thereafter

**PHARMACOKINETICS**
- Molecular weight: 215.7 daltons
- % Protein binding: 50–70
- % Excreted unchanged in urine: 10
- Volume of distribution (L/kg): 5–7
- Half-life – normal/ESRF (hrs): 5–17/16

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>50–75% of normal dose and titrate according to response</td>
<td></td>
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</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Method</th>
<th>Type</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
<td></td>
</tr>
<tr>
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</tr>
<tr>
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<td>Not dialysed. Dose as in normal renal function</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: opioids delay absorption
- Anti-arrhythmics: increased myocardial depression with any combination of anti-arrhythmics
- Antidepressants: metabolism inhibited by fluvoxamine (increased toxicity)
- Antihistamines: increased risk of ventricular arrhythmias with mizolastine – avoid concomitant use
- Antipsychotics: increased risk of ventricular arrhythmias with antipsychotics that prolong the QT interval
- Antivirals: possibly increased risk of arrhythmias with ritonavir
- Beta-blockers: increased myocardial depression
- Diuretics: action of mexiletine antagonised by hypokalaemia
- 5HT₃ antagonists increased risk of ventricular arrhythmias with dolasetron – avoid concomitant use; caution with tropisetron

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**: IV infusion, oral
- **RATE OF ADMINISTRATION**: Variable
- **COMMENTS**: Add 250–500 mg mexiletine to 500 mL of infusion solution, e.g. sodium chloride 0.9%, glucose 5%, sodium bicarbonate 8.4%, sodium lactate, sodium chloride 0.9% with potassium chloride 0.3% or 0.6%

**OTHER INFORMATION**
- Mexiletine has a narrow therapeutic index. Its therapeutic effect has been correlated with plasma concentrations of 0.5–2 micrograms per mL
- Mexiletine is metabolised in the liver and is excreted in the urine, mainly in the form of metabolites
- Rate of elimination increased with acidic urine
- Injection can be given orally; however, due to local anaesthetic effect, care needed with hot foods
Miconazole

**CLINICAL USE**
Antifungal agent

**DOSE IN NORMAL RENAL FUNCTION**
Oral gel: 5–10 mL in mouth, after food, 4 times daily

**PHARMACOKINETICS**
- Molecular weight: 416.1 daltons
- % Protein binding: 90
- % Excreted unchanged in urine: 1
- Volume of distribution (L/kg): 20
- Half-life – normal/ESRF (hrs): 24/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
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<tr>
<th>GFR (mL/min)</th>
<th>Dose in normal renal function</th>
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</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapies</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be significantly dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: effect of coumarins enhanced
- Antidepressants: avoid concomitant use with reboxetine
- Antidiabetics: concentration of sulphonylureas increased
- Anti-epileptics: effect of phenytoin enhanced; possibly increased carbamazepine concentration
- Antihistamines: avoid concomitant use with mizolastine, risk of ventricular arrhythmias
- Antimalarials: avoid concomitant use with arteether and lumefantrine
- Antipsychotics: increased risk of ventricular arrhythmias with pimozide – avoid concomitant use; possibly increased concentration of quetiapine – reduce quetiapine dose; possibly increased risk of ventricular arrhythmias with sertindole – avoid
- Antivirals: concentration of saquinavir possibly increased
- Ciclosporin: possibly increased ciclosporin concentration
- Ergot alkaloids: increased risk of ergotism with ergotamine and methysergide – avoid concomitant use
- Sirolimus: concentration increased by miconazole
- Statins: possibly increased risk of myopathy with atorvastatin and simvastatin – avoid concomitant use with simvastatin
- Tacrolimus: possibly increased tacrolimus concentration

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral gel, topical

**RATE OF ADMINISTRATION**

- **COMMENTS**

**OTHER INFORMATION**
- Miconazole is metabolised in the liver to inactive metabolites; 10–20% of an oral dose is excreted in the urine as metabolites. About 50% of an oral dose may be excreted mainly unchanged in the faeces
- There is little absorption through skin or mucous membranes when miconazole nitrate is applied topically
- 50% removed during haemodialysis
Midazolam

**CLINICAL USE**
Benzodiazepine:
- Sedation with amnesia in conjunction with local anaesthesia, premedication, induction

**DOSE IN NORMAL RENAL FUNCTION**
See SPC for dosing guidelines

**PHARMACOKINETICS**
- Molecular weight (daltons) 325.8 (362.2 as hydrochloride)
- % Protein binding 96–98
- % Excreted unchanged in urine <1
- Volume of distribution (L/kg) 0.7–1.2
- Half-life – normal/ESRF (hrs) 2–7/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/min)**
  - 20–50 Dose as in normal renal function
  - 10–20 Dose as in normal renal function
  - <10 Use sparingly and titrate according to response. Only bolus doses, not continuous infusion

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Unlikely to be dialysed. Dose as in GFR<10mL/min
- HD Not dialysed. Dose as in GFR<10mL/min
- HDF/High flux Unknown dialysability. Dose as in GFR<10mL/min
- CAV/VVHD Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: concentration increased by erythromycin, clarithromycin, telithromycin and quinupristin/dalfopristin (profound sedation); metabolism possibly accelerated by rifampicin
- Antifungals: concentration increased by itraconazole, ketoconazole, posaconazole and fluconazole (prolonged sedative effect)
- Antipsychotics: increased sedative effects; increased risk of hypotension, bradycardia and respiratory depression when parenteral benzodiazepines are given with IM olanzapine
- Antivirals: atazanavir, efavirenz, nelfinavir, saquinavir, ritonavir, amprenavir and indinavir increase risk of prolonged sedation with midazolam, avoid with atazanavir
- Ciclosporin: *in vitro* studies suggested that ciclosporin could inhibit the metabolism of midazolam. However, blood ciclosporin concentrations in patients given ciclosporin to prevent graft rejection were considered too low to result in an interaction
- Sodium oxybate: enhanced effects of sodium oxybate – avoid

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - IV, IM
- **RATE OF ADMINISTRATION**
  - 1–10mL/hour according to response
- **COMMENTS**
  - Can be used undiluted
  - Compatible with glucose 5%, sodium chloride 0.9%

**OTHER INFORMATION**
- Protein binding of midazolam is decreased in ERF; hence more unbound drug is available to produce CNS effects, so a decrease in dose is recommended
- CSM has received reports of respiratory depression, sometimes associated with severe hypotension, following intravenous administration
- Caution when used for sedation in severe renal impairment especially when used with opiates and/or neuromuscular blocking agents – monitor sedation and titrate to response
- Increased CNS sensitivity in patients with renal impairment
- One study reports midazolam as having a sieving coefficient = 0.06 and unlikely to be removed by haemofiltration

RETURN TO CONTENTS
# Midodrine hydrochloride (unlicensed product)

## CLINICAL USE
Treatment of orthostatic hypotension, including dialysis related hypotension

## IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Risk of arrhythmias if given with volatile anaesthetics
- Risk of arrhythmias and hypertension if given with tricyclic antidepressants and MAOIs
- Risk of severe hypertension if given with beta-blockers
- Other drugs which increase blood pressure: enhanced hypertensive effect

## ADMINISTRATION

### RECONSTITUTION
- **ROUTE**
  - Oral

### RATE OF ADMINISTRATION
- **COMMENTS**
  - Take last dose at least 4 hours before bed

## IMPORTANT DRUG INTERACTIONS
Potential adverse drug interactions with other drugs
- Risk of arrhythmias if given with volatile anaesthetics
- Risk of arrhythmias and hypertension if given with tricyclic antidepressants and MAOIs
- Risk of severe hypertension if given with beta-blockers
- Other drugs which increase blood pressure: enhanced hypertensive effect

## PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>290.7</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>Negligible</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>2</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>No data</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>25 minutes (3 hours for active metabolite)/increased (9 for active metabolite)</td>
</tr>
</tbody>
</table>

## DOSE IN NORMAL RENAL FUNCTION

- **Hypotension**: 2.5 mg twice daily up to 10 mg 3 times a day

## DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
<th>Start with a lower dose and titrate according to response</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
</tbody>
</table>

## DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
<th>Start with a lower dose and titrate according to response</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Initial dose, 2.5 mg if &lt;70 kg, 5 mg if &gt;70 kg. See ‘Other Information’</td>
<td></td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Initial dose, 2.5 mg if &lt;70 kg, 5 mg if &gt;70 kg. See ‘Other Information’</td>
<td></td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose as in GFR=10–20mL/min</td>
<td></td>
</tr>
</tbody>
</table>
Minocycline

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
100 mg twice daily
Acne: 100 mg daily in 1 or 2 divided doses

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>457.5</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>75</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>5–10</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1–1.5</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>11–26/12–18</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
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**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
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</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
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<tr>
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<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: possibly enhanced anticoagulant effect of coumarins and phenindione
- Oestrogens: possibly reduced contraceptive effect of oestrogens (risk probably small)
- Retinoids: possibly increased risk of benign intracranial hypertension – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  - Do not take iron preparations, indigestion remedies or phosphate binders at the same time of day as minocycline
Minoxidil

**CLINICAL USE**
- Severe hypertension (in addition to a diuretic and a beta-blocker)
- Male pattern baldness

**DOSE IN NORMAL RENAL FUNCTION**
- Initially 5 mg (elderly 2.5 mg) daily in 1–2 doses increased by 5–10 mg every 3 or more days; maximum 50 mg daily
- Male pattern baldness: 1 mL twice daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 209.2
- % Protein binding: 0
- % Excreted unchanged in urine: 15–20
- Volume of distribution (L/kg): 2–3
- Half-life – normal/ESRF (hrs): 4.2/8.9

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose Prescription</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Start with small doses and titrate according to response. See ‘Other Information’</td>
</tr>
<tr>
<td>10–20</td>
<td>Start with small doses and titrate according to response. See ‘Other Information’</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Start with small doses and titrate according to response. See ‘Other Information’</td>
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</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

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<thead>
<tr>
<th>Therapy</th>
<th>Dose Prescription</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose as in GFR=10-20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- A study of the pharmacokinetics of minoxidil in patients with varying degrees of renal impairment found that the non-renal clearance was also impaired as renal function worsened. Substantial accumulation of minoxidil might occur in these patients during multiple-dose therapy. Recommended that minoxidil therapy be initiated with smaller doses or a longer dose interval in patients with significant renal impairment
- Minoxidil is a peripheral vasodilator and should be given in conjunction with a diuretic to control salt and water retention, and a beta-blocker to control reflex tachycardia. Patients on dialysis do not need to be given minoxidil in conjunction with a diuretic
- Following topical application, between 0.3% and 4.5% of the total applied dose of minoxidil is absorbed from intact scalp
Mircera

**CLINICAL USE**

Management of anaemia associated with renal impairment in pre-dialysis and dialysis patients

**DOSE IN NORMAL RENAL FUNCTION**

- ESA-naive patients: 0.6 mcg/kg every 2 weeks, changing by 25% according to response; once stable change to monthly dosing
- Target haemoglobin usually 10–12 g/dL
- If previously on an ESA: 120–360 mcg monthly depending on previous ESA dose, and adjust according to response

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>60 000</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>No data</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>Unlikely</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>3–5.4 litres</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>IV: 134/Unchanged SC: 139 (142 if not on dialysis)/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
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</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed.</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Risk of hyperkalaemia with ACE inhibitors and angiotensin-II antagonists

**ADMINISTRATION**

**RECONSTITUTION**

- ROUTE
  - SC, IV
- RATE OF ADMINISTRATION
  - COMMENTS

**OTHER INFORMATION**

- Pre-treatment checks and appropriate correction/ treatment needed for iron, folate and B12 deficiencies, infection, inflammation or aluminium toxicity to produce optimum response to therapy
- Concomitant iron therapy (200–300 mg elemental oral iron) needed daily. IV iron may be needed for patients with very low serum ferritin (<100 nanograms/mL)
- May increase heparin requirement during HD
- Reported association of pure red cell aplasia (PRCA) with epoetin therapy – very rare; due to failed production of red blood cell precursors in the bone marrow, resulting in profound anaemia. Possibly due to an immune response to the protein backbone of R-HuEPO. Resulting antibodies render the patient unresponsive to the therapeutic effects of all epoetins and darbepoetin
Mirtazapine

CLINICAL USE
Antidepressant

DOSE IN NORMAL RENAL FUNCTION
15–45 mg daily in 1 or 2 divided doses

PHARMACOKINETICS
Molecular weight (daltons) 265.4
% Protein binding 85
% Excreted unchanged in urine 75
Volume of distribution (L/kg) 107 litres
Half-life – normal/ESRF (hrs) 20–40/Increased

DOSE IN RENAL IMPAIRMENT
GFR (mL/Min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Start at low dose and monitor closely

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unlikely to be dialysed. Dose as in GFR<10 mL/min
HD Unlikely to be dialysed. Dose as in GFR<10 mL/min
HDF/High flux Unknown dialysability. Dose as in GFR<10 mL/min
CAV/ VVHD Unlikely to be dialysed. Dose as in GFR=10–20 mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● Alcohol: increased sedative effect
● Antidepressants: CNS excitation and hypertension with MAOI and moclobemide – avoid concomitant use
● Antimalarials: avoid concomitant use with artemether and lumefantrine
● Sibutramine: increased risk of CNS toxicity – avoid concomitant use

ADMINISTRATION

RECONSTITUTION

ROUTE
● Oral

RATE OF ADMINISTRATION

COMMENTS

Misoprostol

**CLINICAL USE**
- Benign gastric and duodenal ulceration and NSAID associated ulceration
- Prophylaxis of NSAID induced ulceration

**DOSE IN NORMAL RENAL FUNCTION**
Treatment: 800 mcg daily in 2 or 4 divided doses
Prophylaxis: 200 mcg 2–4 times daily

**PHARMACOKINETICS**
- Molecular weight (daltons) 382.5
- % Protein binding <90 (as misoprostol acid)
- % Excreted unchanged in urine <1
- Volume of distribution (L/kg) 858 litres
- Half-life – normal/ESRF (hrs) 20–40 minutes/40–80 minutes (as misoprostol acid)

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**
- **RECONSTITUTION**
  - 
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - 
- **COMMENTS**
  - 

**OTHER INFORMATION**
- Plasma concentrations of misoprostol are generally undetectable due to its rapid metabolic conversion to misoprostol acid
- Dosage adjustment is not usually necessary in patients with varying degrees of renal impairment, even though there is an approximate doubling of half-life, maximum plasma concentration and area under the curve. If renal patients are unable to tolerate it, the dose can be reduced
Mitomycin

**CLINICAL USE**
Cytotoxic antibiotic used in a range of neoplastic conditions

**DOSE IN NORMAL RENAL FUNCTION**
IV: 4–10 mg/m² or 0.06–0.15 mg/kg given every 1–6 weeks, depending on concurrent therapy and bone marrow recovery
For instillation into bladder: 20–40 mg

**PHARMACOKINETICS**
- **Molecular weight**: 334.3 daltons
- **% Protein binding**: No data
- **% Excreted**: 10
  - unchanged in urine
- **Volume of distribution**: 0.5 L/kg
- **Half-life – normal/ESRF (hrs)**: 50 minutes/

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/Min)**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: 75% of normal dose

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**: Unknown dialysability. Dose as in GFR<10 mL/min
- **HD**: Unknown dialysability. Dose as in GFR<10 mL/min
- **HDF/High flux**: Unknown dialysability. Dose as in GFR<10 mL/min
- **CAV/VVHD**: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antipsychotics: avoid concomitant use with clozapine (increased risk of agranulocytosis)

**ADMINISTRATION**

**RECONSTITUTION**
- With water for injection or sodium chloride 0.9%; 5 mL for the 2 mg vial, at least 10 mL for the 10 mg vial and at least 20 mL for the 20 mg vial

**ROUTE**
- IV injection, intra-arterial, bladder instillation

**RATE OF ADMINISTRATION**
- Bolus injection over 3–5 minutes (1 mL/ min)
- Infusion over 15–30 minutes

**OTHER INFORMATION**
- Prodrug, activated in vivo. Metabolism is predominantly in the liver. Rate of clearance is inversely proportional to the maximum serum concentration, due to saturation of the degradative pathways. Approximately 10% is excreted unchanged in the urine. Since metabolic pathways are saturated at low doses, the % dose excreted in the urine increases with increasing dose
- A syndrome of thrombotic microangiopathy resembling haemolytic-uraemic syndrome has been seen in patients receiving mitomycin, either alone or, more frequently, combined with other agents. Symptoms of haemolysis and renal failure may be accompanied by ATN and cardiovascular problems, pulmonary oedema and neurological symptoms
- Principal toxicity of mitomycin-C is bone marrow suppression. The nadir is usually around 4 weeks after treatment and toxicity is cumulative, with increasing risk after each course of treatment
Mitoxantrone

**CLINICAL USE**
Metastatic breast cancer
Non-Hodgkin's lymphoma
Adult acute non-lymphocytic leukaemia

**DOSE IN NORMAL RENAL FUNCTION**
- Metastatic breast cancer, non-Hodgkin's lymphoma and hepatoma: 14 mg/m² every 21 days (12 mg/m² or less if inadequate bone marrow reserves)
- Adult acute non-lymphocytic leukaemia: 12 mg/m² for 5 consecutive days
- Or according to local protocol

**PHARMACOKINETICS**
- Molecular weight 517.4 (as hydrochloride)
- % Protein binding 78
- % Excreted unchanged in urine 7
- Volume of distribution 1000 L/m²
- Half-life – normal/ESRF (hrs) 5–18 days

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Not dialysed. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Other antineoplastic agents: enhanced myelosuppression – when used in combination reduce mitoxantrone dose by 2–4 mg/m²
- Cardiotoxic drugs: increased risk of cardiac toxicity

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
- IV infusion
- RATE OF ADMINISTRATION
- At least 3 minutes
- COMMENTS
- Dilute to at least 50 mL in sodium chloride 0.9%, glucose 5% or sodium chloride 0.18% and glucose 4%

**OTHER INFORMATION**
- Has been administered intraperitoneally at a dose of 28–38 mg/m² every 3–4 weeks although some people advise a maximum dose of only 30 mg/m² per month with a dwell time of 1–4 hours. (Alberts DS, Surwit EA, Peng YM, et al. Phase I clinical and pharmacokinetic study of mitoxantrone given to patients by intraperitoneal administration. Cancer Res. 1988, Oct 15; 48(20): 5874–7)
- Extensive metabolism in the liver. Excretion is predominantly via the bile and faeces. 5–10% of dose is excreted in the urine within 5 days

**RETURN TO CONTENTS**
Mivacurium

**CLINICAL USE**
Non-depolarising muscle relaxant of short duration

**DOSE IN NORMAL RENAL FUNCTION**
- IV injection: 70–250 micrograms/kg; maintenance 100 micrograms/kg every 15 minutes
- IV infusion: maintenance of block 8–10 micrograms/kg/minute, adjusted to maintenance dose of 6–7 micrograms/kg/minute according to response

**PHARMACOKINETICS**
- Molecular weight (daltons): 1029; (1100.2 as chloride)
- % Protein binding: No data
- % Excreted unchanged in urine: <10
- Volume of distribution (L/kg): 0.1–0.3
- Half-life – normal/ESRF (hrs): 2–10 minutes/–

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50 Adjust to response. Slower infusion rate may be required
- 10–20 Adjust to response. Slower infusion rate may be required
- <10 Reduce dose. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Adjust infusion to response
- HD: Unknown dialysability. Adjust infusion to response
- HDF/High flux: Unknown dialysability. Adjust infusion to response
- CAV/VVHD: Unknown dialysability. Adjust infusion to response

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced muscle relaxant effect
- Anti-arrhythmics: procainamide enhances muscle relaxant effect
- Antibacterials: effect enhanced by aminoglycosides, clindamycin, polymyxins and piperacillin
- Botulinum toxin: neuromuscular blockade enhanced, (risk of toxicity)

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - IV bolus, IV infusion
- RATE OF ADMINISTRATION
  - IV bolus: Doses of up to 0.15 mg/kg may be administered over 5–15 seconds. Higher doses should be administered over 30 seconds
- COMMENTS
  - Compatible with sodium chloride 0.9%; glucose 5%; dilute to 500 micrograms/mL
  - Compatible with fentanyl, alfentanil, droperidol and midazolam

**OTHER INFORMATION**
- Spontaneous recovery is complete in approximately 15 minutes and is independent of dose administered
- In patients with CKD 5 the clinically effective duration of block produced by 0.15 mg/kg is approximately 1.5 times longer than in patients with normal renal function; hence, dosage should be adjusted according to individual clinical response
- Results from a study comparing 20 anephric patients with 20 healthy patients highlight the need for reduced dosages of Mivacron in patients with renal failure: patients with renal failure had a slightly shorter time to maximum depression of T1/T0, a slower recovery of T1/T0 to 5% (15.3 vs 9.8 min), required a slower infusion rate (6.3 vs 10.4 micrograms/kg/min) and experienced slower spontaneous recovery (12.2 vs 7.7 min). The drug company has no specific guidelines as to the extent of dose reduction required
Mizolastine

**CLINICAL USE**

Antihistamine:
Symptomatic relief of allergy, e.g. hayfever, urticaria

**DOSE IN NORMAL RENAL FUNCTION**

10 mg daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>432.5</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>98.4</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1.4</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>13</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Anti-arrhythmics: increased risk of ventricular arrhythmias – avoid concomitant use with amiodarone, disopyramide, flecainide, mexiletine, procainamide and propafenone
- Antibacterials: metabolism possibly inhibited by macrolides – avoid concomitant use; increased risk of ventricular arrhythmias with moxifloxacin – avoid concomitant use
- Antifungals: metabolism inhibited by itraconazole and ketoconazole and possibly imidazoles – avoid concomitant use
- Beta-blockers: increased risk of ventricular arrhythmias with sotalol – avoid concomitant use
- Ciclosporin: use with caution due to inhibition of ciclosporin metabolism
- Avoid concomitant treatment with any drug that could prolong QT interval
- Caution with drugs that inhibit cytochrome P450 enzymes (may elevate mizolastine levels)

**ADMINISTRATION**

**CONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**

- Contraindicated in patients with electrolyte imbalances, particularly hypokalaemia
Moclobemide

**CLINICAL USE**
Reversible MAOI:
- Depression
- Social phobia

**DOSE IN NORMAL RENAL FUNCTION**
Depression: 150–600 mg daily in divided doses
Social phobia: 300 mg twice daily

**PHARMACOKINETICS**
Molecular weight 268.7 (daltons)
% Protein binding 50
% Excreted unchanged in urine <1
Volume of distribution 1 (L/kg)
Half-life – normal/ESRF (hrs) 2–4/unchanged

**DOSE IN RENAL IMPAIRMENT**
GFR (mL/Min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
CAPD Likely dialysability. Dose as in normal renal function
HD Likely dialysability. Dose as in normal renal function
HDF/High flux Likely dialysability. Dose as in normal renal function
CAV/VVHD Likely dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: possible CNS excitation or depression with dextromethorphan or pethidine – avoid concomitant use; possible CNS excitation or depression with opioid analgesics
- Antidepressants: avoid concomitant use; possible increased serotonergic effects with duloxetine
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Bupropion: avoid concomitant use
- Dopaminergics: use with caution with entacapone; increased side effects with levodopa; avoid concomitant use with selegiline
- 5HT, agonists: increased CNS toxicity with rizatriptan and sumatriptan – avoid concomitant use; increased CNS toxicity with zolmitriptan – reduce zolmitriptan dose
- Sibutramine: increased CNS toxicity – avoid concomitant use
- Sympathomimetics: risk of hypertensive crisis

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral
  - RATE OF ADMINISTRATION
    - COMMENTS
      - Take after food

**OTHER INFORMATION**
- Hyponatraemia has been reported (especially in elderly patients) due to inappropriate secretion of antidiuretic hormone
Modafinil

**CLINICAL USE**
Excessive daytime drowsiness associated with narcolepsy, obstructive sleep apnoea and chronic shift work

**DOSE IN NORMAL RENAL FUNCTION**
200–400 mg daily in 1 or 2 divided doses
Chronic shift work disorder: 200 mg taken 1 hour before the start of the shift

**PHARMACOKINETICS**
- Molecular weight: 273.4 daltons
- % Protein binding: 60%
- % Excreted unchanged in urine: <10%
- Volume of distribution: 0.9 L/kg
- Half-life – normal/ESRF (hrs): 15/–

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Start at 50% normal dose and increase according to response</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Ciclosporin: reduced ciclosporin concentration
- Oestrogens: metabolism accelerated (reduced contraceptive effect)

**ADMINISTRATION**
- **RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
- **COMMENTS**
- **OTHER INFORMATION**
  - Major metabolite is not pharmacologically active
  - Recommended that modafinil not be used in patients with left ventricular hypertrophy or ischaemic ECG changes
Moexipril hydrochloride

**CLINICAL USE**
Angiotensin-converting enzyme inhibitor:
- Hypertension

**DOSE IN NORMAL RENAL FUNCTION**
3.75–30 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 535
- % Protein binding: 50
- % Excreted unchanged in urine: 1
- Volume of distribution (L/kg): 183 litres
- Half-life – normal/ESRF (hrs): 12 (of active metabolite)/Increased

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–40</td>
<td>Start with low dose and adjust according to response</td>
</tr>
<tr>
<td>10–20</td>
<td>Start with low dose and adjust according to response</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Start with low dose and adjust according to response</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapies</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Anaesthetics: enhanced hypotensive effect
  - Analgesics: antagonism of hypotensive effect and increased risk of renal impairment with NSAIDs; hyperkalaemia with ketorolac and other NSAIDs
  - Ciclosporin: increased risk of hyperkalaemia and nephrotoxicity
  - Diuretics: enhanced hypotensive effect; hyperkalaemia with potassium-sparing diuretics
  - Epoetin: increased risk of hyperkalaemia; antagonism of hypotensive effect
  - Lithium: reduced excretion (possibility of enhanced lithium toxicity)
  - Potassium salts: increased risk of hyperkalaemia
  - Tacrolimus: increased risk of hyperkalaemia and nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- Moexipril is a prodrug that is converted to an active metabolite, moexiprilat
- Close monitoring of renal function during therapy is necessary in those with renal insufficiency
- Renal failure has been reported in association with ACE inhibitors, mainly in patients with severe congestive heart failure, renal artery stenosis, or post renal transplant
- High incidence of anaphylactoid reactions has been reported in patients dialysed with high-flux polyacrylonitrile membranes and treated concomitantly with an ACE inhibitor. This combination should therefore be avoided
- Hyperkalaemia and other side effects are more common in patients with impaired renal function

*It is not licensed for use by anyone else.*
Montelukast

**CLINICAL USE**
Prophylaxis of asthma

**DOSE IN NORMAL RENAL FUNCTION**
10 mg at night

**PHARMACOKINETICS**
- Molecular weight: 608.2 (as sodium salt) (daltons)
- % Protein binding: >99
- % Excreted unchanged in urine: <0.2
- Volume of distribution: 8–11 litres (L/kg)
- Half-life – normal/ESRF (hrs): 2.7–5.5

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAP: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Not dialysed. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**

**COMMENTS**

**OTHER INFORMATION**
Metabolites have minimal therapeutic activity
Morphine

**CLINICAL USE**
Opiate analgesic

**DOSE IN NORMAL RENAL FUNCTION**
5–20 mg every 4 hours (higher in very severe pain or terminal illness)
PR: 15–30 mg every 4 hours

**PHARMACOKINETICS**
- Molecular weight: 285.3 (758.8 as sulphate); (774.8 as tartrate)
- % Protein binding: 20–35
- % Excreted unchanged in urine: 10
- Volume of distribution (L/kg): 3–5

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: 75% of normal dose
  - 10–20: Use small doses, e.g. 2.5–5 mg and extended dosing intervals. Titrate according to response
  - <10: Use small doses, e.g. 1.25–2.5 mg and extended dosing intervals. Titrate according to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Dialysed – active metabolite removed significantly. Dose as in GFR<10 mL/min
- HDF/High flux: Dialysed – active metabolite removed significantly. Dose as in GFR<10 mL/min
- CAV/VVHD: Dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antidepressants: possible CNS excitation or depression with MAOIs – avoid concomitant use, and for 2 weeks after stopping MAOI; possible CNS excitation or depression with moclobemide; increased sedative effects with tricyclics
- Antivirals: concentration possibly increased by ritonavir
- Sodium oxybate: enhanced effect of sodium oxybate – avoid concomitant use

**ADMINISTRATION**
- **RECONSTITUTION**
  - **ROUTE**
    - Oral, SC, IM, IV, PR
  - **RATE OF ADMINISTRATION**
    - 2 mg/minute. (Titrate according to response)

**OTHER INFORMATION**
- Extreme caution with all opiates in patients with impaired renal function
- Potential accumulation of morphine-6-glucuronide (a renally excreted active metabolite, more potent than morphine) and morphine-3-glucuronide. Half-life of morphine-6-glucuronide is increased from 3–5 hours in normal renal function to about 50 hours in ERF
- ENSURE NALOXONE READILY AVAILABLE
- Some units avoid slow release oral preparations as any side effects may be prolonged
Movicol (active ingredient is the osmotic laxative polyethylene glycol)

### CLINICAL USE

Laxative

### DOSE IN NORMAL RENAL FUNCTION

1–3 sachets daily in divided doses in 125 mL of water
Maintenance: 1–2 sachets daily

### PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Molecular weight (daltons)</th>
<th>3350</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Protein binding</td>
<td>Not absorbed</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>Not absorbed</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>Not absorbed</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>Not absorbed</td>
</tr>
</tbody>
</table>

### DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

### DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>CAPD</th>
<th>Not dialysed. Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/ VVHD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

### IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs
- None known

### ADMINISTRATION

RECONSTITUTION
- ROUTE
- Oral
- RATE OF ADMINISTRATION
- COMMENTS
- 

### OTHER INFORMATION

- Movicol contains polyethylene glycol, sodium chloride, sodium bicarbonate and potassium chloride
- Electrolyte content of a sachet when made up with 125 mL water is:
  - Sodium 65 mmol/L
  - Chloride 53 mmol/L
  - Potassium 5.4 mmol/L
  - Bicarbonate 17 mmol/L
- Sachets are formulated to ensure that there is virtually no net gain or loss of sodium, potassium or water
Moxifloxacin

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
400 mg once daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>437.9 (as hydrochloride)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>30–50</td>
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<tr>
<td>% Excreted unchanged in urine</td>
<td>19</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>2</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>12/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–30</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

- Potentially hazardous interactions with other drugs:
  - Analgesics: increased risk of convulsions with NSAIDs
  - Anti-arrhythmics: increased risk of ventricular arrhythmias with amiodarone, disopyramide and procainamide – avoid concomitant use
  - Antibacterials: increased risk of ventricular arrhythmias with parenteral erythromycin – avoid concomitant use
  - Anticoagulants: anticoagulant effect enhanced
  - Antidepressants: increased risk of ventricular arrhythmias with tricyclics – avoid concomitant use
  - Antihistamines: increased risk of ventricular arrhythmias with mizolastine – avoid concomitant use
  - Antimalarials: increased risk of ventricular arrhythmias with chloroquine, hydroxychloroquine, mefloquine or quinine – avoid concomitant use; avoid concomitant use with artemether with lumefantrine
  - Antipsychotics: increased risk of ventricular arrhythmias with haloperidol, phenothiazines, pimozide or sertindole – avoid concomitant use
  - Beta-blockers: increased risk of ventricular arrhythmias with sotalol – avoid concomitant use
  - Ciclosporin: some reports of increased nephrotoxicity
  - Pentamidine: increased risk of ventricular arrhythmias – avoid concomitant use
  - Theophylline: possibly increased risk of convulsions

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
  - Do not take milk, iron preparations, indigestion remedies or phosphate binders at the same time as moxifloxacin

**OTHER INFORMATION**
- Oral bioavailability is 90%
Moxisylyte (thymoxamine)

**CLINICAL USE**
Primary Raynaud’s syndrome

**DOSE IN NORMAL RENAL FUNCTION**
40–80 mg 4 times daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 315.8
- % Protein binding: No data
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): Low
- Half-life – normal/ESRF (hrs): 1–2

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min):
  - 25–50: Dose as in normal renal function
  - 10–25: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux: Unlikely to be dialysed. Dose as in normal renal function
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Alpha-blockers: possibly severe postural hypotension when given in combination
- Beta-blockers: possibly severe postural hypotension when given in combination

**ADMINISTRATION**

**RECONSTITUTION**
- 
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - 
- **COMMENTS**
  - 

**OTHER INFORMATION**
- Theoretically may decrease insulin requirements in diabetics

References:
Moxonidine

CLINICAL USE
Antihypertensive agent (centrally acting agonist at I1 receptor, imidazoline and alpha2 adrenoceptors)

DOSE IN NORMAL RENAL FUNCTION
200–600 mcg daily
(Doses >400 mcg should be in 2 divided doses)

PHARMACOKINETICS
Molecular weight 241.7 (daltons)
% Protein binding 7
% Excreted unchanged in urine 50–75
Volume of distribution (L/kg) 1.8
Half-life – normal/ESRF (hrs) 2–3/6.9 +/–3.7

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
30–60 Dose as in normal renal function
10–30 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Probably dialysed. Dose as in normal renal function
HD Probably dialysed. Dose as in normal renal function
HDF/High flux Probably dialysed. Dose as in normal renal function
CAV/VVHD Probably dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● None known

ADMINISTRATION
RECONSTITUTION
–
ROUTE
● Oral
RATE OF ADMINISTRATION
–
COMMENTS
–

OTHER INFORMATION
● In moderately impaired renal function (GFR=30–60 mL/min) AUC is increased by 85% and clearance decreased by 52%; therefore, monitor patient closely
● Anecdotal evidence suggests that moxonidine can be used safely at standard doses in patients with all degrees of renal impairment
Muromonab-CD3 (OKT3) (unlicensed product)

**CLINICAL USE**
- Steroid resistant acute transplant rejection
- Prophylaxis of rejection in sensitised patients

**DOSE IN NORMAL RENAL FUNCTION**
5 mg daily for 10–14 days (10 days most common)

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>50 000 (Heavy chain) + 25 000 (Light chain)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>No data</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>No data</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.093</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>18–36/—</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/Min)**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**: Unlikely to be dialysed. Dose as in normal renal function
- **HD**: Not dialysed. Dose as in normal renal function
- **HDF/High flux**: Unknown dialysability. Dose as in normal renal function
- **CAV/VVHD**: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Ciclosporin: increases ciclosporin plasma levels
- Indometacin: may increase risk of encephalopathy
- Volatile anaesthetics/drugs that decrease cardiac contractility: increase risk of developing cardiovascular problems

**ADMINISTRATION**
**RECONSTITUTION**
- **ROUTE**
  - IV
- **RATE OF ADMINISTRATION**
  - FAST over less than 1 minute
- **COMMENTS**
  - NB Doctor administration recommended

**OTHER INFORMATION**
- Ensure patient is not fluid overloaded prior to administration
- Possible future scope for dose titration according to CD3 or absolute T-cell count
- Reduce or stop other immunosuppressant therapy during treatment, and resume 3 days prior to cessation of OKT3
- IV methylprednisolone sodium succinate (8 mg/kg given 1–4 hours prior to the first dose of OKT3) is strongly recommended to decrease the incidence and severity of reactions to the first dose. Paracetamol and antihistamines given concomitantly with OKT3 may also help to reduce some early reactions
- Side effects pronounced: WARN PATIENT

RETURN TO CONTENTS
Mycophenolate

**CLINICAL USE**
- Mycophenolate sodium: for renal transplantation
- Mycophenolate mofetil: prophylaxis against acute transplant rejection; autoimmune renal diseases

**DOSE IN NORMAL RENAL FUNCTION**
Mycophenolate sodium: 720 mg twice daily
Mycophenolate mofetil: 1–1.5 g twice a day

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Mycophenolic acid</th>
<th>Mofetil</th>
<th>Sodium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>320.3</td>
<td>433.5</td>
<td>342.3</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>97</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>3.6–4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>12–17.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

- **GFR (mL/min)**
  - 20–50: Dose as in normal renal function
  - 10–20: Mycophenolate mofetil: 1 g twice a day; mycophenolate sodium: dose as in normal renal function
  - <10: Mycophenolate mofetil: 1 g twice a day; mycophenolate sodium: dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapeutic Modality</th>
<th>Mycophenolate mofetil</th>
<th>Mycophenolate sodium</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in normal renal function</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antipsychotics: avoid concomitant use with clozapine (increased risk of agranulocytosis)
- Antivirals: higher concentrations of both mycophenolate acid and aciclovir or ganciclovir when the two are prescribed concomitantly
- Antacids: absorption of mycophenolate decreased in presence of magnesium and aluminium salts
- Colestyramine: 40% reduction in oral bioavailability of mycophenolate
- Ciclosporin: some studies show that ciclosporin decreases plasma MPA AUC levels; other studies show increases – no dose change required
- Iron preparations: may significantly reduce absorption of mycophenolate
- Sevelamer: reduced levels of mycophenolate
- Tacrolimus: increases MPA concentrations – no dose change required but monitor closely

**ADMINISTRATION**

- **RECONSTITUTION**
  - Add 14 mL of glucose 5% per 500 mg vial
- **ROUTE**
  - Oral, IV
- **RATE OF ADMINISTRATION**
  - Over 2 hours
- **COMMENTS**
  - Dilute reconstituted solution further with glucose 5% to achieve a concentration of 6 mg/mL

**OTHER INFORMATION**

- Mycophenolate mofetil (MMF) rapidly undergoes complete presystemic absorption to mycophenolic acid (MPA) which in turn is metabolised to MPA glucuronide. This undergoes extensive enterohepatic recirculation, hence a secondary increase in MPA plasma levels is seen 6–12 hours post dose
- If neutrophil count drops below 1.3 × 10^9/μL, consider suspending MMF therapy
- No dosage reduction is required in the event of a transplant rejection episode
- Mycophenolate sodium 720 mg is approximately equivalent to 1 g mycophenolate mofetil
Nabumetone

CLINICAL USE

NSAID and analgesic

DOSE IN NORMAL RENAL FUNCTION

1 g at night; in severe conditions 0.5–1 g in the morning as well; elderly 0.5–1 g daily

PHARMACOKINETICS

Molecular weight (daltons) 228.3
% Protein binding >99
% Excreted unchanged in urine <1
Volume of distribution (L/kg) 0.11
Half-life – normal/ESRF (hrs) 24/39

DOSE IN RENAL IMPAIRMENT

GFR (mL/min)

20–50 Dose as in normal renal function, but avoid if possible
10–20 0.5–1 g daily, but avoid if possible
<10 0.5–1 g daily, but only use if on dialysis. See ‘Other Information’

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

CAPD Not dialysed. Dose as in GFR<10mL/min
HD Not dialysed. Dose as in GFR<10mL/min
HDF/High flux Not dialysed. Dose as in GFR<10mL/min
CAV/ VVHD Not dialysed. Dose as in GFR=10–20mL/min

IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs
- ACE inhibitors and angiotensin-II antagonists: antagonism of hypotensive effect; increased risk of nephrotoxicity and hyperkalaemia
- Analgesics: avoid concomitant use of 2 or more NSAIDs, including aspirin (increased side effects); avoid with ketorolac (increased risk of side effects and haemorrhage)
- Antibacterials: possibly increased risk of convulsions with quinolones
- Anticoagulants: effects of coumarins enhanced; possibly increased risk of bleeding with heparins and coumarins
- Antidepressants: increased risk of bleeding with SSRIs and venlafaxine
- Antidiabetic agents: effects of sulphonylureas enhanced
- Anti-epileptics: possibly increased phenytoin concentration
- Antivirals: increased risk of haematological toxicity with zidovudine; concentration possibly increased by ritonavir
- Ciclosporin: may potentiate nephrotoxicity
- Cytotoxic agents: reduced excretion of methotrexate; increased risk of bleeding with erlotinib
- Diuretics: increased risk of nephrotoxicity; antagonism of diuretic effect; hyperkalaemia with potassium-sparing diuretics
- Lithium: excretion decreased
- Pentoxifylline: increased risk of bleeding
- Tacrolimus: increased risk of nephrotoxicity

ADMINISTRATION

RECONSTITUTION
- ROUTE
  ● Oral
RANGE OF ADMINISTRATION
- COMMENTS
  -

OTHER INFORMATION

- Nabumetone is absorbed from the GI tract and rapidly metabolised in the liver to the principal active metabolite 6-methoxy-2-naphthylacetic acid (6-MNA). The metabolite is a potent inhibitor of prostaglandin synthesis. Excretion of the metabolite is predominantly in the urine. The SPC recommends a dose reduction if creatinine clearance <30 mL/minute; however, another article concluded that dosage adjustments may not be necessary with decreased renal function. The authors found an increase in the elimination half-life of 6-MNA, but stated that the increased half-life in patients with renal failure is offset by changes in the apparent volume of distribution that prevent the accumulation of 6-MNA. (Brier ME, Sloan RS, Aronoff GR. Population pharmacokinetics of the active metabolite of nabumetone in renal impairment. Br J Clin Pharmacol 2001; 51: 675–682)
Inhibition of renal prostaglandin synthesis by NSAIDs may interfere with renal function, especially in the presence of existing renal disease – avoid if possible; if not, check serum creatinine 48–72 hours after starting NSAID – if increased, discontinue NSAID therapy.

Use normal doses in patients with CKD 5 on dialysis if they do not pass any urine.

Use with caution in renal transplant recipients – can reduce intrarenal autacoid synthesis.

References:
Nadolol

**CLINICAL USE**
Beta-adrenoceptor blocker:
- Hypertension
- Angina
- Arrhythmias
- Migraine
- Thyrotoxicosis

**DOSE IN NORMAL RENAL FUNCTION**
- Hypertension: 80–240 mg per day
- Angina, arrhythmias, migraine: 40–160 mg daily
- Thyrotoxicosis: 80–160 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 309.4
- % Protein binding: 30
- % Excreted unchanged in urine: 73
- Volume of distribution (L/kg): 1.9
- Half-life – normal/ESRF (hrs): 12–24/45

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Start with low dose and increase according to response</td>
</tr>
<tr>
<td>10–20</td>
<td>Start with low dose and increase according to response</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Start with low dose and increase according to response</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Anaesthetics: enhanced hypotensive effect
  - Analgesics: NSAIDs antagonise hypotensive effect
  - Anti-arrhythmics: increased risk of myocardial depression and bradycardia; increased risk of bradycardia, myocardial depression and AV block with amiodarone
  - Antidepressants: enhanced hypotensive effect with MAOIs
  - Antihypertensives; enhanced hypotensive effect; increased risk of withdrawal hypertension with clonidine; increased risk of first dose hypotensive effect with post-synaptic alpha-blockers such as prazosin
  - Antimalarials: increased risk of bradycardia with mefloquine
  - Antipsychotics enhanced hypotensive effect with phenothiazines
  - Calcium-channel blockers: increased risk of bradycardia and AV block with diltiazem; hypotension and heart failure possible with nifedipine and nisoldipine; asystole, severe hypotension and heart failure with verapamil
  - Diuretics: enhanced hypotensive effect
  - Moxisylyte: possible severe postural hypotension
  - Sympathomimetics: severe hypertension with adrenaline and noradrenaline and possibly with dobutamine
  - Tropisetron: increased risk of ventricular arrhythmias – use with caution

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- SPC guidelines for increasing dosing interval for patients with renal impairment may be impractical with respect to patient compliance
- Unlike most other beta-blockers, nadolol is not metabolised and is excreted unchanged mainly by the kidneys

RETURN TO CONTENTS
Naftidrofuryl oxalate

**CLINICAL USE**
Vasodilator:
● Peripheral and cerebral vascular disease

**DOSE IN NORMAL RENAL FUNCTION**
● Peripheral vascular disease: 100–200 mg 3 times daily
● Cerebral vascular disease: 100 mg 3 times daily

**PHARMACOKINETICS**
- Molecular weight: 473.6 daltons
- % Protein binding: 60–65%
- % Excreted unchanged in urine: <1 (mainly as metabolites)
- Volume of distribution: 61.5 litres (L/kg)

**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Dialysed. Dose as in normal renal function
- HDF/High flux: Dialysed. Dose as in normal renal function
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
● None known

**ADMINISTRATION**
- RECONSTITUTION
- ROUTE
  ● Oral
- RATE OF ADMINISTRATION
- COMMENTS
- OTHER INFORMATION
  ● IV preparation was withdrawn due to increased risk of cardiac and neurological toxicity. It has also been associated with acute renal failure secondary to oxalate crystallisation
Nalidixic acid

CLINICAL USE
Antibacterial agent

DOSE IN NORMAL RENAL FUNCTION
600–900 mg every 6 hours

PHARMACOKINETICS
Molecular weight (daltons) 232.2
% Protein binding 93–97
% Excreted unchanged in urine 11–33 (80–90% as inactive metabolites)
Volume of distribution (L/kg) 0.47–0.55
Half-life – normal/ESRF (hrs) 6–8/21

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)

20–50  Dose as in normal renal function
10–20  Dose as in normal renal function
<10   Avoid. See ‘Other Information’

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

CAPD  Unlikely to be dialysed. Dose as in GFR<10mL/min
HD    Unlikely to be dialysed. Dose as in GFR<10mL/min
HDF/High flux Unlikely to be dialysed. Dose as in GFR<10mL/min
CAV/ VVHD  Unknown dialysability. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● Analgesics: increased risk of convulsions with NSAIDs
● Anticoagulants: anticoagulant effect of coumarins enhanced
● Ciclosporin: increased risk of nephrotoxicity
● Antimalarials: manufacturer of artemether with lumefantrine advises avoid concomitant use
● Theophylline: possibly increased risk of convulsions

ADMINISTRATION
RECONSTITUTION
–
ROUTE
● Oral
RATE OF ADMINISTRATION
–
COMMENTS
–

OTHER INFORMATION
Avoid in severe renal impairment because the concentration in the urine is inadequate, and risk of monoglucuronide metabolite toxicity
Naloxone hydrochloride

**CLINICAL USE**
Reversal of opioid induced respiratory depression

**DOSE IN NORMAL RENAL FUNCTION**
See ‘Other Information’

**PHARMACOKINETICS**
- Molecular weight: 363.8 (daltons)
- % Protein binding: 54
- % Excreted unchanged in urine: 0
- Volume of distribution: 3 (L/kg)

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/MIN): 20–50 Dose as in normal renal function
- 10–20 Dose as in normal renal function
- <10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Unknown dialysability. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
- IV, IM, SC. IV more rapid response
- RATE OF ADMINISTRATION
- Rapid if bolus injection

**OTHER INFORMATION**
- IV postoperative use: Give 1.5–3 micrograms/kg; if response inadequate, increments of 100 micrograms every 2 minutes. Further dose by IM injection if needed
- OR dilute 400 micrograms in 100mL sodium chloride 0.9% or glucose 5% (4 micrograms/mL) and give by continuous infusion. Titrate dose according to response
- Opioid overdosage: initial dose of 400–2000 micrograms IV; may be repeated at 2–3 minute intervals if the desired degree of counteraction and improvement in respiratory function is not obtained. (If no response after 10 mg then question the diagnosis of opioid induced toxicity.)
- OR give as an infusion: 4 mg in 20mL (200mcg/mL solution) (unlicensed)
Naproxen

**CLINICAL USE**
NSAID and analgesic

**DOSE IN NORMAL RENAL FUNCTION**
- Rheumatic disease: 0.5–1 g in 1–2 divided doses
- Musculoskeletal disorders and dysmenorrhoea: 250 mg every 6–8 hours; maximum 1.25 g daily
- Gout: 250 mg every 8 hours

**PHARMACOKINETICS**
- Molecular weight: 230.3 (daltons)
- % Protein binding: 99%
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): 0.16

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose in normal renal function, but avoid if possible</th>
<th>Dose in normal renal function, but avoid if possible</th>
<th>Dose in normal renal function, but only use if on dialysis See 'Other Information'</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Slightly dialysed. Dose as in GFR<10mL/min
- HD: Not dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10mL/min
- CAV/VVHD: Slightly dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- ACE inhibitors and angiotensin-II antagonists: antagonism of hypotensive effect; increased risk of nephrotoxicity and hyperkalaemia
- Analgesics: avoid concomitant use of 2 or more NSAIDs, including aspirin (increased side effects); avoid with ketorolac (increased risk of side effects and haemorrhage)
- Antibacterials: possibly increased risk of convulsions with quinolones
- Anticoagulants: effects of coumarins enhanced; possibly increased risk of bleeding with heparins and coumarins
- Antidepressants: increased risk of bleeding with SSRIs and venlafaxine
- Antidiabetic agents: effects of sulphonylureas enhanced
- Anti-epileptics: possibly increased phenytoin concentration
- Antivirals: increased risk of haematological toxicity with zidovudine; concentration possibly increased by ritonavir
- Ciclosporin: may potentiate nephrotoxicity
- Cytotoxic agents: reduced excretion of methotrexate; increased risk of bleeding with erlotinib
- Diuretics: increased risk of nephrotoxicity; antagonism of diuretic effect; hyperkalaemia with potassium-sparing diuretics
- Lithium: excretion decreased
- Pentoxifylline: increased risk of bleeding
- Probencid: excretion reduced by probenecid
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  -
**OTHER INFORMATION**

- Associated with an intermediate risk of side effects
- Eliminated to a large extent (95%) as metabolites by urinary excretion via glomerular filtration. Remainder is excreted via the faeces
- Inhibition of renal prostaglandin synthesis by NSAIDs may interfere with renal function, especially in the presence of existing renal disease – avoid if possible; if not, check serum creatinine 48–72 hours after starting NSAID – if raised, discontinue NSAID therapy
- Use normal doses in patients with CKD 5 on dialysis and who do not pass any urine
- Use with caution in renal transplant recipients (can reduce intrarenal autocoid synthesis)
**Naratriptan**

**CLINICAL USE**
5HT₁ receptor agonist:
- Acute treatment of migraine

**DOSE IN NORMAL RENAL FUNCTION**
2.5 mg. Dose may be repeated after 4 hours; maximum 5 mg/24 hours

**PHARMACOKINETICS**
- Molecular weight: 371.9 (as hydrochloride)
- % Protein binding: 29
- % Excreted unchanged in urine: 50
- Volume of distribution: 170 litres (L/kg)
- Half-life – normal/ESRF (hrs): 6/11

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50: Maximum 2.5 mg daily
  - 15–20: Maximum 2.5 mg daily
  - <15: Use with caution – maximum 2.5 mg daily

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Likely dialysability. Dose as for GFR<15mL/min
- HD: Likely dialysability. Dose as for GFR<15mL/min
- HDF/High flux: Likely dialysability. Dose as for GFR<15mL/min
- CAV/VVHD: Unknown dialysability. Dose as for GFR=15–20mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs:
- Antidepressants: possibly increased serotoninergic effects with duloxetine; increased serotoninergic effects with St John's wort – avoid concomitant use
- Ergot alkaloids: increased risk of vasospasm – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**
- Do not take second dose at 4 hours during an attack if the first dose was ineffectual
- Naratriptan is excreted by glomerular filtration and active secretion into the renal tubules
- Inactive metabolites are renally excreted
- Studies in patients with impaired renal function (GFR=18–115 mL/min) showed an 80% increase in half-life and a 50% decrease in clearance compared with matched individuals with normal renal function
Nateglinide

**CLINICAL USE**
Treatment of type 2 diabetes in combination with metformin

**DOSE IN NORMAL RENAL FUNCTION**
60–180 mg 3 times daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>317.4</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>97–99</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>6–16</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.17–0.2</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1.5/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>15–30</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;15</td>
<td>Start at a low dose and increase according to response</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;15 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;15 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose as in GFR&lt;15 mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>VVHD</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: concentration reduced by rifampicin
- Antifungals: hypoglycaemic effect possibly enhanced by fluconazole
- Lipid-lowering agents: hypoglycaemic effect possibly enhanced by gemfibrozil

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- Although there is a 49% decrease in Cₘₙₙₜ of nateglinide in dialysis patients, the systemic availability and half-life in diabetic subjects with moderate to severe renal insufficiency (creatinine clearance=15–50 mL/min) was comparable between renal subjects requiring haemodialysis and healthy subjects. Although safety was not compromised in this population, dose adjustment may be required in view of low Cₘₙₙₜ.
- Metabolite removed by dialysis
Nebivolol

**CLINICAL USE**

Beta-adrenoceptor blocker:
- Essential hypertension
- Adjunct in heart failure

**DOSE IN NORMAL RENAL FUNCTION**

Hypertension: 2.5–5 mg once daily
Adjunct in heart failure: 1.25–10 mg once daily

**PHARMACOKINETICS**

- Molecular weight: 405.4 (441.9 as hydrochloride)
- % Protein binding: 98
- % Excreted unchanged in urine: <0.5
- Volume of distribution (L/kg): 11.2

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Initial dose 2.5 mg and adjust according to response</td>
</tr>
<tr>
<td>10–20</td>
<td>Initial dose 2.5 mg and adjust according to response</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Initial dose 2.5 mg and adjust according to response</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Not dialysed. Dose as for GFR<10mL/min
- HD: Not dialysed. Dose as for GFR<10mL/min
- HDF/High flux: Unknown dialysability. Dose as for GFR<10mL/min
- CAV/VVHD: Not dialysed. Dose as for GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Analgesics: NSAIDs antagonise hypotensive effect
- Anti-arrhythmics: increased risk of myocardial depression and bradycardia; increased risk of bradycardia, myocardial depression and AV block with amiodarone
- Antidepressants: enhanced hypotensive effect with MAOIs
- Antihypertensives; enhanced hypotensive effect; increased risk of withdrawal hypertension with clonidine; increased risk of first dose hypotensive effect with post-synaptic alpha-blockers such as prazosin
- Antimalarials: increased risk of bradycardia with mefloquine
- Antipsychotics enhanced hypotensive effect with phenothiazines
- Calcium-channel blockers: increased risk of bradycardia and AV block with diltiazem; hypotension and heart failure possible with nifedipine and nisoldipine; asystole, severe hypotension and heart failure with verapamil
- Diuretics: enhanced hypotensive effect
- Moxisylyte: possible severe postural hypotension
- Sympathomimetics: severe hypertension with adrenaline and noradrenaline and possibly with dobutamine
- Tropisetron: increased risk of ventricular arrhythmias – use with caution

**ADMINISTRATION**

**RECONSTITUTION**

- Route
- Oral

**RATE OF ADMINISTRATION**

- Comments

**OTHER INFORMATION**

- 38% of the dose is excreted in the urine as active metabolites
- In a trial of 10 patients with renal artery stenosis given nebivolol 5 mg daily, plasma renin activity significantly decreased, although serum aldosterone levels did not change to any great extent. In addition, there was no change in effective renal plasma flow, GFR, renal blood flow, or renal vascular resistance. Renal function remained well-preserved
Nefopam hydrochloride

CLINICAL USE
Analgesic for moderate pain

DOSE IN NORMAL RENAL FUNCTION
Oral: 30–90mg 3 times a day

PHARMACOKINETICS
Molecular weight 289.8 (daltons)
% Protein binding 73
% Excreted <5 unchanged in urine
Volume of distribution No data (L/kg)
Half-life – normal/ESRF (hrs) 4

DOSE IN RENAL IMPAIRMENT
GFR (mL/Min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function. See ‘Other Information’

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unknown dialysability. Dose as in GFR<10mL/min
HD Unlikely to be dialysed. Dose as in GFR<10mL/min
HDF/High flux Unknown dialysability. Dose as in GFR<10mL/min
CAV/VVHD Unknown dialysability. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● Antidepressants: avoid MAOIs; tricyclics possibly increased risk of side effects

ADMINISTRATION
RECONSTITUTION
–
ROUTE
● Oral
RATE OF ADMINISTRATION
–
COMMENTS
–

OTHER INFORMATION
● Avoid repeated or chronic administration in end stage renal disease and dialysis patients
● In the elderly a dose of 30mg 8 hourly is recommended due to reduced metabolism and increased susceptibility to side effects. Renal patients may also have reduced metabolism and excretion so may also have the same problems – always start with the lower dose
● Active metabolites excreted in the urine
Nelfinavir

**CLINICAL USE**
Protease inhibitor:
- Treatment of HIV infection in combination with other antiretroviral drugs

**DOSE IN NORMAL RENAL FUNCTION**
750 mg 3 times a day, or 1.25 g twice a day

**PHARMACOKINETICS**
- Molecular weight: 663.9 (as mesilate)
- % Protein binding: >98
- % Excreted unchanged in urine: 1–2
- Volume of distribution (L/kg): 2–7
- Half-life – normal/ESRF (hrs): 3.5–5

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10mL/min
- HD: Not dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Not dialysed. Dose as in GFR<10mL/min
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anti-arrhythmics: increased risk of arrhythmias with amiodarone – avoid concomitant use
- Antibacterials: concentration significantly reduced by rifampicin – avoid concomitant use; concentration of rifabutin increased – halve rifabutin dose; avoid with telithromycin in severe renal and hepatic failure
- Antidepressants: concentration reduced by St John’s wort – avoid concomitant use
- Anti-epileptics: concentration possibly reduced by carbamazepine, primidone and barbiturates; concentration of phenytoin reduced
- Antimalarials: avoid concomitant use with artemether/lumezantrine
- Antimuscarinics: avoid concomitant use with tolterodine
- Antipsychotics: possibly increased risk of ventricular arrhythmias with pimozide and sertindole – avoid concomitant use; possibly inhibits aripiprazole metabolism – reduce aripiprazole dose
- Ciclosporin: possibly increased ciclosporin concentration
- Cilostazol: concentration of cilostazol possibly increased – avoid concomitant use
- Diuretics: eplerenone concentration increased – avoid concomitant use
- Ergot alkaloids: risk of ergotism – avoid concomitant use
- Ivabradine: possibly increased ivabradine concentration – avoid concomitant use
- Lipid-regulating drugs: increased risk of myopathy with simvastatin and possibly atorvastatin – avoid concomitant use
- Midazolam: prolonged sedation – avoid concomitant use
- Oestrogens and progestogens: possibly reduced efficacy of oral contraceptives
- Omeprazole: avoid concomitant use due to possible resistance to nelfinavir developing
- 5HT1 agonists: concentration of eletriptan increased – avoid concomitant use
- Tacrolimus: possibly increased tacrolimus concentration

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- No data available on the use of nelfinavir in renal failure but need for dose adjustment is unlikely due to nelfinavir being predominantly metabolised and excreted via the liver. Use with caution.
Neomycin sulphate

**CLINICAL USE**
Antibacterial agent:
- Bowel sterilisation before surgery
- Hepatic coma

**DOSE IN NORMAL RENAL FUNCTION**
- Bowel sterilisation: 1 g every hour for 4 hours, then 1 g every 4 hours for 2–3 days
- Hepatic coma: up to 4 g daily in divided doses usually for a maximum of 14 days

**PHARMACOKINETICS**
- Molecular weight (daltons): 711.7
- % Protein binding: 0–30
- % Excreted unchanged in urine: 30–50
- Volume of distribution (L/kg): 0.25

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function. Use with caution and monitor renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
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<tr>
<td>10–20</td>
<td></td>
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<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Dialysed. Dose as in GFR<10mL/min
- HD: Dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10mL/min
- CAV/VVHD: Dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: altered INR with coumarins or phenindione
- Botulinum toxin: neuromuscular block enhanced (risk of toxicity)
- Ciclosporin: increased risk of nephrotoxicity
- Cytotoxics: possibly reduced methotrexate absorption; increased risk of nephrotoxicity and possibly of ototoxicity with platinum compounds
- Diuretics: increased risk of ototoxicity with loop diuretics
- Muscle relaxants: enhanced effects of suxamethonium and non-depolarising muscle relaxants
- Parasympathomimetics: antagonism of effect of neostigmine and pyridostigmine
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- –

**ROUTE**
- Oral, topical

**RATE OF ADMINISTRATION**
- –

**COMMENTS**
- –

**OTHER INFORMATION**
- Only 3% of an oral dose is absorbed
- About 97% of an orally administered dose is excreted unchanged in the faeces. Impaired GI motility may increase absorption of the drug; therefore, possible that prolonged therapy could result in ototoxicity and nephrotoxicity, particularly in patients with a degree of renal failure
- If renal impairment occurs the dose should be reduced or treatment discontinued
- High doses associated with nephrotoxicity and ototoxicity
- In mild renal failure, i.e. a GFR>50 mL/min, the frequency should be reduced to every 6 hours
Neostigmine

**CLINICAL USE**
- Myasthenia gravis
- Antagonist to non-depolarising neuromuscular blockade

**DOSE IN NORMAL RENAL FUNCTION**
- Myasthenia gravis: neostigmine bromide 15–30 mg at suitable intervals throughout day – total daily dose 75–300 mg; Neostigmine metilsulfate, IM, SC, 1–2.5 mg – usual total daily dose 5–20 mg
- Antagonist to non-depolarising neuromuscular blockade: 50–70 mcg/kg over 1 minute; maximum dose 5 mg

**PHARMACOKINETICS**
- Molecular weight (daltons) 223.3 (303.2 as bromide); (334.4 as metilsulphate)
- % Protein binding 15–25
- % Excreted unchanged in urine 50
- Volume of distribution (L/kg) 0.5–1
- Half-life – normal/ESRF (hrs) 0.8–1.5/3

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min) 20–50 50–100% of normal dose
- GFR (mL/min) 10–20 50–100% of normal dose
- GFR (mL/min) <10 50–100% of normal dose

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Unknown dialysability. Dose as in GFR<10 mL/min
- HD Unknown dialysability. Dose as in GFR<10 mL/min
- HDF/High flux Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD Unknown dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Aminoglycosides, clindamycin and polymyxins antagonise effects of neostigmine

**ADMINISTRATION**
- **RECONSTITUTION**
- **ROUTE**
  - Neostigmine bromide: Oral
  - Neostigmine metilsulfate: SC, IM, IV
- **RATE OF ADMINISTRATION**
  - IV: Very slowly
- **COMMENTS**

**OTHER INFORMATION**
- Neostigmine 0.5 mg IV = 1–1.5 mg IM/SC =15 mg orally
- When used for reversal of non-depolarising neuromuscular blockade, atropine (0.6–1.2 mg IV) or glycopyrronium should be given before or with neostigmine in order to prevent bradycardia, excessive salivation and other muscarinic actions of neostigmine
- The physicochemical nature of neostigmine may tend to encourage its removal by various renal replacement therapies
Netilmicin

CLINICAL USE
Antibacterial agent

DOSE IN NORMAL RENAL FUNCTION
- IM, IV: 4–7.5 mg/kg daily, as a single daily dose or in divided doses every 8 or 12 hours
- Urinary tract infection: 150 mg daily for 5 days

PHARMACOKINETICS
Molecular weight 1441.6 (as sulphate)
% Protein binding <5
% Excreted unchanged in urine 80
Volume of distribution 0.16–0.3 (L/kg)
Half-life – normal/ESRF (hrs) 2–2.5/35–72

DOSE IN RENAL IMPAIRMENT
GFR (mL/MIN)
20–50 4–7.5 mg/kg once daily. Monitor levels
10–20 3–4 mg/kg once daily. Monitor levels
<10 2 mg/kg once daily. Monitor levels

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Dialysed. IV: 2 mg/kg on alternate days
IP: 7.5–10 mg/L per exchange. Monitor levels
HD Dialysed. Administer 2 mg/kg at the end of each dialysis session. Monitor levels
HDF/High flux Dialysed. Administer 2 mg/kg at the end of each dialysis session. Monitor levels
CAV/VVHD Dialysed. Dose as in GFR=10–20 mL/min. Monitor levels

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Botulinum toxin: neuromuscular block enhanced (risk of toxicity)
- Ciclosporin: increased risk of nephrotoxicity
- Cytotoxics: increased risk of nephrotoxicity and possibly of ototoxicity with platinum compounds
- Diuretics: increased risk of ototoxicity with loop diuretics
- Muscle relaxants: effects of non-depolarising muscle relaxants and suxamethonium enhanced
- Parasympathomimetics: antagonism of effect of neostigmine and pyridostigmine
- Tacrolimus: increased risk of nephrotoxicity

ADMINISTRATION
RECONSTITUTION
- ROUTE
- IM, IP, IV bolus or infusion
RATE OF ADMINISTRATION
- IV bolus: Administer over 3–5 minutes
- IV infusion: Administer over 0.5–2 hours
COMMENTS
- Add to 50–200 mL of sterile water for injection, sodium chloride 0.9%, glucose 5% or 10%
- IM and IV dose are identical. Calculate on mg/kg lean body weight, or actual weight, whichever is lower

OTHER INFORMATION
- Netilmicin serum concentrations should be monitored and used for basis of dosage adjustment, otherwise follow guidelines in the SPC according to serum creatinine/creatinine clearance
- Once-daily administration of netilmicin may lead to transient peak concentrations of 20–30 micrograms/mL. Other dosage regimens will result in peak levels not exceeding 12 micrograms/mL. Prolonged levels above 16 micrograms/mL should be avoided. If trough levels are monitored they will usually be 3 micrograms/mL or less with the recommended dosage. Increasing trough concentrations above 4 micrograms/mL should be avoided
Nevirapine

**CLINICAL USE**
Non-nucleoside reverse transcriptase inhibitor:
- Treatment of progressive or advanced HIV infection in combination with at least two other antivirals

**DOSE IN NORMAL RENAL FUNCTION**
200 mg daily, increasing to twice daily after 14 days if tolerated

**PHARMACOKINETICS**
- Molecular weight (daltons) 266.3
- % Protein binding 60
- % Excreted unchanged in urine <3
- Volume of distribution (L/kg) 1.12–1.3
- Half-life – normal/ESRF (hrs) 45 (single dose) 25–30 (multiple dosing)/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
<td>See 'Other Information'</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
<td></td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
<td></td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: concentration decreased by rifampicin – avoid concomitant use; possibly increased rifabutin concentration
- Anticoagulants: may increase or reduce effect of warfarin
- Antidepressants: concentration reduced by St John’s wart – avoid concomitant use
- Antifungals: concentration of ketoconazole reduced – avoid concomitant use; concentration increased by fluconazole; possibly reduced caspofungin concentration – may need to increase caspofungin dose
- Antipsychotics: possibly reduced aripiprazole concentration – increase aripiprazole dose
- Antivirals: concentration of indinavir and efavirenz reduced and possibly amprenavir, lopinavir and atazanavir – avoid concomitant use with atazanavir
- Oestrogens and progestogens: accelerated metabolism (reduced contraceptive effect)

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  -

**OTHER INFORMATION**
- Little data available on the use of nevirapine in renal failure, but need for dose adjustment is unlikely due to nevirapine being predominantly metabolised in the liver, and the inactive metabolites excreted in the urine. Use with caution
- There was a preliminary study of haemodialysis patients which showed that a normal dose was not associated with increased side effects. (Izzedine H, Launay-Vacher V, Aymard G, et al. Pharmacokinetic of nevirapine in haemodialysis. Nephrol Dial Transplant. 2001, Jan; 16: 192–3)
Nicardipine hydrochloride

CLINICAL USE
Calcium-channel blocker:
- Prophylaxis and treatment of angina
- Mild to moderate hypertension

DOSE IN NORMAL RENAL FUNCTION
20–40 mg 3 times daily

PHARMACOKINETICS
- Molecular weight (daltons) 516
- % Protein binding >99
- % Excreted unchanged in urine <1
- Volume of distribution (L/kg) 0.8
- Half-life – normal/ESRF (hrs) 8.6/Unchanged

DOSE IN RENAL IMPAIRMENT
<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function. Start with small doses</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function. Start with small doses</td>
</tr>
</tbody>
</table>

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–20 mL/min

ADMINISTRATION
- RECONSTITUTION
  - ROUTE
    - Oral
    - RATE OF ADMINISTRATION
    - COMMENTS
      - Administration of nicardipine with food appears to reduce the bioavailability and delay the achievement of peak plasma concentrations

OTHER INFORMATION
- Extensively metabolised in the liver and excreted in the urine and faeces, mainly as inactive metabolites
- Nicardipine blood levels may be elevated in some renally impaired patients. Therefore, start with a low dose and titrate to BP and response. The dose interval may also need to be extended to 12 hourly

IMPORTANT DRUG INTERACTIONS
- Potentially hazardous interactions with other drugs:
  - Anaesthetics: enhanced hypotensive effect
  - Antibacterials: metabolism possibly accelerated by rifampicin
  - Anti-epileptics: effect reduced by carbamazepine, barbiturates, phenytoin and primidone
  - Antifungals: metabolism possibly inhibited by itraconazole and ketoconazole
  - Antihypertensives: enhanced hypotensive effect, increased risk of first dose hypotensive effect of post-synaptic alpha-blockers
  - Antivirals: concentration possibly increased by ritonavir
  - Cardiac glycosides: digoxin concentration increased
  - Ciclosporin: concentration of ciclosporin increased
  - Grapefruit juice: concentration increased – avoid concomitant use
  - Tacrolimus: may increase tacrolimus levels
  - Theophylline: possibly increased theophylline concentration

RETURN TO CONTENTS
Nicorandil

**CLINICAL USE**
Prevention and treatment of chronic stable angina

**DOSE IN NORMAL RENAL FUNCTION**
5–30 mg twice daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Molecular weight (daltons)</th>
<th>211.2</th>
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</thead>
<tbody>
<tr>
<td>% Protein binding</td>
<td>Slightly</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>1</td>
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<tr>
<td>Volume of distribution (L/kg)</td>
<td>No data</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1/Unchanged</td>
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</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
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<tr>
<td>10–20</td>
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<tr>
<td>&lt;10</td>
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</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose as in normal renal function</th>
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</thead>
<tbody>
<tr>
<td>CAP</td>
<td>Unknown dialysability.</td>
</tr>
<tr>
<td>HD</td>
<td>Unknown dialysability.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability.</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unknown dialysability.</td>
</tr>
<tr>
<td>VVHD</td>
<td>Unknown dialysability.</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Sildenafil, tadalafil and vardenafil:
  enhanced hypotensive effect, avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
-
Nicotinic acid

**CLINICAL USE**
Hyperlipidaemia

**DOSE IN NORMAL RENAL FUNCTION**
375 mg – 2 g daily at night

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>123.1</td>
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<tr>
<td>% Protein binding</td>
<td>High</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>12</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>Very high</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1–5</td>
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**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose and Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>50% of dose and increase according to response</td>
</tr>
<tr>
<td>15–30</td>
<td>50% of dose and increase according to response</td>
</tr>
<tr>
<td>&lt;15</td>
<td>25% of dose and increase according to response</td>
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</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Dialysed. Dose as in GFR&lt;15 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;15 mL/min</td>
</tr>
<tr>
<td>HD/High flux</td>
<td>Dialysed. Dose as in GFR&lt;15 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose as in GFR=15–30 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Lipid-regulating drugs: increased risk of myopathy when used in combination with statins
- Aspirin: increased flushing

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**

- Use with caution in renal failure due to increased risk of rhabdomyolysis
- Toxic reactions are frequent in CKD 5
- Nicotinic acid and its metabolites are renally excreted and the metabolites account for some of the side effects of nicotinic acid
- One study showed that once daily nicotinic acid used in patients with a GFR<60 mL/min (average 61 mL/min) was safe and effective. (McGovern ME, Stanek E, Malott C, et al. Once-daily niacin extended-release is effective and safe for treatment of dyslipidaemia associated with chronic kidney disease. J Am Coll Cardiol. 2004; 43(5) Suppl. 2: A487: 820–6)
Nifedipine

**CLINICAL USE**
Calcium-channel blocker:
- Prophylaxis and treatment of angina
- Hypertension
- Raynaud's phenomenon

**DOSE IN NORMAL RENAL FUNCTION**
Capsules: 5–20 mg 3 times daily
Tablets: 20–40 mg twice daily
MR: 20–90 mg daily

**PHARMACOKINETICS**
Molecular weight 346.3 (daltons)
% Protein binding 92–98
% Excreted unchanged in urine <1
Volume of distribution (L/kg) 1.4
Half-life – normal/ESRF (hrs) 1.4–11 (depends on preparation)/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Start with small doses</td>
</tr>
<tr>
<td>10–20</td>
<td>Start with small doses</td>
</tr>
<tr>
<td>&lt;10</td>
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</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD** Not dialysed. Dose as in GFR<10 mL/min
- **HD** Not dialysed. Dose as in GFR<10 mL/min
- **HDF/High flux** Unknown dialysability. Dose as in GFR<10 mL/min
- **CAV/VVHD** Unknown dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Antibacterials: metabolism accelerated by rifampicin; concentration increased by quinupristin/dalfopristin
- Anti-epileptics: effect reduced by carbamazepine, barbiturates, phenytoin and primidone
- Antifungals: metabolism possibly inhibited by itraconazole and ketoconazole
- Antihypertensives: enhanced hypotensive effect, increased risk of first dose hypotensive effect of post-synaptic alpha-blockers; occasionally severe hypotension and heart failure with beta-blockers
- Antivirals: concentration possibly increased by ritonavir
- Cardiac glycosides: digoxin concentration possibly increased
- Ciclosporin: may increase ciclosporin level, but not a problem in practice; nifedipine concentration may be increased
- Grapefruit juice: concentration increased – avoid concomitant use
- Insulin: may impair glucose tolerance
- Magnesium salts: profound hypotension with IV magnesium
- Tacrolimus: increased tacrolimus levels
- Theophylline: possibly increased theophylline concentration

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE** Oral
- **RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- Protein binding decreased in severe renal impairment
- Acute renal dysfunction reported
- Increased incidence of side effects (headache, flushing, dizziness and peripheral oedema) in patients with ERF
- For acute use, bite capsule then swallow contents with 10–50 mL water

RETURN TO CONTENTS
Nimodipine

**CLINICAL USE**
Calcium-channel blocker:
- Prevention and treatment of ischaemic neurological deficits following subarachnoid haemorrhage

**DOSE IN NORMAL RENAL FUNCTION**
- Prevention: 60 mg orally every 4 hours
- Treatment via central catheter: 1 mg/hour initially, increased after 2 hours to 2 mg/hour. If BP unstable, weight <70 kg, start with 0.5 mg/hour or less if necessary

**PHARMACOKINETICS**
- Molecular weight (daltons) 418.4
- % Protein binding 98
- % Excreted unchanged in urine <1
- Volume of distribution (L/kg) 0.9–1.6
- Half-life – normal/ESRF (hrs) 1.1–1.7/22

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
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<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>CAPD</th>
<th>Not dialysed. Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: enhanced hypotensive effect
- Antibacterials: metabolism accelerated by rifampicin
- Anti-epileptics: effect reduced by carbamazepine, barbiturates, phenytoin and primidone
- Antifungals: metabolism possibly inhibited by itraconazole and ketoconazole
- Antihypertensives: enhanced hypotensive effect, increased risk of first dose hypotensive effect of post-synaptic alpha-blockers
- Antivirals: concentration possibly increased by ritonavir
- Grapefruit juice: concentration increased – avoid concomitant use
- Theophylline: possibly increased theophylline concentration

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral, IV
- **RATE OF ADMINISTRATION**
  - IV – First 2 hours: 1 mg (5 mL) nimodipine per hour
  - After 2 hours: Infuse 2 mg (10 mL) nimodipine per hour
- **COMMENTS**
  - Nimodipine solution must not be added to an infusion bag or bottle and must not be mixed with other drugs
  - Nimodipine solution should be administered only via a bypass into a running drip (40 mL/hour) of either sodium chloride 0.9% or glucose 5%
  - In the event of nimodipine tablets and solution being administered sequentially, the total duration of treatment should not exceed 21 days

**OTHER INFORMATION**
- Nimodipine solution reacts with PVC. Polyethylene tubes are supplied
- Patients with known renal disease and/or receiving nephrotoxic drugs should have renal function monitored closely during IV treatment

RETURN TO CONTENTS
Nisoldipine

**CLINICAL USE**
Calcium-channel blocker:
- Hypertension
- Angina

**DOSE IN NORMAL RENAL FUNCTION**
10–40 mg daily (varies, depending on indication)

**PHARMACOKINETICS**
- Molecular weight (daltons): 388.4
- % Protein binding: >99
- % Excreted unchanged in urine: <10
- Volume of distribution (L/kg): 2.3–7.1

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/MIN): 20–50
  - Dose as in normal renal function
- 10–20
  - Dose as in normal renal function
- <10
  - Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Not dialysed. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Antibacterials: metabolism accelerated by rifampicin
- Anti-epileptics: concentration reduced by phenytoin and possibly carbamazepine, barbiturates and primidone
- Antifungals: metabolism possibly inhibited by itraconazole and ketoconazole avoid; avoid with fluconazole
- Antihypertensives: enhanced hypotensive effect, increased risk of first-dose hypotensive effect of post-synaptic alpha-blockers; occasionally severe hypotension and heart failure with beta-blockers
- Antivirals: concentration possibly increased by ritonavir
- Grapefruit juice: concentration increased — avoid concomitant use
- Theophylline: possibly increased theophylline concentration

**ADMINISTRATION**

**RECONSTITUTION**

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**

**COMMENTS**

---

RETURN TO CONTENTS
Nitrazepam

**CLINICAL USE**
Benzodiazepine:
- Hypnotic

**DOSE IN NORMAL RENAL FUNCTION**
5–10 mg at bedtime; elderly (or debilitated) 2.5–5 mg

**PHARMACOKINETICS**
- Molecular weight (daltons): 281.3
- % Protein binding: 87
- % Excreted unchanged in urine: <5
- Volume of distribution (L/kg): 2

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/Min)**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function. Start with small doses

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**
  - Unlikely to be dialysed. Dose as in GFR<10mL/min
- **HD**
  - Unlikely to be dialysed. Dose as in GFR<10mL/min
- **HDF/High flux**
  - Unknown dialysability. Dose as in GFR<10mL/min
- **CAV/VVHD**
  - Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: metabolism possibly increased by rifampicin
- Antipsychotics: increased sedative effects
- Antivirals: concentration possibly increased by ritonavir
- Disulfiram: metabolism of nitrazepam inhibited, increased sedative effects
- Sodium oxybate: enhanced effects of sodium oxybate – avoid

**ADMINISTRATION**
**RECONSTITUTION**
- 
**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 
**COMMENTS**
- 
**OTHER INFORMATION**
- Mild to moderate renal insufficiency does not alter the kinetics of nitrazepam
- CKD 5 patients will be more susceptible to adverse effects (drowsiness, sedation, unsteadiness)
Nitrofurantoin

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
Treatment: 50–100 mg every 6 hours
Prophylaxis: 50–100 mg at night

**PHARMACOKINETICS**
- Molecular weight (daltons): 238.2
- % Protein binding: 60–90
- % Excreted unchanged in urine: 30–40
- Volume of distribution (L/kg): 0.3–0.7
- Half-life – normal/ESRF (hrs): 0.3–1/1

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min):
  - 20–50: Dose as in normal renal function. Use with caution
  - 10–20: Contraindicated. See ‘Other Information’
  - <10: Contraindicated. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Dialysed. Avoid – contraindicated
- HD: Dialysed. Avoid – contraindicated
- HDF/High flux: Dialysed. Avoid – contraindicated
- CAV/VVHD: Dialysed. Avoid – contraindicated

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  - Urine may be coloured a dark yellow or brown
  - Macrocystalline form has slower dissolution and absorption rates, produces lower serum concentration and takes longer to achieve peak concentration in the urine

**OTHER INFORMATION**
- Avoid nitrofurantoin in patients with impaired renal function (GFR<20 mL/min) as the drug is ineffective due to inadequate urine concentration; toxic plasma concentrations can occur causing adverse effects, e.g. neuropathy, blood dyscrasias
- Nitrofurantoin gives false positive urinary glucose (if testing for reducing substances)
Nizatidine

**CLINICAL USE**
H₂-receptor antagonist

**DOSE IN NORMAL RENAL FUNCTION**
Oral: 150–600 mg daily
IV: 300–480 mg daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>331.5</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>35</td>
</tr>
<tr>
<td>% Excreted in urine</td>
<td>60</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.8–1.3</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1–2/3.5–11</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose (mg daily)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>150–300</td>
</tr>
<tr>
<td>&lt;20</td>
<td>150</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapeutic Modality</th>
<th>Dose (mg daily)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;20 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;20 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;20 mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unknown dialysability. Dose as in GFR&lt;20 mL/min</td>
</tr>
<tr>
<td>VVHD</td>
<td>GFR&lt;20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antifungals: absorption of itraconazole and ketoconazole reduced

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral, IV
- **RATE OF ADMINISTRATION**
  - Continuous IV infusion: Dilute 300 mg in 150 mL. Rate 10 mg/hour. Bolus: Dilute 100 mg in 50 mL and give over 15 minutes

**COMMENTS**
- Compatible with sodium chloride 0.9% or glucose 5%.
- To maintain gastric pH ≥4, a continuous infusion of 10 mg/hour is recommended

**OTHER INFORMATION**
- The effect of haemodialysis is unproven. It is not expected to be efficient since nizatidine has a large volume of distribution
Noradrenaline acid tartrate (norepinephrine bitartrate)

**CLINICAL USE**
- Hypotension
- Cardiac arrest (sympathomimetic)

**DOSE IN NORMAL RENAL FUNCTION**
(Doses expressed as noradrenaline acid tartrate)
- Acute hypotension: 80 mcg/mL solution, initially 0.16–0.33 mL/minute; adjust according to response
- Cardiac arrest: 200 mcg/mL solution, 0.5–0.75 mL

**PHARMACOKINETICS**
- Molecular weight: 337.3 daltons
- % Protein binding: ~50%
- % Excreted unchanged in urine: ~16%
- Volume of distribution: 0.09–0.4 (L/kg)
- Half-life – normal/ESRF (hrs): 1 minute/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Adrenergic neurone blockers: antagonise hypotensive effect
  - Antidepressants: tricyclics may cause hypertension and arrhythmias; MAOIs and moclobemide may cause hypertensive crisis
  - Beta-blockers: can cause severe hypertension
  - Clonidine: possibly increased risk of hypertension
  - Dopaminergics: effects possibly increased by entacapone; avoid concomitant use with rasagiline
  - Sympathomimetics: effects possibly enhanced by dopexamine

**ADMINISTRATION**
- **RECONSTITUTION**
  - **ROUTE**
    - IV
  - **RATE OF ADMINISTRATION**
    - According to response
  - **COMMENTS**
    - Preferably give centrally (low pH)
    - Dilute 1–4 mg in 100 mL glucose 5%
    - Can be given undiluted

**OTHER INFORMATION**
- Do not mix with alkaline drugs/solutions
- The pharmacokinetics of noradrenaline are not significantly affected by renal or hepatic disease
Norfloxacin

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
400 mg twice daily, duration of course depends on indication

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>319.3</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>14</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>30</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>2.5–3.1</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>3–4/6.5–8</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td></td>
</tr>
<tr>
<td>10–30</td>
<td>400 mg every 12 to 24 hours</td>
</tr>
<tr>
<td>&lt;10</td>
<td>400 mg daily</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in Normal Renal Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in GFR=10–30 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: increased risk of convulsions with NSAIDs
- Anticoagulants: anticoagulant effect of coumarins enhanced
- Antimalarials: manufacturer of artemether with lumefantrine advises avoid concomitant use
- Ciclosporin: increased risk of nephrotoxicity
- Theophylline: possibly increased risk of convulsion; increased levels of theophylline

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
-
Normal human immunoglobulin

**CLINICAL USE**
- Replacement therapy in primary and secondary immunodeficiency
- Idiopathic thrombocytopenic purpura
- Guillain Barré syndrome
- Kawasaki disease
- Allogeneic bone marrow transplantation
- Treatment of infections and prophylaxis of graft versus host disease

**DOSE IN NORMAL RENAL FUNCTION**
Variable according to preparation and indication. See individual SPC

**PHARMACOKINETICS**
- Molecular weight (daltons): 150,000
- % Protein binding: –
- % Excreted unchanged in urine: –
- Volume of distribution (L/kg): –
- Half-life – normal/ESRF (hrs): 24–36 days

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose as normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as normal renal function. See ‘Other Information’</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose as normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Probably not dialysed.</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Probably not dialysed.</td>
</tr>
</tbody>
</table>

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
- IV

**RATE OF ADMINISTRATION**
- Variable – see individual SPC

**COMMENTS**

**OTHER INFORMATION**
- IgG and IgG-complexes are broken down in the cells of the reticuloendothelial system
- Cases of acute renal failure have been reported in patients receiving IVIg therapy. In most cases, risk factors have been identified, such as pre-existing renal insufficiency, diabetes mellitus, hypovolaemia, overweight, concomitant nephrotoxic medicinal products or, aged over 65. In all patients, IVIg administration requires:
  - adequate hydration prior to the initiation of the infusion of IVIg;
  - monitoring of urine output;
  - monitoring of serum creatinine levels;
  - avoidance of concomitant use of loop diuretics
- In case of renal impairment, IVIg discontinuation should be considered. While reports of renal dysfunction and acute renal failure have been associated with the use of many of the licensed IVIg products, those containing sucrose (compared to glycine, maltose or sorbitol) as a stabiliser accounted for a disproportionate share of the total number. In patients at risk, the use of IVIg products that do not contain sucrose may be considered. In addition, the product should be administered at the minimum concentration and infusion rate practicable
- Overdose may lead to fluid overload and hyperviscosity, particularly in patients at risk, including elderly patients or patients with renal impairment
- The MHRA has issued a Medical Device Alert relating to the following point of care and home-use blood glucose meters: Roche Accu-Chek and Glucotrend, Abbott Diabetes Care FreeStyle

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Immunoglobulin administration may impair (for a period of at least 6 weeks and up to 3 months) the efficacy of live attenuated virus vaccines such as measles, rubella, mumps and varicella

RETURN TO CONTENTS
There is a risk of overestimation of blood glucose results when these meters are used for samples from patients on treatments that contain (or are metabolised to) maltose, xylose or galactose. The MHRA advises that the affected meters should not be used to measure blood glucose in patients receiving such treatments. Treatments that are known to contain (or that are metabolised to) maltose, xylose or galactose include (Extraneal®) icodextrin (used in peritoneal dialysis, PD), and certain immunoglobulin preparations (including Octagam®)
Nortriptyline

CLINICAL USE
Tricyclic antidepressant

DOSE IN NORMAL RENAL FUNCTION
30–150 mg daily in single or divided doses

PHARMACOKINETICS
Molecular weight (daltons) 263.4 (299.8 as hydrochloride)
% Protein binding 95
% Excreted unchanged in urine <5
Volume of distribution (L/kg) 15–23
Half-life – normal/ESRF (hrs) 25–38/15–66

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function. Start with small dose

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Not dialysed. Dose as in GFR<10 mL/min
HD Not dialysed. Dose as in GFR<10 mL/min
HDF/High flux Unknown dialysability. Dose as in GFR<10 mL/min
CAV/VVHD Not dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
Alcohol: increased sedative effect
Analgesics: increased risk of CNS toxicity with tramadol; possibly increased risk of side effects with nefopam; possibly increased sedative effects with opioids
Anti-arrhythmics: increased risk of ventricular arrhythmias with amiodarone – avoid concomitant use; increased risk of ventricular arrhythmias with drugs that prolong the QT interval; increased risk of arrhythmias with propafenone
Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin – avoid concomitant use; concentration reduced by rifampicin
Anticoagulants: may alter anticoagulant effect of coumarins
Antidepressants: enhanced CNS excitation and hypertension with MAOIs and moclobemide – avoid concomitant use; concentration possibly increased with SSRIs
Anti-epileptics: convulsive threshold lowered; concentration reduced by carbamazepine, primidone, barbiturates and possibly phenytoin
Antimalarials: avoid concomitant use with artemether/lumefantrine
Antipsychotics: increased risk of ventricular arrhythmias especially with pimozone; increased antimuscarinic effects with clozapine and phenothiazines; concentration increased by antipsychotics
Antivirals: increased TAD side effects with amphenavir; concentration possibly increased with ritonavir
Atomoxetine: increased risk of ventricular arrhythmias and possibly convulsions
Beta-blockers: increased risk of ventricular arrhythmias with sotalol
Clonidine: tricyclics antagonise hypotensive effect; increased risk of hypertension on clonidine withdrawal
Dopaminergics: avoid use with entacapone; CNS toxicity reported with selegiline and rasagiline
Pentamidine: increased risk of ventricular arrhythmias
Sibutramine: increased risk of CNS toxicity – avoid concomitant use
Sympathomimetics: increased risk of hypertension and arrhythmias with adrenaline and noradrenaline; metabolism possibly inhibited by methylphenidate

ADMINISTRATION
RECONSTITUTION
ROUTE Oral
RATE OF ADMINISTRATION
COMMENTS

OTHER INFORMATION
All metabolites are highly lipophilic
Nystatin

**CLINICAL USE**
Antifungal agent

**DOSE IN NORMAL RENAL FUNCTION**
Oral: 100,000–1,000,000 units (1–10 mL) every 6 hours
Topical: Apply 2–4 times daily (depends on formulation)

**PHARMACOKINETICS**
- Molecular weight (daltons): 926.1
- % Protein binding: No data
- % Excreted unchanged in urine: No data
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): No data

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Not dialysed. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral, topical

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- Not absorbed from intact skin or mucous membranes
- No significant gastrointestinal absorption

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Octreotide

CLINICAL USE
Relief of symptoms of gastroenteropancreatic endocrine tumours and acromegaly

DOSE IN NORMAL RENAL FUNCTION
50 micrograms – 1.2 mg daily

PHARMACOKINETICS
- Molecular weight: 1019.2 (as acetate)
- % Protein binding: 65
- % Excreted unchanged in urine: 32
- Volume of distribution: 0.27 L/kg
- Half-life – normal/ESRF (hrs): 1.5/Increased

DOSE IN RENAL IMPAIRMENT
GFR (mL/MIN)
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Dialysed. Dose as in normal renal function
- HDF/High flux: Dialysed. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Ciclosporin: ciclosporin concentration reduced

ADMINISTRATION
RECONSTITUTION
- ROUTE
  - SC, IV
- RATE OF ADMINISTRATION
  - IV bolus with ECG monitoring
- COMMENTS
  - IV: sodium chloride 0.9% to a ratio of not less than 1:1 and not more than 1:9

OTHER INFORMATION
- SC: to reduce local discomfort, warm to room temperature before injection
- For multiple injections, use different sites
- Patients with reduced renal function have been shown to have a reduced clearance of the drug (75 mL/minute vs. 175 mL/minute)
Oestrogen, conjugated (unlicensed product)

**CLINICAL USE**
Second line haemostatic agent for uraemic bleeding

**DOSE IN NORMAL RENAL FUNCTION**
0.6 mg/kg/day for 5 days

**PHARMACOKINETICS**
Molecular weight (daltons) –
% Protein binding –
% Excreted unchanged in urine –
Volume of distribution (L/kg) –
Half-life – normal/ESRF (hrs) –

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>CAPD</th>
<th>Unknown dialysability. Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>VVHD</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Ciclosporin: concentration of ciclosporin increased
- Anticoagulants: antagonism of anticoagulant effect of coumarins and phenindione
- Anti-epileptics: accelerate metabolism of oestrogens

**ADMINISTRATION**

**RECONSTITUTION**
- To 50 mL with sodium chloride 0.9%

**ROUTE**
- IV

**RATE OF ADMINISTRATION**
- Over a minimum of 30 minutes

**COMMENTS**
- 

**OTHER INFORMATION**
- Duration of effect about 14 days
- Used in association with desmopressin (DDAVP) in intractable cases
- Orally 10–20 mg daily for 5–7 days
- Conjugated oestrogens are a mixture of sodium oestrone sulphate and sodium equilin sulphate and other oestrogenic substances of the type excreted by pregnant mares
Ofloxacin

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
Oral: 200–400 mg daily, increased if necessary to 400 mg twice daily
IV: 200–400 mg twice daily

**PHARMACOKINETICS**
Molecular weight (daltons) 361.4
% Protein binding 25
% Excreted unchanged in urine 65–80
Volume of distribution (L/kg) 1.5–2.5
Half-life – normal/ESRF (hrs) 4–6/15–60

**DOSE IN RENAL IMPAIRMENT**
GFR (mL/Min)
20–50 200–400 mg once daily
10–20 200–400 mg once daily
<10 200 mg once daily

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
CAPD Not significantly dialysed. Dose as in GFR<10mL/min
HD Dialysed. Dose as in GFR<10mL/min
HDF/High flux Dialysed. Dose as in GFR<10mL/min
CAV/VVHD Dialysed. Dose as in GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: increased risk of convulsions with NSAIDs
- Anticoagulants: effect of acenocoumarol and warfarin enhanced
- Antimalarials: manufacturer of artemether with lumefantrine advises avoid concomitant use
- Ciclosporin: increased risk of nephrotoxicity
- Theophylline: possibly increased risk of convulsions

**ADMINISTRATION**

**RECONSTITUTION**
-

**ROUTE**
- Oral, IV

**RATE OF ADMINISTRATION**
- 200mg over 30 minutes

**COMMENTS**
-
Olanzapine

CLINICAL USE
- Schizophrenia
- Moderate to severe mania

DOSE IN NORMAL RENAL FUNCTION
- Oral: 5–20 mg daily
- IM: 5–10 mg repeated after 2 hours if required; maximum 3 doses daily for 3 days
- Maximum dose of combined routes: 20 mg per day

PHARMACOKINETICS
- Molecular weight (daltons) 312.4
- % Protein binding 93
- % Excreted unchanged in urine 7 (57% as metabolites and unchanged drug)
- Volume of distribution (L/kg) 10–20
- Half-life – normal/ESRF (hrs) 30–38/Unchanged

DOSE IN RENAL IMPAIRMENT GFR (mL/min)
- 20–50 Initial dose 5 mg daily and titrate as necessary
- 10–20 Initial dose 5 mg daily and titrate as necessary
- <10 Initial dose 5 mg daily and titrate as necessary

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD Not dialysed. Dose as in GFR<10 mL/min
- HD Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/ Not dialysed. Dose as in GFR=10–20 mL/min
- VVHD Unknown dialysability. Dose as in GFR=10–20 mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Analgesics: increased risk of convulsions with tramadol; enhanced hypotensive and sedative effects with opioids
- Antibacterials: concentration possibly increased by ciprofloxacin
- Antidepressants: fluvoxamine increases concentration of olanzapine
- Anti-epileptics: antagonism (convulsive threshold lowered); carbamazepine increases metabolism of olanzapine; increased risk of neutropenia with valproate
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antivirals: concentration reduced by ritonavir
- Anxiolytics and hypnotics: increased sedative effects; increased risk of hypotension, bradycardia and respiratory depression with IM olanzapine and parenteral benzodiazepines
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use

ADMINISTRATION
RECONSTITUTION
- 2.1 mL water for injection
ROUTE
- Oral, IM
RATE OF ADMINISTRATION
- COMMENTS
-
Olmesartan medoxomil

**CLINICAL USE**
Angiotensin-II receptor antagonist:
● Hypertension

**DOSE IN NORMAL RENAL FUNCTION**
10–40 mg once daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 558.6
- % Protein binding: 99.7
- % Excreted unchanged in urine: 35–50
- Volume of distribution (L/kg): 0.24

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>In renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function.</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function. Start with low doses</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function. Initial dose 10 mg daily and gradually increase</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
● Anaesthetics: enhanced hypotensive effect

- Analgesics: antagonism of hypotensive effect and increased risk of renal impairment with NSAIDs; hyperkalaemia with ketorolac and other NSAIDs
- Ciclosporin: increased risk of hyperkalaemia and nephrotoxicity
- Diuretics: enhanced hypotensive effect; hyperkalaemia with potassium-sparing diuretics
- Epoetin: increased risk of hyperkalaemia; antagonism of hypotensive effect
- Lithium: reduced excretion (possibility of enhanced lithium toxicity)
- Potassium salts: increased risk of hyperkalaemia
- Tacrolimus: increased risk of hyperkalaemia and nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- Hyperkalaemia and other side effects are more common in patients with impaired renal function
- Renal failure has been reported in association with angiotensin-II antagonists in patients with renal artery stenosis, post renal transplant, and in those with congestive heart failure
- Close monitoring of renal function during therapy is necessary in those with renal insufficiency
- In mild, moderate and severe renal failure, the AUC is increased by 62, 82 and 179% respectively

RETURN TO CONTENTS
Olsalazine sodium

**CLINICAL USE**
Induction and maintenance of remission in ulcerative colitis

**DOSE IN NORMAL RENAL FUNCTION**
1–3 g daily
Maintenance: 500 mg twice daily

**PHARMACOKINETICS**
- Molecular weight (daltons) 346.2
- % Protein binding >99
- % Excreted unchanged in urine 1–2
- Volume of distribution (L/kg) 6 litres
- Half-life – normal/ESRF (hrs) 1/Unchanged

**DOSE IN RENAL IMPAIRMENT (GFR (mL/Min))**
- 20–50 Caution – use only if necessary; start with low dose and increase according to response
- 10–20 Caution – use only if necessary; start with low dose and increase according to response
- <10 Caution – use only if necessary; start with low dose and increase according to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HD Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HDF/High flux Unlikely to be dialysed. Dose as in GFR<10 mL/min
- CAV/Unknown dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - COMMENTS
  -

**OTHER INFORMATION**
- Potential to be nephrotoxic due to 5-aminosalicylic acid (5-ASA) component. Both 5-ASA and its acetylated metabolite are rapidly excreted in the urine
- Half-life of metabolite is 7 days
- Less than 3% of an oral dose is absorbed before the drug reaches the colon
- Unlikely that renal dysfunction will have any important effect on the kinetics of the drug
- Manufacturers recommend that the use of olsalazine in patients with significant renal impairment is contraindicated due to lack of experience of its use in this patient population

---

PRESCRIBING INFORMATION

- **INDICATIONS**
  - Ulcerative colitis

- **CONTRAINDICATIONS**
  - Known hypersensitivity to this drug
  - Acute ulcerative colitis

- **WARNING**
  - Use with caution in patients with a history of gastrointestinal bleeding or stomach disease.

- **SIDE EFFECTS**
  - Gastrointestinal: Nausea, vomiting, abdominal pain, diarrhea
  - Dermatological: Rash, urticaria

- **INTERACTIONS**
  - Potentially hazardous interactions with other drugs
  - None known

- **ADVERSE REACTIONS**
  - Gastrointestinal: Nausea, vomiting, abdominal pain, diarrhea
  - Dermatological: Rash, urticaria

- **PHARMACOKINETICS**
  - Molecular weight (daltons) 346.2
  - % Protein binding >99
  - % Excreted unchanged in urine 1–2
  - Volume of distribution (L/kg) 6 litres
  - Half-life – normal/ESRF (hrs) 1/Unchanged

- **DOSE IN RENAL IMPAIRMENT (GFR (mL/Min))**
  - 20–50 Caution – use only if necessary; start with low dose and increase according to response
  - 10–20 Caution – use only if necessary; start with low dose and increase according to response
  - <10 Caution – use only if necessary; start with low dose and increase according to response

- **DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
  - CAPD Unlikely to be dialysed. Dose as in GFR<10 mL/min
  - HD Unlikely to be dialysed. Dose as in GFR<10 mL/min
  - HDF/High flux Unlikely to be dialysed. Dose as in GFR<10 mL/min
  - CAV/Unknown dialysability. Dose as in GFR=10–20 mL/min

---

**RECONSTITUTION**
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - COMMENTS
  -

**OTHER INFORMATION**
- Potential to be nephrotoxic due to 5-aminosalicylic acid (5-ASA) component. Both 5-ASA and its acetylated metabolite are rapidly excreted in the urine
- Half-life of metabolite is 7 days
- Less than 3% of an oral dose is absorbed before the drug reaches the colon
- Unlikely that renal dysfunction will have any important effect on the kinetics of the drug
- Manufacturers recommend that the use of olsalazine in patients with significant renal impairment is contraindicated due to lack of experience of its use in this patient population
Omalizumab

**CLINICAL USE**
Monoclonal antibody:
- Add-on therapy to improve asthma control

**DOSE IN NORMAL RENAL FUNCTION**
- Usually 75–375mg in 1 to 3 injections, dependent on baseline IgE levels and body weight every 2–4 weeks
- Maximum dose is 375 mg every 2 weeks
- See SPC for more information

**PHARMACOKINETICS**
- Molecular weight: 149000 (daltons)
- % Protein binding: 0
- % Excreted unchanged in urine: No data
- Volume of distribution (L/kg): 0.046–0.11
- Half-life – normal/ESRF (hrs): 20–26 days

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/Min)**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function. Use with caution
  - <10: Dose as in normal renal function. Use with caution

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely dialysability. Dose as in GFR<10mL/min
- HD: Unlikely dialysability. Dose as in GFR<10mL/min
- HDF/High flux: Unlikely dialysability. Dose as in GFR<10mL/min
- CAV/VVHD: Unlikely dialysability. Dose as in GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**
- **RECONSTITUTION**
  - Water for injection
- **ROUTE**
  - SC
- **RATE OF ADMINISTRATION**
  - COMMENTS
  - Preferably administer in the deltoid region of arm; alternatively in the thigh
  - Do not give more than 150 mg at one injection site
  - After reconstitution, chemically and physically stable for 8 hours at 2–8°C and 4 hours at 30°C

**OTHER INFORMATION**
- Has a bioavailability of 62%; peak concentrations occur after 7–8 days
- Metabolised by the liver
- Contraindicated in dialysis patients due to lack of information, therefore suggest use with caution and monitor patients closely
Omeprazole

**CLINICAL USE**
Gastric acid suppression

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: 10–120 mg daily
- IV: 40 mg once daily for up to 5 days
- Patients with recent bleeding on endoscopy: 80 mg stat followed by 8 mg/hour for 72 hours (British Society of Gastroenterology)

**PHARMACOKINETICS**
- Molecular weight (daltons): 345.4
- % Protein binding: 95%
- % Excreted unchanged in urine: Minimal
- Volume of distribution (L/kg): 0.3
- Half-life – normal/ESRF (hrs): 0.5–3/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: effect of coumarins possibly enhanced
- Anti-epileptics: effects of phenytoin possibly enhanced
- Antivirals: reduced atazanavir concentration – avoid concomitant use; AUC of saquinavir increased by 82% (increased risk of toxicity)
- Ciclosporin: variable response; mostly increase in ciclosporin level
- Cilostazol: increased cilostazol concentration – avoid concomitant use
- Tacrolimus: may increase tacrolimus concentration

**ADMINISTRATION**

**RECONSTITUTION**
- 5 mL solvent provided per 40 mg vial

**ROUTE**
- Oral, IV

**RATE OF ADMINISTRATION**
- Bolus: over 5 minutes
- Infusion: 40 mg over 20–30 minutes
- Continuous infusion: 8 mg/hour

**COMMENTS**
- Add to 100 mL sodium chloride 0.9% or glucose 5%
- Once diluted stable for 12 hours in sodium chloride 0.9% and 3 hours in glucose 5%
- Use oral as soon as possible
- 200 mg in 50 mL for 8 mg/hour infusion. (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006)

**OTHER INFORMATION**
- Omeprazole clearance is not limited by renal disease
Ondansetron

**CLINICAL USE**
Anti-emetic

**DOSE IN NORMAL RENAL FUNCTION**
Oral: 4–24 mg daily in 2–3 divided doses
IV: 8–32 mg daily
PR: 16 mg pre-chemotherapy

**PHARMACOKINETICS**
- Molecular weight (daltons) 293.4
- % Protein binding 70–76
- % Excreted unchanged in urine <5
- Volume of distribution (L/kg) 2
- Half-life – normal/ESRF (hrs) 3–6/5.4

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>As normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>As normal renal function</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>As normal renal function</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral, IV, IM, rectal
- RATE OF ADMINISTRATION
  - IV bolus over 3–5 minutes
  - IV infusion: over 15 minutes
  - Continuous infusion: 1 mg/hour

**COMMENTS**
- Dilute in 50–100 mL of sodium chloride 0.9% or glucose 5%

**OTHER INFORMATION**
- Can be used to treat uraemic pruritus
- Renal clearance of ondansetron is low
Orlistat

**CLINICAL USE**
Adjunct in obesity

**DOSE IN NORMAL RENAL FUNCTION**
120 mg taken immediately before, during or up to 1 hour after each meal; maximum 360 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 495.7
- % Protein binding: >99%
- % Excreted unchanged in urine: 0–4%
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 1–2/unchanged

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux: Unlikely to be dialysed. Dose as in normal renal function
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Acarbose: avoid concomitant administration
- Anticoagulants: monitor INR more frequently
- Ciclosporin: possibly reduces absorption of ciclosporin
- Vitamins: may reduce the absorption of fat soluble vitamins

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- If the meal doesn’t contain any fat, omit orlistat
- Orlistat is poorly absorbed; bioavailability of less than 5%
Orphenadrine hydrochloride

**CLINICAL USE**
Anti-muscarinic:
- Parkinsonism
- Drug induced extrapyramidal symptoms

**DOSE IN NORMAL RENAL FUNCTION**
150–400 mg daily in divided doses

**PHARMACOKINETICS**
- Molecular weight (daltons): 305.8
- % Protein binding: 95
- % Excreted unchanged in urine: 8
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 14/–

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose in normal renal function</th>
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<tr>
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<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD** Unlikely dialysability. Dose as in normal renal function
- **HD** Unlikely dialysability. Dose as in normal renal function
- **HDF/High flux** Unlikely dialysability. Dose as in normal renal function
- **CAV/VVHD** Unlikely dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs:
  - None known

**ADMINISTRATION**

- **RECONSTITUTION**
  -
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  -
- **COMMENTS**
  -
Oseltamivir

CLINICAL USE
Treatment and post-exposure prevention of influenza

DOSE IN NORMAL RENAL FUNCTION
- Treatment: 75 mg twice daily for 5 days
- Post-exposure prevention: 75 mg once daily for at least 10 days; up to 6 weeks if epidemic in community

PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>410.4 (as phosphate)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>42 (3 as carboxylate)</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>Negligible (99% excreted as carboxylate metabolite in urine)</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.3–0.4</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1–3, (6–10 as metabolite)/&gt;20</td>
</tr>
</tbody>
</table>

DOSE IN RENAL IMPAIRMENT GFR (mL/min)

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–30</td>
<td>Treatment: 75 mg once daily or 30 mg twice daily</td>
</tr>
<tr>
<td></td>
<td>Prophylaxis: 75 mg every 48 hours or 30 mg once daily</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Treatment: 30 mg once off dose</td>
</tr>
<tr>
<td></td>
<td>Prophylaxis: 30 mg every 10 days¹</td>
</tr>
</tbody>
</table>

¹ See ‘Other Information’

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Dialysed. Treatment: 30 mg stat; prophyaxlis: 30 mg weekly²</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Treatment: 30 mg stat; prophyaxlis: 30 mg after alternate dialysis sessions²</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Treatment: 30 mg stat; prophyaxlis: 30 mg after alternate dialysis sessions²</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–30 mL/min</td>
</tr>
</tbody>
</table>

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- None known

ADMINISTRATION

RECONSTITUTION
- ROUTE
  - Oral

RATE OF ADMINISTRATION
- COMMENTS

OTHER INFORMATION
- Oseltamivir is a prodrug; extensively metabolised in the liver to the active carboxylate metabolite
- At least 75% of the oral dose reaches the systemic circulation as the carboxylate
- All the active metabolite is excreted in the urine
- A lower dose is required in severe renal disease due to the active metabolite accumulating

References:
1. Draft briefing and guidance for adult renal units in the UK during an influenza pandemic. Prepared for the Renal Association Clinical Affairs Board. 28/8/07
Oxaliplatin

**CLINICAL USE**

Treatment of metastatic colorectal cancer in combination with fluorouracil and folinic acid

**DOSE IN NORMAL RENAL FUNCTION**

85 mg/m²; can be repeated at intervals of 2 weeks if toxicity permits

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Molecular weight (daltons)</th>
<th>397.3</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Protein binding</td>
<td>33%</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>54%</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>330 +/- 40.9 litres</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>273/Increased</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

GFR (mL/min)

<table>
<thead>
<tr>
<th>20–50</th>
<th>10–20</th>
<th>&lt;10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose as in normal renal function</td>
<td>Dose as in normal renal function</td>
<td>No information on use, therefore use with great caution and monitor closely</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>CAPD</th>
<th>HD</th>
<th>HDF/High flux</th>
<th>CAV/VVHD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Aminoglycosides: increased risk of nephrotoxicity and possibly ototoxicity with aminoglycosides, capreomycin, polymyxins or vancomycin
- Antipsychotics: avoid concomitant use with clozapine (increased risk of agranulocytosis)

**ADMINISTRATION**

**RECONSTITUTION**

- Glucose 5% or water for injection to give a concentration of 5 mg/mL

**ROUTE**

- IV infusion

**RATE OF ADMINISTRATION**

- 2–6 hours

**COMMENTS**

- Dilute with 250–500 mL glucose 5% to a concentration 0.2–0.7 mg/mL

**OTHER INFORMATION**

- No in vitro evidence of cytochrome P450 metabolism. Extensive nonenzymatic biotransformation occurs. Platinum removal is mainly by renal excretion and tissue distribution; platinum metabolites mainly by renal excretion. By day 5, approximately 54% of the total dose was recovered in the urine and <3% in the faeces
- Binds irreversibly to red blood cells, which can prolong the half-life of the drug
- Reduced renal clearance and volume of distribution in renal impairment
- There is a 38–44% reduction of platinum clearance in mild-moderate renal impairment (GFR=20–39 mL/min) but no increased incidence of side effects has been reported.

References:
**Oxazepam**

**CLINICAL USE**

Benzodiazepine:
- Anxiolytic
- Insomnia

**DOSE IN NORMAL RENAL FUNCTION**

Anxiolytic: 15–30 mg 3 or 4 times a day
Insomnia: 15–50 mg at night

**PHARMACOKINETICS**

- Molecular weight (daltons): 286.7
- % Protein binding: 85–97
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): 0.6–1.6

**DOSE IN RENAL IMPAIRMENT**

- GFR (mL/min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Start at low dose and increase according to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Antibacterials: metabolism possibly increased by rifampicin
- Antipsychotics: enhanced sedative effects
- Antivirals: possibly increased concentration with ritonavir
- Sodium oxybate: enhanced effects of sodium oxybate – avoid
- Ulcer-healing drugs: metabolism inhibited by cimetidine

**ADMINISTRATION**

**RECONSTITUTION**
- Route: Oral

**RATE OF ADMINISTRATION**
- Comments:

**OTHER INFORMATION**

- Protein binding decreased and volume of distribution increased in ERF
- Inactive glucuronide metabolite accumulates in CKD 5; significance of this unknown

RETURN TO CONTENTS
Oxcarbazepine

**CLINICAL USE**
- Anti-epileptic agent
- Trigeminal neuralgia (unlicensed indication)

**DOSE IN NORMAL RENAL FUNCTION**
- Epilepsy: 600 mg–2.4 g daily in divided doses
- Trigeminal neuralgia: 400–2.4 g in 2–4 divided doses

**PHARMACOKINETICS**
- Molecular weight (daltons): 252.3
- % Protein binding: 40–60 (metabolite)
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): 0.7–0.8
- Half-life – normal/ESRF (hrs): 1.3–2.3 (9 for metabolite)/Unchanged (16–19 for metabolite)

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 30–50: Dose as in normal renal function
  - 10–30: Dose as in normal renal function. Start with 300 mg daily and titrate slowly
  - <10: Dose as in normal renal function. Start with 300 mg daily and titrate slowly

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR < 10 mL/min
- HD: Unknown dialysability. Dose as in GFR < 10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR < 10 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in GFR = 10–30 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Ciclosporin: metabolism accelerated (reduced ciclosporin concentration)
- Antidepressants: antagonism of anticonvulsant effect; avoid concomitant use with MAOIs
- Antimalarials: possibly increased risk of convulsions with chloroquine and hydroxychloroquine; anticonvulsant effect antagonised by mefloquine
- Antipsychotics: antagonism of anticonvulsant effect
- Oestrogens and progestogens: metabolism accelerated (reduced contraceptive effect)
- Tacrolimus: metabolism accelerated (reduced tacrolimus concentration)

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**
- Metabolised to active monohydroxy metabolite
- Hyponatraemia is more common with oxcarbazepine than carbamazepine, monitoring is recommended
- Maximum plasma concentrations reached after about 1 hour
Oxprenolol hydrochloride

**CLINICAL USE**
Beta-1 adrenoceptor blocker:
- Hypertension
- Angina
- Arrhythmias
- Anxiety

**DOSE IN NORMAL RENAL FUNCTION**
- Hypertension, angina: 80–160 mg daily in 2–3 divided doses; maximum 320 mg daily
- Arrhythmias: 40–240 mg daily in 2–3 divided doses
- Anxiety: 40–80 mg daily in 1–2 divided doses

**PHARMACOKINETICS**
- Molecular weight (daltons) 301.8
- % Protein binding 70–80
- % Excreted unchanged in urine <3
- Volume of distribution (L/kg) 1.2
- Half-life – normal/ESRF (hrs) 1–2/unchanged

**DOSE IN RENAL IMPAIRMENT**
GFR (mL/MIN)
- 20–50 Dose as in normal renal function
- 10–20 Dose as in normal renal function
- <10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Unlikely dialysability. Dose as in normal renal function.
- HD Unlikely dialysability. Dose as in normal renal function.
- HDF/High flux Unknown dialysability. Dose as in normal renal function.
- CAV/ VVHD Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: NSAIDs antagonise hypotensive effect
- Anti-arrhythmics: increased risk of myocardial depression and bradycardia; increased risk of bradycardia, myocardial depression and AV block with amiodarone
- Antidepressants: enhanced hypotensive effect with MAOIs
- Antihypertensives: enhanced hypotensive effect; increased risk of first dose hypotensive effect with post-synaptic alpha-blockers such as prazosin; increased risk of withdrawal hypertension with clonidine; increased risk of bradycardia and AV block with diltiazem; severe hypotension and heart failure occasionally with nifedipine; asystole, severe hypotension and heart failure with verapamil
- Antimalarials: increased risk of bradycardia with mefloquine
- Antipsychotics: enhanced hypotensive effect with phenothiazines
- Diuretics: enhanced hypotensive effect
- Moxisylyte: possibly severe postural hypotension
- Severe hypertension with adrenaline and noradrenaline (especially with non-selective beta-blockers) and possibly with dopamine
- Tropisetron: increased risk of ventricular arrhythmias – use with caution

**ADMINISTRATION**
- RECONSTITUTION
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
- COMMENTS

**OTHER INFORMATION**
- Use with caution in patients with chronic obstructive airways disease, asthma or diabetes
- Rhabdomyolysis with myoglobinuria has been reported in severe overdosage with oxprenolol
Oxybutynin hydrochloride

**CLINICAL USE**
- Urinary frequency, urgency and incontinence
- Neurogenic bladder instability and nocturnal enuresis

**DOSE IN NORMAL RENAL FUNCTION**
- 2.5–5 mg 2 to 3 times a day; maximum 5 mg 4 times a day
- XL: 5–20 mg once daily
- Patches: 1 patch (36 mg) twice weekly

**PHARMACOKINETICS**
- Molecular weight (daltons): 393.9
- % Protein binding: 83–85
- % Excreted unchanged in urine: <0.1
- Volume of distribution (L/kg): 193 litres

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Dialysed</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td></td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
- Other antimuscarinic agents: increased antimuscarinic effects

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral, topical

**COMMENTS**
- **OTHER INFORMATION**
  - Start with a low dose in elderly patients and those with renal impairment, and increase according to response
Oxycodone hydrochloride

**CLINICAL USE**
Opioid analgesic for moderate to severe pain

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: 5 mg 4–6 hourly; usual maximum dose 400 mg daily
- M/R: 10 mg 12 hourly; usual maximum dose 200 mg 12 hourly
- IV: 1–10 mg every 4 hours
- SC: initially 5 mg every 4 hours
- SC infusion: initially 7.5 mg over 24 hours

**PHARMACOKINETICS**
- Molecular weight (daltons) 351.8
- % Protein binding 45
- % Excreted unchanged in urine <10
- Volume of distribution (L/kg) 1.2–6.31
- Half-life – normal/ESRF (hrs) 2–4 (4.5, M/R)/3–5 (5.5 M/R)

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Start with small doses. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR<10 mL/min
- HD: Unknown dialysability. Dose as in GFR<10 mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anti-arrhythmics: delayed absorption of mexiletine
- Antidepressants: CNS excitation or depression with MAOIs – avoid concomitant use; possible CNS excitation or depression with moclobemide; increased sedative effects with tricyclics
- Antivirals: concentration possibly increased by ritonavir
- Sodium oxybate: enhanced effect of sodium oxybate – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral, IV, IM, SC
- RATE OF ADMINISTRATION
  - Infusion over 24 hours

**OTHER INFORMATION**
- Has been used in CKD 5 patients; start with lowest dose and gradually increase dose according to response
- Limited accumulation of metabolites in renal failure compared with morphine
- 2 mg of oral oxycodone is approximately equivalent to 1 mg of parenteral oxycodone

**RETURN TO CONTENTS**
Oxytetracycline

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
250–500 mg 4 times a day
Acne: 500 mg twice daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 460.4
- % Protein binding: 20–40
- % Excreted unchanged in urine: 10–35
- Volume of distribution (L/kg): 1.5
- Half-life – normal/ESRF (hrs): 9/66

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: 250 mg 4 times a day

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10mL/min
- HD: Not dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10mL/min
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: possibly enhanced anticoagulant effect of coumarins and phenindione
- Oestrogens: possibly reduced contraceptive effects of oestrogens (risk probably small)
- Retinoids: possible increased risk of benign intracranial hypertension with tetracyclines and retinoids – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- Avoid if possible in renal impairment, due to potential nephrotoxicity and increased risk of azotaemia, hyperphosphataemia and acidosis
- May cause an increase in blood urea which is dose related
- Avoid in SLE

RETURN TO CONTENTS
Paclitaxel

**CLINICAL USE**
- Ovarian and breast cancer
- Non-small cell lung carcinoma
- AIDS-related Kaposi’s sarcoma

**DOSE IN NORMAL RENAL FUNCTION**
100–220 mg/m² every 3 weeks depending on local regime and duration of infusion

**PHARMACOKINETICS**
- Molecular weight: 853.9 daltons
- % Protein binding: 89–98%
- % Excreted unchanged in urine: 1.3–12.6%
- Volume of distribution: 198–688 litres/m²

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/MIN)**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**: Unlikely to be dialysed. Dose as in normal renal function
- **HD**: Not dialysed. Dose as in normal renal function
- **HDF/High flux**: Unknown dialysability. Dose as in normal renal function
- **CAV/VVHD**: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antidiabetics: metabolism of rosiglitazone possibly inhibited
- Antipsychotics: avoid concomitant use with clozapine (increased risk of agranulocytosis)

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - IV
- **RATE OF ADMINISTRATION**
  - 3 hours depending on regime
- **COMMENTS**
  - Dilute to a concentration of 0.3–1.2 mg/mL with sodium chloride 0.9% or glucose 5%
  - Stable for 27 hours at room temperature

**OTHER INFORMATION**
- Administer through a 0.22µm in line filter
- Use non-PVC infusion bags
- Hepatic metabolism and biliary clearance are the principal mechanisms for disposal. Mean values for cumulative urinary recovery of unchanged drug ranged from 1.3 to 12.6% of the dose, indicating extensive non-renal clearance
Paliperidone

**CLINICAL USE**
Atypical antipsychotic for schizophrenia

**DOSE IN NORMAL RENAL FUNCTION**
3–12 mg once daily

**PHARMACOKINETICS**
- Molecular weight (daltons) 426.5
- % Protein binding 74
- % Excreted unchanged in urine 59
- Volume of distribution (L/kg) 487 litres
- Half-life – normal/ESRF (hrs) 23/51

**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**
- 50–80 3mg once daily and increase according to response
- 30–50 3mg once daily and increase according to response
- 10–30 3mg alternate days, increasing to 3mg daily according to response
- <10 3mg alternate days, increasing to 3mg daily according to response. Use with caution

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Unknown dialysability. Dose as in GFR<10mL/min
- HD Unknown dialysability. Dose as in GFR<10mL/min
- HDF/High flux Unknown dialysability. Dose as in GFR<10mL/min
- CAV/VVHD Unknown dialysability. Dose as in GFR=10–30mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Anti-arrhythmics: increased risk of ventricular arrhythmias when given with anti-arrhythmics that prolong the QT interval
- Antidepressants: increases concentration of tricyclics (possibly increased risk of ventricular arrhythmias)
- Antimalarials: avoidance of antipsychotics advised by manufacturer of artemether/lumefantrine
- Atomoxetine: increased risk of ventricular arrhythmias with atomoxetine
- Anti-epileptics: antagonise anticonvulsant effect (convulsive threshold lowered)
- Antivirals: concentration possibly increased by ritonavir
- Sibutramine: increased risk of CNS toxicity – manufacturer of sibutramine advises avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  -

**OTHER INFORMATION**
- Clearance is reduced by 71% in ERF
- Contraindicated (by manufacturer) in patients with GFR<10mL/min, due to lack of experience
Palonosetron

**CLINICAL USE**

Anti-emetic:
- For use with cancer chemotherapy

**DOSE IN NORMAL RENAL FUNCTION**

250 mcg as a single dose approximately 30 minutes before chemotherapy

**PHARMACOKINETICS**

- Molecular weight: 332.9 (as hydrochloride)
- % Protein binding: 62
- % Excreted unchanged in urine: 40
- Volume of distribution: 6.9–7.9 (L/kg)
- Half-life – normal/ESRF (hrs): 40

**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**

- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

- Potentially hazardous interactions with other drugs: None

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - IV bolus

**RATE OF ADMINISTRATION**

- 30 seconds

**COMMENTS**

- **OTHER INFORMATION**
  - Repeated doses within 7 days are not recommended
  - Use with caution in people at risk of QT prolongation
### Pancreatin

#### CLINICAL USE
Pancreatic enzyme replacement

#### DOSE IN NORMAL RENAL FUNCTION
1–6 capsules (depends on preparation) with meals, adjusted according to response (1 capsule if using the strong preparation)

#### PHARMACOKINETICS
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>No data</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>No data</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>No data</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>No data</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>No data</td>
</tr>
</tbody>
</table>

#### DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose in Normal Renal Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

#### IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- None known

#### ADMINISTRATION

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

#### OTHER INFORMATION
- Not absorbed from GI tract
Pancuronium bromide

**CLINICAL USE**
Non-depolarising muscle relaxant of long duration

**DOSE IN NORMAL RENAL FUNCTION**
Initial dose: 50–100 micrograms/kg
Incremental dose: 10–20 micrograms/kg

**PHARMACOKINETICS**
- Molecular weight (daltons): 732.7
- % Protein binding: 80–90
- % Excreted unchanged in urine: 40–60
- Volume of distribution (L/kg): 0.15–0.38
- Half-life – normal/ESRF (hrs): 2/4.3–8.2

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/Min)**
  - 20–50 Dose as in normal renal function
  - 10–20 Initial dose: 25–50 micrograms/kg
  - Incremental dose: 5–10 micrograms/kg
  - <10 Initial dose: 10–25 micrograms/kg
  - Incremental dose: 2.5–5 micrograms/kg

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Unknown dialysability. Dose as in GFR<10mL/min
- HD Unknown dialysability. Dose as in GFR<10mL/min
- HDF/High flux Unknown dialysability. Dose as in GFR<10mL/min
- CAV/ VVHD Unknown dialysability. Dose as in GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced muscle relaxant effect
- Anti-arrhythmics: procainamide enhances muscle relaxant effect
- Antibacterials: effect enhanced by aminoglycosides, clindamycin, polymyxins and piperacillin
- Botulinum toxin: neuromuscular block enhanced (risk of toxicity)

**ADMINISTRATION**
- **RECONSTITUTION**
  - –
- **ROUTE**
  - IV
- **RATE OF ADMINISTRATION**
  - Bolus
- **COMMENTS**
  - –

**OTHER INFORMATION**
- Active metabolites accumulate in CKD 5; duration of action prolonged

RETURN TO CONTENTS
Pantoprazole

**CLINICAL USE**
Gastric acid suppression

**DOSE IN NORMAL RENAL FUNCTION**
Oral: 20–80 mg in the morning
IV: 40–160 mg daily; doses >80 mg in 2 divided doses

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>383.4</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>98</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>80 (as metabolites)</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.15</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1/2–3</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
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<tr>
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</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**: Not dialysed. Dose as in normal renal function
- **HD**: Not dialysed. Dose as in normal renal function
- **HDF/High flux**: Unknown dialysability. Dose as in normal renal function
- **CAV/VVHD**: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

- Potentially hazardous interactions with other drugs
  - Antifungals: absorption of itraconazole and ketoconazole reduced

**ADMINISTRATION**

**RECONSTITUTION**
- 10 mL sodium chloride 0.9%

**ROUTE**
- Oral, IV

**RATE OF ADMINISTRATION**
- 2–15 minutes

**COMMENTS**
- Use within 12 hours of reconstitution
- Dilute to 100 mL with sodium chloride 0.9% or glucose 5%
Papaveretum

(15.4 mg/mL) 1 mL contains 10 mg anhydrous morphine, 1.2 mg papaverine HCl, and 1.04 mg codeine HCl

CLINICAL USE

Opiate analgesia

DOSE IN NORMAL RENAL FUNCTION

SC/IM: 0.5–1 mL every 4 hours
IV: 25–50% of dose

PHARMACOKINETICS

<table>
<thead>
<tr>
<th></th>
<th>Papaverine HCl</th>
<th>Morphine HCl</th>
<th>Codeine HCl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>375.8</td>
<td>375.8</td>
<td>371.9</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>90</td>
<td>20–35</td>
<td>7</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;1</td>
<td>10</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.99–1.52</td>
<td>3–5</td>
<td>3–4</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1.2–2.2/–</td>
<td>2–3/–</td>
<td>2.5–4/–</td>
</tr>
</tbody>
</table>

DOSE IN RENAL IMPAIRMENT

GFR (mL/min)

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>0.4–0.75 mL every 6–8 hours</td>
</tr>
<tr>
<td>&lt;10</td>
<td>0.25–0.5 mL every 6–8 hours. Avoid if possible</td>
</tr>
</tbody>
</table>

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unknown dialysability. Dose as in GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs
- Anti-arrhythmics: delayed absorption of mexiletine
- Antidepressants: possible CNS excitation or depression with MAOIs – avoid concomitant use; possible CNS excitation or depression with moclobemide; increased sedative effects with tricyclics
- Antivirals: concentration possibly increased with ritonavir
- Sodium oxybate: enhanced effect of sodium oxybate – avoid concomitant use

ADMINISTRATION

RECONSTITUTION
- ROUTE
  - SC, IM, IV
- RATE OF ADMINISTRATION
  - IV bolus or continuous infusion (1 mg/mL)

OTHER INFORMATION

- As with all opiates, use with extreme caution in patients with impaired renal function
- May cause excessive sedation and respiratory depression
- Papaveretum 15.4 mg =1 mL = 10 mg morphine
**Paracetamol**

**CLINICAL USE**
Analgesia and antipyretic

**DOSE IN NORMAL RENAL FUNCTION**
500 mg – 1 g every 4–6 hours
(IV: if <50 kg, dose is 15 mg/kg)

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>151.2</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>20–30%</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1–2</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1–4/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>500 mg – 1 g every 6–8 hours</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Dialysis Method</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral, rectal, IV

**RATE OF ADMINISTRATION**
- 15 minutes

**OTHER INFORMATION**

- Beware sodium content of soluble tablets (1 tablet = 18.6 mmol sodium)
- Nephrotoxic in overdose due to a reactive alkylating metabolite
- Metabolites may accumulate in CKD 5; normal doses are used in CKD 5
- IV preparation starts working within 5 to 10 minutes with peak activity after 60 minutes
Parecoxib

**CLINICAL USE**
Cox 2 inhibitor:
- Short-term treatment of postoperative pain

**DOSE IN NORMAL RENAL FUNCTION**
40 mg initially then 20–40 mg every 6–12 hours if required; maximum dose 80 mg daily

**PHARMACOKINETICS**
- Molecular weight: 392.4 (as sodium salt)
- % Protein binding: 98
- % Excreted unchanged in urine: <5 (as valdecoxib)
- Volume of distribution: 55 litres
- Half-life – normal/ESRF (hrs): 8 (as valdecoxib)/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function.</th>
<th>Use with caution</th>
<th>Dose as in normal renal function, but avoid if possible</th>
<th>Dose as in normal renal function, but only use if ERF on dialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–30</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Not dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Not dialysed. Dose as in GFR=10–30 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- ACE inhibitors and angiotensin-II antagonists: antagonism of hypotensive effect; increased risk of nephrotoxicity and hyperkalaemia
- Analgesics: avoid concomitant use of 2 or more NSAIDs, including aspirin (increased side effects); avoid with ketorolac (increased risk of side effects and haemorrhage)
- Antibacterials: possible increased risk of convulsions with quinolones
- Anticoagulants: enhanced anticoagulant effect of coumarins and phenindione; increased risk of bleeding with heparin
- Antidepressants: increased risk of bleeding with SSRIs and venlafaxine
- Antidiabetics: possibly enhanced effect of sulphonylureas
- Anti-epileptics: possibly enhanced effect of phenytoin
- Antifungals: if used with fluconazole reduce the dose of parecoxib
- Antivirals: increased risk of haematological toxicity with zidovudine; concentration possibly increased by ritonavir
- Ciclosporin: potential for increased risk of nephrotoxicity
- Cytotoxic agents: reduced excretion of methotrexate (possible increased risk of toxicity); increased risk of bleeding with erlotinib
- Diuretics: increased risk of nephrotoxicity; possible antagonism of diuretic effect; increased risk of hyperkalaemia with potassium-sparing diuretics
- Lithium: reduced excretion of lithium (risk of toxicity)
- Pentoxifylline: possibly increased risk of bleeding
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- 2 mL sodium chloride 0.9%

**ROUTE**
- IV, IM

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**
- Clinical trials have shown renal effects similar to those observed with comparative NSAIDs. Monitor patient for deterioration in renal function and fluid retention
Inhibition of renal prostaglandin synthesis by NSAIDs may interfere with renal function, especially in the presence of existing renal disease – avoid if possible; if not, check serum creatinine 48–72 hours after starting NSAID – if raised, discontinue NSAID therapy

Use normal doses in patients with ERF on dialysis

Use with caution in renal transplant recipients (can reduce intrarenal autocoid synthesis)

Parecoxib should be used with caution in uraemic patients predisposed to gastrointestinal bleeding or uraemic coagulopathies

Works within 30 minutes

Rapidly converted to valdecoxib

Contraindicated in patients with ischaemic heart disease or cerebrovascular disease and class II-IV NYHA congestive heart failure
Paricalcitol

**CLINICAL USE**
Vitamin D analogue:
- Treatment and prevention of secondary hyperparathyroidism associated with chronic renal failure

**DOSE IN NORMAL RENAL FUNCTION**
- IV: Give dose every other day or post dialysis; dose is dependent on PTH levels. See SPC for details
- Oral: 1–4 mcg either daily or 3×/week according to PTH levels

**PHARMACOKINETICS**
- Molecular weight (daltons): 416.6
- % Protein binding: >99
- % Excreted unchanged in urine: 0 (16% as metabolites)
- Volume of distribution (L/kg): 17–25 litres (6 litres in haemodialysis patients)

**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - IV, oral
- **RATE OF ADMINISTRATION**
  - Not less than 30 seconds
- **COMMENTS**
  -

**OTHER INFORMATION**
- Monitor calcium and phosphate levels at least monthly, more frequently during dose titration
- Paricalcitol solution for injection contains 30% v/v of propyleneglycol as an excipient. Isolated cases of central nervous system depression, haemolysis, and lactic acidosis have been reported as toxic effect associated with propyleneglycol administration at high doses. Although they are not expected to be found with paricalcitol administration (as propyleneglycol is eliminated during the dialysis process), the risk of toxic effect in overdosing situations has to be taken into account
- Paricalcitol injection contains 20% v/v of ethanol (alcohol). Each dose may contain up to 1.3 g ethanol. Harmful for those suffering from alcoholism
Paroxetine

**CLINICAL USE**

Antidepressant:
- Panic disorders
- Obsessive compulsive disorder
- Social anxiety
- Post traumatic stress disorder

**DOSE IN NORMAL RENAL FUNCTION**

10–60 mg daily depending on indication

**PHARMACOKINETICS**

- Molecular weight: 329.4 (daltons)
- % Protein binding: 95
- % Excreted unchanged in urine: <2
- Volume of distribution: 13 (L/kg)
- Half-life – normal/ESRF (hrs): 24/30

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>Dose as in normal renal function</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–30</td>
<td>10 mg daily and titrate slowly</td>
<td>20 mg daily and titrate slowly</td>
</tr>
<tr>
<td>&lt;10</td>
<td>20 mg daily and titrate slowly</td>
<td>20 mg daily and titrate slowly</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Unlikely to be dialysed. Dose as in GFR<10mL/min
- HD: Not dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Dose as in GFR<10mL/min
- CAV/VVHD: Dose as for GFR=10–30mL/min

**IMPORTANT DRUG INTERACTIONS**

- Potentially hazardous interactions with other drugs
  - Analgesics: increased risk of bleeding with aspirin and NSAIDs; increased risk of CNS toxicity with tramadol
  - Anti-arrhythmics: possibly inhibits propafenone metabolism (increased risk of toxicity)
  - Anticoagulants: effect of coumarins possibly enhanced
  - Antidepressants: avoid concomitant use with MAOIs and moclobemide (increased risk of toxicity); avoid concomitant use with St John’s wort; possibly enhanced serotonergic effects with duloxetine; can increase tricyclic antidepressant concentration; increased agitation and nausea with tryptophan
  - Anti-epileptics: antagonism (lowered convulsive threshold); concentration reduced by carbamazepine, phenytoin and primidone
  - Antimalarials: avoid concomitant use with artemether/lumefantrine
  - Antipsychotics: concentration of clozapine, sertindole and possibly risperidone increased; metabolism of perphenazine inhibited, reduce dose of perphenazine; possibly inhibit aripiprazole metabolism, reduce aripiprazole dose
  - Antivirals: concentration increased by ritonavir
  - Dopaminergics: use entacapone with caution; increased risk of hypertension and CNS excitation with selegiline – avoid concomitant use; increased risk of CNS toxicity with rasagiline – avoid concomitant use
  - 5HT\_1 agonist: risk of CNS toxicity increased by sumatriptan – avoid concomitant use; possibly increased risk of serotonergic effects with frovatriptan
  - Lithium: increased risk of CNS effects – monitor levels
  - Sibutramine: increased risk of CNS toxicity – avoid concomitant use

**ADMINISTRATION**

- RECONSTITUTION –
- ROUTE – Oral
- RATE OF ADMINISTRATION –
- COMMENTS –

RETURN TO CONTENTS
Pegfilgrastim

CLINICAL USE
Pegylated recombinant human granulocyte-colony stimulating factor (rhG-CSF):
● Reduction of duration of neutropenia (except in chronic myeloid leukaemia and myelodysplastic syndromes)

DOSE IN NORMAL RENAL FUNCTION
6 mg given approximately 24 hours post chemotherapy

PHARMACOKINETICS
Molecular weight (daltons) 39,000
% Protein binding Very high (filgrastim)
% Excreted unchanged in urine Minimal
Volume of distribution (L/kg) 0.15 (filgrastim)
Half-life – normal/ESRF (hrs) 15–80/Unchanged

DOSE IN RENAL IMPAIRMENT GFR (mL/Min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Not dialysed. Dose as in normal renal function
HD Not dialysed. Dose as in normal renal function
HDF/High flux Unlikely to be dialysed. Dose as in normal renal function
CAV/VVHD Not dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● Cytotoxics: neutropenia possibly exacerbated if administered with fluorouracil

ADMINISTRATION
RECONSTITUTION
–
ROUTE
● SC
RATE OF ADMINISTRATION
–
COMMENTS
● Incompatible with sodium chloride solutions
● Discard after 72 hours if left at room temperature

OTHER INFORMATION
● Pegfilgrastim is a sustained-release form of filgrastim
Peginterferon alfa

**CLINICAL USE**

Treatment of chronic hepatitis B and C infection with or without ribavirin

**DOSE IN NORMAL RENAL FUNCTION**

- ViraferonPeg: 1.5 mcg/kg once weekly in combination with ribavirin
- Monotherapy: 0.5–1 mcg/kg once weekly
- Pegasys: 180 mcg weekly

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>40 000</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>No data</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>30</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.99</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>40–80/increased by about 25–45%</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

- GFR (mL/min)
  - 20–50: Dose as in normal renal function. See ‘Other Information’
  - 10–20: 135 mcg (Pegasys) once weekly. See ‘Other Information’
  - <10: 135 mcg (Pegasys) once weekly. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Unlikely to be dialysed. Dose as in GFR<10mL/min
- HD: Dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10mL/min
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs

- Immunosuppressants: (e.g. ciclosporin, tacrolimus, sirolimus) may have an antagonistic effect
- Theophylline: inhibits metabolism of theophylline (enhanced effect)

**ADMINISTRATION**

**RECONSTITUTION**

- 0.7 mL water for injection or pre-filled syringes

**ROUTE**

- SC

**RATE OF ADMINISTRATION**

- COMMENTS

- Stable for 24 hours at 2–8°C after reconstitution

**OTHER INFORMATION**

- Administer 12 hours after haemodialysis
- ViraferonPeg is contraindicated once GFR<50mL/min – monitor closely and reduce dose if required
- In haemodialysis patients, 135 mcg Pegasys is equivalent to a 180 mcg dose in the general population
- In patients with CKD 5 undergoing haemodialysis there is a 25–45% reduction in clearance compared with patients with normal renal function
Pemetrexed

**CLINICAL USE**
- Treatment of chemotherapy naive patients with unresectable malignant pleural mesothelioma in combination with cisplatin
- Monotherapy for non-small cell lung cancer

**DOSE IN NORMAL RENAL FUNCTION**
500 mg/m² on the first day of each 21 day cycle

**PHARMACOKINETICS**
- Molecular weight: 471.4 (as disodium)
- % Protein binding: 81
- % Excreted unchanged in urine: 70–90
- Volume of distribution: 6–9 litres/m²
- Half-life – normal/ESRF: 2–4/Increased

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 45–50: Dose as in normal renal function
  - 20–45: Use with caution, at a lower dose. See 'Other Information'
  - <20: Use with caution, at a lower dose. See 'Other Information'

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in GFR<20 mL/min
- HD: Not dialysed. Dose as in GFR<20 mL/min
- HDF/High flux: Unlikely to be dialysed. Dose as in GFR<20 mL/min
- CAV/ VVHD: Not dialysed. Dose as in GFR=20–45 mL/min

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
- Nephrotoxic agents: may reduce clearance of pemetrexed – use with caution
- Live vaccines: avoid use; YELLOW FEVER VACCINE ABSOLUTELY CONTRAINDICATED

**ADMINISTRATION**
- **RECONSTITUTION**
- 20 mL sodium chloride 0.9% per 500 mg vial
- **ROUTE**
- IV infusion
- **RATE OF ADMINISTRATION**
- Over 10 minutes
- **COMMENTS**
- Dilute in 100 mL preservative-free sodium chloride 0.9%
- Incompatible with calcium containing fluids

**OTHER INFORMATION**
- To reduce the incidence and severity of skin reactions, a steroid (equivalent to 4 mg of dexamethasone) should be given the day before, the day of, and the day after pemetrexed therapy. Patients should also take a vitamin preparation containing folic acid and IM vitamin B₁₂
- 25% of patients get reversible mild renal dysfunction
- In one study, pemetrexed was discontinued in patients with a GFR<30 mL/min after a patient with a GFR=19 mL/min died due to drug related toxicities. (Mita C, Sweeney CJ, Baker SD, et al. Phase I and pharmacokinetic study of pemetrexed administered every 3 weeks to advanced cancer patients with normal and impaired renal function. *J Clin Oncol*. 2006 Feb 1; 24(4): 552–62.)

**References:**
Penicillamine

**CLINICAL USE**
Rheumatoid arthritis

**DOSE IN NORMAL RENAL FUNCTION**
- 125–250 mg daily for first month; increase by same amount every 4–12 weeks until remission occurs
- Maintenance dose: usually 500–750 mg daily in divided doses
- Maximum 1.5 g daily

**PHARMACOKINETICS**
- Molecular weight (daltons) 149.2
- % Protein binding 80
- % Excreted 10–40 unchanged in urine
- Volume of distribution (L/kg) 0.8
- Half-life – normal/ESRF (hrs) 1–3/Increased

**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**
- 20–50 Avoid if possible or reduce dose. 125 mg for first 12 weeks. Increase by same amount every 12 weeks
- 10–20 Avoid – nephrotoxic
- <10 Avoid – nephrotoxic

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD** Unknown dialysability. Avoid – nephrotoxic
- **HD** Dialysed. 125–250 mg 3 times a week after HD
- **HDF/High flux** Dialysed. 125–250 mg 3 times a week after HD
- **CAV/VVHD** Unknown dialysability. Avoid – nephrotoxic

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antipsychotics: avoid concomitant use with clozapine (increased risk of agranulocytosis)

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
  - **RATE OF ADMINISTRATION**
  - **COMMENTS**

**OTHER INFORMATION**
- Proteinuria occurs frequently and is partially dose-related. In some patients it may progress to glomerulonephritis or nephrotic syndrome
- Urinalysis should be carried out weekly for the first two months of treatment, after any change in dosage, and monthly thereafter. Increasing proteinuria may necessitate withdrawal of treatment
Pentamidine isetionate

**CLINICAL USE**

Antibacterial agent:
- Pneumocystis treatment and prophylaxis
- Visceral leishmaniasis
- Cutaneous leishmaniasis
-Trypanosomiasis

**DOSE IN NORMAL RENAL FUNCTION**

- Pneumocystis:
  - Treatment: Nebuliser: 600 mg daily for 3 weeks; IV: 4 mg/kg/day for at least 14 days
  - Prophylaxis: 300 mg monthly or 150 mg every 2 weeks
- Visceral leishmaniasis: 3–4 mg/kg on alternate days to a maximum of 10 doses (deep IM)
- Cutaneous leishmaniasis: 3–4 mg/kg once or twice weekly (deep IM)
- Trypanosomiasis: 4 mg/kg daily, or alternate days to a total of 7–10 doses (deep IM or IV)

**PHARMACOKINETICS**

- Molecular weight (daltons) 592.7
- % Protein binding 69
- % Excreted unchanged in urine <5
- Volume of distribution (L/kg) 3–4
- Half-life – normal/ESRF (hrs) 6–9/9

**DOSE IN RENAL IMPAIRMENT**

**GFR (mL/Min)**
- 20–50 Dose as in normal renal function
- 10–20 Depending on severity of infection: 4 mg/kg/day IV for 7–10 days, then on alternate days to complete minimum 14 doses, OR, 4 mg/kg on alternate days to complete minimum 14 doses
- <10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD Not dialysed. Dose as in GFR<10 mL/min
- HD Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/ VVHD GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Anti-arrhythmics: increased risk of ventricular arrhythmias with amiodarone – avoid concomitant use
- Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin and parenteral erythromycin – avoid concomitant use with moxifloxacin
- Antidepressants: increased risk of ventricular arrhythmias with tricyclics
- Antipsychotics: increased risk of ventricular arrhythmias with amisulpride and phenothiazines – avoid concomitant use with amisulpride
- Ivabradine: increased risk of ventricular arrhythmias

**ADMINISTRATION**

**RECONSTITUTION**
- IV: 300 mg with 3–5 mL water for injection
- IM: 300 mg with 3 mL water for injection
- Inhalation: 600 mg with 6 mL water for injection

**ROUTE**
- IV, IM, nebulised

**RATE OF ADMINISTRATION**
- Over at least 1 hour

**COMMENTS**
- Dilute calculated dose in 50–250 mL sodium chloride 0.9% or glucose 5%
OTHER INFORMATION

- Monitor patients closely
- Patient must be lying down when drug is administered
- If given by IV infusion, patient should be monitored closely: heart rate, blood pressure, blood glucose
- IV prophylaxis (unlicensed): 4–5 mg/kg over a minimum of 1 hour every 4 weeks
- Nebulise over 20 minutes using Respigard II or other suitable nebuliser, oxygen flow rate 6–10 L/minute
- 5 mg nebulised salbutamol may be given prior to pentamidine nebulisation to reduce risk of bronchospasm. Do not mix together in nebuliser
- May produce reversible impairment of renal function
- Renal clearance accounts for <5% of the plasma clearance of pentamidine
Pentostatin

**CLINICAL USE**
Antineoplastic agent used in hairy cell leukaemia

**DOSE IN NORMAL RENAL FUNCTION**
4 mg/m² every other week

**PHARMACOKINETICS**
- Molecular weight: 268.3 daltons
- % Protein binding: 4%
- % Excreted unchanged in urine: 50–96%
- Volume of distribution (L/kg): 36.1 litres
- Half-life – normal/ESRF (hrs): 2.6–10/18

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>50–60</td>
<td>50% of dose. See ‘Other Information’</td>
</tr>
<tr>
<td>10–50</td>
<td>See ‘Other Information’</td>
</tr>
<tr>
<td>&lt;10</td>
<td>See ‘Other Information’</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dialysability</th>
<th>Dose as in</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown</td>
<td>GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unknown</td>
<td>GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Likely</td>
<td>GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown</td>
<td>GFR=10–50 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antipsychotics: avoid concomitant use with clozapine (increased risk of agranulocytosis)
- Cytotoxics: increased risk of toxicity with high-dose cyclophosphamide – avoid concomitant use; increased pulmonary toxicity with fludarabine (unacceptably high incidence of fatalities)

**ADMINISTRATION**

**RECONSTITUTION**
- 5 mL water for injections

**ROUTE**
- IV bolus or infusion

**RATE OF ADMINISTRATION**
- 20–30 minutes

**COMMENTS**
- Add to 25–50 mL glucose 5% or sodium chloride 0.9% (final concentration 180–330 mcg/mL)

**OTHER INFORMATION**
- Only a small amount is metabolised. It is primarily excreted unchanged by the kidneys (30–90% excreted by kidneys within 24 hours)
- Patients with CKD are at a greater risk of toxicity with pentostatin
- Another study used it in a haemodialysis patient at increasing doses of 1, 2, then 3 mg/m². Treatment was then continued at a dose of 2 mg/m². The patient was dialysed for 4 hours 1–2 hours after receiving the pentostatin to remove any remaining drug. The main complication was anorexia. Tumour lysis syndrome also occurred 4 days after the 3 mg/m² dose. (Arima N, Sugiyama T. Pentostatin treatment for a patient with chronic type adult T-cell leukaemia undergoing haemodialysis. *Rinsho Ketsueki.* 2005 Nov; 46(11): 1191–5.)
- Hydration with 500–1000 mL of fluid is recommended before treatment and another 500 mL after treatment
  - GFR=60 mL/min, give 70% of dose
  - GFR=45 mL/min, give 60% of dose
  - GFR<30 mL/min, avoid

RETURN TO CONTENTS
## Pentoxifylline (oxpentifylline)

### Clinical Use
- Peripheral vascular disease
- Venous leg ulcers (unlicensed indication)

### Dose in Normal Renal Function
400 mg 2 to 3 times daily

### Pharmacokinetics
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>278.3</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>0</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>0 (95% as active metabolites)</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>2.4–4.2</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>0.4–1/Unchanged (see ‘Other Information’)</td>
</tr>
</tbody>
</table>

### Dose in Renal Impairment

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–30</td>
<td>Reduce dose by 30–50% depending on individual tolerance (400 mg once or twice daily)</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Reduce dose by 30–50% depending on individual tolerance (400 mg once or twice daily)</td>
</tr>
</tbody>
</table>

### Dose in Patients Undergoing Renal Replacement Therapies
<table>
<thead>
<tr>
<th>Type</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. 400 mg daily, slowly increasing if necessary</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. 400 mg daily, slowly increasing if necessary</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. 400 mg daily, slowly increasing if necessary</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in GFR=10–30 mL/min</td>
</tr>
</tbody>
</table>

### Important Drug Interactions
Potentially hazardous interactions with other drugs
- Analgesics: possibly increased risk of bleeding when administered in combination with NSAIDs; increased risk of bleeding with ketorolac – avoid concomitant use

### Administration

<table>
<thead>
<tr>
<th>Reconstitution</th>
<th>Route</th>
<th>Rate of Administration</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Oral</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Other Information
- May enhance hypoglycaemia
- Avoid in porphyria
- Active metabolites are renally excreted and have an extended half-life in renal impairment
Perindopril erbumine

**CLINICAL USE**
Angiotensin-converting enzyme inhibitor:
- Hypertension
- Heart failure

**DOSE IN NORMAL RENAL FUNCTION**
2–8 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 441.6
- % Protein binding: 60 (10–20 as perindoprilat)
- % Excreted unchanged in urine: 4–12
- Volume of distribution (L/kg): 0.2
- Half-life – normal/ESRF (hrs): 1/27

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose in renal impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Initially 2 mg daily, adjust according to response</td>
</tr>
<tr>
<td>10–20</td>
<td>Initially 2 mg daily, adjust according to response</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Initially 2 mg daily, adjust according to response</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Dialysis</th>
<th>Dose in renal impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/ VVHD</td>
<td>Dialysed. Dose as in GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs:
- Anaesthetics: enhanced hypotensive effect
- Analgesics: antagonism of hypotensive effect and increased risk of renal impairment with NSAIDs; hyperkalaemia with ketorolac and other NSAIDs
- Ciclosporin: increased risk of hyperkalaemia and nephrotoxicity
- Diuretics: enhanced hypotensive effect; hyperkalaemia with potassium-sparing diuretics
- Epinephrine: increased risk of hyperkalaemia; antagonism of hypotensive effect
- Lithium: reduced excretion (possibility of enhanced lithium toxicity)
- Potassium salts: increased risk of hyperkalaemia
- Tacrolimus: increased risk of hyperkalaemia and nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- Active metabolite perindoprilat has a half-life of 25–30 hours
- Titrate dose according to response; normal doses have been used in CKD 5
- Small volume of distribution due to low lipophilicity
- Close monitoring of renal function during therapy is necessary in those with renal insufficiency
- Renal failure has been reported in association with ACE inhibitors in patients with renal artery stenosis, post renal transplant and those with severe congestive heart failure
- High incidence of anaphylactoid reactions has been reported in patients dialysed with high-flux polyacrylonitrile membranes and treated concomitantly with an ACE inhibitor – this combination should therefore be avoided
- Hyperkalaemia and other side-effects are more common in patients with renal impairment
Pethidine hydrochloride

**CLINICAL USE**

Opiate analgesia

**DOSE IN NORMAL RENAL FUNCTION**

**IV:** 25–50 mg every 4 hours  
**Oral:** 50–150 mg every 4 hours  
**S/C, IM:** 25–100 mg every 4 hours

**PHARMACOKINETICS**

- **Molecular weight (daltons):** 283.8  
- **% Protein binding:** 60–80  
- **% Excreted unchanged in urine:** 5  
- **Volume of distribution (L/kg):** 4.17  
- **Half-life – normal/ESRF (hrs):** 3–6/7–32

**DOSE IN RENAL IMPAIRMENT**

- **GFR (mL/min):**
  - **20–50:** Dose as in normal renal function  
  - **10–20:** Use small doses – increase dosing interval to 6 hours and decrease dose by 25%  
  - **<10:** Avoid if possible. If not, use small doses: increase dosing interval to 8 hours and decrease dose by 50%

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD:** Unknown dialysability. Dose as in GFR<10 mL/min  
- **HD:** Not dialysed. Dose as in GFR<10 mL/min  
- **HDF/High flux:** Unknown dialysability. Dose as in GFR<10 mL/min  
- **CAV/VVHD:** Unlikely dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:

- Anti-arrhythmics: delayed absorption of mexiletine  
- Antidepressants: possible CNS excitation or depression with MAOIs and moclobemide – avoid concomitant use; possibly increased serotonergic effects with duloxetine; increased sedative effects with tricyclics  
- Antipsychotics: enhanced sedative and hypotensive effect  
- Antivirals: concentration reduced by ritonavir but concentration of toxic pethidine metabolite increased – avoid concomitant use  
- Dopaminergics: risk of CNS toxicity with rasagiline – avoid concomitant use; hyperpyrexia and CNS toxicity reported with selegiline – avoid concomitant use  
- Sodium oxybate: enhanced effect of sodium oxybate – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - IV, oral, SC, IM

**RATE OF ADMINISTRATION**

- **IV:** Bolus 3–4 minutes

**COMMENTS**

- **OTHER INFORMATION**
  - Risk of CNS and respiratory depression or convulsions, particularly in ERF patients receiving regular doses, due to accumulation of active metabolite, norpethidine. Norpethidine levels can be measured

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Phenelzine

**CLINICAL USE**
MAOI antidepressant

**DOSE IN NORMAL RENAL FUNCTION**
15 mg 3 times daily; maximum: 30 mg 3 times daily

**PHARMACOKINETICS**
- Molecular weight: 136 (234.3 as sulphate)
- % Protein binding: No data
- % Excreted unchanged in urine: 0.25–1.1
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 1.2/–

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Possibly dialysed. Dose as in normal renal function
- HD: Possibly dialysed. Dose as in normal renal function
- HDF/High flux: Possibly dialysed. Dose as in normal renal function
- CAV/ VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potential hazardous interactions with other drugs
- Alcohol: some alcoholic and dealcoholised drinks contain tyramine which can cause hypertensive crisis
- Alpha-blockers: avoid concomitant use with indoramin; enhanced hypotensive effect
- Anaesthetics: avoid concomitant use
- Analgesics: CNS excitation or depression with pethidine, other opioids and nefopam – avoid concomitant use
- Antidepressants: enhancement of CNS effects and toxicity. Care with all antidepressants including drug free periods when changing therapies
- Anti-epileptics: antagonism of anticonvulsant effect; avoid carbamazepine with or within 2 weeks of MAOIs
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: effects enhanced by clozapine
- Atomoxetine: avoid concomitant use and for 2 weeks after use
- Bupropion: avoid with or for 2 weeks after MAOIs
- Dopaminergics: avoid concomitant use with entacapone and tolcapone; hypertensive crisis with levodopa and rasagline – avoid for at least 2 weeks after stopping MAOI; hypotension with selegiline
- 5HT1 agonist: risk of CNS toxicity with sumatriptan, rizatriptan and zolmitriptan – avoid sumatriptan and rizatriptan for 2 weeks after MAOI
- Methyldopa: avoid concomitant use
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use
- Sympathomimetics: hypertensive crisis with dexamfetamine, other amphetamines, dopamine, dopexamine, ephedrine, isomethphetamine, methylphenidate, phenylephrine, phenylpropanolamine, pseudoephedrine or sympathomimetics
- Tetrabenazine: risk of CNS excitation and hypertension

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
- Oral
- **RATE OF ADMINISTRATION**
- COMMENTS
-
Phenindione

**CLINICAL USE**
Anticoagulant

**DOSE IN NORMAL RENAL FUNCTION**
Day 1: 200 mg  
Day 2: 100 mg  
Maintenance dose: 50–150 mg daily according to INR

**PHARMACOKINETICS**
- Molecular weight (daltons): 222.2
- % Protein binding: >97
- % Excreted unchanged in urine: No data
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 5–6/

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Unknown dialysability. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - There Are Many Significant Interactions With Coumarins. Prescribe With Care With Regard To The Following:
    - Anticoagulant effect enhanced by: alcohol, amiodarone, anabolic steroids, aspirin, azithromycin, aztreonam, bicalutamide, cephalosporins, chloramphenicol, cimetidine, ciprofloxacin, clarithromycin, clopidogrel, cranberry juice, danazol, dextropropoxyphene, dipyriramole, disulfiram, erythromycin, esomeprazole, ezetimibe, fibrates, fluconazole, flutamide, fluvastatin, grapefruit juice,itraconazole, ketoconazole, levamisole, levofloxacin, macrolides, methylphenidate, metronidazole, miconazole, nalidixic acid, neomycin, norfloxacin, NSAIDs, ofloxacin, omeprazole, pantoprazole, paracetamol, penicillins, propafenone, ritonavir, rosuvastatin, SSRIs, simvastatin, sitaxentan, sulfinpyrazone, sulphonamides, tamoxifen, testosterone, tetracyclines, thyroxine, tigecycline, toremifene, tramadol, trimethoprim, valproate, voriconazole

- Anticoagulant effect decreased by: acitretin, azathioprine, barbiturates, carbamazepine, griseofulvin, mercaptopurine, mitotane, oral contraceptives, phenytoin, primidone, rifampicin, St John’s wort – avoid concomitant use, sucralfate, vitamin K

- Anticoagulant effects enhanced/reduced by: amprenavir, anion exchange resins, corticosteroids, dietary changes, tricyclics

- Analgesics: increased risk of bleeding with IV diclofenac and ketorolac – avoid concomitant use

- Antidiabetic agents: enhanced hypoglycaemic effect with sulphonylureas

- Ciclosporin: there have been a few reports of altered anticoagulant effect; decreased ciclosporin levels have been seen rarely

- Cytotoxics: increased risk of bleeding with erlotinib and imatinib; enhanced effect with etoposide, fluorouracil, ifosfamide and sorafenib

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**
- Titrate dose to INR
- Enhanced anticoagulant effect in renal impairment, due to reduced protein binding
- Metabolites of phenindione often colour the urine pink or orange
**Phenobarbital (phenobarbitone)**

**CLINICAL USE**
Anti-epileptic agent

**DOSE IN NORMAL RENAL FUNCTION**
Oral: 60–180 mg at night
Status epilepticus: 10 mg/kg, max 1 g IV

**PHARMACOKINETICS**
- Molecular weight: 232.2 (254.2 as sodium salt)
- % Protein binding: 45–60
- % Excreted unchanged in urine: 25
- Volume of distribution (L/kg): 1
- Half-life – normal/ESRF (hrs): 75–120/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function, but avoid very large doses</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Reduce dose by 25–50% and avoid very large single doses</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**: Dialysed. Dose as in GFR<10mL/min
- **HD**: Dialysed. Dose as in GFR<10mL/min
- **HDF/High flux**: Dialysed. Dose as in GFR<10mL/min
- **CAV/VVHD**: Not dialysed. Dose as in GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**

- Potentially hazardous interactions with other drugs
  - Antibacterials: reduced concentration of chloramphenicol, doxycycline, metronidazole, telithromycin and possibly rifampicin – avoid with telithromycin
  - Anticoagulants: increased metabolism of coumarins (reduced effect)
  - Antidepressants: antagonise anticonvulsant effect; reduces concentration of paroxetine, mianserin and tricyclics; concentration reduced by St John's wort – avoid concomitant use
  - Antifungals: possibly reduced concentration of itraconazole, posaconazole and voriconazole – avoid concomitant use with voriconazole; reduced absorption of griseofulvin (reduced effect)
  - Antipsychotics: antagonise anticonvulsant effect; metabolism of haloperidol increased; possibly reduces aripiprazole concentration – increase aripiprazole dose; concentration of both drugs reduced with chlorpromazine
  - Antivirals: concentration of abacavir, amprenavir, darunavir, indinavir, lopinavir, nelfinavir and saquinavir possibly reduced
  - Calcium-channel blockers: effect of felodipine, isradipine and probably dihydropyridines, diltiazem and verapamil reduced
  - Ciclosporin: reduced ciclosporin levels
  - Corticosteroids: metabolism of corticosteroids accelerated, reduced effect
  - Diuretics: concentration of eplerenone reduced – avoid concomitant use; increased risk of osteomalacia with carbonic anhydrase inhibitors
  - Oestrogens and progestogens: metabolism accelerated, reduced contraceptive effect
  - Sodium oxybate: enhanced effects of sodium oxybate – avoid
  - Tacrolimus: concentration of tacrolimus reduced

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - IV, oral
- **RATE OF ADMINISTRATION**
  - Not more than 100mg/minute
- **COMMENTS**
  - For IV administration, dilute 1 in 10 with water for injection
OTHER INFORMATION

- Aim for plasma concentration of 15–40 mg/L (65–170 µmol/L) for optimum response
- May cause excessive sedation and increased osteomalacia in ERF
- Charcoal haemoperfusion and haemodialysis more effective than peritoneal dialysis for poisoning
- Up to 50% unchanged drug excreted in urine with alkaline diuresis
Phenoxymethylpenicillin (penicillin V)

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
500–1000 mg every 6 hours

**PHARMACOKINETICS**
- Molecular weight (daltons) 350.4
- % Protein binding 80
- % Excreted unchanged in urine 60–90
- Volume of distribution (L/kg) 0.5
- Half-life – normal/ESRF (hrs) 0.5–1/4

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50 Dose as in normal renal function
  - 10–20 Dose as in normal renal function
  - <10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Not dialysed. Dose as normal renal function
- HD Dialysed. Dose as in normal renal function
- HDF/High flux Dialysed. Dose as in normal renal function
- CAV/ VVHD Dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Reduces excretion of methotrexate

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**
  -

**OTHER INFORMATION**
- Renal failure prolongs half-life of phenoxymethylpenicillin, but as it has a wide therapeutic index no dose adjustment is necessary
Phentolamine mesilate

**CLINICAL USE**
Alpha-adrenoceptor blocker:
- Hypertensive crisis

**DOSE IN NORMAL RENAL FUNCTION**
2–5 mg repeated if necessary

**PHARMACOKINETICS**
- Molecular weight: 377.5 daltons
- % Protein binding: 54%
- % Excreted unchanged in urine: 13%
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 19 minutes/–

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td></td>
<td>Titrate dose to end point, i.e. lower BP</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
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<td>CAPD</td>
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</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Antidepressants: additive hypotensive effect with MAOIs – avoid concomitant use
- Antihypertensives: enhanced hypotensive effect
- Diuretics: enhanced hypotensive effect
- Linezolid: additive hypotensive effect
- Moxisylyte: possibly severe postural hypotension
- Vardenafil, sildenafil and tadalafil: enhanced hypotensive effect – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - IV
  - RATE OF ADMINISTRATION
    - COMMENTS
    -

**OTHER INFORMATION**
- Titrate according to response
Phenytoin

**CLINICAL USE**
- Anti-epileptic agent
- Diabetic neuropathy
- Trigeminal neuralgia

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: 150–500 mg/day or 3–4 mg/kg/day in 1–2 divided doses; higher doses can be used in exceptional cases
- Status epilepticus (IV): 10–18 mg/kg (with BP and ECG monitoring) then 100 mg every 6–8 hours according to levels

**PHARMACOKINETICS**
- Molecular weight: 252.3 (274.2 as sodium salt)
- % Protein binding: 90
- % Excreted unchanged in urine: up to 5
- Volume of distribution (L/kg): 0.52–1.19

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Dialysed. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Analgesics: enhanced effect with NSAIDs; metabolism of methadone accelerated
  - Anti-arrhythmics: increased concentration with amiodarone; concentration of disopyramide and mexiletine reduced
  - Antibacterials: level increased by clarithromycin, chloramphenicol, isoniazid, metronidazole, co-trimoxazole and trimethoprim (+ antifolate effect); concentration increased or decreased by ciprofloxacin; concentration of doxycycline and telithromycin reduced; concentration reduced by rifampicin
  - Anticoagulants: increased metabolism of coumarins (reduced effect but also reports of enhancement)
  - Antidepressants: MAOIs, SSRIs and tricyclics antagonise anticonvulsant effect, concentration increased by fluoxetine and fluvoxamine; concentration of mianserin, mirtazepine and paroxetine and possibly tricyclics reduced; concentration reduced by St John's wort – avoid
  - Anti-epileptics: concentration of both drugs reduced with carbamazepine, concentration may also be increased by carbamazepine, ethosuximide, oxcarbazepine and topiramate; concentration of ethosuximide, active oxcarbazepine metabolite, primidone (but active metabolite increased), topiramate and valproate possibly reduced; concentration of lamotrigine, tiagabine and zonisamide reduced; concentration reduced by vigabatrin
  - Antifungals: concentration of ketoconazole, itraconazole, posaconazole, voriconazole and possibly caspofungin reduced – avoid with itraconazole, increase voriconazole dose and possibly caspofungin; levels increased by fluconazole, miconazole and voriconazole
  - Antimalarials: antagonise anticonvulsant effect; possibly reduced aripiprazole concentration – increase aripiprazole dose; metabolism of clozapine, quetiapine and sertindole increased
  - Antipsychotics: antagonise anticonvulsant effect; possibly reduced aripiprazole concentration – increase aripiprazole dose; metabolism of clozapine, quetiapine and sertindole increased
  - Calcium-channel blockers: levels increased by diltiazem; concentration of diltiazem, felodipine, isradipine, nisoldipine and verapamil and possibly dihydropyridines, nicardipine and nifedipine reduced
  - Ciclosporin: reduced ciclosporin levels
  - Corticosteroids: metabolism accelerated (effect reduced)
  - Cytotoxics: metabolism inhibited by fluorouracil; increased antifolate effect
with methotrexate; reduced phenytoin absorption; concentration of busulfan, etoposide and imatinib reduced—avoid with imatinib

- Disulfiram: levels of phenytoin increased
- Diuretics: concentration of eplerenone reduced—avoid concomitant use; increased risk of osteomalacia with carbonic anhydrase inhibitors; antagonises effect of furosemide
- Oestrogens and progestogens: metabolism increased (reduced contraceptive effect)
- Sulfinpyrazone: concentration increased by sulfinpyrazone
- Theophylline: concentration of both drugs reduced
- Ulcer-healing drugs: metabolism inhibited by cimetidine; absorption reduced by sucralfate; enhanced effect with esomeprazole and omeprazole

**ADMINISTRATION**

**RECONSTITUTION**

**ROUTE**

- IV, oral

**RATE OF ADMINISTRATION**

- IV infusion and bolus: not greater than 50 mg/minute

**COMMENTS**

- Infusion: dilute in 50–100 mL sodium chloride 0.9%; final concentration not exceeding 10 mg/mL
- Give by slow IV injection into large vein followed by sodium chloride 0.9% flush, to avoid irritation. Cardiac monitoring recommended

**OTHER INFORMATION**

- Aim for phenytoin levels of 10–20 mg/L (40–80 micromol/L)
- Total phenytoin levels must be adjusted for hypoalbuminaemia and uraemia (levels of 5–12 mcg/mL may be enough)
- Decreased protein binding and volume of distribution in renal failure
- Free fraction of phenytoin is increased in uraemia to approximately 0.2
- Request free phenytoin serum levels, if possible
- Loading dose 15 mg/kg IV or oral, then 5 mg/kg/day. Steady state reached in 3–5 days if loading dose given
- Increase dose gradually (25–50 mg/day at weekly intervals); demonstrates saturation kinetics
- Phenytoin absorption is markedly reduced by concurrent nasogastric enteral nutrition administration. Avoid concomitant administration with divalent cations
- May cause folate deficiency
- A useful equation:
  
  \[
  \frac{C_{\text{normal}}}{C_{\text{observed}}} = [(0.48) \times (1 - 0.1) \times \text{albumin}] + 0.1
  \]
  
  \[
  \frac{4.4 (\text{g/dl})}{4.4 (\text{g/dl})}
  \]

- Reduced phenytoin absorption; concentration of busulfan, etoposide and imatinib reduced—avoid with imatinib

- May cause folate deficiency
- A useful equation:
  
  \[
  \frac{C_{\text{normal}}}{C_{\text{observed}}} = [(0.48) \times (1 - 0.1) \times \text{albumin}] + 0.1
  \]
  
  \[
  \frac{4.4 (\text{g/dl})}{4.4 (\text{g/dl})}
  \]

**RETURN TO CONTENTS**
Phosphate supplements

**CLINICAL USE**
Hypophosphataemia

**DOSE IN NORMAL RENAL FUNCTION**
Oral: According to response; maximum oral dose = 100 mmol in 24 hours
IV: 9–30 mmol/day (maximum 500 micromols/kg in critically ill patients); see ‘Other Information’

**PHARMACOKINETICS**
- Molecular weight: 94–97 (Phosphate)
- % Protein binding: No data
- % Excreted unchanged in urine: High
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): No data

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Dialysed. Dose as in normal renal function
- HD: Dialysed. Dose as in normal renal function
- HDF/High flux: Dialysed. Dose as in normal renal function
- CAV/VVHD: Dialysed. Dose as in normal renal function

**ADMINISTRATION**

**RECONSTITUTION**

**ROUTE**
- 1V, oral

**RATE OF ADMINISTRATION**
- Usually over 6–12 hours

**COMMENTS**
- Phosphatepolyfusor: give undiluted over 24 hours, peripherally
- Addiphos: peripherally – give each vial (20 mL) diluted to 250–500 mL with glucose 5% over 6–12 hours, minimum volume 100 mL (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006); centrally – 20 mL vial made up to 60 mL with glucose 5% over 6–8 hours via syringe driver

**OTHER INFORMATION**
- Oral dosing: Phosphate Sandoz – 16.1 mmol phosphate, 20.4 mmol sodium, 3.1 mmol potassium per tablet
- IV dosing: (i) Phosphate Polyfusor (500 mL) containing: 50 mmol phosphate, 81 mmol sodium, 9.5 mmol potassium. (ii) Addiphos (20 mL) containing: 40 mmol phosphate, 30 mmol sodium, 30 mmol potassium
- HD patients usually need 15–20 mmol/day in TPN
- CAV/VVHD patients usually need 30–40 mmol/day
- During IV phosphate replacement, serum calcium, potassium and phosphate should be monitored 6–12 hourly. Repeat the dose within 24 hours if an adequate level has not been achieved. Urinary output should also be monitored
- There is experience giving 15 mmol over 2 hours up to 3 times a day
- Excessive doses of phosphate may cause hypocalcaemia and metastatic calcification

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Avoid insoluble incompatibilities, e.g. calcium salts
Phytomenadione (vitamin K<sub>1</sub>)

**CLINICAL USE**
- Vitamin K deficiency
- Antidote to oral anticoagulants

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: 10–20 mg daily
- IV: 5–40 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 450.7
- % Protein binding: 90
- % Excreted unchanged in urine: <10
- Volume of distribution (L/kg): 0.05–0.13

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux: Dialysed. Dose as in normal renal function
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Antagonises effect of coumarins and phenindione

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - IV, IM, oral
- **RATE OF ADMINISTRATION**
  - Konakion® – very slow injection (1 mg/min)
  - Konakion MM® – dilute each 10 mg with 55 mL of glucose 5% and give by slow infusion over 15–30 minutes

**COMMENTS**
- Risk of anaphylaxis if IV injected too rapidly
- Protect infusion from light
- Konakion® should not be diluted (non-micellar)
- Only Konakion® can be given IM

**OTHER INFORMATION**
- Konakion MM® recommended for severe haemorrhage
- Anticoagulation antidote: re-test prothrombin time 8–12 hours after Konakion®, 3 hours after Konakion MM® – repeat dose if inadequate
- Patients with obstructive jaundice requiring oral vitamin K should be prescribed the water-soluble preparation menadion sodium diphosphate – dosage range is similar
Pimozide

CLINICAL USE
Antipsychotic

DOSE IN NORMAL RENAL FUNCTION
2–20 mg daily

PHARMACOKINETICS
Molecular weight 461.5 (daltons)
% Protein binding 99
% Excreted unchanged in urine <1
Volume of distribution No data (L/kg)
Half-life – normal/ESRF (hrs) 55–150/

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Start with low dose and increase according to response

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unknown dialysability. Dose as in GFR<10 mL/min
HD Unknown dialysability. Dose as in GFR<10 mL/min
HDF/High flux Unknown dialysability. Dose as in GFR<10 mL/min
CAV/VVHD Unknown dialysability. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Antibacterials: avoid concomitant use with macrolides and moxifloxacin (increased risk of ventricular arrhythmias)
- Antidepressants: concentration increased by sertraline and possibly paroxetine – avoid with paroxetine; increased risk of ventricular arrhythmias with maprotiline and tricyclics – avoid concomitant use; increased plasma level of tricyclics
- Anti-epileptics: antagonises anticonvulsant effect
- Antifungals: avoid concomitant use with imidazole and triazole
- Antimalarials: avoid concomitant use with artemether/lumefantrine; increased risk of ventricular arrhythmias with mefloquine and quinine – avoid concomitant use
- Antipsychotics: increased risk of ventricular arrhythmias with phenothiazines – avoid concomitant use
- Antivirals: concentration increased by amprenavir, atazanavir, efavirenz, indinavir, nelfinavir, ritonavir and saquinavir, increased risk of ventricular arrhythmias – avoid concomitant use
- Anxiolytics and hypnotics: increased sedative effects
- Aprepitant: avoid concomitant use
- Atomoxetine: increased risk of ventricular arrhythmias
- Beta-blockers: increased risk of ventricular arrhythmias with sotalol
- Diuretics: increased risk of ventricular arrhythmias due to hypokalaemia
- Ivabradine: increased risk of ventricular arrhythmias
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use

ADMINISTRATION
RECONSTITUTION
- ROUTE
  - Oral
RATE OF ADMINISTRATION
- COMMENTS
  -

OTHER INFORMATION
- ECG required before treatment. To be repeated annually
Pindolol

**CLINICAL USE**

Beta-blocker:
- Hypertension
- Angina

**DOSE IN NORMAL RENAL FUNCTION**

- Hypertension: 15–45 mg daily in divided doses (15 mg can be given as a single dose.)
- Angina: 2.5–5 mg 3 times daily

**PHARMACOKINETICS**

- Molecular weight (daltons) 248.3
- % Protein binding 40–60
- % Excreted unchanged in urine 30–40
- Volume of distribution (L/kg) 2–3
- Half-life – normal/ESRF (hrs) 3–4/Increased

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Anaesthetics: enhanced hypotensive effect
- Analgesics: NSAIDs antagonise hypotensive effect
- Anti-arrhythmics: increased risk of myocardial depression and bradycardia; increased risk of bradycardia, myocardial depression and AV block with amiodarone
- Antidepressants: enhanced hypotensive effect with MAOIs
- Antihypertensives: enhanced hypotensive effect; increased risk of withdrawal hypertension with clonidine; increased risk of first dose hypotensive effect with post-synaptic alpha-blockers such as prazosin
- Antimalarials: increased risk of bradycardia with mefloquine
- Antipsychotics: enhanced hypotensive effect with phenothiazines
- Calcium-channel blockers: increased risk of bradycardia and AV block with diltiazem; hypotension and heart failure possible with nifedipine and nisoldipine; asystole, severe hypotension and heart failure with verapamil
- Diuretics: enhanced hypotensive effect
- Moxisylyte: possible severe postural hypotension
- Sympathomimetics: severe hypertension with adrenaline and noradrenaline and possibly with dobutamine
- Tropisetron: increased risk of ventricular arrhythmias – use with caution

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
  - **OTHER INFORMATION**
    - The fate of metabolites, even if they are inactive, is unknown
Pioglitazone

**CLINICAL USE**
Treatment of type 2 diabetes mellitus

**DOSE IN NORMAL RENAL FUNCTION**
15–45 mg daily

**PHARMACOKINETICS**
- Molecular weight: 392.9 (as hydrochloride)
- % Protein binding: >99
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): 0.25
- Half-life: 5–6 (active metabolites: 16–23) / Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose in renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose Instructions</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function and monitor carefully</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function and monitor carefully</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function and monitor carefully</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unknown dialysability. Dose as in normal renal function and monitor carefully</td>
</tr>
<tr>
<td>VVHD</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  -

**OTHER INFORMATION**
- Liver function tests should be measured prior to initiation of therapy and then every 2 months for the first 12 months, and thereafter at regular intervals
- Pioglitazone should not be used in patients with heart failure or history of heart failure; incidence of heart failure is increased when pioglitazone is combined with insulin. Patients should be closely monitored for signs of heart failure
Piperazine

**CLINICAL USE**

Treatment of threadworm and roundworm infections

**DOSE IN NORMAL RENAL FUNCTION**

- **Threadworm:** 4 g sachet stirred into a glass of milk or water and drunk immediately; repeat after 14 days
- **Roundworms:** 4 g sachet stirred into a glass of milk or water and drunk immediately; repeat at monthly intervals for up to 3 months if re-infection risk

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>86.14 (202.1 as phosphate); (642.7 as citrate)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>No data</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>5–30</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>No data</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>No data</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function but avoid repeated administration</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose in GFR&lt;10 mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs

- Pyrantel: antagonises effect of piperazine

**ADMINISTRATION**

- **Reconstitution**
- **Route**
  - Oral
- **Rate of Administration**
- **Comments**

**OTHER INFORMATION**

- May accumulate in severe renal impairment causing neurotoxicity
- Acts within the lumen of the gastrointestinal tract which is independent of any systemic absorption
Piracetam

**CLINICAL USE**
Myoclonus

**DOSE IN NORMAL RENAL FUNCTION**
7.2 g daily in 2–3 divided doses titrated to a maximum of 20 g daily

**PHARMACOKINETICS**
- Molecular weight: 142.2 daltons
- % Protein binding: 15
- % Excreted: >90
- Unchanged in urine
- Volume of distribution: 0.7 L/kg
- Half-life – normal/ESRF (hrs): 5/Increased

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>4.8 g in 2–3 divided doses</th>
<th>1.2 g daily</th>
<th>1.2 g daily</th>
<th>Contraindicated</th>
</tr>
</thead>
<tbody>
<tr>
<td>50–80</td>
<td>4.8 g in 2–3 divided doses</td>
<td>1.2 g twice daily</td>
<td>1.2 g daily</td>
<td>Contraindicated</td>
</tr>
<tr>
<td>30–50</td>
<td>1.2 g twice daily</td>
<td>1.2 g daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–30</td>
<td>1.2 g daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Likely dialysability. Avoid. Contraindicated
- HD: Dialysed. Avoid. Contraindicated
- HDF/High flux: Dialysed. Avoid. Contraindicated
- CAV: Unknown dialysability. Dose as in GFR=20–30 mL/min
- VVHD: Dialysed. Avoid. Contraindicated

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**
- **RECONSTITUTION**
  - 
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - 
- **COMMENTS**
  - 

**RETURN TO CONTENTS**
Piroxicam

**CLINICAL USE**

NSAID and analgesic

**DOSE IN NORMAL RENAL FUNCTION**

- Rheumatic disease: 20–30 mg daily
- Acute gout: 40 mg in single or divided doses
- Acute musculoskeletal disorders: 40 mg daily for 2 days, then 20 mg daily

**PHARMACOKINETICS**

- Molecular weight: 331.3 daltons
- % Protein binding: 99%
- % Excreted unchanged in urine: <5
- Volume of distribution (L/kg): 0.14
- Half-life – normal/ESRF (hrs): 50/Unchanged

**DOSE IN RENAL IMPAIRMENT**

- **GFR (mL/min)**
  - 20–50: Dose as in normal renal function, but avoid if possible
  - 10–20: Dose as in normal renal function, but avoid if possible
  - <10: Dose as in normal renal function, but only use if on dialysis

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Not dialysed. Dose as in GFR<10 mL/min. See ‘Other Information’
- HD: Not dialysed. Dose as in GFR<10 mL/min. See ‘Other Information’
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min. See ‘Other Information’
- CAV/VVHD: Not dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs

- ACE inhibitors and angiotensin-II antagonists: antagonism of hypotensive effect; increased risk of nephrotoxicity and hyperkalaemia

- Analgesics: avoid concomitant use of 2 or more NSAIDs, including aspirin (increased side effects); avoid with ketorolac (increased risk of side effects and haemorrhage)

- Antibacterials: possibly increased risk of convulsions with quinolones

- Anticoagulants: effects of coumarins enhanced; possibly increased risk of bleeding with heparins and coumarins

- Antidepressants: increased risk of bleeding with SSRIs and venlafaxine

- Antidiabetic agents: effects of sulphonylureas enhanced

- Anti-epileptics: possibly increased phenytoin concentration

- Antivirals: increased risk of haematological toxicity with zidovudine; concentration increased by ritonavir

- Ciclosporin: may potentiate nephrotoxicity

- Cytotoxic agents: reduced excretion of methotrexate; increased risk of bleeding with erlotinib

- Diuretics: increased risk of nephrotoxicity; antagonism of diuretic effect; hyperkalaemia with potassium-sparing diuretics

- Lithium: excretion decreased

- Pentoxifylline: increased risk of bleeding

- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral, IM, topical

- **RATE OF ADMINISTRATION**
  - 

- **COMMENTS**
  - 

**OTHER INFORMATION**

- Inhibition of renal prostaglandin synthesis by NSAIDs may interfere with renal function, especially in the presence of existing renal disease – avoid if possible; if not, check serum creatinine 48–72 hours after starting NSAID – if serum creatinine is increased, stop NSAID

- Use normal doses in patients with CKD 5 if on dialysis and do not pass any urine

- Use with caution in renal transplant recipients – can reduce intrarenal autacoid synthesis

- Water soluble inactive metabolites may be removed by HD and CAPD
### Pivmecillinam hydrochloride

#### CLINICAL USE
Antibacterial agent

#### DOSE IN NORMAL RENAL FUNCTION
- Acute uncomplicated cystitis: 400 mg initially, then 200 mg 3 times a day
- Chronic or recurrent bacteriuria: 400 mg every 6–8 hours
- Enteric fever (typhoid): 1.2–2.4 g daily for 14 days

#### PHARMACOKINETICS
- Molecular weight (daltons): 476
- % Protein binding: 5–10
- % Excreted unchanged in urine: 45–50 (as mecillinam)
- Volume of distribution (L/kg): 0.2–0.4 (as mecillinam)
- Half-life – normal/ESRF (hrs): 1.2/Increased

#### DOSE IN RENAL IMPAIRMENT
<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function. See ‘Other Information’</td>
</tr>
</tbody>
</table>

#### IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Methotrexate: penicillins can reduce the excretion of methotrexate (increased risk of toxicity)
- Probenecid: reduces excretion of penicillins

#### ADMINISTRATION
**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  - Take with food

#### OTHER INFORMATION
- Hydrolysed to mecillinam which is the active drug
- Contraindicated in carnitine deficiency as it can cause carnitine deficiency
- Can cause oesophageal injury, take with water and food while standing up
- Can cause porphyria
- Accumulation may occur in patients with severe renal impairment, so use the lower dose if using for extended periods of time
- Unlikely to work in people with little residual kidney function as works by renal excretion into the bladder, where its site of action is

#### DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD: Likely dialysability. Dose as in GFR<10 mL/min
- HD: Likely dialysability. Dose as in GFR<10 mL/min
- HDF/High flux: Likely dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Likely dialysability. Dose as in normal renal function
Pizotifen

CLINICAL USE
Prophylactic treatment of vascular headaches including migraine

DOSE IN NORMAL RENAL FUNCTION
1.5 mg at night or 500 mcg 3 times a day adjusted according to response
Maximum single dose: 3 mg
Maximum daily dose: 4.5 mg

PHARMACOKINETICS
Molecular weight 429.5 (as maleate)
% Protein binding >90
% Excreted unchanged in urine <1 (55% as metabolites)
Volume of distribution (L/kg) 6–8
Half-life – normal/ESRF (hrs) 1 (metabolite 23 hours)

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unlikely to be dialysed. Dose as in GFR<10 mL/min
HD Unlikely to be dialysed. Dose as in GFR<10 mL/min
HDF/High flux Unknown dialysability. Dose as in GFR<10 mL/min
CAV/VVHD Unlikely to be dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● Adrenergic neurone blockers: pizotifen antagonises hypotensive effect

ADMINISTRATION

RECONSTITUTION
–

ROUTE
● Oral

RATE OF ADMINISTRATION
–

COMMENTS
–

OTHER INFORMATION
● Use with caution in people with a predisposition for urinary retention or closed angle glaucoma
● Pizotifen has appetite stimulating properties
Posaconazole

**CLINICAL USE**
Triazole antifungal agent

**DOSE IN NORMAL RENAL FUNCTION**
- 400 mg twice daily with food or 240 mL of a nutritional supplement
- Or 200 mg 4 times a day without food
- Oropharyngeal candidiasis severe infection or in immunocompromised patients: Loading dose of 200 mg once a day on the first day, then 100 mg once a day for 13 days
- Prophylaxis of invasive fungal infections: 200 mg 3 times a day

**PHARMACOKINETICS**
Molecular weight (daltons) 700.8
% Protein binding >98
% Excreted unchanged in urine <0.2
Volume of distribution (L/kg) 1774 litres
Half-life – normal/ESRF (hrs) 20–66 (average 35)/Unchanged

**DOSE IN RENAL IMPAIRMENT**
GFR (mL/MIN)
- 20–50 Dose as in normal renal function
- 10–20 Dose as in normal renal function
- <10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
CAPD Not dialysed. Dose as in normal renal function
HD Not dialysed. Dose as in normal renal function
HDF/High flux Unknown dialysability. Dose as in normal renal function
CAV/ VVHD Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antidepressants: avoid concomitant use with reboxetine
- Antibacterials: rifamycins may reduce posaconazole concentration; avoid concomitant administration unless benefit outweighs risk; rifabutin concentration increased
- Anti-epileptics: phenytoin, carbamazepine, phenobarbital and primidone may reduce posaconazole concentration – avoid concomitant administration unless benefit outweighs risk
- Antimalarials: avoid concomitant administration with artemether/ lumefantrine
- Antipsychotics: increased risk of ventricular arrhythmias with pimozide and sertindole – avoid concomitant use; possibly increase quetiapine levels – reduce dose of quetiapine
- Antivirals: possibly increases saquinavir levels
- Anxiolytics and hypnotics: increases midazolam levels
- Ciclosporin: increases posaconazole concentration. Posaconazole can increase ciclosporin concentration, – dose reduction may be required
- Ergot alkaloids: may increase ergot alkaloid concentration leading to ergotism – avoid concomitant administration
- Lipid-lowering drugs: possibly increased risk of myopathy with atorvastatin or simvastatin
- Sirolimus: may increase concentration of sirolimus – adjust sirolimus dose as required according to levels
- Sulphonylureas: posaconazole can decrease glucose concentrations, monitor glucose levels in diabetic patients
- Tacrolimus: concentration of tacrolimus increased – reduce dose of tacrolimus
- Ulcer-healing drugs: cimetidine may reduce posaconazole concentration by 39% – avoid concomitant administration unless benefit outweighs risk; drugs which reduce gastric acidity may reduce bioavailability of posaconazole
- Vinca alkaloids: may increase vinca alkaloid concentration leading to neurotoxicity – avoid concomitant administration unless benefit outweighs risk. It is advised to reduce the dose of the vinca alkaloid
- Tacrolimus: increases $C_{\text{max}}$ and AUC by 121% and 358% respectively of tacrolimus – reduce tacrolimus dose to about a third of current dose and adjust as required
<table>
<thead>
<tr>
<th>ADMINISTRATION</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>RECONSTITUTION</td>
<td></td>
</tr>
<tr>
<td>ROUTE</td>
<td>• Oral</td>
</tr>
<tr>
<td>RATE OF ADMINISTRATION</td>
<td></td>
</tr>
<tr>
<td>COMMENTS</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>OTHER INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use with caution in people with arrhythmias, electrolyte disturbances QT prolongation, sinus bradycardia and cardiomyopathy</td>
</tr>
<tr>
<td>Contains 7 g of glucose per 800 mg daily dose</td>
</tr>
<tr>
<td>Measure liver function tests as moderate increases have been noted</td>
</tr>
</tbody>
</table>
Potassium chloride

**CLINICAL USE**
Hypokalaemia

**DOSE IN NORMAL RENAL FUNCTION**
2–4 g (25–50 mmol) daily

**PHARMACOKINETICS**
- Molecular weight (daltons) 74.6
- % Protein binding N/A
- % Excreted unchanged in urine N/A
- Volume of distribution (L/kg) N/A
- Half-life – normal/ESRF (hrs) N/A

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>According to response</td>
</tr>
<tr>
<td>10–20</td>
<td>According to response</td>
</tr>
<tr>
<td>&lt;10</td>
<td>According to response</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD** Dialysed. Dose according to response
- **HD** Dialysed. Dose according to response
- **HDF/High flux** Dialysed. Dose according to response
- **CAV/VVHD** Dialysed. Dose according to response

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- ACE inhibitors and angiotensin-II antagonists: increased risk of hyperkalaemia
- Ciclosporin: increased risk of hyperkalaemia
- Potassium-sparing diuretics: increased risk of hyperkalaemia
- Tacrolimus: increased risk of hyperkalaemia

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral, IV

**RATE OF ADMINISTRATION**
- Infusion up to 20 mmol potassium per hour except in extreme hypokalaemic emergency where some units give up to 40 mmol/hour with cardiac monitoring

**COMMENTS**
- Give IV solution well diluted (not exceeding 40 mmol/500 mL) for peripheral administration
- Mix IV solutions thoroughly to avoid layering effect
- Some units give more concentrated solution centrally: 100–200 mmol/100 mL sodium chloride 0.9% or glucose 5%, but at a rate not more than 20 mmol/hour
- Cardiac monitoring mandatory

**OTHER INFORMATION**
- Potassium chloride injection MUST NOT be injected undiluted
- Monitor serum potassium levels
- Sando K: 12 mmol potassium per tablet
- Slow K: 8 mmol potassium per tablet
- Kay-Cee-L Syrup: 1 mmol potassium per mL
- Potassium chloride strong 15% injection: 20 mmol potassium /10 mL
Pramipexole

**CLINICAL USE**
- Parkinson's disease
- Symptomatic treatment of restless legs

**DOSE IN NORMAL RENAL FUNCTION**
- Parkinson's disease: 88 – 1100 mcg 3 times a day
- Restless legs: 88–540 mcg taken 2–3 hours before bedtime

**PHARMACOKINETICS**
- Molecular weight: 302.3 (as hydrochloride)
- % Protein binding: <20
- % Excreted unchanged in urine: <90
- Volume of distribution: 400–500 litres
- Half-life – normal/ESRF (hrs): 8–14/36

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Initially 88 mcg twice daily and titrate slowly</td>
</tr>
<tr>
<td>10–20</td>
<td>Initially 88 mcg once daily and titrate slowly</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Initially 88 mcg once daily and titrate slowly</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/HD: Not dialysed. Dose as in GFR=10–20 mL/min
- VVHD: Not dialysed.

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
- Avoid concomitant use with antipsychotics

**ADMINISTRATION**
- **RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- 88 mcg of base = 125 mcg of salt, 180 mcg = 250 mcg, 350 mcg = 500 mcg, 700 mcg = 1 mg, 1.1 mg = 1.5 mg
- Less than 9% of dose is removed by haemodialysis
- Drowsiness is a common side effect especially at higher doses
- For restless legs, dose as in normal renal function

**RETURN TO CONTENTS**
Pravastatin sodium

**CLINICAL USE**
HMG CoA reductase inhibitor:
- Hypercholesterolaemia

**DOSE IN NORMAL RENAL FUNCTION**
10–40 mg daily at night

**PHARMACOKINETICS**
- **Molecular weight (daltons)**: 446.5
- **% Protein binding**: Approx 50
- **% Excreted unchanged in urine**: 20
- **Volume of distribution (L/kg)**: 0.5
- **Half-life – normal/ESRF (hrs)**: 1.5–2/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/min)**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**: Unlikely to be dialysed. Dose as in normal renal function
- **HD**: Not dialysed. Dose as in normal renal function
- **HDF/High flux**: Unknown dialysability. Dose as in normal renal function
- **CAV/VVHD**: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: increased risk of myopathy with daptomycin
- Antivirals: concentration reduced by efavirenz
- Ciclosporin: increased risk of myopathy
- Lipid lowering agents: increased risk of myopathy with fibrates, gemfibrozil (avoid) and nicotinic acid

**ADMINISTRATION**
**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- Rhabdomyolysis with acute renal failure, secondary to statin-induced myoglobinaemia, has been reported
- Inactive polar metabolite accumulates but is readily removed by haemodialysis
Praziquantel (unlicensed product)

**CLINICAL USE**
- Treatment of tapeworm
- *Hymenolepis nana*
- *Schistosoma haematobium* worms
- *S. japonicum* infections

**DOSE IN NORMAL RENAL FUNCTION**
- Tapeworm: 5–10 mg/kg after a light breakfast
- *Hymenolepis nana*: 25 mg/kg
- *Schistosomiasis*: 20 mg/kg repeated after 4–6 hours
- *S. japonicum*: 60 mg/kg in 3 divided doses on 1 day

**PHARMACOKINETICS**
- Molecular weight (daltons): 312.4
- % Protein binding: 80
- % Excreted unchanged in urine: 80% as metabolites
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 1–1.5 (metabolites 4 hours)/Slightly increased

**DOSE IN RENAL IMPAIRMENT**
- 20–50 GFR (mL/min): Dose as in normal renal function
- 10–20 GFR (mL/min): Dose as in normal renal function
- <10 GFR (mL/min): Dose as in normal renal function Use lower dose with caution

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**: Not dialysed. Dose as in GFR<10 mL/min
- **HD**: Not dialysed. Dose as in GFR<10 mL/min
- **HDF/High flux**: Unknown dialysability. Dose as in GFR<10 mL/min
- **CAV/HD**: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Carbamazepine, phenytoin, chloroquine: reduce bioavailability of praziquantel
- Cimetidine and albendazole: increases bioavailability

**ADMINISTRATION**
- **RECONSTITUTION**
  - **ROUTE**: Oral
  - **RATE OF ADMINISTRATION**
  - **COMMENTS**

**OTHER INFORMATION**
- Available on a named patient basis from Merck (Cysticide)
- One study did not show any adverse effects in a haemodialysis patient
Prazosin

**CLINICAL USE**
Alpha-adrenoceptor blocker:
- Hypertension
- Congestive heart failure
- Raynaud’s syndrome
- Benign prostatic hyperplasia (BPH)

**DOSE IN NORMAL RENAL FUNCTION**
- 0.5–20 mg daily in 2–3 divided doses
- Raynaud’s syndrome, BPH: 0.5–2 mg twice daily

**PHARMACOKINETICS**
- Molecular weight (daltons) 419.9
- % Protein binding 97
- % Excreted unchanged in urine <10
- Volume of distribution (L/kg) 1.2–1.5
- Half-life – normal/ESRF (hrs) 2–4/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/MIN)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Antidepressants: enhanced hypotensive effect with MAOIs
- Beta-blockers: enhanced hypotensive effect, increased risk of first dose hypotensive effect
- Calcium-channel blockers: enhanced hypotensive effect, increased risk of first dose hypotensive effect
- Diuretics: enhanced hypotensive effect, increased risk of first dose hypotensive effect
- Moxisylyte: possibly severe postural hypotension when used in combination
- Vardenafil, sildenafil and tadalafil: enhanced hypotensive effect – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
  -
Prednisolone

**CLINICAL USE**
Corticosteroid:
- Immunosuppression
- Anti-inflammatory

**DOSE IN NORMAL RENAL FUNCTION**
Oral: variable
IM: 25–100 mg once or twice weekly (as prednisolone acetate)

**PHARMACOKINETICS**
- Molecular weight: 360.4 (daltons)
- % Protein binding: 70–95 saturable
- % Excreted unchanged in urine: 11–30
- Volume of distribution: 1.3–1.7 (L/kg)
- Half-life – normal/ESRF (hrs): 2–4/Increased

**DOSE IN RENAL IMPAIRMENT**
GFR (mL/Min)
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
CAPD: Not dialysed. Dose as in normal renal function
HD: Not dialysed. Dose as in normal renal function
HDF/High flux: Not dialysed. Dose as in normal renal function
CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: metabolism accelerated by rifamycins; metabolism possibly inhibited by erythromycin
- Anticoagulants: efficacy of coumarins may be altered
- Anti-epileptics: metabolism accelerated by carbamazepine, barbiturates, phenytoin and primidone
- Antifungals: increased risk of hypokalaemia with amphotericin – avoid concomitant use; metabolism possibly inhibited by itraconazole and ketoconazole
- Antivirals: concentration possibly increased by ritonavir
- Ciclosporin: rare reports of convulsions in patients on ciclosporin and high-dose corticosteroids; increased levels of prednisolone; increased ciclosporin levels reported with prednisolone
- Cytotoxics: increased risk of haematological toxicity with methotrexate
- Diuretics: enhanced hypokalaemic effects of acetazolamide, loop diuretics and thiazide diuretics
- Vaccines: high dose corticosteroids can impair immune response to vaccines – avoid concomitant use with live vaccines

**ADMINISTRATION**

**RECONSTITUTION**

**ROUTE**
- Oral, IM, rectal

**RATE OF ADMINISTRATION**

**COMMENTS**

**OTHER INFORMATION**
- Evidence of unpredictable bioavailability from enteric coated tablets – avoid if possible
Pregabalin

CLINICAL USE
- Anti-epileptic agent
- Neuropathic pain
- Generalised anxiety disorder

DOSE IN NORMAL RENAL FUNCTION
150–600 mg daily in 2 or 3 divided doses

PHARMACOKINETICS
- Molecular weight (daltons) 159.2
- % Protein binding 0
- % Excreted unchanged in urine 92–99
- Volume of distribution (L/kg) 0.56
- Half-life – normal/ESRF (hrs) 5–6.5/ Increased

DOSE IN RENAL IMPAIRMENT
- GFR (mL/Min)
  - 30–60 Initial dose 75 mg daily and titrate according to tolerability and response
  - 15–30 Initial dose 25–50 mg daily and titrate according to tolerability and response
  - <15 Initial dose 25 mg daily and titrate according to tolerability and response

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD Dialysed. Dose as in GFR<15 mL/min
- HD Dialysed. Dose as in GFR<15 mL/min
- HDF/High Flux Dialysed. Dose as in GFR<15 mL/min
- CAV/VVHD Dialysed. Dose as in GFR=15–30 mL/min

IMPORTANT DRUG INTERACTIONS
- Potentially hazardous interactions with other drugs
  - None known

ADMINISTRATION
- RECONSTITUTION
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
- COMMENTS
- OTHER INFORMATION
- Oral bioavailability >90%
- 50% of dose is removed after a 4 hour haemodialysis session
- Use with caution in people with severe congestive heart failure
- May cause reversible deterioration in renal function
Primaquine phosphate

**CLINICAL USE**
- Treatment of malaria (Plasmodium vivax and Plasmodium ovale), in combination with chloroquine
- Treatment of Pneumocystis jiroveci pneumonia (PCP), in combination with clindamycin

**DOSE IN NORMAL RENAL FUNCTION**
- Malaria: 15–30 mg once daily for 14 days
- PCP: 30 mg once daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 455.3
- % Protein binding: No data
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): 3–4

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Antimalarials: avoid concomitant use with artemether/lumefantrine

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  -

**OTHER INFORMATION**
- Primaquine base 7.5 mg is approximately equivalent to 13.2 mg primaquine phosphate
- Major metabolite, 8-(3-carboxyl-1-methylpropylamino)-6-methoxyquinolone, possesses less antimalarial activity than the parent compound
- Contraindicated in acutely ill patients with rheumatoid arthritis or SLE – increased risk of developing granulocytopenia
- Risk of haemolytic anaemia in patients with G-6-PD deficiency; haemolysis generally appears 2–3 days after primaquine administration
- Risk of methaemoglobinemia at high doses

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Primaquine phosphate is not licensed for use by anyone else.
**Primaxin (imipenem/cilastatin)**

### CLINICAL USE
Antibacterial agent

### DOSE IN NORMAL RENAL FUNCTION
- **IV:** 1–4 g daily in 3–4 divided doses (as imipenem)
- **IM:** mild-moderate infections: 500–750 mg every 12 hours

### PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Property</th>
<th>Imipenem (daltons)</th>
<th>Cilastatin (daltons)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight</td>
<td>317.4</td>
<td>380.4</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>20–70</td>
<td>75</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.23</td>
<td>0.22</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1/4</td>
<td>1/12</td>
</tr>
</tbody>
</table>

### DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>31–70</td>
<td>500 mg every 6–8 hours</td>
</tr>
<tr>
<td>21–30</td>
<td>500 mg every 8–12 hours</td>
</tr>
<tr>
<td>&lt;20</td>
<td>250–500 mg (or 3.5 mg/kg whichever is lower) every 12 hours</td>
</tr>
</tbody>
</table>

### DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Dosed as in GFR&lt;20 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dosed as in GFR&lt;20 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dosed as in GFR&lt;20 mL/min</td>
</tr>
<tr>
<td>CAV/VVH</td>
<td>Dosed. 250 mg every 6 hours or 500 mg every 8 hours¹</td>
</tr>
<tr>
<td>CVVHD/HDF</td>
<td>Dosed. 250 mg every 6 hours or 500 mg every 6–8 hours¹</td>
</tr>
</tbody>
</table>

### IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Ciclosporin: variable reports of increase/no change in ciclosporin levels, and of neurotoxicity
- Convulsions reported with concomitant administration of ganciclovir

### ADMINISTRATION

#### RECONSTITUTION
- 250 mg with 50 mL, 500 mg with 100 mL sodium chloride 0.9% (in some units 500 mg with 50 mL)
- IM: 2 mL lidocaine 1%

#### ROUTE
- IM, IV peripherally or centrally (500 mg/50 mL – given centrally)

#### RATE OF ADMINISTRATION
- 250 or 500 mg dose over 20–30 minutes
- 1 g over 40–60 minutes

### OTHER INFORMATION
- Risk of adverse neurological effects, e.g. convulsions. Extreme caution required in patients with history of CNS disease
- Cilastatin can accumulate in patients with impaired renal function
- Sodium content 1.72 mmol/500 mg
- Imipenem is administered with cilastatin to prevent metabolism of imipenem within the kidney
- Non-renal clearance in acute renal failure is less than in chronic renal failure
- Patients with GFR<5 mL/min should not receive drug unless HD is started within 48 hours
- Metabolised to inactive, nephrotoxic metabolites

References:

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1 is not licensed for use by anyone else.
Primidone

**CLINICAL USE**
- Anti-epileptic agent
- Also used for essential tremor

**DOSE IN NORMAL RENAL FUNCTION**
- Epilepsy: 500 mg–1.5 g daily in 2 divided doses
- Essential tremor: 62.5–750 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 218.3
- % Protein binding: 20
- % Excreted unchanged in urine: 40
- Volume of distribution (L/kg): 0.4–1

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function, but avoid very large doses
  - <10: Reduce dose by 25–50% initially, and avoid very large single doses

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR<10mL/min
- HD: Dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10mL/min
- CAV/VVHD: Dialysed. Dose as in GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Antibacterials: reduced concentrations of chloramphenicol, doxycycline, metronidazole and telithromycin
  - Anticoagulants: increased metabolism of coumarins (reduced effect)
  - Antidepressants: antagonise anticonvulsant effect; reduces concentration of paroxetine, mianserin and tricyclics; St John's wort reduces active primidone metabolite concentration – avoid concomitant use
  - Anti-epileptics: reduces concentration of carbamazepine; carbamazepine reduces primidone concentration but increases metabolite concentration; possibly reduces concentration of ethosuximide; reduces concentration of lamotrigine and tiagabine; primidone concentration possibly reduced by phenytoin, but active metabolite increased and concentration of phenytoin may be altered; primidone concentration possibly increased by valproate, valproate concentration reduced; concentration of primidone possibly reduced by vigabatrin
  - Antifungals: possibly reduces concentration of posaconazole and voriconazole – avoid concomitant use; reduces absorption of griseofulvin (reduced effect)
  - Antimalarials: possibly increased risk of convulsions with chloroquine and hydroxychloroquine; anticonvulsant effect antagonised by mefloquine
  - Antipsychotics: anticonvulsant effect antagonised; metabolism of haloperidol accelerated; possibly reduces aripiprazole concentration – increase aripiprazole dose
  - Antivirals: concentration of indinavir, lopinavir, nelfinavir and saquinavir possibly reduced
  - Calcium-channel blockers: effect of felodipine, isradipine and probably other dihydropyridines, diltiazem and verapamil reduced
  - Ciclosporin: reduces ciclosporin blood levels
  - Corticosteroids: metabolism of corticosteroids accelerated, reduced effect
  - Oestrogens and progestogens: metabolism accelerated, reduced contraceptive effect

**ADMINISTRATION**
- **RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
- **COMMENTS**

RETURN TO CONTENTS
OTHER INFORMATION

- Plasma concentrations of 5–12 mcg/L (23–55 µmol/L) have been loosely correlated with optimum response.

- Partially converted to phenobarbital and phenylethylmalonamide with long half-lives (metabolites may accumulate in renal impairment).

- May cause excessive sedation and osteomalacia.
Procainamide hydrochloride

**CLINICAL USE**

Anti-arrhythmic agent:
- Treatment of ventricular arrhythmias, especially after myocardial infarction
- Atrial tachycardia

**DOSE IN NORMAL RENAL FUNCTION**

- Slow IV injection: 50 mg/min (100 mg with ECG monitoring), repeated at 5-minute intervals until arrhythmia is controlled; max dose 1 g
- Infusion: 500–600 mg over 25–30 minutes with ECG monitoring, then maintenance of 2–6 mg/minute. If required start oral anti-arrhythmics 3–4 hours after infusion

**PHARMACOKINETICS**

- Molecular weight (daltons) 271.8
- % Protein binding 15–20
- % Excreted unchanged in urine 30–70
- Volume of distribution (L/kg) 1.48–4.3
- Half-life – normal/ESRF (hrs) 2.5–5/9.6–11.3

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
<th>Dose as in normal renal function</th>
<th>Normal loading dose. Maintenance dose according to response, lower doses or longer dosage intervals may be required</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>CAPD</th>
<th>Dialysed. Dose as in GFR&lt;10 mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Anti-arrhythmics: amiodarone increases procainamide levels, increased risk of ventricular arrhythmias – avoid concomitant use; increased myocardial depression with other anti-arrhythmics
- Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin – avoid concomitant use; concentration increased by trimethoprim
- Antidepressants: increased risk of ventricular arrhythmias with tricyclics
- Antihistamines: increased risk of ventricular arrhythmias with mizolastine – avoid concomitant use
- Antimalarials: increased risk of ventricular arrhythmias with artemether/lumefantrine – avoid concomitant use
- Antipsychotics: increased risk of ventricular arrhythmias with phenothiazines and any antipsychotics that prolong the QT interval; avoid with amisulpride, pimozide and sertindole
- Atomoxetine: increased risk of ventricular arrhythmias
- Beta-blockers: increased myocardial depression; increased risk of ventricular arrhythmias with sotalol – avoid concomitant use
- 5HT<sub>3</sub> antagonists: increased risk of ventricular arrhythmias with dolasetron – avoid concomitant use; avoid with tropisetron
- Muscle relaxants: enhanced effect of muscle relaxants
- Ulcer-healing drugs: levels increased by cimetidine

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - IV bolus, IV infusion, IM
- **RATE OF ADMINISTRATION**
  - Bolus: 50–100 mg/minute
  - Infusion: 2–6 mg/minute
- **COMMENTS**
  - Stable in glucose 5%
  - Dilute to a concentration of 2 mg/mL and give at a rate of 1–3 mL/minute, or to a
concentration of 4 mg/mL and give at a rate of 0.5–1.5 mL/minute
- Stability of solution can be improved by adding sodium bicarbonate to glucose solution

OTHER INFORMATION
- For optimum response, plasma concentration should be 3–10 mg/L; severe toxicity has been noted at concentrations above 12 mg/L
- Active metabolite is N-acetyl-procainamide (NAPA) which is 80% renally excreted
- Haemofiltration can be used in cases of procainamide poisoning
- Half-life depends on acetylator status of patient
- Can cause systemic lupus erythematosus in up to 30% of patients with long-term use
- CAPD removes 19% of procainamide and 24% of NAPA
Procarbazine

**CLINICAL USE**
Antineoplastic agent:
- Main indication is Hodgkin's disease

**DOSE IN NORMAL RENAL FUNCTION**
250–300 mg daily in divided doses; begin with small doses
Maintenance: 50–150 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 257.8 (as hydrochloride)
- % Protein binding: No data
- % Excreted unchanged in urine: 5
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 10 minutes/Increased

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>20–50</th>
<th>50–100% of dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>10–20</td>
<td>50–100% of dose. Use with caution</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>50–100% of dose. Use with caution</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose in GFR&lt;10 mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Alcohol: may produce a disulfiram reaction
- Antipsychotics: avoid concomitant use with clozapine (increased risk of agranulocytosis)

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- After oral absorption, the drug appears to be rapidly and completely absorbed
- Procarbazine is metabolised to an active alkylating agent by microsomal enzymes in the liver. After 24 hrs up to 70% of a dose is recovered in the urine
- Nadir for bone-marrow depression is 4 weeks with recovery within 6 weeks
- For 48 hours after dose, wear protective clothing to handle urine
- Increased toxicity reported in patients with renal impairment
Prochlorperazine

**CLINICAL USE**
- Nausea and vomiting
- Labyrinthine disorders
- Psychoses
- Severe anxiety

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: 5–10 mg 2–3 times daily
- Buccal: 1–2 tablets twice daily
- IM/IV: 12.5 mg (unlicensed IV)
- Psychoses: Oral: 75–100 mg daily, IM: 12.5–25 mg 2–3 times daily
- Severe anxiety: 15–20 mg daily by mouth, in divided doses; maximum 40 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 373.9
- % Protein binding: 96
- % Excreted unchanged in urine: Minimal
- Volume of distribution (L/kg): 23
- Half-life – normal/ESRF (hrs): 6–9/

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Start with small doses, i.e. 6.25 mg IM or 5 mg orally

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/ VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Anaesthetics: enhanced hypotensive effect
  - Analgesics: increased risk of convulsions with tramadol; enhanced hypotensive and sedative effects with opioids
  - Anti-arrhythmics increased risk of ventricular arrhythmias with anti-arrhythmics that prolong the QT interval, e.g. procainamide, disopyramide and amiodarone – avoid concomitant use with amiodarone
  - Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin – avoid concomitant use
  - Antidepressants: increase concentrations and additive antimuscarinic effects, notably with tricyclics
  - Anti-epileptics: antagonised (convulsive threshold lowered)
  - Antimalarials: avoid concomitant use with artemether/lumefantrine
  - Antipsychotics: increased risk of ventricular arrhythmias with pimozide – avoid concomitant use
  - Antivirals: increased risk of ventricular arrhythmias with pimozide – avoid concomitant use
  - Anti-arrhythmics increased risk of ventricular arrhythmias with anti-arrhythmics that prolong the QT interval, e.g. procainamide, disopyramide and amiodarone – avoid concomitant use with amiodarone
  - Beta-blockers: increased risk of ventricular arrhythmias with sotalol
  - Desferrioxamine: avoid concomitant use
  - Diuretics: enhanced hypotensive effect
  - Lithium: increased risk of extrapyramidal side effects and possibly neurotoxicity
  - Pentamidine: increased risk of ventricular arrhythmias
  - Sibutramine: increased risk of CNS toxicity – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**

**ROUTE**
- IM, IV (unlicensed), oral, buccal

**RATE OF ADMINISTRATION**
- IM or IV over 3–4 minutes

**COMMENTS**
- Unlicensed IV administration methods:
  - Either: dilute with water for injection to 5 times its own volume, and administer slowly over not less than 5 minutes,
  - Or dilute to 1 mg/mL and administer at rate not greater than 1 mg/minute

**OTHER INFORMATION**
- Increased CNS sensitivity in severe renal impairment
## Procyclidine hydrochloride

### CLINICAL USE
- Control of extrapyramidal symptoms
- Acute dystonias

### DOSE IN NORMAL RENAL FUNCTION

**Oral:** 2.5–10 mg 3 times a day; maximum 60 mg daily  
**Acute dystonias:** IM/IV: 5–10 mg

### PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>323.9</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>No data</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>12/–</td>
</tr>
</tbody>
</table>

### DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

### IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs  
- None known

### ADMINISTRATION

**RECONSTITUTION**
- **ROUTE**
  - IV, IM, oral
- **RATE OF ADMINISTRATION**
  - Bolus over 3–5 minutes
- **COMMENTS**
  - Unknown dialysability. Dose as in normal renal function
  - Not dialysed. Dose as in normal renal function
  - Unknown dialysability. Dose as in normal renal function
  - Unknown dialysability. Dose as in normal renal function

**RETURN TO CONTENTS**
Proguanil hydrochloride

**CLINICAL USE**
Malaria chemoprophylaxis

**DOSE IN NORMAL RENAL FUNCTION**
200 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 290.2
- % Protein binding: 75
- % Excreted unchanged in urine: 60
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 20

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–60: 100 mg daily
- 10–20: 50 mg every 48 hours
- <10: 50 mg weekly

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: effect of warfarin possibly enhanced
- Antimalarials: avoid concomitant use with artemether/lumefantrine; increased antifolate effect with pyrimethamine

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral
  - RATE OF ADMINISTRATION
  - COMMENTS

**OTHER INFORMATION**
- Rare reports of haematological changes (e.g. megaloblastic anaemia and pancytopenia) in patients with severe renal impairment
Promazine hydrochloride

**CLINICAL USE**
Antipsychotic for agitation and restlessness

**DOSE IN NORMAL RENAL FUNCTION**
- Psychomotor agitation: 100–200 mg 4 times a day
- Agitation and restlessness in elderly: 25–50 mg 4 times a day

**PHARMACOKINETICS**
As for chlorpromazine
- Molecular weight: 320.9 daltons
- % Protein binding: 95–98%
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): 7–20

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in normal renal function</th>
<th>Dose in normal renal function</th>
<th>Start with low doses and titrate slowly</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antihistamines: enhanced hypotensive effect
- Analgesics: increased risk of convulsions with tramadol; enhanced hypotensive and sedative effects with opioids
- Anti-arrhythmics: increased risk of ventricular arrhythmias with anti-arrhythmics that prolong the QT interval – avoid concomitant use with amiodarone
- Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin – avoid concomitant use
- Antidepressants: increased level of tricyclics (possibly increased risk of ventricular arrhythmias and antimuscarinic side effects)
- Anticonvulsant: antagonises anticonvulsant effect
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: increased risk of ventricular arrhythmias with pimozide – avoid concomitant use
- Antivirals: concentration possibly increased with ritonavir
- Benzodiazepines: increased sedative effect
- Beta-blockers: enhanced hypotensive effect; increased risk of ventricular arrhythmias with sotalol
- Diuretics: enhanced hypotensive effect
- Lithium: increased risk of extrapyramidal side effects and possibly neurotoxicity
- Pentamidine: increased risk of ventricular arrhythmias
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use with drugs that prolong the QT interval

**ADMINISTRATION**

**RECONSTITUTION**

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**

**COMMENTS**

**OTHER INFORMATION**

References:

RETURN TO CONTENTS
Promethazine hydrochloride

**CLINICAL USE**
Antihistamine

**DOSE IN NORMAL RENAL FUNCTION**
Oral: 25 mg at night increased to twice daily, or 10–20 mg 2–3 times a day
Slow IV/IM: 25–100 mg

**PHARMACOKINETICS**
Molecular weight (daltons) 320.9
% Protein binding 76–93
% Excreted unchanged in urine 0
Volume of distribution (L/kg) 13.5
Half-life – normal/ESRF (hrs) 5–14/

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
CAPD Unknown dialysability. Dose as in normal renal function
HD Not dialysed. Dose as in normal renal function
HDF/High flux Unknown dialysability. Dose as in normal renal function
CAV/VVHD Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
● None known

**ADMINISTRATION**
RECONSTITUTION

**ROUTE**
● IV, IM, oral

**RATE OF ADMINISTRATION**
● Bolus over 3–5 minutes

**COMMENTS**
● Administer in 10 mL water for injection for slow IV injection (2.5 mg/mL)

**OTHER INFORMATION**
● Excessive sedation may occur in CKD 5

RETURN TO CONTENTS
Propafenone hydrochloride

**CLINICAL USE**

Anti-arrhythmic agent:
- Ventricular arrhythmias
- Paroxysmal supraventricular tachyarrhythmias, (including paroxysmal atrial flutter or fibrillation, and paroxysmal re-entrant tachycardias involving the AV node or accessory pathway) where standard therapy has failed or is unsuitable

**DOSE IN NORMAL RENAL FUNCTION**

- >70 kg: 150–300 mg 3 times daily
- If <70 kg start with a lower dose

**PHARMACOKINETICS**

- Molecular weight (daltons): 377.9
- % Protein binding: >95
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): 1.9–3
- Half-life – normal/ESRF (hrs): 2–10 (10–32 hours in slow metabolisers)/Unchanged

**DOSE IN RENAL IMPAIRMENT**

- GFR (mL/min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function. Use with caution

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Not dialysed. Dose as in GFR<10mL/min
- HD: Not dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10mL/min
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Anti-arrhythmics: increased myocardial depression with other anti-arrhythmics
- Antibacterials: increased metabolism with rifampicin (reduced effect)
- Anticoagulants: enhanced anticoagulant effect of coumarins
- Antidepressants: increased risk of arrhythmias with tricyclics; metabolism of propafenone possibly inhibited by paroxetine (increased risk of toxicity)
- Antihistamines: increased risk of ventricular arrhythmias with mizolastine—avoid concomitant use
- Antipsychotics: increased risk of ventricular arrhythmias with antipsychotics that prolong the QT interval
- Antivirals: concentration of propafenone increased by amprenavir and ritonavir, increased risk of ventricular arrhythmias – avoid concomitant use
- Beta-blockers: increased myocardial depression; increased concentration of metoprolol and propranolol
- Cardiac glycosides: increased digoxin concentration – halve digoxin dose
- Ciclosporin: possibly increased ciclosporin concentration
- 5HT3 antagonists: increased risk of ventricular arrhythmias with dolasetron – avoid concomitant use; avoid with tropisetron
- Ulcer-healing drugs: levels increased by cimetidine

**ADMINISTRATION**

**RECONSTITUTION**

- ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - COMMENTS

**OTHER INFORMATION**

- Half-life depends on acetylator status of patient
- Ensure that electrolyte disturbances are corrected before commencing treatment
- Metabolised by CYP2D6 isoenzyme
- Therapeutic plasma concentrations are 150–1500 ng/mL
## Propiverine hydrochloride

### CLINICAL USE
- Treatment of urinary frequency, urgency, and incontinence
- Neurogenic bladder instability

### DOSE IN NORMAL RENAL FUNCTION

<table>
<thead>
<tr>
<th>Dose</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 mg</td>
<td>2–4 times a day</td>
</tr>
<tr>
<td>XL: 30 mg</td>
<td>once daily</td>
</tr>
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</table>

### PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>403.9</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>90–95</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>125–473 litres (Average: 279 litres)</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>20</td>
</tr>
</tbody>
</table>

### DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–30</td>
<td>Dose as in normal renal function. Maximum 30 mg daily</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function. Maximum 30 mg daily</td>
<td></td>
</tr>
</tbody>
</table>

### IMPORTANT DRUG INTERACTIONS

Potential interactions with other drugs:
- None known

### ADMINISTRATION

**RECONSTITUTION**

- **ROUTE**
  - Oral

- **RATE OF ADMINISTRATION**
  - 

- **COMMENTS**
  - 

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Return to Contents
Propofol

**CLINICAL USE**
- Induction and maintenance of general anaesthesia
- Sedation of ventilated patients for up to 3 days

**DOSE IN NORMAL RENAL FUNCTION**
- Induction: 1.5–2.5 mg/kg at a rate of 20–40 mg every 10 seconds
- Maintenance: 25–50 mg repeated according to response or 4–12 mg/kg/hour
- Sedation: 0.3–4 mg/kg/hour
- Sedation for surgical and diagnostic procedures: 0.5–1 mg/kg over 1–5 minutes then maintenance: 1.5–4.5 mg/kg/hour or 10–20 mg/kg

**PHARMACOKINETICS**
- Molecular weight (daltons): 178.3
- % Protein binding: >95
- % Excreted unchanged in urine: <0.3
- Volume of distribution (L/kg): 8–19

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux: Unlikely to be dialysed. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Adrenergic-neurone blockers: enhanced hypotensive effect
- Antihypertensives: enhanced hypotensive effect
- Antidepressants: avoid MAOIs for 2 weeks before surgery; increased risk of arrhythmias and hypotension with tricyclics
- Antipsychotics: enhanced hypotensive effect
- Muscle relaxants: increased risk of myocardial depression and bradycardia with suxamethonium

**ADMINISTRATION**
- **RECONSTITUTION**
- **ROUTE**
  - IV
- **RATE OF ADMINISTRATION**
  - See local protocols
- **COMMENTS**

RETURN TO CONTENTS
Propranolol hydrochloride

**Clinical Use**

Beta-adrenoceptor blocker:
- Hypertension
- Phaeochromocytoma
- Angina
- Arrhythmias
- Anxiety
- Migraine prophylaxis

**Dose in Normal Renal Function**

- Hypertension: 40–160 mg twice daily
- Phaeochromocytoma: 60 mg daily for 3 days before surgery, or 30 mg daily if unsuitable for surgery
- Angina: 120–240 mg daily in divided doses
- Arrhythmias: 10–40 mg 3–4 times daily
- Anxiety: 40 mg 1–3 times daily
- Prophylaxis after an MI: 40 mg 4 times daily then 80 mg twice daily
- Migraine and essential tremor: 80–160 mg daily
- IV: 1 mg over 1 minute repeated after 2 minutes to a maximum of 10 mg (5 mg with anaesthesia)

**Pharmacokinetics**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>295.8</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>80–95</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>4</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>2–6/Unchanged</td>
</tr>
</tbody>
</table>

**Dose in Renal Impairment**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td>Start with small doses and increase according to response</td>
</tr>
<tr>
<td>10–20</td>
<td>Start with small doses and increase according to response</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Start with small doses and increase according to response</td>
<td></td>
</tr>
</tbody>
</table>

**Dose in Patients Undergoing Renal Replacement Therapies**

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**Important Drug Interactions**

Potentially hazardous interactions with other drugs:
- Anaesthetics: enhanced hypotensive effect; risk of bupivacaine toxicity increased
- Analgesics: NSAIDs antagonise hypotensive effect
- Anti-arrhythmics: increased risk of myocardial depression and bradycardia; increased risk of bradycardia, myocardial depression and AV block with amiodarone; concentration increased by propafenone
- Antibacterials: metabolism increased by rifampicin
- Antidepressants: enhanced hypotensive effect with MAOIs; concentration increased by fluvoxamine; concentration of imipramine increased
- Antihypertensives: enhanced hypotensive effect; increased risk of withdrawal hypertension with clonidine; increased risk of first dose hypotensive effect with post-synaptic alpha-blockers such as prazosin
- Antimalarials: increased risk of bradycardia with mefloquine
- Antipsychotics enhanced hypotensive effect with phenothiazines; concentration of both drugs increased with chlorpromazine
- Calcium-channel blockers: increased risk of bradycardia and AV block with diltiazem; hypotension and heart failure possible with nifedipine and nisoldipine; asystole, severe hypotension and heart failure with verapamil
- Diuretics: enhanced hypotensive effect
- Moxisylyte: possible severe postural hypotension
It is not licensed for use by anyone else.

- Sympathomimetics: severe hypertension with adrenaline and noradrenaline and possibly with dobutamine
- Tropisetron: increased risk of ventricular arrhythmias – use with caution

**ADMINISTRATION**

<table>
<thead>
<tr>
<th>RECONSTITUTION</th>
<th>RATE OF ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral, IV</td>
<td></td>
</tr>
</tbody>
</table>

**OTHER INFORMATION**

- Non-selective active metabolites accumulate in renal impairment. Consider metoprolol or atenolol
- May reduce renal blood flow in severe renal impairment
Propylthiouracil

**CLINICAL USE**
Hyperthyroidism

**DOSE IN NORMAL RENAL FUNCTION**
Initially: 200–400 mg daily
Maintenance dose: 50–150 mg daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Molecular weight (daltons)</th>
<th>170.2</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Protein binding</td>
<td>80</td>
</tr>
<tr>
<td>% Excreted</td>
<td>&lt;2</td>
</tr>
<tr>
<td>unchanged in urine</td>
<td></td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.3–0.4</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1–2/8.5</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>20–50</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>10–20</td>
<td>75% of normal dose and titrate to response</td>
</tr>
<tr>
<td></td>
<td>&lt;10</td>
<td>50% of normal dose and titrate to response</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unknown dialysability. Dose as in GFR=10–20 mL/min</td>
</tr>
<tr>
<td>VVHD</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
● None known

**ADMINISTRATION**

**REconstitution**

● Oral

**Rate of Administration**

● Oral

**Other Information**

● Renally impaired patients are at a greater risk of cardiotoxicity and leucopenia
Protamine sulphate

**CLINICAL USE**
Counteract anticoagulant effect of heparin

**DOSE IN NORMAL RENAL FUNCTION**
Depends on time since stopping IV/subcutaneous heparin and dose of heparin given

**PHARMACOKINETICS**
- Molecular weight (daltons): Approx 4500
- % Protein binding: 1
- % Excreted unchanged in urine: No data
- Volume of distribution (L/kg): 12.3 litres
- Half-life – normal/ESRF (hrs): 7.4 minutes/

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/MIN):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Unknown dialysability. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
- RATE OF ADMINISTRATION
  - 5 mg/minute

**OTHER INFORMATION**
- Counteracting the anticoagulant effect of heparin during extra-corporeal treatments requires approximately 1.5 mg protamine per 100 IU heparin
- Most clinicians recommend a dose of 1–1.5 mg protamine sulphate for each 100 units heparin given depending on the length of time since heparin administration
- May be used topically to stop bleeding fistulae
Pseudoephedrine hydrochloride

**CLINICAL USE**
Nasal decongestant

**DOSE IN NORMAL RENAL FUNCTION**
60mg 4 times a day

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>201.7</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>No data</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>90–98</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>2–3</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>5.5 (depends on pH of urine)</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td>Use caution</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
<td>Use caution</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
<td>Use caution</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely dialysability. Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>CAV/ VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Adrenergic neurone blockers: antagonise hypotensive effect of adrenergic neurone blockers
- Antibacterials: risk of hypertensive crisis with linezolid
- Antidepressants: risk of hypertensive crisis with MAOIs and moclobemide
- Dopaminergics: avoid concomitant use with rasagiline

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  -

**OTHER INFORMATION**

- 5–20% is removed by haemodialysis
- Increased risk of developing hypertension in patients with GFR<20mL/min
**Pyrazinamide (unlicensed product)**

### CLINICAL USE
Antimicrobial agent for tuberculosis

### DOSE IN NORMAL RENAL FUNCTION
1.5–2 g per day

### PHARMACOKINETICS
- Molecular weight (daltons) 123.1
- % Protein binding 10
- % Excreted unchanged in urine 4
- Volume of distribution (L/kg) 0.75–1.3
- Half-life – normal/ESRF (hrs) 9–10/26

### DOSE IN RENAL IMPAIRMENT
- GFR (mL/min)
  - 20–50 Dose as in normal renal function
  - 10–20 Dose as in normal renal function
  - <10 Use 50–100% of dose

### DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD Not dialysed. Dose as in GFR<10 mL/min
- HD 50–100% dialysed. Dose as in GFR<10 mL/min or 25–30 mg/kg post dialysis
- HDF/High flux Dialysed. Dose as in GFR<10 mL/min or 25–30 mg/kg post dialysis
- CAV/VVHD Unknown dialysability. Dose as in normal renal function

### IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Ciclosporin: on limited evidence, pyrazinamide appears to reduce ciclosporin levels

### ADMINISTRATION
- RECONSTITUTION
  - –
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - –
- COMMENTS
  - –

### OTHER INFORMATION
- Available from IDIS on a named patient basis
- Can precipitate gout as impairs urate excretion

References:
Pyridostigmine bromide

CLINICAL USE
Myasthenia gravis

DOSE IN NORMAL RENAL FUNCTION
0.3–1.2 g per day in divided doses

PHARMACOKINETICS
Molecular weight (daltons) 261.1
% Protein binding No data
% Excreted unchanged in urine 80–90
Volume of distribution (L/kg) 0.8–1.4
Half-life – normal/ESRF (hrs) 3–4/6

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>% of daily dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–30</td>
<td>35% of daily dose</td>
</tr>
<tr>
<td>10–20</td>
<td>35% of daily dose</td>
</tr>
<tr>
<td>&lt;10</td>
<td>20% of daily dose</td>
</tr>
</tbody>
</table>

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● Aminoglycosides, clindamycin and polymyxins antagonise effects of pyridostigmine

ADMINISTRATION

RECONSTITUTION –
ROUTE ● Oral
RATE OF ADMINISTRATION –
COMMENTS –
Pyridoxine hydrochloride

**CLINICAL USE**

Vitamin B₆

**DOSE IN NORMAL RENAL FUNCTION**

- Deficiency: 20–50 mg up to 3 times daily
- Prophylaxis against isoniazid neuropathy: 10–20 mg daily; 50 mg 3 times daily for treatment
- Idiopathic sideroblastic anaemia: 100–400 mg daily in divided doses
- Premenstrual syndrome: 50–100 mg daily

**PHARMACOKINETICS**

- Molecular weight (daltons): 205.6
- % Protein binding: High (as pyridoxal and pyridoxal phosphate)
- % Excreted unchanged in urine: No data
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 15–20 days

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

RECONSTITUTION
- ROUTE
  - Oral
 RATE OF ADMINISTRATION
- COMMENTS
- OTHER INFORMATION
  - Long-term use of pyridoxine in doses greater than 200 mg daily has been associated with neuropathy
Pyrimethamine

**CLINICAL USE**
Antiprotozoal agent:
- Malaria
- Toxoplasmosis

**DOSE IN NORMAL RENAL FUNCTION**
- Malaria: used in dual drug combinations
- Malaria prophylaxis: 25 mg weekly
- Toxoplasmosis: 100–200 mg daily for 2–3 days then 25–100 mg daily for 2–6 weeks (in combination with sulfadiazine)

**PHARMACOKINETICS**
- Molecular weight (daltons): 248.7
- % Protein binding: 80–90
- % Excreted unchanged in urine: 15–30
- Volume of distribution (L/kg): 2
- Half-life – normal/ESRF (hrs): 35–175/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs:
- Increased antifolate effect with sulphonamides, trimethoprim and methotrexate
- Anti-epileptics: anticonvulsant effect antagonised; increased antifolate effect with phenytoin
- Antimalarials: avoid concomitant use with artemether/lumefantrine; increased antifolate effect with proguanil

**ADMINISTRATION**
- **RECONSTITUTION**
  - **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**
  -

**OTHER INFORMATION**
- Pyrimethamine should always be administered with a folate supplement to reduce the risk of bone marrow depression
Quetiapine

**CLINICAL USE**
- Schizophrenia
- Mania

**DOSE IN NORMAL RENAL FUNCTION**
- Schizophrenia: 50–750 mg daily in 2 divided doses
- Mania: 50–400 mg twice daily

**PHARMACOKINETICS**
- Molecular weight: 883.1 (as fumarate)
- % Protein binding: 83
- % Excreted unchanged in urine: <5
- Volume of distribution (L/kg): 6–14

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Initial dose and increments (mg/day)</th>
<th>According to response</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>25 mg/day and increase in increments of 25–50 mg/day</td>
<td>according to response</td>
</tr>
<tr>
<td>10–20</td>
<td>25 mg/day and increase in increments of 25–50 mg/day</td>
<td>according to response</td>
</tr>
<tr>
<td>&lt;10</td>
<td>25 mg/day and increase in increments of 25–50 mg/day</td>
<td>according to response</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**
  - Unknown dialysability. Dose as in GFR<10mL/min
- **HD**
  - Unknown dialysability. Dose as in GFR<10mL/min
- **HDF/High flux**
  - Unknown dialysability. Dose as in GFR<10mL/min
- **CAV/VVHD**
  - Unknown dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs:
  - Anaesthetics: enhanced hypotensive effect
  - Analgesics: increased risk of convulsions with tramadol; enhanced hypotensive and sedative effects with opioids
  - Antibacterials: concentration possibly increased by macrolides – reduce dose of quetiapine
  - Antidepressants: concentration of tricyclics possibly increased
  - Anti-epileptics: antagonism of convulsive threshold; metabolism accelerated by carbamazepine and phenytoin
  - Antifungals: concentration possibly increased by imidazoles and triazoles – reduce quetiapine dose
  - Antimalarials: manufacturer advises avoid use with artesunate and lumefantrine
  - Antivirals: ritonavir possibly increases concentration
  - Anxiolytics and hypnotics: enhanced sedative effects
  - Sibutramine: increased risk of CNS toxicity – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- Plasma clearance is reduced by 25% in severe renal impairment
- Absorption is increased by food so it should be taken consistently either with or without food
Quinagolide

**CLINICAL USE**
Hyperprolactinaemia

**DOSE IN NORMAL RENAL FUNCTION**
75–150 micrograms daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>432 (as hydrochloride)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>90</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>Very little, most is excreted as metabolites in faeces and urine</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>100 litres</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>17</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Use with caution Start with low dose and titrate according to response</td>
</tr>
<tr>
<td>10–20</td>
<td>Use with caution Start with low dose and titrate according to response</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Use with caution Start with low dose and titrate according to response</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unknown dialysability. Dose as in GFR=10–20mL/min</td>
</tr>
<tr>
<td>VVHD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- Manufacturer advises to avoid use in renal impairment due to lack of data
- Renally excreted metabolites (glucuronide and sulphate) are inactive
Quinapril

**CLINICAL USE**
Angiotensin converting enzyme inhibitor:
- Hypertension
- Heart failure

**DOSE IN NORMAL RENAL FUNCTION**
- 2.5–80 mg daily in 1–2 divided doses
- In heart failure 40 mg is normal maximum dose

**PHARMACOKINETICS**
- Molecular weight (daltons) 475 (as hydrochloride)
- % Protein binding 97
- % Excreted unchanged in urine 30
- Volume of distribution (L/kg) 1.5
- Half-life – normal/ESRF (hrs) 1/12–14

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50 Start with low dose, adjust according to response
- 10–20 Start with low dose, adjust according to response
- <10 Start with low dose, adjust according to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Not dialysed. Dose as in GFR<10 mL/min
- HD 25% dialysed. Dose as in GFR<10 mL/min
- HDF/High flux Dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD Unknown dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Analgesics: antagonism of hypotensive effect and increased risk of renal impairment with NSAIDs; hyperkalaemia with ketorolac and other NSAIDs
- Ciclosporin: increased risk of hyperkalaemia and nephrotoxicity
- Diuretics: enhanced hypotensive effect; hyperkalaemia with potassium-sparing diuretics
- Epoetin: increased risk of hyperkalaemia; antagonism of hypotensive effect
- Lithium: reduced excretion (possibility of enhanced lithium toxicity)
- Potassium salts: increased risk of hyperkalaemia
- Tacrolimus: increased risk of hyperkalaemia and nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- Renal failure has been reported with ACE inhibitors: mainly in patients with renal artery stenosis, post renal transplant and those with severe congestive heart failure
- A high incidence of anaphylactoid reactions has been reported in patients dialysed with high-flux polyacrylonitrile membranes and treated concomitantly with an ACE inhibitor – this combination should be avoided
- Hyperkalaemia and other side effects more common in patients with renal impairment
- Close monitoring of renal function during therapy is necessary in those patients with known renal insufficiency

RETURN TO CONTENTS
Quinine

CLINICAL USE

- Severe and complicated falciparum malaria
- Nocturnal cramp

DOSE IN NORMAL RENAL FUNCTION

- IV: Quinine dihydrochloride: Loading dose 20 mg/kg to maximum 1.4 g, then after 8 hours, maintenance 10 mg/kg (up to maximum 700 mg) 8 hourly, reduced to 5–7 mg/kg if parenteral treatment required for more than 48 hours
- Oral: Quinine sulphate 600 mg every 8 hours for 5–7 days
- Nocturnal cramp: Quinine sulphate 200–300 mg at night

PHARMACOKINETICS

Molecular weight (daltons) 324.4 (397.3 as dihydrochloride); (782.9 as sulphate)
% Protein binding 70–90
% Excreted unchanged in urine 5–20
Volume of distribution (L/kg) 2.5–7.1
Half-life – normal/ESRF (hrs) 11 (healthy), 18 (malaria)/26

DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)

20–50 Malaria: 5–7 mg/kg every 8 hours Cramp: Dose as in normal renal function
10–20 Malaria: 5–7 mg/kg every 8–12 hours Cramp: Dose as in normal renal function
<10 Malaria: 5–7 mg/kg every 24 hours Cramp: Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

- CAPD: Dialysed. Dose as in GFR<10mL/min
- HD: Dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10mL/min

IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs
- Anti-arrhythmics: flecainide levels increased; increased risk of ventricular arrhythmias with amiodarone – avoid concomitant use
- Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin – avoid concomitant use
- Antimalarials: increased risk of convulsions with mefloquine; avoid concomitant use with arteether/lumefantrine
- Antipsychotics: increased risk of ventricular arrhythmias with pimozide – avoid concomitant use
- Cardiac glycosides: levels of digoxin increased (halve maintenance dose)
- Ciclosporin: decreased ciclosporin levels reported
- Cimetidine: may increase plasma levels of quinine

ADMINISTRATION

RECONSTITUTION

ROUTE

- IV infusion, oral

RATE OF ADMINISTRATION

- 4 hours

COMMENTS

- Add to sodium chloride 0.9% or glucose 5% for infusion
- Loading dose of 20 mg/kg may be required in some cases (refer to specialist treatment). Not to be given if patient has had quinine or mefloquine in previous 12–24 hours

OTHER INFORMATION

- Quinine dihydrochloride injection is available as a special order
- Monitor for signs of cardiotoxicity
- Give doses after haemodialysis on dialysis days
- Monitor quinine levels if patient exhibits any symptoms of toxicity
Rabeprazole sodium

**CLINICAL USE**
Gastric acid suppression

**DOSE IN NORMAL RENAL FUNCTION**
10–120 mg daily, doses >100 mg in 2 divided doses

**PHARMACOKINETICS**
- Molecular weight (daltons): 381.4
- % Protein binding: 97
- % Excreted unchanged in urine: 0 (90 as metabolites)
- Volume of distribution (L/kg): 0.34
- Half-life – normal/ESRF (hrs): 0.7–1.5/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**: Unlikely to be dialysed. Dose as in normal renal function
- **HD**: Not dialysed. Dose as in normal renal function
- **HDF/High flux**: Unlikely to be dialysed. Dose as in normal renal function
- **CAV/VVHD**: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antifungals: absorption of itraconazole and ketoconazole reduced

**ADMINISTRATION**
- **RECONSTITUTION**
  - **ROUTE**: Oral
  - **RATE OF ADMINISTRATION**
    - **COMMENTS**
    - **OTHER INFORMATION**
      - Interstitial nephritis has been reported with rabeprazole
# Raloxifene hydrochloride

## CLINICAL USE
Treatment and prevention of osteoporosis in post-menopausal women

## IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Anticoagulants: antagonism of anticoagulant effect of coumarins
- Colestyramine: reduced absorption of raloxifene – avoid concomitant use

## ADMINISTRATION

### RECONSTITUTION
- **ROUTE**
  - Oral

### RATE OF ADMINISTRATION
- **COMMENTS**
  -

## PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>510</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>98–99</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;0.2</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>2348</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>27.7/Unchanged</td>
</tr>
</tbody>
</table>

## DOSE IN NORMAL RENAL FUNCTION
- 60 mg daily

## DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

## DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>VVHD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

## OTHER INFORMATION
- There are case reports of it being beneficial in females on haemodialysis and also a benefit to the lipid profile. (Hernandez E, Valera R, Alonzo E, et al. Effects of raloxifene on bone metabolism and serum lipids in post-menopausal women on chronic haemodialysis. *Kidney Int*. 2003; 63(6): 2269–74.)
- This study showed that raloxifene could reduce vertebral fractures although they were more likely to suffer from side effects. (Ishani A, Blackwell T, Jamal SA, et al. The effect of raloxifene treatment in post-menopausal women with CKD. *J Am Soc Nephrol*. 2008; 19:1430–8.)
- Manufacturer advises use is contraindicated in severe renal impairment due to lack of data rather than known toxicity
- < 6% of dose is excreted in the urine
Raltitrexed

**CLINICAL USE**
Treatment of colorectal cancer when fluorouracil and folinic acid cannot be used

**DOSE IN NORMAL RENAL FUNCTION**
3 mg/m² every 3 weeks

**PHARMACOKINETICS**
- Molecular weight (daltons) 458.5
- % Protein binding 93
- % Excreted unchanged in urine 40–50
- Volume of distribution (L/kg) 548 litres
- Half-life – normal/ESRF (hrs) 198/Increased

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>55–65</td>
<td>Use 75% of the dose (2.25 mg/m²) every 4 weeks</td>
</tr>
<tr>
<td>25–54</td>
<td>Use 50% of the dose (1.5 mg/m²) every 4 weeks</td>
</tr>
<tr>
<td>&lt;25</td>
<td>Avoid. See ‘Other Information’</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;25mL/min.</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;25mL/min.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;25mL/min.</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;25mL/min.</td>
</tr>
<tr>
<td>VVHD</td>
<td>GFR&lt;25mL/min.</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Folic and folinic acid: impairs cytotoxic action

**ADMINISTRATION**

**RECONSTITUTION**
- 4 mL water for injection

**ROUTE**
- IV infusion

**RATE OF ADMINISTRATION**
- Over 15 minutes

**COMMENTS**
- Dilute in 50–250 ml sodium chloride 0.9% or glucose 5%
- Stable for 24 hours at 2–8°C

**OTHER INFORMATION**
- Doses above 3 mg/m² have an increased incidence of life-threatening/fatal toxicity
- Increased risk of treatment-related toxicity if CrCl<65 mL/min
- Anecdotal reports of using 30–40% of the dose every 4 weeks in patients with severe renal impairment and closely monitoring haematological parameters. Risk of severe and prolonged side effects – use if risk of not treating the patient outweighs the risk of adverse effects
- Not metabolised. 40–50% is excreted unchanged in the urine and 15% of dose is excreted in the faeces over a 10-day period. Active tubular secretion may contribute to the renal excretion
Ramipril

**CLINICAL USE**

Angiotensin-converting enzyme inhibitor:
- Hypertension
- Secondary prevention of myocardial infarction (MI), stroke or cardiovascular death
- Heart failure

**DOSE IN NORMAL RENAL FUNCTION**

1.25–10 mg once a day
Prophylaxis after a MI: 2.5–5 mg twice daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>416.5</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>56 (as ramiprilat)</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;2</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1.2</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>13–17/Increased (as ramiprilat)</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in normal renal function</th>
<th>Initial dose 1.25 mg daily and increase according to response</th>
<th>Initial dose 1.25 mg daily and increase according to response</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Initial dose 1.25 mg daily and increase according to response</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Initial dose 1.25 mg daily and increase according to response</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapeutic Modality</th>
<th>Dose as in normal renal function</th>
<th>Initial dose 1.25 mg daily and increase according to response</th>
<th>Initial dose 1.25 mg daily and increase according to response</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose as in GFR=10–20 mL/min</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Analgesics: antagonism of hypotensive effect and increased risk of renal impairment with NSAIDs; hyperkalaemia with ketorolac and other NSAIDs
- Ciclosporin: increased risk of hyperkalaemia and nephrotoxicity
- Diuretics: enhanced hypotensive effect; hyperkalaemia with potassium-sparing diuretics
- Epoetin: increased risk of hyperkalaemia; antagonism of hypotensive effect
- Lithium: reduced excretion (possibility of enhanced lithium toxicity)
- Potassium salts: increased risk of hyperkalaemia
- Tacrolimus: increased risk of hyperkalaemia and nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**

- Metabolised to active metabolite, ramiprilat
- Renal failure has been reported in association with ACE inhibitors in patients with renal artery stenosis, post renal transplant, and those with congestive heart failure
- A high incidence of anaphylactoid reactions has been reported in patients dialysed with high-flux polyacrylonitrile membranes and treated concomitantly with an ACE inhibitor – this combination should therefore be avoided
- Hyperkalaemia and other side effects more common in patients with impaired renal function
- Close monitoring of renal function during therapy is necessary in those patients with known renal insufficiency
- Normal doses have been used in CKD 5
Ranitidine

**CLINICAL USE**

H₂ antagonist:
- Conditions associated with hyperacidity

**DOSE IN NORMAL RENAL FUNCTION**

- Oral: 150–300 mg once or twice daily
- Zollinger Ellison: 150 mg 3 times daily up to 6 g/day
- IM/Slow IV injection: 50 mg every 6–8 hours
- IV infusion: 25 mg/hour for 2 hours, 6–8 hourly; or for stress ulceration prophylaxis 125–250 mcg/kg/hour

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>314.4</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>15</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>Oral: 30–35; IV: 80</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1.4</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>2–3/6–9</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>50–100% of normal dose</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Probably dialysed. 50 mg every 8–12 hours. Oral: dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Alpha-blockers: effects of tolazoline antagonised
- Antifungals: absorption of itraconazole and ketoconazole reduced
- Ciclosporin: may increase or not change ciclosporin levels; nephrotoxicity, additive hepatotoxicity and thrombocytopenia reported

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral, IV peripherally, IM (undiluted)
- **RATE OF ADMINISTRATION**
  - Bolus: 50 mg made up to 20 mL, over at least 2 minutes
  - Intermittent infusion: 50 mg to 100 mL of appropriate intravenous solution run over 2 hours
  - Continuous infusion: required dose in 250 mL of intravenous fluid over 24 hours

**COMMENTS**

- Compatible with sodium chloride 0.9%, glucose 5% and other fluids
- Admixtures stable for 24 hours
- Minimum volume: can be used undiluted as a bolus over at least 2 minutes. (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006)

**OTHER INFORMATION**

- In CKD 5 usually twice daily for IV preparation and normal dose for oral

References:
1. Dose from CVVH Initial Drug Dosing Guidelines on [www.thedrugmonitor.com](http://www.thedrugmonitor.com)
Rasagiline

**CLINICAL USE**
Treatment of Parkinson’s disease

**DOSE IN NORMAL RENAL FUNCTION**
1 mg daily

**PHARMACOKINETICS**
- Molecular weight: 267.3 (as mesilate)
- % Protein binding: 60–70
- % Excreted unchanged in urine: <1
- Volume of distribution: 243 litres
- Half-life – normal/ESRF (hrs): 0.6–2/unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min): 20–50 Dose as in normal renal function
- 10–20 Dose as in normal renal function
- <10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Unknown dialysability. Dose as in normal renal function
- HDF/High flux: Likely to be dialysed. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: avoid concomitant use with dextromethorphan; avoid concomitant use with pethidine (risk of serious adverse reactions) – allow at least 14 days before starting pethidine
- Antidepressants: avoid concomitant use with other MAOIs (can lead to hypertensive crisis) – allow at least 14 days before starting a MAOI; avoid concomitant use with fluoxetine and fluvoxamine; allow 5 weeks between stopping fluoxetine and starting rasagiline; allow 14 days between stopping rasagiline and starting fluoxetine or fluvoxamine; increased CNS toxicity with SSRIs and tricyclics
- Sympathomimetics: concomitant use is not recommended

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**
  -

**OTHER INFORMATION**
- Rasagiline is an irreversible selective inhibitor of monoamine oxidase type B
Rasburicase

**CLINICAL USE**
Prophylaxis and treatment of acute hyperuricaemia with initial chemotherapy for haematological malignancy

**DOSE IN NORMAL RENAL FUNCTION**
200 mcg/kg once daily for up to 7 days

**PHARMACOKINETICS**
- Molecular weight: 34 000 (daltons)
- % Protein binding: 0
- % Excreted unchanged in urine: 0
- Volume of distribution: 0.11–0.127 (L/kg)
- Half-life – normal/ESRF (hrs): 19/–

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux: Unlikely to be dialysed. Dose as in normal renal function
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- With solvent provided
- IV

**RATE OF ADMINISTRATION**
- Over 30 minutes

**COMMENTS**
- Add appropriate volume to 50 mL sodium chloride 0.9%

**OTHER INFORMATION**
- Renal elimination of rasburicase is considered to be a minor pathway for rasburicase clearance
- Rasburicase is a protein; it is expected that metabolic degradation will follow the pathways of other proteins, i.e. peptide hydrolysis
- After infusion of rasburicase at a dose of 0.20 mg/kg/day, steady state is achieved at day 2–3
Reboxetine

**CLINICAL USE**
Antidepressant

**DOSE IN NORMAL RENAL FUNCTION**
4–5 mg twice daily; maximum 12 mg daily

**PHARMACOKINETICS**
- Molecular weight: 409.5 (as mesilate)
- % Protein binding: 97 (92% in elderly)
- % Excreted unchanged in urine: 10
- Volume of distribution (L/kg): 26–63 litres
- Half-life – normal/ESRF (hrs): 13/26

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: 2 mg twice daily and adjust according to response
  - <10: 2 mg twice daily and adjust according to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR<10 mL/min
- HD: Unknown dialysability. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV: Unknown dialysability. Dose as in GFR=10–20 mL/min
- VVHD: Unknown dialysability. Dose as in

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: avoid concomitant use with macrolides and linezolid
- Antidepressants: risk of increased toxicity with concomitant use with MAOI’s; avoid concomitant use with fluvoxamine
- Antifungals: avoid concomitant use with imidazoles and triazoles
- Antimalarials: avoid concomitant use with artemether with lumefantrine
- Ciclosporin: use with caution as high concentrations of reboxetine inhibit CYP3A4 and CYP2D6
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - COMMENTS
  -

RETURN TO CONTENTS
Remifentanil

**CLINICAL USE**
- Analgesic
- Induction of anaesthesia

**DOSE IN NORMAL RENAL FUNCTION**
- Induction: 0.5–1 microgram/kg/min
- Maintenance:
  - Ventilated patients: 0.05–2 mcg/kg/min
  - Spontaneous respiration: 25–100 nanograms/kg/min
- Analgesia and sedation in ventilated, intensive care patients: 6–740 nanograms/kg/minute
- Additional analgesia during painful procedures in ventilated, intensive care patients: 100–750 nanograms/kg/minute

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>412.9 (as hydrochloride)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>70</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>95 (as metabolites)</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.35</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>3–10 minutes (biological activity)/unchanged Terminal elimination 10–20 minutes</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anti-arrhythmics: delayed absorption of mexiletine
- Antidepressants: possible CNS excitation or depression (hypertension or hypotension) in patients also receiving MAOIs (including moclobemide) – avoid concomitant use; possibly increased sedative effects with tricyclics
- Antipsychotics: enhanced sedative and hypotensive effect
- Antivirals: concentration possibly increased by ritonavir (risk of toxicity) – avoid
- Sodium oxybate: enhanced effect of sodium oxybate – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- To 1 mg/mL with infusion fluid

**ROUTE**
- IV

**RATE OF ADMINISTRATION**
- Dependent on indication

**COMMENTS**
- Dilute to 20–250 mcg/mL with glucose 5%, sodium chloride 0.9% or water for injection; usually 50 micrograms/mL for general anaesthesia

**OTHER INFORMATION**
- Half-life of metabolite is increased to 30 hours in renal failure compared with 90 minutes in patients with normal renal function
- Metabolite is essentially inactive
- Remifentanil would be expected to be metabolised before patient needs to be dialysed
- 25–35% of metabolites are removed by dialysis

RETURN TO CONTENTS
Repaglinide

**CLINICAL USE**
Type 2 diabetes mellitus

**DOSE IN NORMAL RENAL FUNCTION**
0.5–16 mg daily, doses given 15–30 minutes before a meal; doses up to 4 mg can be given as a single dose

**PHARMACOKINETICS**
- Molecular weight: 452.6 daltons
- % Protein binding: >98%
- % Excreted unchanged in urine: <8 (mainly as metabolites)
- Volume of distribution: 30 litres
- Half-life – normal/ESRF (hrs): 1/2

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/min)**
  - 30–80: Dose as in normal renal function
  - 5–29: Start at a low dose and gradually increase according to response
  - <5: Start at a low dose and gradually increase according to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in GFR<5 mL/min.
- HD: Not dialysed. Dose as in GFR<5 mL/min.
- HDF/High flux: Not dialysed. Dose as in GFR<5 mL/min.
- CAV: Unlikely to be dialysed. Dose as in GFR=5–29 mL/min.

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: effects enhanced by clarithromycin and possibly trimethoprim; hypoglycaemic effect antagonised by rifampicin
- Antifungals: effect possibly enhanced by itraconazole
- Ciclosporin: possibly enhanced hypoglycaemic effect
- Lipid-lowering agents: increased risk of severe hypoglycaemia with gemfibrozil – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- Route
  - Oral

**RATE OF ADMINISTRATION**
- Comments

**OTHER INFORMATION**
- Major route of elimination is hepatic metabolism to inactive metabolites which are excreted via the bile
Reteplase

**CLINICAL USE**
Thrombolytic, used for acute myocardial infarction

**DOSE IN NORMAL RENAL FUNCTION**
10 units over 2 minutes; second dose of 10 units given 30 minutes later

**PHARMACOKINETICS**
- Molecular weight (daltons): 39571.1
- % Protein binding: No data
- % Excreted unchanged in urine: Negligible
- Volume of distribution (L/kg): 6–6.5 litres
- Half-life – normal/ESRF (hrs): Fibrinolytic half-life is 1.6 hours./Increased Dominant (α) half-life is 14.6 ± 6.7 minutes Terminal (β) half-life is 1.6 hrs ± 39 minutes

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min) 20–50: Dose as in normal renal function
- GFR (mL/min) 10–20: Dose as in normal renal function
- GFR (mL/min) <10: Dose as in normal renal function. Use with caution

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR<10mL/min
- HD: Unknown dialysability. Dose as in GFR<10mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10mL/min
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antiplatelets, heparin, vitamin K antagonists: increased risk of bleeding

**ADMINISTRATION**
- RECONSTITUTION
  - With diluent provided
- ROUTE
  - Slow IV
- RATE OF ADMINISTRATION
  - Over not more than 2 minutes
- COMMENTS
  - Use immediately once reconstituted
  - Do not mix with heparin in the same line

**OTHER INFORMATION**
- Heparin and aspirin should be given before and after reteplase therapy to reduce the risk of re-thrombosis but may increase the risk of bleeding
- Half-life is increased in severe renal failure in animal models
- Possible increased risk of bleeding complications in severe renal impairment
Ribavirin (tribavirin)

**CLINICAL USE**

Antiviral agent:
- Severe respiratory syncytial virus bronchiolitis
- Chronic Hepatitis C in combination with Interferon α or Peginterferon α

**DOSE IN NORMAL RENAL FUNCTION**

Bronchiolitis: 6g nebulised daily for 12–18 hours for 3–7 days

Hepatitis C:
- Rebetol: <65 kg: 400mg twice daily 65–85 kg: 400mg in the morning and 600mg at 6 pm >85 kg: 600mg twice daily
- Copegus:
  - <75 kg: 400mg in the morning and 600mg at 6 pm
  - >75 kg: 600mg twice daily

**PHARMACOKINETICS**

- Molecular weight (daltons): 244.2
- % Protein binding: 0
- % Excreted unchanged in urine: 10–40
- Volume of distribution (L/kg): Nebulised: 647 litres; Oral: 5000 litres

**DOSE IN RENAL IMPAIRMENT**

20–50 GFR (mL/min)
- Dose as in normal renal function. Avoid oral. See ‘Other Information’

10–20 GFR (mL/min)
- Dose as in normal renal function. Avoid oral. See ‘Other Information’

<10 GFR (mL/min)
- Dose as in normal renal function. Avoid oral. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/
- VVHD: GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Antivirals: ribavirin may antagonise the effects of stavudine; increased side effects with didanosine

**ADMINISTRATION**

- RECONSTITUTION
  - Dissolve contents of one vial in water for injection
- ROUTE
  - Nebulised, oral, IV
- RATE OF ADMINISTRATION
  - IV: over 10–15 minutes
- COMMENTS
  - Nebulised: further dilute to a volume of 300mL

**OTHER INFORMATION**

- Oral: Administer ribavirin with interferon α 3 MIU 3 times a week or peginterferon α 1.5 mcg/kg/week
- Contraindicated by the company due to reduced clearance leading to increased side effects
- Ribavirin is metabolised by reversible phosphorylation and a degradative pathway involving deribosylation and amide hydrolysis to produce renally excreted active metabolites
- There are two studies using ribavirin (200–400 mg a day) in combination with interferon in haemodialysis and peritoneal dialysis patients. Anaemia was one of the main problems, resulting in either increased doses of erythropoietin or discontinuation of ribavirin therapy. Most patients were stabilised on a dose of 200 mg daily or 200 mg 3 times a week. A dose of 200 mg daily gave troughs comparable to those in patients with normal renal function taking 1200 mg daily. (Bruchfeld A, Stahle L, Andersson J, et al. Ribavirin treatment in dialysis patients with chronic hepatitis C virus infection – a pilot study. J Viral Hepat. 2001, Jul 8(4): 287–92 and Tan AC, Brouwer JT, Glue P, et al. Safety of interferon and ribavirin therapy in haemodialysis patients with chronic hepatitis C: results of a pilot study. Nephrol Dial Transplant. 2001, Jan; 16: 193–5.)
After stopping therapy the half-life was approximately 298 hours, due to slow elimination from non-plasma compartments.

Ribavirin is also available (on named patient basis) as an intravenous infusion, from ICN Pharmaceuticals.

Recommended dosing schedule in patients with normal renal function is:
- Initial loading dose: 33 mg/kg
- Six hours after the initial dose: 16 mg/kg every 6 hours during 4 days (16 doses)
- Eight hours following the last of these doses: 8 mg/kg every 8 hours during 3 days (9 doses)

Patients with impaired renal function should be carefully monitored during therapy with ribavirin for signs and symptoms of toxicity, such as haemolytic anaemia.

Available clinical experience suggests that patients with renal insufficiency and creatinine clearance of 50–80 mL/min tolerate the usual dosage regimen of ribavirin.

Individuals with moderate to severe renal insufficiency (creatinine clearance 30–50 mL/min) have tolerated, without reports of complications, a dose regimen with an initial loading dose of 20–25 mg/kg, followed by single daily doses of 10 mg/kg during 9–10 consecutive days.

There is no experience in patients with end-stage renal disease.

See SPC for further information.
Rifabutin

**CLINICAL USE**

Antibacterial agent:
- Tuberculosis
- Mycobacterial infection

**DOSE IN NORMAL RENAL FUNCTION**

- Prophylaxis of *Mycobacterium avium* in patients with low CD4 count: 300 mg daily
- Treatment of non-tuberculous mycobacterial disease, in combination with other drugs: 450–600 mg daily
- Treatment of pulmonary tuberculosis, in combination with other drugs: 150–450 mg daily

**PHARMACOKINETICS**

- Molecular weight (daltons) 847
- % Protein binding 70
- % Excreted unchanged in urine 5
- Volume of distribution (L/kg) 8–9
- Half-life – normal/ESRF (hrs) 35–40/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in normal renal function</th>
<th>Maximum 300 mg daily</th>
<th>Maximum 300 mg daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>Dose as in normal renal function</td>
<td>Maximum 300 mg daily</td>
<td>Maximum 300 mg daily</td>
</tr>
<tr>
<td>10–30</td>
<td>Maximum 300 mg daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
<td>Maximum 300 mg daily</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Not dialysed. Dose as in GFR<10 mL/min
- CAV: Unknown dialysability. Dose as in GFR=10–30 mL/min
- VVHD: GFR=10–30 mL/min

**IMPORTANT DRUG INTERACTIONS**

- Antibacterials: clarithromycin and other macrolides increase concentration of rifabutin, resulting in increased risk of uveitis – reduce rifabutin dose; reduced concentration of dapsone and clarithromycin
- Anticoagulants: reduced anticoagulant effect of coumarins
- Antidiabetics: reduced anti-diabetic effect of chlorpropamide and tolbutamide; possibly reduced anti-diabetic effect with sulphonylureas
- Anti-epileptics: reduced concentration of phenytoin and carbamazepine
- Antifungals: fluconazole, triazoles, posaconazole and voriconazole increase the concentration of rifabutin resulting in increased risk of uveitis – reduce rifabutin dose; rifabutin reduces concentration of posaconazole, voriconazole and itraconazole – increase voriconazole dose, avoid with itraconazole
- Antipsychotics: possibly reduced aripiprazole concentration – increase dose of aripiprazole
- Antivirals: amprenavir, atazanavir darunavir, nelfinavir and tipranavir and possibly nevirapine increase concentration of rifabutin – halve or reduce dose of rifabutin; efavirenz reduces the concentration of rifabutin – increase dose of rifabutin; indinavir increases rifabutin concentration – reduce dose of rifabutin; concentration of indinavir reduced when given together – increase indinavir dose; ritonavir increases the concentration of rifabutin resulting in increased risk of uveitis – avoid concomitant use; concentration of saquinavir reduced – avoid concomitant use unless another protease inhibitor is also given
- Atovaquone: concentration of atovaquone reduced (possible therapeutic failure of atovaquone)
- Ciclosporin: possibly reduced ciclosporin levels
- Corticosteroids: reduced level of corticosteroids – double steroid dose. Give as twice daily dosage
- Oestrogens and progestogens: reduced contraceptive effect due to increased metabolism
- Sirolimus: reduced sirolimus concentration – avoid
- Tacrolimus: possibly reduced tacrolimus trough concentration
## ADMINISTRATION

<table>
<thead>
<tr>
<th>RECONSTITUTION</th>
<th>OTHER INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Can cause an orange-tan skin pigmentation as well as discoloured urine</td>
</tr>
<tr>
<td></td>
<td>Can cause abnormal LFTs and hepatitis</td>
</tr>
<tr>
<td></td>
<td>Can cause uveitis especially in combination with clarithromycin and fluconazole</td>
</tr>
<tr>
<td></td>
<td>Rifabutin is a less potent CYP4503A enzyme inducer than rifampicin but similar interactions may occur</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>RATE OF ADMINISTRATION</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>COMMENTS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Rifampicin

CLINICAL USE
Antibacterial agent:
- Tuberculosis
- Staphylococcal infection

DOSE IN NORMAL RENAL FUNCTION
600–1200 mg daily in 2–4 divided doses

PHARMACOKINETICS
Molecular weight (daltons) 822.9
% Protein binding 80
% Excreted unchanged in urine 15–30
Volume of distribution (L/kg) 0.64–0.66
Half-life – normal/ESRF (hrs) 2–5/1.8–11

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 50% – 100% of normal dose

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Not dialysed. Dose as in GFR<10 mL/min
HD Not dialysed. Dose as in GFR<10 mL/min
HDF/High flux Not dialysed. Dose as in GFR<10 mL/min
CAV/VVHD Unknown dialysability. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Anti-arrhythmics: metabolism of disopyramide, mexiletine and propafenone accelerated
- Antibacterials: reduced concentration of chloramphenicol, clarithromycin, dapsone, trimethoprim and telithromycin – avoid with telithromycin; monitor LFTs in combination with quinupristin/dalfopristin; concentration increased by clarithromycin and other macrolides
- Anticoagulants: reduced anticoagulant effect of coumarins
- Antidiabetics: reduced antidiabetic effect of chlorpropamide and tolbutamide; concentration of rosiglitazone, nateglinide and repaglinide reduced – may need to increase dose of rosiglitazone; possibly reduced antidiabetic effect with sulphonylureas
- Anti-epileptics: reduced concentration of phenytoin and lamotrigine
- Antifungals: concentration of both drugs may be reduced with ketoconazole; reduced concentration of fluconazole, itraconazole, posaconazole and terbinafine; concentration of voriconazole reduced – avoid concomitant use; initially increases then reduces caspofungin concentration
- Antipsychotics: reduced concentration of haloperidol, aripiprazole and clozapine – increase dose of aripiprazole
- Antivirals: concentration of abacavir and tipranavir possibly reduced – avoid with tipranavir; concentration of amprenavir, atazanavir, darunavir, indinavir, lopinavir, nelfinavir, nevirapine and saquinavir reduced – avoid; concentration of efavirenz reduced – increase dose of efavirenz; avoid with zidovudine
- Atovaquone: concentration of atovaquone reduced (possible therapeutic failure of atovaquone)
- Bosentan: reduced bosentan concentration – avoid
- Calcium-channel blockers: metabolism of diltiazem, verapamil, irsoprol, nicardipine, nifedipine, nisoldipine and nimodipine accelerated
- Ciclosporin: markedly reduced levels (danger of transplant rejection); ciclosporin dose may need increasing 5-fold or more
- Corticosteroids: reduced level of corticosteroids – double steroid dose. Give as twice daily dosage
- Cytotoxics: reduced concentration of erlotinib, sunitinib, dasatinib and imatinib – avoid with imatinib
- Diuretics: concentration of eplerenone reduced – avoid
- Oestrogens and progestogens: reduced contraceptive effect due to increased metabolism
- Tacrolimus: reduced tacrolimus concentration
- Sirolimus: reduced sirolimus concentration
**ADMINISTRATION**

- Use solvent provided
- Oral, IV

**RATE OF ADMINISTRATION**

- 2–3 hours

**COMMENTS**

- Dilute in 500 mL glucose 5% or sodium chloride 0.9%
- For central administration, 600 mg in 100 mL glucose 5% over 0.5–2 hours has been used (unlicensed).
- Stable for up to 24 hours at room temperature

**OTHER INFORMATION**

- Some units give dose in concentrations up to 60 mg/mL (in its own solvent) over 10 minutes, on prescriber’s responsibility
- May cause acute interstitial nephritis, potassium wasting or renal tubular defects
- Reduce dose if LFTs are abnormal or patient <45 kg
- Absorption from gastrointestinal tract can be reduced by up to 80% by the presence of food in the gastrointestinal tract
- CAPD exit site infections: 300 mg twice daily for 4 weeks has been used
- Rifampicin is excreted into CAPD fluid causing an orange/yellow colour
- Monitor rifampicin levels if necessary
- In severe renal impairment there is no increase in half-life at doses less than 600 mg daily
Rimonabant

**CLINICAL USE**
Treatment for obesity in conjunction with diet and exercise

**DOSE IN NORMAL RENAL FUNCTION**
20 mg daily before breakfast

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>463.8</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>&gt;99.9</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>3</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>Depends on body weight (higher in obese patients)</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>9 days (16 days in obese patients)</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function. Use with caution</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High</td>
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</tr>
<tr>
<td>CAV/</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Ketoconazole: concentration of rimonabant increased

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- Manufacturer states use contraindicated in CKD 5 due to lack of data
- Do not use in patients with major depression or who are on an antidepressant as there is a high risk of depression reported with rimonabant

RETURN TO CONTENTS
Risedronate sodium

CLINICAL USE

- Treatment and prevention of post-menopausal osteoporosis (including corticosteroid induced)
- Paget’s disease

DOSE IN NORMAL RENAL FUNCTION

- Post-menopausal osteoporosis: 5 mg daily or 35 mg weekly
- Paget’s disease: 30 mg daily for 2 months

PHARMACOKINETICS

- Molecular weight (daltons): 305.1
- % Protein binding: 24
- % Excreted unchanged in urine: 50
- Volume of distribution (L/kg): 6.3
- Half-life – normal/ESRF (hrs): 480/Increased

DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>See ‘Other Information’</td>
</tr>
<tr>
<td>&lt;10</td>
<td>See ‘Other Information’</td>
</tr>
</tbody>
</table>

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>CAPD</th>
<th>Unknown dialysability. Dose as in GFR&lt;10mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unknown dialysability. Dose as in GFR=10–20mL/min</td>
</tr>
<tr>
<td>VVHD</td>
<td></td>
</tr>
</tbody>
</table>

IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs

Calcium-containing substances: avoid for 2 hours before and after administration

ADMINISTRATION

RECONSTITUTION
- ROUTE
  - Oral
RATE OF ADMINISTRATION
- COMMENTS
- OTHER INFORMATION

- Swallow whole with a glass of water 30 minutes before food. Sit or stand upright for 30 minutes after administration
- Renal clearance is decreased by 70% in patients with creatinine clearance <30 mL/min
- One paper reviewed all the information available and concluded that 50% of the recommended dose may be possible in ERF, but more trials are required, and osteomalacia and adynamic bone disease must first be excluded. (Miller PD. Treatment of osteoporosis in chronic kidney disease and end-stage renal disease. Curr Osteoporos Rep. 2005; 3: 5–12.)
- Examples of use in other units in HD patients: Normal doses; 5 mg once weekly
Risperidone

**CLINICAL USE**
- Schizophrenia
- Psychoses
- Mania

**DOSE IN NORMAL RENAL FUNCTION**
Oral: 2–16 mg daily in divided doses
IM: 25–50 mg every 2 weeks

**PHARMACOKINETICS**
- Molecular weight: 410.5 daltons
- % Protein binding: 90
- % Excreted unchanged in urine: 70
- Volume of distribution (L/kg): 1–2
- Half-life – normal/ESRF (hrs): 19.5/Increased

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in Renal Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Initially 0.5 mg twice daily, increasing by 0.5 mg BD to 1–2 mg twice daily. Use with caution. See ‘Other Information’ for IM dosing</td>
</tr>
<tr>
<td>10–20</td>
<td>Initially 0.5 mg twice daily, increasing by 0.5 mg BD to 1–2 mg twice daily. Use with caution. See ‘Other Information’ for IM dosing</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Initially 0.5 mg twice daily, increasing by 0.5 mg BD to 1–2 mg twice daily. Use with caution. See ‘Other Information’ for IM dosing</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Type</th>
<th>Dose in Renal Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/ VVHD</td>
<td>Unlikely to be dialysed. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Analgesics: increased risk of convulsions with tramadol; enhanced hypotensive and sedative effects with opioids
- Antidepressants: concentration increased by fluoxetine and possibly paroxetine; concentration of tricyclics possibly increased
- Anti-epileptics: antagonism, convulsive threshold may be lowered; metabolism accelerated by carbamazepine
- Antimalarials: avoid concomitant use with artemether with lumefantrine
- Antipsychotics: avoid concomitant use of depot formulations with clozapine (cannot be withdrawn quickly if neutropenia occurs)
- Antivirals: ritonavir may increase concentration of risperidone
- Anxiolytics and hypnotics: enhanced sedative effects
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- With solvent provided

**ROUTE**
- Oral, deep IM

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**
- At a dose of 3 mg twice daily, 1.5 mg (i.e. 25%) of risperidone is removed after a 5 hour dialysis session with a dialysate flow of 500mL/min
- In overdose, rare cases of QT prolongation have been reported
- Clearance of risperidone and active metabolites decreased by 60% in severe renal impairment
- If a dose of 2 mg daily orally is tolerated then a dose of 25 mg (IM) every 2 weeks can be used initially in renal impairment
Ritonavir

**CLINICAL USE**

Protease inhibitor:
- Treatment of HIV-1 infection in combination with other antiretrovirals

**DOSE IN NORMAL RENAL FUNCTION**

600 mg twice daily
As low dose booster with other protease inhibitors: 100–200 mg once or twice daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>720.9</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>98–99</td>
</tr>
<tr>
<td>% Excreted in urine</td>
<td>3.5</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.4</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>3–5/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Alfuzosin: avoid concomitant use
- Analgesics: opioid and NSAID levels may be increased (risk of toxicity) – avoid dextropropoxyphene and piroxicam; methadone and pethidine levels reduced; increased fentanyl and toxic pethidine metabolite concentration – avoid with pethidine
- Anti-arrhythmics: increased concentration of amiodarone, flecainide and propafenone (increased risk of ventricular arrhythmias) – avoid concomitant use; possible increased risk of arrhythmias with disopyramide and mexiletine
- Antibacterials: rifabutin concentration increased (risk of uveitis) – avoid; concentration of clarithromycin and other macrolides increased – reduce dose of clarithromycin in renal impairment; concentration of both drugs may be increased in combination with fusidic acid; avoid with telithromycin in renal and hepatic failure
- Anticoagulants: anticoagulant effect of coumarins and phenindione possibly increased; effect of warfarin may be enhanced or reduced
- Antidepressants: SSRIs and tricyclic concentrations possibly increased; concentration reduced by St John's wort; possibly reduced paroxetine concentration; increased side effects with trazodone
- Anti-epileptics: carbamazepine and phenytoin concentration may be increased; concentration reduced by phenytoin
- Antifungals: in combination with itraconazole or ketoconazole concentration of both drugs may be increased; concentration increased by fluconazole; voriconazole concentration reduced – avoid
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: concentration of pimozide, sertindole, clozapine and possibly other antipsychotics may be increased (risk of toxicity) – avoid concomitant use; possibly inhibits metabolism of aripiprazole – reduce aripiprazole dose; olanzapine concentration reduced
- Antivirals: levels of both nelfinavir and ritonavir may be increased if used in combination; amprenavir, indinavir and saquinavir levels increased; increased risk of toxicity with efavirenz – monitor LFTs
- Anxiolytics and hypnotics: levels of many of them increased (risk of extreme sedation and respiratory depression) – avoid alprazolam, diazepam, flurazepam, midazolam, zolpidem; concentration of buspirone increased
- Bupropion: bupropion levels increased (risk of toxicity) – avoid
- Calcium-channel blockers: levels of blockers possibly increased – avoid with lercanidipine
● Ciclosporin: levels possibly increased by ritonavir
● Cilostazol: concentration of cilostazol possibly increased – avoid concomitant use
● Corticosteroids: possibly increased corticosteroid concentration; increased concentration of inhaled/intranasal budesonide and fluticasone
● Diuretics: eplerenone concentration increased – avoid concomitant use
● Ergot alkaloids: risk of ergotism – avoid
● Ivabradine: ivabradine concentration possibly increased – avoid concomitant use
● Lipid-lowering drugs: increased risk of myopathy with simvastatin – avoid; possibly increased risk of myopathy with atorvastatin
● Oestrogens and progestogens: metabolism accelerated (contraceptive effect reduced)
● 5HT1 agonists: concentration of eletriptan increased – avoid
● Sildenafil: concentrations of sildenafil significantly increased – avoid
● Theophylline: metabolism accelerated, theophylline levels reduced
● Tacrolimus: levels possibly increased by ritonavir
● Vardenafil: possibly increased vardenafil concentration – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**

–

**ROUTE**

● Oral

**RATE OF ADMINISTRATION**

–

**COMMENTS**

–

**OTHER INFORMATION**

● Administer with food
Rituximab

**CLINICAL USE**
Monoclonal antibody:
- Lymphomas
- Diffuse large B-cell non-Hodgkin's lymphoma in combination with other chemotherapy
- Rheumatoid arthritis
- Lupus nephritis (unlicensed)

**DOSE IN NORMAL RENAL FUNCTION**
- 375 mg/m² weekly for 4 weeks
- Follicular lymphoma: 375 mg/m² once every 3 months for up to 2 years
- Rheumatoid arthritis: two 1 g doses 2 weeks apart
- Lupus nephritis: 375 mg/m² for 1–2 doses, two weeks apart

**PHARMACOKINETICS**
- Molecular weight (daltons): 144,000
- % Protein binding: No data
- % Excreted unchanged in urine: No data
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 76.3 (after 1st infusion)/–
  205.8 (after 4th infusion)/–

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Use with caution
  - 10–20: Use with caution
  - <10: Use with caution

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Use with caution
- HD: Not dialysed. Use with caution
- HDF/High flux: Unlikely to be dialysed. Use with caution
- CAV/VVHD: Unknown dialysability. Use with caution

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - IV infusion

**RATE OF ADMINISTRATION**
- 1st dose: 50 mg/hour, then increase the rate every 30 minutes by 50 mg/hour to achieve a maximum rate of 400 mg/hour
- Further doses: 100 mg/hour, increasing by 100 mg/hour every 30 minutes to achieve a maximum rate of 400 mg/hour

**COMMENTS**
- Add to sodium chloride 0.9% or glucose 5% to achieve a concentration of 1–4 mg/mL, and gently invert to prevent foaming
- Use immediately after dilution. Infusion solution is stable for 12 hours at room temperature
- Prepared solution has 24 hrs chemical stability at 2–8°C

**OTHER INFORMATION**
- Always give a premedication of paracetamol and an antihistamine before infusion
- Mean serum half-life increases with dose and repeated dosing (76.3 hours after 1st infusion and 205.8 hours after 4th infusion). Detectable in body for 3–6 months
- Alternative regime for vasculitis (anecdotal): 1 g/m² on days 1 and 14, repeated at relapse or after 6 months
- Patients with high tumour burden or malignant cells >50,000/mm³ may be at risk of severe cytokine release syndrome which may be associated with acute renal failure – treat with caution
- Rituximab has been used to reduce alloreactive antibodies pre-transplant, to treat focal segmental glomerulosclerosis, mixed essential cryoglobulinaemia, SLE, primary systemic vasculitis, PRCA, HUS, and PTLD. (Salama AD, Pusey CD. Drug insight: rituximab in renal disease and transplantation. Nat Clin Pract Nephrol. 2006; 2(4): 221–30)
Rivastigmine

CLINICAL USE
- Mild-moderate dementia in Alzheimer’s disease
- Idiopathic Parkinson’s disease

DOSE IN NORMAL RENAL FUNCTION
3–6 mg twice daily (initially 1.5 mg twice daily)

PHARMACOKINETICS
- Molecular weight (daltons): 250.3 (400.4 as hydrogen tartrate)
- % Protein binding: 40
- % Excreted unchanged in urine: 0 (>90 as pharmacologically inactive metabolites)
- Volume of distribution (L/kg): 1.8–2.7
- Half-life – normal/ESRF (hrs): 1/–

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
- 20–50 Start at a low dose and gradually increase
- 10–20 Start at a low dose and gradually increase
- <10 Start at a low dose and gradually increase

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD: Likely dialysability. Dose as in GFR<10 mL/min
- HD: Likely dialysability. Dose as in GFR<10 mL/min
- HDF/High flux: Likely dialysability. Dose as in GFR<10 mL/min
- CAV/CAVHD: Likely dialysability. Dose as in GFR=10-20 mL/min

IMPORTANT DRUG INTERACTIONS
- Potentially hazardous interactions with other drugs
  - Muscle relaxants: enhances effect of suxamethonium; antagonises effect of non-depolarising muscle relaxants

ADMINISTRATION
- RECONSTITUTION
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
- COMMENTS
- OTHER INFORMATION
  - Administer with food. Swallow whole
Rizatriptan

**CLINICAL USE**
Acute treatment of migraine

**DOSE IN NORMAL RENAL FUNCTION**
10 mg, repeated after 2 hours if required; maximum of 2 doses in 24 hours

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Molecular weight (daltons)</th>
<th>391.5 (as benzoate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Protein binding</td>
<td>14</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>14</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>110 litres (females), 140 litres (males)</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>2–3/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Use with caution 5 mg, repeated after 2 hours; maximum 15 mg daily</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>CAPD</th>
<th>Unknown dialysability. Dose as in GFR&lt;10mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous drug interactions with other drugs

- Antidepressants: risk of CNS toxicity with MAOIs and linezolid – avoid for 2 weeks after discontinuation of MAOI; possibly increased serotonergic effects with duloxetine; increased serotonergic effects with St John's wort – avoid concomitant use
- Ergot alkaloids: increased risk of vasospasm – avoid concomitant use
- Propranolol: rizatriptan levels increased, reduce dose of rizatriptan to 5 mg (max 10 mg in 24 hours)

**ADMINISTRATION**

**ROUTE**

- Oral

**RATE OF ADMINISTRATION**

- 

**COMMENTS**

- 

**OTHER INFORMATION**

- Administration with food delays absorption by approximately 1 hour
- Metabolised to mainly inactive metabolites
- <1% excreted in the urine as active N-monodesmethyl metabolite
- AUC increases by 44% in haemodialysis patients
Rocuronium bromide

**CLINICAL USE**
Muscle relaxant in general anaesthesia, medium duration

**DOSE IN NORMAL RENAL FUNCTION**
IV injection: intubation dose: 0.6 mg/kg; maintenance: 0.15 mg/kg
IV infusion: 0.6 mg/kg loading dose, followed by 0.3–0.6 mg/kg/hour

**PHARMACOKINETICS**
- Molecular weight: 609.7 daltons
- % Protein binding: 25–30
- % Excreted unchanged in urine: 40
- Volume of distribution: 0.2 L/kg
- Half-life – normal/ESRF (hrs): 1.2–1.4 /Unchanged

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function. See ‘Other Information’
- <10: Dose as in normal renal function. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR<10 mL/min
- HD: Unknown dialysability. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced muscle relaxant effect
- Anti-arrhythmics: procainamide enhances muscle relaxant effect
- Antibacterials: effect enhanced by aminoglycosides, clindamycin, polymyxins and piperacillin
- Botulinum toxin: neuromuscular block enhanced (risk of toxicity)

**ADMINISTRATION**
**RECONSTITUTION**
-

**RATE OF ADMINISTRATION**
- IV

**COMMENTS**
- Compatible with sodium chloride 0.9% and glucose 5%

**OTHER INFORMATION**
- Use with caution in renal failure: variable duration of action (range: 22–90 minutes)
- Use the lowest possible dose in patients with GFR<20 mL/min, as at risk of prolonged paralysis
Ropinirole

**CLINICAL USE**
- Anti-Parkinson agent
- Restless legs syndrome

**DOSE IN NORMAL RENAL FUNCTION**
- Parkinson’s disease: 9–24 mg daily in divided doses
- Restless legs syndrome: 0.25 mg daily initially, increasing to a maximum of 4 mg daily

**PHARMACOKINETICS**
- Molecular weight: 260.4 (296.8 as hydrochloride)
- % Protein binding: 10–40
- % Excreted: <10 in urine
- Volume of distribution: 8 (L/kg)
- Half-life – normal/ESRF (hrs): 6/–

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Use with caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapies</th>
<th>Dose as in normal renal function</th>
<th>Use with caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely dialysability. Dose as in GFR&lt;10mL/min</td>
<td></td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
<td></td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely dialysability. Dose as in GFR=10–20mL/min</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Antipsychotics: antagonism of anti-Parkinsonian effect – avoid concomitant use
  - Metoclopramide: antagonism of anti-Parkinsonian effect – avoid concomitant use
  - Oestrogens and progestogens: concentration increased

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  -

**OTHER INFORMATION**
- If administered with L-dopa, decrease the dose of L-dopa by 20%
- Take with meals to improve GI tolerance, but Cmax increases by 2.6 hours
- No data in renal impairment
- Ropinirole is hepatically metabolised to inactive metabolites
- For use in restless legs syndrome in CKD 5, start with a low dose and increase according to tolerability
Rosiglitazone

<table>
<thead>
<tr>
<th>CLINICAL USE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 2 diabetes mellitus</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DOSE IN NORMAL RENAL FUNCTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>4–8 mg daily in 1–2 divided doses</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PHARMACOKINETICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
</tr>
<tr>
<td>% Protein binding</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DOSE IN RENAL IMPAIRMENT</th>
</tr>
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<tbody>
<tr>
<td>GFR (mL/Min)</td>
</tr>
<tr>
<td>20–50 Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20 Dose as in normal renal function. Use with caution</td>
</tr>
<tr>
<td>&lt;10 Dose as in normal renal function. Use with caution</td>
</tr>
</tbody>
</table>

<table>
<thead>
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<td>HDF/High flux</td>
</tr>
<tr>
<td>CAV/</td>
</tr>
<tr>
<td>VVHD</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IMPORTANT DRUG INTERACTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potentially hazardous interactions with other drugs</td>
</tr>
<tr>
<td>Antibacterials: concentration reduced by rifampicin – consider increasing rosiglitazone dose</td>
</tr>
<tr>
<td>Lipid-lowering agents: concentration increased by gemfibrozil – consider reducing rosiglitazone dose</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>RECONSTITUTION</td>
</tr>
<tr>
<td>ROUTE</td>
</tr>
<tr>
<td>Oral</td>
</tr>
<tr>
<td>RATE OF ADMINISTRATION</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>COMMENTS</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>OTHER INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measure liver function prior to initiating therapy, and then at regular intervals</td>
</tr>
<tr>
<td>Should not be used in patients with heart failure or history of heart failure; incidence of heart failure is increased when rosiglitazone is combined with insulin</td>
</tr>
<tr>
<td>Should not be used in patients with acute coronary syndrome. Patients should be closely monitored for signs of heart failure</td>
</tr>
<tr>
<td>May be associated with a small increased risk of cardiac ischaemia particularly in combination with insulin. The combination of rosiglitazone and insulin should be used only in exceptional cases, and under close supervision</td>
</tr>
<tr>
<td>Rosiglitazone is contraindicated for co-administration with insulin in the UK but not in the USA</td>
</tr>
<tr>
<td>Not recommended for use in patients with ischaemic heart disease or peripheral arterial disease; in patients with history of ischaemic heart disease rosiglitazone should only be used after careful evaluation of the patient's individual risk</td>
</tr>
<tr>
<td>Rosiglitazone is extensively metabolised in the liver. Some of the metabolites are active, and are largely excreted in the urine</td>
</tr>
</tbody>
</table>
Rosuvastatin

**CLINICAL USE**

HMG CoA reductase inhibitor:
- Hyperlipidaemia

**DOSE IN NORMAL RENAL FUNCTION**

- 5–40 mg daily
- Asians, people at increased risk of myopathy, and in combination with fibrates: 5–20 mg daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>1001.1 (as calcium salt)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>90</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>5</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>134 litres</td>
</tr>
</tbody>
</table>
| Half-life – normal/ESRF (hrs)         | 19/Increased           

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–60</td>
<td>5–20 mg daily</td>
</tr>
<tr>
<td>10–20</td>
<td>5–20 mg daily</td>
</tr>
<tr>
<td>&lt;10</td>
<td>5–20 mg daily</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapeutic Modality</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely dialysability. Dose as in GFR&lt;10 mL/min.</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unknown dialysability. Dose as in GFR=10–20 mL/min</td>
</tr>
<tr>
<td>VVHD</td>
<td>GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Antibacterials: erythromycin reduces concentration of rosuvastatin; increased risk of myopathy with daptomycin
- Anticoagulants: effect of coumarins and phenindione enhanced
- Ciclosporin: increased risk of myopathy – avoid concomitant use
- Lipid-lowering agents: increased risk of myopathy with fibrates, gemfibrozil (avoid) and nicotinic acid

**ADMINISTRATION**

**RECONSTITUTION**

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**

**COMMENTS**

**OTHER INFORMATION**

- In renal impairment, doses above 20 mg should not be used due to risk of myopathy
- Do not use doses greater than 20 mg in Asian patients
- Always start at a dose of 5 mg
- The 40 mg dose should only be used under specialist supervision
- Increased risk of proteinuria with doses above 40 mg
- Case studies from Glasgow have shown that statins in combination with fusidic acid have an increased risk of causing myopathy in diabetic patients

RETURN TO CONTENTS
Rotigotine

**CLINICAL USE**
Treatment of Parkinson’s disease

**DOSE IN NORMAL RENAL FUNCTION**
- 2–8 mg every 24 hours
- With levodopa: max 16 mg every 24 hours

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>315.5</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>92</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>71</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>84</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>5–7/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Antipsychotics: avoid concomitant use (antagonism of effect)
- Metoclopramide: avoid concomitant use (antagonism of effect)

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
- Topical

**RATE OF ADMINISTRATION**
- COMMENTS
- 

**OTHER INFORMATION**

- Discontinue gradually at a rate of 2 mg/24 hours, every other day
- Apply to intact skin on the abdomen, thigh, hip, flank, shoulder or upper arm
- If a patch falls off replace with a new one
- Backing layer contains aluminium and should be removed prior to MRIs or cardioversion
- Rotigotine is being investigated for its use in restless legs syndrome
Salbutamol

CLINICAL USE
Beta₂-adrenoceptor agonist:
- Reversible airways disease

DOSE IN NORMAL RENAL FUNCTION
- Oral: 2–4 mg 3–4 times daily
- SC/IM: 500 micrograms, repeated 4 hourly if necessary
- IV: 250 micrograms slow bolus, repeated if required
- Infusion: start with 5 micrograms/minute, adjust according to response, usually 3–20 micrograms/minute
- Aerosol: 100–200 micrograms (1–2 puffs) 4 times daily
- Powder: 200–400 micrograms 4 times daily
- Nebulisation: 2.5–5 mg 4 times daily, or more frequently

PHARMACOKINETICS
- Molecular weight: 239.3 daltons
- % Protein binding: 10
- % Excreted unchanged in urine: 51–64
- Volume of distribution (L/kg): 2–2.5

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Unknown dialysability. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Increased risk of hypokalaemia when diuretics, theophylline or large doses of corticosteroids are given with high doses of salbutamol
- Antihypertensives: acute hypotension with IV infusion of salbutamol and methyldopa

ADMINISTRATION
- RECONSTITUTION
  - ROUTE
    - IV, SC, IM, oral, inhaled, nebulised
  - RATE OF ADMINISTRATION
    - IV slow bolus; IV infusion 3–20 micrograms/minute
  - COMMENTS
    - Infusion: dilute 10 mL (10 mg) to 500 mL with sodium chloride 0.9% or glucose 5% (20 micrograms/mL)
    - Via syringe pump: dilute 10 mL (10 mg) to 50 mL with sodium chloride 0.9% or glucose 5% (200 micrograms/mL)

OTHER INFORMATION
- Monitor ECG/BP/pulse
- Nebulised salbutamol may be prescribed for hypokalaemic effect in acute hyperkalaemia (unlicensed)
Saquinavir

CLINICAL USE
Protease inhibitor:
- Treatment of HIV infection in combination with other antiviral drugs

DOSE IN NORMAL RENAL FUNCTION
With low dose ritonavir: 1 g twice daily

PHARMACOKINETICS
Molecular weight (daltons) 670.8
% Protein binding 98
% Excreted unchanged in urine <4
Volume of distribution (L/kg) 10
Half-life – normal/ESRF (hrs) 13.2

DOSE IN RENAL IMPAIRMENT
GFR (mL/Min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unlikely to be dialysed. Dose as in normal renal function
HD Unlikely to be dialysed. Dose as in normal renal function
HDF/High flux Not dialysed. Dose as in normal renal function
CAV/ VVHD Unknown dialysability. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Antibacterials: rifampicin and rifabutin can reduce saquinavir levels by 80% and 40% respectively (metabolism accelerated); increased hepatotoxicity with rifampicin; concentration possibly increased by quinupristin/dalfopristin; avoid with telithromycin in severe renal and hepatic failure
- Antidepressants: concentration reduced by St John’s wort – avoid
- Anti-epileptics: carbamazepine, phenobarbital, primidone and phenytoin can reduce saquinavir levels
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: possibly increased risk of ventricular arrhythmias with pimozide and sertindole – avoid concomitant use; possibly inhibits aripiprazole metabolism – reduce aripiprazole dose
- Antivirals: tipranavir and efavirenz can reduce saquinavir levels; nelfinavir can cause an increase in levels of both nelfinavir and saquinavir; concentration increased by atazanavir, indinavir, lopinavir and ritonavir; reduced darunavir concentration
- Anxiolytics and hypnotics: midazolam plasma concentration possibly increased (prolonged sedation) – avoid
- Ciclosporin: concentration of both drugs increased
- Cilostazol: concentration of cilostazol possibly increased – avoid concomitant use
- Ergot alkaloids: risk of ergotism – avoid
- Lipid-lowering drugs: increased risk of myopathy with simvastatin – avoid; possibly increased myopathy with atorvastatin
- Omeprazole: AUC of saquinavir increased by 82% (increased risk of toxicity)
- Tacrolimus: possibly increased tacrolimus concentration – may need to reduce dose

ADMINISTRATION
RECONSTITUTION
- 
ROUTE
- Oral
RATE OF ADMINISTRATION
- 
COMMENTS
- Administer within 2 hours after meal

OTHER INFORMATION
- Therapeutic drug monitoring is available from HIV Focus Roche Products UK and the University of Liverpool, but this service is not available to all patients
Senna

**CLINICAL USE**
Constipation

**DOSE IN NORMAL RENAL FUNCTION**
Tablets: 15–30 mg (2–4 tablets) at night
Granules: 5–10 mL at night
Syrup: 10–20 mL at night
Manevac granules: 5–10 mL every 6–12 hours

**PHARMACOKINETICS**
- Molecular weight: 862.7
- % Protein binding: Systemic bioavailability less than 5%
- % Excreted unchanged in urine: No data
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): No data

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Unknown dialysability. Dose as in normal renal function
- HDF/High Flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - None known

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- Acts in 8–12 hours
- Syrup available, 5 mL = 1 tablet
- Granules available, 1 × 5 mL spoonful = 2 tablets
- Diabetic patients should use the tablets as these have negligible sugar content
Sertindole

**CLINICAL USE**
Atypical antipsychotic:
- Schizophrenia

**DOSE IN NORMAL RENAL FUNCTION**
12–20 mg once daily; maximum 24 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 440.9
- % Protein binding: 99.5
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): 20
- Half-life – normal/ESRF (hrs): 72

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Start at low dose and increase according to response</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/ VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs:
- Anaesthetics: enhanced hypotensive effect
- Analgesics: increased risk of convulsions with tramadol; enhanced hypotensive and sedative effects with opioids
- Anti-arrhythmics: increased risk of ventricular arrhythmias with anti-arrhythmics that prolong the QT interval; avoid concomitant use with amiodarone, disopyramide and procainamide (risk of ventricular arrhythmias)
- Antibacterials: avoid concomitant use with macrolides and moxifloxacin (increased risk of ventricular arrhythmias)
- Antidepressants: fluoxetine and paroxetine increase sertindole concentration; increased plasma level of tricyclics
- Anti-epileptics: antagonises anticonvulsant effect; metabolism accelerated by carbamazepine and phenytoin
- Antifungals: avoid concomitant use with imidazoles and triazoles
- Antimalarial: avoid concomitant use with pyrimethamine/sulfadoxine
- Antipsychotics: increased risk of ventricular arrhythmias with amisulpride – avoid concomitant use
- Antivirals: concentration increased by amprenavir, indinavir, ritonavir and saquinavir (increased risk of ventricular arrhythmias) – avoid concomitant use
- Anxiolytics and hypnotics: increased sedative effects
- Beta-blockers: increased risk of ventricular arrhythmias with sotalol
- Diuretics increased risk of ventricular arrhythmias due to hypokalaemia
- Ivabradine: increased risk of ventricular arrhythmias
- Lithium: increased risk of ventricular arrhythmias
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use
- Ulcer-healing drugs: increased risk of ventricular arrhythmias with cimetidine

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  -
OTHER INFORMATION

- Available on a named patient basis
- Can cause peripheral oedema
- Associated with cardiac arrhythmias, QT interval prolongation, and sudden cardiac death
- Patients should have an ECG pre and during treatment
- Hypokalaemia and hypomagnesaemia should be corrected before starting therapy
Sertraline

**CLINICAL USE**

SSRI:
- Antidepressant
- Post-traumatic stress disorder
- Obsessive compulsive disorder

**DOSE IN NORMAL RENAL FUNCTION**

25–200 mg daily depending on indication

**PHARMACOKINETICS**

Molecular weight 342.7 (as hydrochloride)
% Protein binding >98
% Excreted unchanged in urine
Volume of distribution (L/kg) 25
Half-life – normal/ESRF (hrs) 26/Probably unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Analgesics: increased risk of bleeding with aspirin and NSAIDs; risk of CNS toxicity increased with tramadol
- Anticoagulants: effect of coumarins possibly enhanced
- Antidepressants: increased risk of toxic CNS effects of MAOIs and moclobemide; sertraline and MAOIs should not be prescribed within a 2 week period of each other; avoid concomitant use with St John's wort; possibly enhanced serotonergic effects with duloxetine; can increase tricyclics antidepressant concentration; increased agitation and nausea with tryptophan
- Anti-epileptics: antagonism (lowered convulsive threshold)
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: concentration of clozapine and pimozide increased – avoid concomitant use with pimozide
- Antivirals: concentration reduced by efavirenz and darunavir; possibly increased concentration with ritonavir
- Ciclosporin: may increase serotonin syndrome
- Dopaminergics: increased risk of hypertension and CNS excitation with selegiline – avoid concomitant use; increased risk of CNS toxicity with rasagiline – avoid concomitant use
- Linezolid: use with caution
- Lithium: increased risk of CNS effects; lithium toxicity reported
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**

- Sertraline is extensively metabolised by the liver. It can be used in renal failure at normal doses with caution
Sevelamer (Renagel®)

**CLINICAL USE**
Phosphate-binding agent

**DOSE IN NORMAL RENAL FUNCTION**
1–5 tablets (average: 3–5) 3 times a day with meals; adjust according to serum phosphate level

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>Large</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>No data</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>No data</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>No data</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>No data</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT GFR (mL/min)**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Type</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed.</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unlikely to be dialysed.</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be dialysed.</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Mycophenolate: may reduce mycophenolate levels

**ADMINISTRATION**

**RECONSTITUTION**
- 
**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 
**COMMENTS**
- 

**OTHER INFORMATION**
- Do not use if the patient has swallowing disorders or untreated or severe gastroparesis
- Renagel is not systemically absorbed
- One tablet = 800mg of poly(allylamine hydrochloride) polymer
- Can be dispersed in 10mL sodium bicarbonate 8.4% injection if patient is unable to take the tablets. (Info from the Royal Hospital for Sick Children, Yorkhill, Glasgow)
Sibutramine hydrochloride

**CLINICAL USE**
Treatment of obesity for patients who have not responded to appropriate weight reducing methods

**DOSE IN NORMAL RENAL FUNCTION**
10–15 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 334.3
- % Protein binding: 97
- % Excreted unchanged in urine: Only inactive metabolites
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 14–16

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function. Use with caution</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function. Use with caution</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function. Use with caution</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs:
- Antidepressants: increased risk of CNS toxicity; avoid concomitant administration with MAOIs and moclobemide – avoid for at least 2 weeks after stopping sibutramine; increased CNS toxicity with noradrenaline re-uptake inhibitors, tricyclics, SSRIs, mirtazapine and tryptophan – avoid concomitant use with tryptophan
- Antipsychotics: increased risk of CNS toxicity – avoid concomitant use
- Avoid use with drugs which increase heart rate or blood pressure

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

- **RATE OF ADMINISTRATION**
  -

- **COMMENTS**
  -

**OTHER INFORMATION**

- Do not use in patients with uncontrolled hypertension, i.e. BP >145/90 mmHg
- Initiation of therapy is associated with a mean increase in resting systolic and diastolic BP of 2–3 mmHg
Sildenafil

**CLINICAL USE**
- Treatment of erectile dysfunction (ED)
- To increase exercise ability in pulmonary arterial hypertension

**DOSE IN NORMAL RENAL FUNCTION**
- ED: 25–100 mg 0.5–4 hours before sexual intercourse (ideally, about 1 hour); no more than 1 dose per day
- Pulmonary arterial hypertension: 20 mg 3 times daily

**PHARMACOKINETICS**
- Molecular weight: 666.7 (as citrate)
- % Protein binding: 96%
- Volume of distribution: 1–2 L/kg
- Half-life – normal/ESRF (hrs): 4/Increased

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 30–50: Dose as in normal renal function
  - 10–30: Dose as in normal renal function
  - <10: ED: Initial dose 25 mg and increase if required

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in GFR<10mL/min
- HD: Unlikely to be dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Not dialysed. Dose as in GFR<10mL/min
- CAV/ VVHD: Unlikely to be dialysed. Dose as in GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Alpha-blockers: enhanced hypotensive effect – avoid for 4 hours after sildenafil
  - Antivirals: ritonavir significantly increases sildenafil concentration – avoid concomitant use; concentration possibly increased by saquinavir, amprenavir, indinavir and nelfinavir – reduce dose of sildenafil; side effects possibly increased by atazanavir
  - Nicorandil: enhanced hypotensive effect – avoid concomitant use
  - Nitrates: enhanced hypotensive effect – absolutely contraindicated

**ADMINISTRATION**
- **RECONSTITUTION**
  - **ROUTE**
    - Oral
  - **RATE OF ADMINISTRATION**
    - 
  - **COMMENTS**
    - 

**OTHER INFORMATION**
- Dialysis is not expected to increase clearance as sildenafil is highly protein bound
- Patients should seek prompt medical advice if their erections last for more than 4 hours
- Recommend use on non-dialysis days due to hypotension. In peritoneal dialysis, treatment with sildenafil is well tolerated
- Anecdotally it has been used at Guy’s hospital, London for diabetic gastroparesis at a dose of 25 mg 3 times a day
- The use of sildenafil is potentially hazardous in patients with active coronary ischaemia, those with congestive heart failure, and those with complicated multi-drug antihypertensive therapy regimens
- In 9 patients on maintenance haemodialysis, sildenafil 50 mg appeared to produce firmer erections and greater sexual satisfaction, but the effects were prolonged for up to 48 hours after administration

RETURN TO CONTENTS
Simple linctus

**CLINICAL USE**
Relief of dry, irritating coughs

**DOSE IN NORMAL RENAL FUNCTION**
5 mL 3–4 times daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Molecular weight (daltons)</th>
<th>210.1 (Citric acid monohydrate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Protein binding</td>
<td>No data</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>No data</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>No data</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>No data</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Unknown dialysability. Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td></td>
</tr>
<tr>
<td>HDF/High Flux</td>
<td></td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- Sugar content has not been found to alter diabetics’ insulin requirements. Use diabetic cough preparations whenever possible.
Simvastatin

**CLINICAL USE**

HMG CoA reductase inhibitor:
- Primary hypercholesterolaemia

**DOSE IN NORMAL RENAL FUNCTION**

10–80 mg at night

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Molecular weight (daltons)</th>
<th>418.6</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Protein binding</td>
<td>&gt;95</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>13</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>54</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1.9/–</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Dose as in normal renal function</th>
<th>10–20 mg daily. In severe renal impairment doses above 10 mg should be used with caution (doses up to 40 mg have been used)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

| CAPD | Unlikely to be dialysed. Dose as in GFR<10mL/min |
| HD   | Unlikely to be dialysed. Dose as in GFR<10mL/min |
| HDF/High flux | Unknown dialysability. Dose as in GFR<10mL/min |
| CAV/VVHD | Unknown dialysability. Dose as in normal renal function |

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Anti-arrhythmics: increased risk of myopathy with amiodarone – do not exceed 20 mg of simvastatin.¹
- Antibacterials: increased risk of myopathy with clarithromycin, daptomycin, telithromycin and erythromycin – avoid concomitant use; increased risk of myopathy with fusidic acid
- Anticoagulants: effects of coumarins enhanced
- Antifungals: increased risk of myopathy with itraconazole, posaconazole or ketoconazole and possibly miconazole – avoid concomitant use; possibly increased risk of myopathy with imidazoles and triazoles
- Antivirals: increased risk of myopathy with atazanavir, indinavir, nelfinavir, ritonavir or saquinavir and possibly amprenavir or lopinavir – avoid concomitant use; concentration reduced by efavirenz
- Calcium-channel blockers: increased risk of myopathy with verapamil and possibly diltiazem – do not exceed 20 mg of simvastatin with verapamil or 40 mg with diltiazem.¹
- Ciclosporin: increased risk of myopathy – do not exceed 10 mg of simvastatin.¹
- Grapefruit: increased risk of myopathy – avoid concomitant use
- Hormone antagonists: possibly increased risk of myopathy with danazol – do not exceed 10 mg of simvastatin.¹
- Lipid-lowering agents: increased risk of myopathy with fibrates – do not exceed 10 mg of simvastatin except with fenofibrate; gemfibrozil – avoid; and nicotinic acid

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

- **RATE OF ADMINISTRATION**
  - **COMMENTS**
  -

**OTHER INFORMATION**

References:
Sirolimus

**CLINICAL USE**
Immunosuppressant:
- Prophylaxis of transplant allograft rejection

**DOSE IN NORMAL RENAL FUNCTION**
6 mg loading dose followed by 2 mg daily, adjusted according to levels – see ‘Other Information’

**PHARMACOKINETICS**
- Molecular weight: 914.2 daltons
- % Protein binding: 92
- % Excreted unchanged in urine: 2.2
- Volume of distribution: 4–20 (L/kg)

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/min)**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**: Unlikely to be dialysed. Dose as in normal renal function
- **HD**: Not dialysed. Dose as in normal renal function
- **HDF/High flux**: Unknown dialysability. Dose as in normal renal function
- **CAV/VVHD**: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Antibacterials: concentration increased by clarithromycin and telithromycin – avoid; concentration of both drugs increased with erythromycin; concentration reduced by rifampicin and rifabutin – avoid
  - Antifungals: concentration increased by itraconazole, ketoconazole, miconazole, posaconazole and voriconazole
  - Antivirals: concentration possibly increased by atazanavir and lopinavir
  - Calcium-channel blockers: concentration increased by diltiazem; concentration of both drugs increased with verapamil
  - Ciclosporin: increased absorption of sirolimus – give sirolimus 4 hours after ciclosporin; sirolimus concentration increased; long-term concomitant administration may be associated with a deterioration in renal function
  - Grapefruit juice: concentration of sirolimus increased – avoid concomitant use
  - Mycophenolate: concomitant use of mycophenolate and sirolimus increases plasma levels of both sirolimus and mycophenolic acid

**ADMINISTRATION**
- **RECONSTITUTION**
  - 
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - 
- **COMMENTS**
  - 

**OTHER INFORMATION**
- Aim for trough levels of 4–12 ng/mL where sirolimus is used in combination with low dose ciclosporin
- In cases of delayed graft function or where a calcineurin inhibitor is not tolerated or contraindicated, sirolimus may be used with steroids alone. A loading dose of 10–15 mg may be given, followed by maintenance dose of 3–6 mg daily and adjust according to levels. Aim for trough levels of 8–20 ng/mL
- May be used in combination with MMF, but can lead to delayed wound healing post surgery. Sirolimus can increase levels of mycophenolate mofetil leading to anaemia
- Some centres successfully using level-controlled sirolimus in conjunction with low dose tacrolimus
- Anecdotally, has been used for encapsulating sclerosing peritonitis in a CAPD patient at Guy’s Hospital, London. Acts by interfering with various growth factors and their effect on impairing wound healing
Pneumonitis appears to be more common with sirolimus than initially thought, especially if the trough levels are on the high side. (Glare J. Adverse effect report – pneumonitis with sirolimus. Ann Intern Med. 2006; 144: 505–09.)

If changing from tablets to solution, give the same dose and monitor trough levels 1–2 weeks later.

Tablet has a 27% increased bioavailability compared with the solution.

Sirolimus has been associated with anaphylactic/anaphylactoid reactions, angioedema and hypersensitivity vasculitis.
Sitagliptin

**CLINICAL USE**
Treatment of type 2 diabetes in combination with metformin or a thiazolidinedione

**DOSE IN NORMAL RENAL FUNCTION**
100 mg once daily

**PHARMACOKINETICS**
- **Molecular weight (daltons):** 523.3 (as phosphate)
- **% Protein binding:** 38
- **% Excreted unchanged in urine:** 79
- **Volume of distribution (L/kg):** 198 litres
- **Half-life – normal/ESRF (hrs):** 12.4/Probably increased

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- **30–50:** 50 mg once daily
- **<30:** 25 mg once daily

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD:** Not dialysed. Dose as in GFR>30 mL/min
- **HD:** Not dialysed. Dose as in GFR>30 mL/min
- **HDF/High flux:** Dialysed. Dose as in GFR>30 mL/min
- **CAV/VVHD:** Unknown dialysability. Dose as in GFR>30 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**
  -

**OTHER INFORMATION**
- 13.5% of dose is removed during a 3–4 hour haemodialysis session
- In severe renal impairment (GFR<30 mL/min) the AUC was increased 4-fold
- 50 mg and 25 mg tablets are only available in the USA at present
Sodium bicarbonate

**CLINICAL USE**
- Metabolic acidosis
- Alkalisation of urine
- Renoprotection against contrast media

**DOSE IN NORMAL RENAL FUNCTION**
Oral: 0.5–1.5 g 3 times daily (or more may be required)
IV: 8.4%, 60–120 mL per hour; 4.2%, up to 120 mL per hour; 1.26% or 1.4% - see 'Other Information'

**PHARMACOKINETICS**
- Molecular weight (daltons): 84
- % Protein binding: 0
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): Dependent on the physical state of the patient at the time
- Half-life – normal/ESRF (hrs): No data

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Dialysed. Dose as in normal renal function
- HD: Dialysed. Dose as in normal renal function
- HDF/High flux: Dialysed. Dose as in normal renal function
- CAV/VVHD: Dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Increases lithium excretion

**ADMINISTRATION**
**RECONSTITUTION**
- **ROUTE**
  - Oral, IV, central administration for undiluted infusion
  - **RATE OF ADMINISTRATION**
  - **COMMENTS**

**OTHER INFORMATION**
- Caution – may result in sodium retention and oedema
- Sodium bicarbonate 1.26% or 1.4% may be given IV to prevent the nephrotoxicity associated with scans or procedures involving radiological contrast media. A typical hydration regimen is 3 ml/kg/hour for 1 hour prior to the procedure, followed by 1 mL/kg/hour for 6 hours afterwards
- 8.4% ≡ 1 mmol bicarbonate + 1 mmol sodium per mL
- 500 mg sodium bicarbonate tablet ≡ 6 mmol sodium + 6 mmol bicarbonate
- Sodium bicarbonate reduces serum potassium concentrations by inducing a shift of potassium ions into the cell
- A sugar free raspberry flavoured oral solution of 8.4% sodium bicarbonate is available from Martindale
# Sodium chloride

## CLINICAL USE
Treatment and prophylaxis of sodium chloride deficiency

## DOSE IN NORMAL RENAL FUNCTION
- **Oral prophylaxis:** 40–80 mmol sodium daily, up to a maximum of 200 mmol sodium daily IV: in severe deficiency 2–3 litres over 2–3 hours then reduce

## PHARMACOKINETICS
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>58.4</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>0</td>
</tr>
<tr>
<td>% Excreted</td>
<td>No data</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>Dependent on the physiological state of the patient at the time</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>No data</td>
</tr>
</tbody>
</table>

## DOSE IN RENAL IMPAIRMENT
- **GFR (mL/Min):**
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

## IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- May impair the efficacy of antihypertensive drugs in chronic renal failure

## ADMINISTRATION

### RECONSTITUTION
- **ROUTE**
  - Oral, IV

### RATE OF ADMINISTRATION
- **COMMENTS**

## OTHER INFORMATION
- **Other regimens:** for acute muscular cramps post haemodialysis, 10 mL sodium chloride 30% injection diluted in 100 mL sodium chloride 0.9%, and infused over 30 minutes or in dialysis washback
- **Sodium salts should be administered with caution to patients with congestive heart failure, peripheral or pulmonary oedema, or impaired renal function**
- Slow sodium® 600 mg tablet approximately 10 mmol sodium and 10 mmol chloride

## DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>
Sodium clodronate

**CLINICAL USE**

Bisphosphonate:
1. Management of osteolytic lesions, hypercalcaemia and bone pain associated with skeletal metastases in patients with breast cancer or multiple myeloma
2. Hypercalcaemia of malignancy

**DOSE IN NORMAL RENAL FUNCTION**

1. Oral: 1.6–3.2 g daily in single or 2 divided doses
   - Loron-520: 2–4 tablets daily
2. Slow IV infusion: 300 mg daily for 7–10 days or a single dose infusion of 1.5 g

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Molecular weight (daltons)</th>
<th>360.9 (as disodium salt)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Protein binding</td>
<td>36</td>
</tr>
<tr>
<td>% Excreted</td>
<td>&gt;70</td>
</tr>
<tr>
<td>unchanged in urine</td>
<td></td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.3</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1st phase: 2; 2nd phase: 13/51</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td></td>
</tr>
<tr>
<td>10–30</td>
<td>50% of normal dose</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Avoid</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

| CAPD | Not dialysed. Dose as in GFR<10mL/min |
| HD   | Dialysed. Dose as in GFR<10mL/min    |
| HDF/High flux | Dialysed. Dose as in GFR<10mL/min |
| CAV/ | Unknown dialysability. Dose as in GFR=10–30mL/min |
| VVHD |                                  |

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>Oral, IV infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>RATE OF ADMINISTRATION</td>
<td>(1) Single infusion: 1500 mg over 4 hours</td>
</tr>
<tr>
<td></td>
<td>(2) Multiple infusions: 300 mg over at least 2 hours</td>
</tr>
</tbody>
</table>

**COMMENTS**

- (1) Single infusion: 1500 mg sodium clodronate to 500 mL sodium chloride 0.9% or glucose 5%
- (2) Multiple infusions: 300 mg sodium clodronate to 500 mL sodium chloride 0.9% or glucose 5%
- Multiple infusions should be repeated on successive days until normocalcaemia is achieved or to a maximum of 7–10 days
- Whichever method of infusion is employed, most patients will achieve normocalcaemia within 5 days

**OTHER INFORMATION**

- Renal failure has been associated with IV use of bisphosphonates. Smaller doses (up to 300 mg daily) over 2–3 hours are less likely to be associated with renal impairment than high doses by short IV infusion
- Reversible elevations of creatinine have been reported. Renal function should be monitored during treatment
- Orally: avoid food for one hour before and after treatment, particularly calcium-containing products; also avoid iron, mineral supplements and antacids
Sodium fusidate

CLINICAL USE
Antibacterial agent

DOSE IN NORMAL RENAL FUNCTION
- Oral: 0.5–1 g (as sodium fusidate) every 8 hours
- Suspension: 750 mg every 8 hours (as fusidic acid)
- IV: 500 mg (as sodium fusidate) every 8 hours

PHARMACOKINETICS
- Molecular weight: 538.7 daltons
- % Protein binding: 95
- % Excreted unchanged in urine: <1
- Volume of distribution: 0.2 L/kg

DOSE IN RENAL IMPAIRMENT
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Antivirals: concentration of both drugs increased in combination with ritonavir – avoid concomitant use
- Statins: increased risk of myopathy with simvastatin and atorvastatin especially in diabetics

ADMINISTRATION
RECONSTITUTION
- Use buffered solution provided, then dilute in 500 mL sodium chloride 0.9%

ROUTE
- IV (peripherally), oral

RATE OF ADMINISTRATION
- Over 6 hours

COMMENTS
- Unlicensed administration: 500 mg/10 mL buffered solution diluted to 100 mL and given via a central line over 2–6 hours

OTHER INFORMATION
- 500 mg reconstituted with buffer contains 3.1 mmol sodium and 1.1 mmol of phosphate
- Can be administered neat via central line (unlicensed)
Sodium nitroprusside

**CLINICAL USE**
- Hypertensive crisis
- Heart failure
- Controlled hypotension in surgery

**DOSE IN NORMAL RENAL FUNCTION**
- 0.3–8 micrograms/kg/minute
- Maintenance of blood pressure: 20–400 mcg/minute
- Heart failure: 10–200 mcg/minute
- Controlled blood pressure in surgery: maximum 1.5 mcg/kg/minute

**PHARMACOKINETICS**
- Molecular weight (daltons) 297.9
- % Protein binding 0
- % Excreted unchanged in urine <10
- Volume of distribution (L/kg) 0.2
- Half-life – normal/ESRF (hrs) 2–10 minutes/Unchanged

**DOSE IN RENAL IMPAIRMENT**
| GFR (mL/min) | Dose as in normal renal function | Avoid prolonged use
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Dialysed. Dose as in GFR<10 mL/min
- HD: Dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect

**ADMINISTRATION**

**RECONSTITUTION**
- 2–3 mL glucose 5%

**ROUTE**
- IV

**RATE OF ADMINISTRATION**
- 10–400 micrograms/minute, adjusted according to response

**COMMENTS**
- Dilute 50 mg in 250–1000 mL glucose 5% to give a concentration of 50–200 mcg/mL
- Minimum volume is 1 mg/mL via central line. (UK Critical Care Group Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006)
- Wrap syringes and lines in foil to protect from light

**OTHER INFORMATION**
- Sodium nitroprusside is rapidly metabolised to cyanogen which is converted to thiocyanate
- Avoid prolonged use in renal impairment because accumulation of thiocyanate (which is dialysable) may cause seizures or a coma
- Monitor thiocyanate and cyanide levels
- Do not stop infusion abruptly – tail off over 10–30 minutes
SODIUM VALPROATE

Sodium valproate

**CLINICAL USE**

All forms of epilepsy

**DOSE IN NORMAL RENAL FUNCTION**

- Oral: 600 mg – 2.5 g daily in divided doses
- IV:
  - For continuation of existing oral therapy, IV and oral doses are equivalent, give the same dose.
  - For initiation of new therapy: give a loading dose of 400–800 mg (up to 10 mg/kg), followed by either a constant infusion or intermittent doses up to a cumulative daily dose of 2.5 g

**PHARMACOKINETICS**

- Molecular weight (daltons) 166.2
- % Protein binding 90–95
- % Excreted unchanged in urine 3–7
- Volume of distribution (L/kg) 0.1–0.4
- Half-life – normal/ESRF (hrs) 6–15/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Dialysed. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Antidepressants: antagonise anticonvulsant effect
- Anti-epileptics: concentration reduced by carbamazepine; concentration of active carbamazepine metabolite increased; increased concentration of lamotrigine, primidone, active metabolite of primidone, and possibly ethosuximide; sometimes reduces concentration of active metabolite of oxcarbazepine; alters phenytoin concentration; phenytoin and primidone reduce valproate concentration
- Antimalarials: mefloquine antagonises anticonvulsant effect; increased convulsions with chloroquine and hydroxychloroquine
- Antipsychotics: antagonise anticonvulsant effect; increased neutropenia with olanzapine
- Ciclosporin: variable ciclosporin blood level response
- Ulcer-healing drugs: metabolism inhibited by cimetidine, increased concentration

**ADMINISTRATION**

**RECONSTITUTION**
- Use solvent provided

**ROUTE**
- IV, oral, PR (unlicensed)

**RATE OF ADMINISTRATION**
- 3–5 minutes bolus, or continuous infusion

**COMMENTS**

**OTHER INFORMATION**

- Increases ketones in urine. May give false positive urine tests for ketones
- Sodium valproate serum levels do not correlate with anti-epileptic activity
- Monitor serum levels to ensure not greater than 100 micrograms/mL, or if non-compliance is suspected
- Suppositories are available on a named patient basis

References:
Sorafenib

**CLINICAL USE**
Treatment of advanced renal cell carcinoma

**DOSE IN NORMAL RENAL FUNCTION**
400 mg twice daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
</table>
| Molecular weight               | 464.8 (637 as tosylate) daltons |%
| % Protein binding              | 99.5                           |
| % Excreted unchanged in urine  | 0                              |
| Volume of distribution (L/kg)  | No data                        |
| Half-life – normal/ESRF (hrs)  | 25–48                          |

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–30</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unlikely to be dialysed. Dose as in GFR=10–30mL/min</td>
</tr>
<tr>
<td>VVHD</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: may enhance effect of coumarins
- Antipsychotics: avoid concomitant use with clozapine (increased risk of agranulocytosis)

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- Administer preferably without food

**OTHER INFORMATION**
- Increased amylase and lipase and hypophosphataemia are common
- Most common side effects are diarrhoea and dermatological effects
- Sorafenib is metabolised primarily in the liver and undergoes oxidative metabolism mediated by CYP3A4, as well as glucuronidation mediated by UGT1A9
- Following oral administration of a 100 mg dose of a solution formulation of sorafenib, 96% of the dose was recovered within 14 days, with 77% of the dose excreted in faeces, and 19% of the dose excreted in urine as glucuronidated metabolites. Unchanged sorafenib, accounting for 51% of the dose, was found in faeces but not in urine, indicating that biliary excretion of unchanged drug might contribute to the elimination of sorafenib
- A case report of interstitial nephritis has been reported in a patient with CRF due to FSGS. (Izzedine H. Interstitial nephritis in a patient taking sorafenib. *Nephrol Dial Transplant.* 2007; 22: 2411)
Sotalol hydrochloride

**CLINICAL USE**

Beta-adrenoceptor blocker:
- Treatment of life-threatening ventricular arrhythmias
- Prophylaxis of SVT

**DOSE IN NORMAL RENAL FUNCTION**

- Oral: 80–640 mg per day in single or divided doses (480–640 mg under specialist supervision)
- IV: 20–120 mg every 6 hours

**PHARMACOKINETICS**

- Molecular weight (daltons): 308.8
- % Protein binding: 0
- % Excreted unchanged in urine: >90
- Volume of distribution (L/kg): 1.6–2.4

**DOSE IN RENAL IMPAIRMENT**

- GFR (mL/min):
  - 20–50: 50% of normal dose
  - 10–20: 25% of normal dose
  - <10: 25% of normal dose and use with caution

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HD: Dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**

- Potentially hazardous interactions with other drugs
  - Anaesthetics: enhanced hypotensive effect
  - Analgesics: NSAIDs antagonise hypotensive effect
  - Anti-arrhythmics: increased risk of myocardial depression and bradycardia; increased risk of bradycardia, myocardial depression and AV block with amiodarone; increased risk of ventricular arrhythmias with amiodarone, disopyramide or procainamide – avoid
  - Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin – avoid
  - Antidepressants: enhanced hypotensive effect with MAOIs; increased risk of ventricular arrhythmias with tricyclics
  - Antihistamines: increased risk of ventricular arrhythmias with mizolastine – avoid
  - Antihypertensives: enhanced hypotensive effect; increased risk of withdrawal hypertension with clonidine; increased risk of first dose hypotensive effect with post-synaptic alpha-blockers such as prazosin
  - Antimalarials: increased risk of bradycardia with mefloquine; avoid with artemether and lumefantrine
  - Antipsychotics: enhanced hypotensive effect with phenothiazines; increased risk of ventricular arrhythmias with amisulpride, phenothiazines, pimozide or sertindole
  - Atomoxetine: increased risk of ventricular arrhythmias
  - Calcium-channel blockers: increased risk of bradycardia and AV block with diltiazem; hypotension and heart failure possible with nifedipine and nisoldipine; asystole, severe hypotension and heart failure with verapamil
  - Diuretics: enhanced hypotensive effect; increased risk of ventricular arrhythmias due to hypokalaemia
  - 5HT3 antagonists: increased risk of ventricular arrhythmias due to hypokalaemia
  - Moxisylyte: possible severe postural hypotension
  - Sympathomimetics: severe hypertension with adrenaline and noradrenaline and possibly with dobutamine

**RETURN TO CONTENTS**
## ADMINISTRATION

**RECONSTITUTION**

- 

**ROUTE**

- IV, oral

**RATE OF ADMINISTRATION**

- Slow IV bolus with ECG monitoring
- Over 10 minutes

**COMMENTS**

- 

## OTHER INFORMATION

- Sotalol prolongs the QT interval, which predisposes to the development of *torsades de pointes*
- If used in haemodialysis, give lowest possible dose, after dialysis
Spironolactone

**CLINICAL USE**
Diuretic, aldosterone antagonist

**DOSE IN NORMAL RENAL FUNCTION**
25–400 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 416.6
- % Protein binding: 90
- % Excreted unchanged in urine: 0 (47–57 as metabolites)
- Volume of distribution (L/kg): No data

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50: 50% of normal dose
- 10–20: 50% of normal dose
- <10: Use with caution See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/: Not dialysed. Dose as in GFR=10–20 mL/min
- VVHD: GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- ACE inhibitors or angiotensin-II antagonists: enhanced hypotensive effect; risk of severe hyperkalaemia
- Antibacterials: avoid concomitant use with lymecycline
- Antidepressants: increased risk of postural hypotension with tricyclics
- Antihypertensives: enhanced hypotensive effect; increased risk of first dose hypotensive effect with post-synaptic alpha-blockers
- Cardiac glycosides: increased digoxin concentration; possibly increased digitoxin concentration
- Ciclosporin: increased risk of hyperkalaemia
- Lithium: reduced lithium excretion
- NSAIDs: increased risk of hyperkalaemia (especially with indometacin); increased risk of nephrotoxicity; diuretic effect of spironolactone antagonised by aspirin
- Potassium salts: increased risk of hyperkalaemia
- Tacrolimus: increased risk of hyperkalaemia

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**
- Renal patients are at an increased risk of hyperkalaemia and therefore spironolactone should be used with caution. It has active metabolites with long half-lives
- Small studies have shown that doses of 25 mg of spironolactone 3 times a week can be safely used in haemodialysis patients although unknown whether that dose would be therapeutic – potassium levels should be monitored closely. (Sauden. 2003.)
- Another small study used 25 mg daily but the potassium was monitored 3 times a week. (Hussain. 2003)
Stavudine

**CLINICAL USE**
Nucleoside reverse transcriptase inhibitor:
- Treatment of HIV in combination with other antiretroviral drugs

**DOSE IN NORMAL RENAL FUNCTION**
- <60 kg: 30 mg twice daily
- >60 kg: 40 mg twice daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 224.2
- % Protein binding: <1
- % Excreted unchanged in urine: 40
- Volume of distribution (L/kg): 0.5
- Half-life – normal/ESRF (hrs): 1–1.5/5.5–8

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/min)**
  - 26–50: <60 kg: 15 mg twice daily
    >60 kg: 20 mg twice daily
  - <25: <60 kg: 15 mg daily
    >60 kg: 20 mg daily

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**
  - Unknown dialysability. Dose as in GFR<25 mL/min
- **HD**
  - Dialysed. Dose as in GFR<25 mL/min
- **HDF/High flux**
  - Dialysed. Dose as in GFR<25 mL/min
- **CAV/VVHD**
  - Unknown dialysability. Dose as in GFR=26–50 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs:
- Antivirals: zidovudine may inhibit intracellular activation – avoid concomitant use; increased risk of side effects with didanosine; effects possibly inhibited by ribavirin
- Cytotoxics: effects possibly inhibited by doxorubicin; increased risk of toxicity with hydroxycarbamide – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
  - Administer at least an hour before food

**OTHER INFORMATION**
- Clearance by haemodialysis is 120 mL/min
- Lactic acidosis, sometimes fatal, has been reported with the use of nucleoside analogues
- Patients with ERF are more likely to develop peripheral neuropathy
Streptokinase

**CLINICAL USE**

Fibrinolytic:
- Thrombolysis in DVT, PE, acute arterial thromboembolism, acute MI, thrombosed A-V shunts

**DOSE IN NORMAL RENAL FUNCTION**

- Loading dose: 250,000 IU followed by 100,000 IU/hour for 12–72 hours (refer to SPC)
- Myocardial Infarction: 1.5 MIU followed by aspirin
- Thrombosed HD shunts: 10–25,000 IU sealed in shunt and repeated after 30–45 minutes

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>47,408</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>No data</td>
</tr>
<tr>
<td>% Excreted</td>
<td>0 unchanged in urine</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.02–0.08</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>18 minutes/–</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unlikely to be dialysed.</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed.</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Anticoagulants should not be given with streptokinase
- Heparin infusions should be stopped 4 hours before streptokinase infusion. If this is not possible, protamine sulphate should be used to neutralise the heparin; heparin infusions can be restarted 4 hours post streptokinase infusion followed by oral anticoagulants

**ADMINISTRATION**

**RECONSTITUTION**
- See manufacturer’s literature

**ROUTE**
- IV

**RATE OF ADMINISTRATION**
- Give loading dose of 250,000 IU in 100 mL fluid over 30 minutes, followed by an appropriate volume for the maintenance dose
- Give 1.5 MIU for acute MI in 50–200 mL fluid over 1 hour

**COMMENTS**
- For occluded HD shunts, add 100,000 IU to 100 mL sodium chloride 0.9% and put 10–25 mL into the clotted portion of the shunt

**OTHER INFORMATION**

- There are no significant changes in pharmacokinetics in patients with renal insufficiency. Dosage reduction is therefore not necessary
Streptomycin (unlicensed product)

**CLINICAL USE**
Antibacterial agent:
- Tuberculosis, in combination with other drugs
- Adjunct to doxycycline in brucellosis
- Enterococcal endocarditis

**DOSE IN NORMAL RENAL FUNCTION**
- <40 years and weight >50 kg: 15 mg/kg (maximum 1 g) daily or 3 times a week
- >40 years and weight <50 kg: 0.5–0.75 g daily or 0.75 g 3 times a week
- Non-tuberculosis infections: 1–2 g daily in divided doses
- Adjust doses according to levels

**PHARMACOKINETICS**
- Molecular weight: 581.6 (1457.4 as sulphate)
- % Protein binding: 34–35
- % Excreted unchanged in urine: 29–89
- Volume of distribution (L/kg): 0.26
- Half-life – normal/ESRF (hrs): 2.5/100

**DOSE IN RENAL IMPAIRMENT GFR (mL/Min)**
- 20–50: Give every 24–72 hours. Dose according to levels
- 10–20: Give every 24–72 hours. Dose according to levels
- <10: Give every 72–96 hours. Dose according to levels

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Dialysed. Dose as in GFR<10 mL/min
- HD: Dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Botulinum toxin: neuromuscular block enhanced
- Ciclosporin: increased risk of nephrotoxicity
- Cytotoxics: increased risk of nephrotoxicity and ototoxicity with platinum compounds
- Loop diuretics: increased risk of ototoxicity
- Muscle relaxants: enhanced effects of non-depolarising muscle relaxants and suxamethonium
- Parasympathomimetics: neostigmine and pyridostigmine antagonised by aminoglycosides
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**
**RECONSTITUTION**
- Dissolve 1 g in 2 or 3 mL water for injection
**ROUTE**
- IM, IV
**RATE OF ADMINISTRATION**
- In 100 mL sodium chloride 0.9% or glucose 5% over 30 minutes

**COMMENTS**
- In patients who experience tingling sensations or dizziness during administration, increase the infusion time to 60 minutes

**OTHER INFORMATION**
- Available on a named patient basis from Pfizer
- Peak level taken 1 hour post dose and should be in the range 15–40 mg/litre; trough level (taken pre dose) should be <5 mg/litre, or <1 mg/litre in renal impairment or those over 50 years of age
- May be less nephrotoxic than other aminoglycosides
- PD peritonitis dose is 20–40 mg/litre/day
- Risk of side effects increases after a cumulative dose of 100 g
A study in 4 patients used IV streptomycin at a dose of 7–15 mg/kg over 30–60 minutes without any problems, although IV administration did increase risk of toxicity.

Due to the efficacy of twice weekly therapy, it is recommended that tuberculosis patients with severe renal impairment be given a dose of 750 mg 2–3 times a week for the first 2 months of treatment; trough levels should not exceed 4 mg/L. (Ellard GA. Cerebrospinal fluid drug concentrations and the treatment of tuberculous meningitis. Am Rev Respir Dis. 1993; 148: 650–5.)

Peak serum concentrations in individuals with renal impairment should not exceed 20–25 mcg/mL.

Risk of severe neurotoxicity, irreversible vestibular damage and cochlear reactions is greatly increased in patients with impaired renal function; optic nerve dysfunction, peripheral neuritis, arachnoiditis and encephalopathy may also occur.
Strontium ranelate

**CLINICAL USE**
Treatment of post-menopausal osteoporosis

**DOSE IN NORMAL RENAL FUNCTION**

2 g once daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>513.5</td>
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<tr>
<td>% Protein binding</td>
<td>25</td>
</tr>
<tr>
<td>% Excreted in urine unchanged</td>
<td>66</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>60/Increased</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–30</td>
<td>See ‘Other Information’</td>
</tr>
<tr>
<td>&lt;10</td>
<td>See ‘Other Information’</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Dialysis Type</th>
<th>Dose as in Normal Renal Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–30mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

- Antibiotics: strontium can reduce absorption of oral tetracycline and quinolones – suspend strontium therapy during treatment

**ADMINISTRATION**

**RECONSTITUTION**

- Glass of water

**ROUTE**

- Oral

**RATE OF ADMINISTRATION**

- COMMENTS

**OTHER INFORMATION**

- Give between meals as the absorption of strontium is reduced by food and milk products
- Interferes with colorimetric methods of blood and urinary calcium concentrations
- Give with calcium and vitamin D supplements
- Steady state strontium levels are approximately 50% higher in patients with a GFR<25 mL/min compared to patients with normal renal function. No specific treatment effect was detected in patients with renal impairment (Cohen-Solal ME, et al. Fluoride and strontium accumulation in bone does not correlate with osteoid tissue in dialysis patients. *Nephrol Dial Transplant*. 2002; 17: 449–54.)
- Another study found that haemodialysis patients with osteomalacia developed high bone-strontium levels. (D’Haese PC, et al. Increased bone strontium levels in hemodialysis patients with osteomalacia. *Kidney Int*. 2000, Mar; 57: 1107–14.)
- There is no evidence of high levels of bone strontium in dialysis patients being related to osteomalacia. (Data from Servier. Meunier PJ, et al. The effects of strontium ranelate on the risk of vertebral fracture in women with post-menopausal osteoporosis. *NEJM*. 2004; 350(5): 459–68.)
- Oral bioavailability is about 25%

**RETURN TO CONTENTS**
Sucralfate (aluminium sucrose sulphate)

**CLINICAL USE**
- Treatment of peptic ulcer and chronic gastritis
- Prophylaxis of stress ulceration in seriously ill patients

**DOSE IN NORMAL RENAL FUNCTION**
- 4 g daily in 2–4 divided doses
- Prophylaxis of stress ulceration: 1 g 6 times daily
- Maximum 8 g daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 2086.7
- % Protein binding: No data
- % Excreted unchanged in urine: 3.5
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): No data

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min):
  - 20–50: 4 g daily
  - 10–20: 2–4 g daily
  - <10: 2–4 g daily

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Not dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
- Reduced absorption of digoxin, tetracyclines, quinolones, coumarins and phenytoin – give 2 hours after sucralfate

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  - Sucralfate exerts its action at the site of the ulcer, and is minimally absorbed (3–5%) from the GI tract as sucrose sulphate
  - In normal renal function, any aluminium which is absorbed is excreted in the urine
  - Tablets may be dispersed in 10–15 mL of water

**OTHER INFORMATION**
- Sucralfate should be used with caution in renal impairment as aluminium may be absorbed and accumulate
- In severe renal impairment and patients receiving dialysis, sucralfate should be used with extreme caution and only for short periods
- Absorbed aluminium is bound to plasma proteins and is not dialysable
- Use of other aluminium-containing products with sucralfate can increase the total body burden of aluminium
Sulfadiazine

**CLINICAL USE**

Antimicrobial agent:
- Toxoplasmosis in AIDS patients (unlicensed indication)
- Prevention of rheumatic fever

**DOSE IN NORMAL RENAL FUNCTION**

Loading dose: 2–4 g
Maintenance dose: 2–6 g daily in divided doses

**PHARMACOKINETICS**

- Molecular weight: 250.3; 272.3 (as sodium salt)
- % Protein binding: 20–55%
- % Excreted unchanged in urine: 80 – See ‘Other Information’
- Volume of distribution (L/kg): 0.29
- Half-life – normal/ESRF (hrs): 17/Prolonged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Use 50% of dose and monitor levels</th>
<th>Use 25% of dose and monitor levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Renal Replacement Therapy</th>
<th>Dose as in normal renal function</th>
<th>Use 50% of dose and monitor levels</th>
<th>Use 25% of dose and monitor levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose as in GFR=10–20mL/min</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Antibacterials: increased risk of crystalluria with methenamine
- Anticoagulants: effect of coumarins enhanced
- Anti-epileptics: antifolate effect and concentration of phenytoin increased
- Antimalarials: increased risk of antifolate effect with pyrimethamine
- Antipsychotics: avoid concomitant use with clozapine (increased risk of agranulocytosis)
- Ciclosporin: reduced levels of ciclosporin; increased risk of nephrotoxicity
- Cytotoxics: increase risk of methotrexate toxicity

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

- **RATE OF ADMINISTRATION**
  - **COMMENTS**
  -

**OTHER INFORMATION**

- Penetrates into the CSF within 4 hours of oral administration to produce therapeutic concentrations which may be more than half those in the blood
- Metabolised in the liver to the acetylated form, with elimination predominantly via the kidneys
- Urinary excretion of sulfadiazine and its acetyl derivative is dependent on pH; when the urine is acidic about 30% is excreted unchanged in both fast and slow acetylators, whereas when the urine is alkaline about 75% is excreted unchanged by slow acetylators
- Crystalluria may be avoided by adequate hydration and alkalinising the urine to a pH >7.15
- Blood concentrations of 100–150 micrograms/mL are desirable
- For treatment of toxoplasmosis, use sulfadiazine in conjunction with pyrimethamine 25–100 mg daily
Sulfasalazine (sulphasalazine)

**CLINICAL USE**
- Ulcerative colitis
- Crohn's disease
- Rheumatoid arthritis

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: 1–2 g 4 times daily, reduced to 0.5 g 4 times daily
- Enema: 3 g at night
- Suppositories: 0.5–1 g twice daily
- Rheumatoid arthritis: 0.5 g daily, increased to 1.5 g twice daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>398.4</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>95–99</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>10–15</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>5.9–9.1</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>18/–</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function.</th>
<th>Use with caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Start at very low dose and monitor. Use with caution</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapies</th>
<th>Dose as in GFR&lt;10 mL/min</th>
<th>Use with caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed.</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed.</td>
<td></td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unlikely to be dialysed.</td>
<td></td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>GFR=10–20 mL/min</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
- Ciclosporin: may reduce ciclosporin levels

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral, rectal
- **RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- 15% of a dose of sulfasalazine is absorbed in the small intestine and becomes highly bound to plasma proteins. The remainder is split into sulfapyridine and 5-ASA by colonic bacteria. Sulfapyridine is rapidly absorbed from the colon, whereas 5-ASA is poorly absorbed
- Most of a dose of sulfasalazine is excreted in the urine. Unchanged sulfasalazine accounts for 15% of the original dose, sulfapyridine and its metabolites 60%, and 5-ASA and its metabolites 20–33%
- Unabsorbed drug is excreted in the faeces
- In patients with moderate to severe renal impairment, toxicity includes increased risk of crystalluria – ensure high fluid intake
Sulfinpyrazone

**CLINICAL USE**
- Gout prophylaxis
- Hyperuricaemia

**DOSE IN NORMAL RENAL FUNCTION**
100–200 mg daily with food (or milk); maximum dose 600–800 mg

**PHARMACOKINETICS**
- Molecular weight: 404.5 daltons
- % Protein binding: 98
- % Excreted unchanged in urine: 22–42
- Volume of distribution: 0.06 L/kg

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function. Use lower dose range
  - <10: Avoid

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Avoid. See ‘Other Information’
- HD: Not dialysed. Avoid. See ‘Other Information’
- HDF/High flux: Unknown dialysability. Avoid. See ‘Other Information’
- CAV/VVHD: Not dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: enhances anticoagulant effect of coumarins
- Antidiabetics: enhances effect of sulphonylureas
- Anti-epileptics: increases plasma concentration of phenytoin
- Ciclosporin: may reduce ciclosporin levels

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  -

**OTHER INFORMATION**
- An adequate fluid intake of 2–3 litres daily should be taken to reduce risk of uric acid renal calculi
- Uricosuric effects are lost when GFR<10 mL/min
- Reversible acute renal failure may occur especially with high initial doses
- Can cause salt and water retention
- In combination with aspirin, has been shown to improve vascular access thrombosis in haemodialysis patients, but there was an increased occurrence of gastrointestinal bleeding (Domoto DT, Bauman JE, Joist JH. Combined aspirin and sulfinpyrazone in the prevention of recurrent hemodialysis vascular access thrombosis. *Thromb Res.* 1991, Jun 15; 62(6): 737–43)
Sulindac

**CLINICAL USE**

NSAID and analgesic

**DOSE IN NORMAL RENAL FUNCTION**

200 mg twice daily

**PHARMACOKINETICS**

- Molecular weight: 356.4 daltons
- % Protein binding: 95
- % Excreted unchanged in urine: 7
- Volume of distribution: No data
- Half-life – normal/ESRF (hrs): 7.8/16.4 (metabolite)/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function. Avoid if possible</td>
</tr>
<tr>
<td>10–20</td>
<td>Give 50–100% of normal dose. Avoid if possible</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Give 50–100% of normal dose. Avoid if possible</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Type</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

- Anticoagulants: effects of coumarins enhanced; possibly increased risk of bleeding with heparins and coumarins
- Antidepressants: increased risk of bleeding with SSRIs and venlafaxine
- Antidiabetic agents: effects of sulphonylureas enhanced
- Anti-epileptics: possibly increased phenytoin concentration
- Antivirals: increased risk of haematological toxicity with zidovudine; concentration possibly increased by ritonavir
- Ciclosporin: may potentiate nephrotoxicity
- Cytotoxic agents: reduced excretion of methotrexate; increased risk of bleeding with erlotinib
- Diuretics: increased risk of nephrotoxicity; antagonism of diuretic effect; hyperkalaemia with potassium-sparing diuretics
- Lithium: excretion decreased
- Pentoxifylline: increased risk of bleeding
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**

- **COMMENTS**
  -

**OTHER INFORMATION**

- Sulindac has become the NSAID of choice in some centres for patients with renal impairment because of reports of its renal sparing effects. There is evidence that this sparing effect is dose-related and is lost if doses above 100 mg twice daily are used
- Inhibition of renal prostaglandin synthesis by NSAIDs may interfere with renal function, especially in the presence of existing renal disease – avoid NSAIDs if possible; if not, check serum creatinine 48–72 hours after starting NSAID – if increased, discontinue therapy
- Use normal doses in patients with CKD 5 on dialysis if they do not pass any urine
- Use with caution in renal transplant recipients (can reduce intrarenal autacoid synthesis)
Sulpiride

**CLINICAL USE**

Antipsychotic:
- Acute and chronic schizophrenia

**DOSE IN NORMAL RENAL FUNCTION**

400–800 mg daily increasing to maximum 2.4 g daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>341.4</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>40%</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>90–95%</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1.2–1.7</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>8–9/26</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Give 66% of normal dose, or increase dosing interval by factor of 1.5</td>
</tr>
<tr>
<td>10–20</td>
<td>Give 50% of normal dose, or increase dosing interval by factor of 2</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Give 30% of normal dose, or increase dosing interval by factor of 3</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapeutic modality</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Partly dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Anaesthetics: enhanced hypotensive effect
- Analgesics: increased risk of convulsions with tramadol; enhanced hypotensive and sedative effects with opioids
- Anti-arrhythmics: increased risk of ventricular arrhythmias with anti-arrhythmics that prolong the QT interval, e.g. procainamide, disopyramide and amiodarone – avoid concomitant use with amiodarone
- Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin – avoid concomitant use
- Antidepressants: increased level of tricyclics; possibly increased risk of ventricular arrhythmias and antimuscarinic side effects
- Anti-epileptics: antagonism (convulsive threshold lowered)
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: increased risk of ventricular arrhythmias with pimozide – avoid concomitant use
- Antivirals: concentration possibly increased with ritonavir
- Anxiolytics and hypnotics: increased sedative effects
- Beta-blockers: enhanced hypotensive effect; increased risk of ventricular arrhythmias with sotalol
- Diuretics: enhanced hypotensive effect
- Lithium: increased risk of extrapyramidal side effects and possibly neurotoxicity
- Penicillin: increased risk of ventricular arrhythmias
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**

- **COMMENTS**

**OTHER INFORMATION**

- Sulpiride is almost entirely excreted in the urine as unchanged drug. Administer with caution and decrease the dose in renal impairment
Sumatriptan

**CLINICAL USE**
Acute relief of migraine

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: 50–100 mg; maximum 300 mg in 24 hours
- SC: 6 mg; maximum 12 mg in 24 hours
- Intranasally: 10–20 mg; maximum 40 mg in 24 hours

**PHARMACOKINETICS**
- Molecular weight: 295.4; 413.5 (as succinate)
- % Protein binding: 14–21
- % Excreted unchanged in urine: <20
- Volume of distribution (L/kg): 170 litres
- Half-life – normal/ESRF (hrs): 2/Probably unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function, use with caution</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function, use with caution</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Device</th>
<th>Dose</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
<td></td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
<td></td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function. Use with caution</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antidepressants: risk of CNS toxicity with MAOIs, moclobemide, SSRIs, sertraline, St John's wort – avoid concomitant use; possibly increased serotonergic effects with duloxetine
- Ergot alkaloids: increased risk of vasospasm – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- Injection is pre-filled into syringes ready for administration

**ROUTE**
- Oral, SC, nasal spray

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- Non-renal clearance accounts for about 80% of the total clearance. The remaining 20% is excreted in urine, mainly as metabolites, by active renal tubular secretion
Suxamethonium chloride

**CLINICAL USE**
Depolarising muscle relaxant used in short procedures and ECT

**DOSE IN NORMAL RENAL FUNCTION**
- IV injection: 0.5–1 mg/kg
- IV infusion: 2.5–4 mg/minute; maximum 500 mg/hour

**PHARMACOKINETICS**
- Molecular weight: 397.3 daltons
- % Protein binding: 70
- % Excreted unchanged in urine: <10
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 2–3 minutes/–

**DOSE IN RENAL IMPAIRMENT**
<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function. Use with caution. See ‘Other Information’</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**
  - Unknown dialysability. Dose as in GFR<10mL/min
- **HD**
  - Unknown dialysability. Dose as in GFR<10mL/min
- **HDF/High flux**
  - Unknown dialysability. Dose as in GFR<10mL/min
- **CAV/VVHD**
  - Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: increased risk of myocardial depression and bradycardia with propofol; enhanced effect with volatile liquid general anaesthetics
- Anti-arrhythmics: lidocaine and procainamide enhance muscle relaxant effect
- Antibacterials: effect enhanced by aminoglycosides, clindamycin, polymyxins, vancomycin and piperacillin
- Cardiac glycosides: increased risk of cardiac arrhythmias with digoxin

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - **IV**
  - **RATE OF ADMINISTRATION**
    - Over 10–30 seconds
    - Infusion: 2.5–4 mg/minute, maximum 500 mg/hour

**COMMENTS**
- For continuous infusion add 10 mL to 500 mL glucose 5% or sodium chloride 0.9% = 0.1% solution

**OTHER INFORMATION**
- Suxamethonium is predominantly excreted in the urine as active and inactive metabolites. Patients on dialysis may require a dose at the lower end of the range due to reduced plasma cholinesterase activity
- Use with caution in hyperkalaemia as potassium is released from depolarised muscle
- Hyperkalaemia may occur when suxamethonium is used in CKD 5
Synercid (quinupristin 150 mg/dalfopristin 350 mg)

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
7.5 mg/kg every 8 hours

**PHARMACOKINETICS**
- Molecular weight: 1118.3 (quinupristin); 787 (dalfopristin) – as mesilate
- % Protein binding: 55–78 (quinupristin); 11–26 (dalfopristin)
- % Excreted unchanged in urine: 15 (quinupristin); 19 (dalfopristin)
- Volume of distribution: 0.45 (quinupristin); 0.24 (dalfopristin)
- Half-life – normal/ESRF (hrs): 0.9 (quinupristin); 0.7 (dalfopristin)

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>5–7.5 mg/kg 8–12 hourly</td>
<td>Over 60 minutes</td>
</tr>
<tr>
<td>10–20</td>
<td>5–7.5 mg/kg 8–12 hourly</td>
<td>Central access is recommended: Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>&lt;10</td>
<td>5 mg/kg 8–12 hourly</td>
<td>Stable for 5 hours at room temperature and 24 hours if refrigerated</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. 10–20 mg/kg/day in 2 divided doses
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VHVD: Unlikely to be dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs:
  - Anti-arrhythmics: increased risk of ventricular arrhythmias with disopyramide and lidocaine – avoid concomitant use
  - Anxiolytics and hypnotics: increased concentration of midazolam (risk of profound sedation); metabolism of zopiclone inhibited
  - Calcium-channel blockers: increased concentration of nifedipine
  - Ciclosporin: increased levels of ciclosporin
  - Ergot alkaloids: avoid concomitant use with ergotamine and methysergide
  - Tacrolimus: tacrolimus levels increased by 15%

**ADMINISTRATION**
- Reconstitution:
  - With 5 mL glucose 5% or water for injection
- Route:
  - IV infusion through a central line
- Rate of Administration:
  - Over 60 minutes

**RECOMMENDATIONS**
- Central access is recommended:
  - Dilute reconstituted solution further in 100 mL glucose 5% for central access
  - Or 250 mL for peripheral access (for emergency administration of 1st dose only).

**OTHER INFORMATION**
- After the infusion, flush the line with glucose 5% to minimise venous irritation
- Has been administered intraperitoneally at a dose of 25 mg/L in alternate bags, in combination with intravenous treatment
- Synercid is an inhibitor of CYP 3A4: caution is recommended when co-administering any drug also metabolised by this route

References:
Tacrolimus

**CLINICAL USE**
Immunosuppressive agent:
- Prophylaxis and treatment of acute rejection in liver, heart and kidney transplantation
- Treatment of moderate to severe atopic eczema

**DOSE IN NORMAL RENAL FUNCTION**
Oral:
- Liver transplantation: 100–200 mcg/kg/day in 2 divided doses
- Kidney transplantation: 150–300 mcg/kg/day in 2 divided doses
- Heart transplantation: 75 mcg/kg/day in 2 divided doses

IV:
- Liver transplantation: 10–50 mcg/kg as a continuous 24 hour infusion, starting 6 hours post surgery
- Kidney transplantation: 50–100 mcg/kg as a continuous 24 hour infusion, starting within 24 hours of surgery
- Heart transplantation: 10–20 mcg/kg as a continuous 24 hour infusion

**PHARMACOKINETICS**
- Molecular weight (daltons): 822
- % Protein binding: >98
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): 1300 litres
- Half-life – normal/ESRF (hrs): 12–16/Probably unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min):
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Ciclosporin: may increase the half-life of ciclosporin and exacerbate any toxic effects. The two should not be prescribed concomitantly. Care should be taken when converting from ciclosporin to tacrolimus
- Tacrolimus levels increased by: atazanavir, basiliximab, bromocriptine, caspofungin, chloramphenicol, cimetidine, cortisone, danazol, dapsone, diltiazem, ergotamine, ethinyloestradiol, gestodene, grapefruit juice, imidazole and triazole antifungals, lidocaine, felodipine, lansoprazole, possibly levofloxacin, macrolides, midazolam, nelfinavir, nicardipine, nifedipine, omeprazole, pantoprazole, quinidine, quinupristin/dalfopristin, ritonavir, saquinavir, tamoxifen, telithromycin, theophylline, verapamil and voriconazole
- Tacrolimus levels decreased by: carbamazepine, caspofungin, isoniazid, phenobarbital, phenytoin (phenytoin levels possibly increased), rifampicin and St John’s wort
- Increased nephrotoxicity with: aciclovir, aminoglycosides, amphotericin, co-trimoxazole, ganciclovir, NSAIDs and vancomycin
- Increased risk of hyperkalaemia with: potassium-sparing-diuretics and potassium salts
- Clotrimazole: more than doubles the bioavailability of tacrolimus (US-based researchers report that concomitant clotrimazole substantially increases the relative oral bioavailability of tacrolimus in renal transplant recipients. *Inpharma*. 2005, Dec 10; 1517: 15)
ADMINISTRATION

RECONSTITUTION

ROUTE
- IV, oral, topical

RATE OF ADMINISTRATION
- Continuous infusion over 24 hours

COMMENTS
- Dilute in glucose 5% or sodium chloride 0.9% to a concentration of 4–100 micrograms/mL, i.e. 5 mg in 50–1000 mL
- Incompatible with PVC. Add to either glucose 5% in polyethylene or glass containers or to sodium chloride 0.9% in polyethylene containers
- Contains polyethoxylated castor oil which has been associated with anaphylaxis

OTHER INFORMATION
- When converting from oral to IV, give one fifth of the total daily dose over 24 hours and monitor levels
- Also available as a 0.03% and 0.1% ointment for eczema and anal Crohn’s disease
- Approximate whole blood ranges:
  - Initially: liver: 5–10 ng/mL, renal: 8–15 ng/mL
  - Maintenance: 5–15 ng/mL
Tadalafil

**CLINICAL USE**
Treatment of erectile dysfunction

**DOSE IN NORMAL RENAL FUNCTION**
10–20 mg, 30 minutes to 12 hours before sexual activity

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>389.4</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>94</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>36</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>63 litres</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>17.5/ Increased</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>10 mg initially and use with caution</td>
</tr>
<tr>
<td>&lt;10</td>
<td>10 mg initially and use with caution</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be dialysed. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Alpha-blockers: enhanced hypotensive effect – avoid concomitant use
- Nicorandil: possibly enhanced hypotensive effect – avoid concomitant use
- Nitrates: enhanced hypotensive effect – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- Maximum dosing frequency is once daily
- Due to lack of trial data, maximum recommended dose is 10 mg in severe renal impairment; in practice a higher dose may be used with caution
- Protein binding is not affected by renal impairment

**RETURN TO CONTENTS**
Tamoxifen

CLINICAL USE
● Treatment of breast cancer
● Anovulatory infertility

DOSE IN NORMAL RENAL FUNCTION
● Breast cancer: 20 mg daily
● Anovulatory infertility: 20–80 mg daily

PHARMACOKINETICS
Molecular weight (daltons) 371.5; (563.6 as citrate)
% Protein binding >99
% Excreted unchanged in urine 0
Volume of distribution (L/kg) 20
Half-life – normal/ESRF (hrs) 7 days/Probably unchanged

DOSE IN RENAL IMPAIRMENT
GFR (mL/Min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unknown dialysability. Dose as in normal renal function
HD Unknown dialysability. Dose as in normal renal function
HDF/High flux Unknown dialysability. Dose as in normal renal function
CAV/VVHD Unknown dialysability. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● Anticoagulants: effects of coumarins enhanced

ADMINISTRATION
RECONSTITUTION
–
ROUTE
● Oral
RATE OF ADMINISTRATION
–
COMMENTS
–

OTHER INFORMATION
● Tamoxifen has been used for the treatment of encapsulating peritoneal sclerosis, at a dose of 20 mg daily. (Eltoum MA. Four consecutive cases of peritoneal dialysis-related encapsulating peritoneal sclerosis treated successfully with tamoxifen. Perit Dial Int. 2006, Mar-Apr; 26(2): 183–4)
Tamsulosin hydrochloride

**CLINICAL USE**
Treatment of benign prostatic hyperplasia

**DOSE IN NORMAL RENAL FUNCTION**
400 mcg in the morning after breakfast

**PHARMACOKINETICS**
- Molecular weight (daltons): 445
- % Protein binding: 99
- % Excreted unchanged in urine: 9
- Volume of distribution (L/kg): 0.2
- Half-life – normal/ESRF (hrs): 4–5.5 (M/R: 10–15)/Increased

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function. Use with caution</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Type</th>
<th>Dose/Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Antidepressants: enhanced hypotensive effect with MAOIs
- Beta-blockers: enhanced hypotensive effect; increased risk of first dose hypotensive effect
- Calcium-channel blockers: enhanced hypotensive effect; increased risk of first dose hypotensive effect
- Diuretics: enhanced hypotensive effect; increased risk of first dose hypotensive effect
- Moxisylyte: possibly severe postural hypotension
- Vardenafil, sildenafil and tadalafil: enhanced hypotensive effect, avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - 
- **COMMENTS**
  - 

**OTHER INFORMATION**
- Swallow whole with 150 mL of water while sitting or standing
- Protein binding is increased in renal impairment
## Tazocin (piperacillin/tazobactam)

### Clinical Use

Antibacterial agent

### Dose in Normal Renal Function

2.25–4.5 g every 6–8 hours

### Pharmacokinetics

<table>
<thead>
<tr>
<th>Property</th>
<th>Piperacillin</th>
<th>Tazobactam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>539.5</td>
<td>322.3</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>20–30</td>
<td>20–30</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>60–80</td>
<td>80</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.18–0.3</td>
<td>0.18–0.33</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1/4–6</td>
<td>1/7</td>
</tr>
</tbody>
</table>

### Dose in Renal Impairment

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>4.5 g every 8–12 hours, or 2.25 g every 6 hours</th>
<th>4.5 g every 12 hours, or 2.25 g every 8 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>4.5 g every 8–12 hours, or 2.25 g every 6 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>4.5 g every 12 hours, or 2.25 g every 8 hours</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Dose in Patients Undergoing Renal Replacement Therapies

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed.</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed.</td>
</tr>
<tr>
<td>CVVHD/HDF</td>
<td>Dialysed: 2.25–3.375 g every 6 hours, or 4.5 g every 8 hours</td>
</tr>
</tbody>
</table>

### Important Drug Interactions

Potentially hazardous interactions with other drugs

- Reduced excretion of methotrexate – monitor methotrexate levels during concomitant treatment
- Enhanced action of vecuronium and similar neuromuscular blocking agents

### Administration

#### Reconstitution

- Reconstitute each 4.5 g with 20 mL sterile water for injection or sodium chloride 0.9%.

#### Route

- IV

#### Rate of Administration

- IV bolus over 3–5 minutes
- IV infusion over 20–30 minutes

#### Comments

- May be given as an infusion in glucose 5% or sodium chloride 0.9%

### Other Information

- Sodium content is 2.79 mmol/g of injection
- Has been used intraperitoneally for treatment of PD peritonitis at a concentration of 250 mg/L
- Patients with renal impairment are at a greater risk of neuromuscular excitability or convulsions that are associated with overdose
- May cause in vitro inactivation of aminoglycosides
- 6–21% is removed by peritoneal dialysis and 30–50% by haemodialysis plus an extra 5% as the metabolite

References:

Teicoplanin

**CLINICAL USE**

Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**

Loading dose: 400 mg every 12 hours for 3 doses, then
IM/IV: 200–400 mg daily, or 3–6 mg/kg/day (up to 10 mg/kg/day in some reports) in life-threatening infections

**PHARMACOKINETICS**

Molecular weight 1875–1891 (daltons)

% Protein binding 90–95

% Excreted >97

unchanged in urine

Volume of distribution 0.94–1.4 (L/kg)

Half-life – normal/ESRF (hrs) 150/62–230

**DOSE IN RENAL IMPAIRMENT**

GFR (mL/min)

<table>
<thead>
<tr>
<th>GFR</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Give normal loading dose, then dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Give normal loading dose, then 200–400 mg every 24–48 hours</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Give normal loading dose, then 200–400 mg every 48–72 hours</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed.(^1) Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/ VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs

- None known

**ADMINISTRATION**

**RECONSTITUTION**

- Use water for injection provided
- IV, IM

**RATE OF ADMINISTRATION**

- IV bolus: 2–3 minutes; IV infusion: 30 minutes

**COMMENTS**

- USE IN CAPD
- Give 400 mg IV stat dose, then 20 mg/L/bag IP for 7 days, then 20 mg/L/alternate-bag for 7 days, then 20 mg/L/night-bag only for 7 days

**OTHER INFORMATION**

- TDM optimises therapy, but not essential.
- Troughs not less than 10 mg/L. Peaks 1 hour after: 20–50 mg/L
- Relationship between blood level and toxicity not established
- Long-term concurrent use of gentamicin and teicoplanin causes additive ototoxicity

References:

Telbivudine

**CLINICAL USE**
Treatment of chronic hepatitis B infection

**DOSE IN NORMAL RENAL FUNCTION**
600 mg daily

**PHARMACOKINETICS**
- Molecular weight: 242.2 daltons
- % Protein binding: 3.3
- % Excreted unchanged in urine: 42
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 30–53.6/Increased

**DOSE IN RENAL IMPAIRMENT**

- GFR (mL/min):
  - 30–50: 600 mg every 48 hours
  - <30: 600 mg every 72 hours

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Dialysed. 600 mg every 96 hours
- HD: Dialysed. 600 mg every 96 hours
- HDF/High flux: Dialysed. 600 mg every 96 hours
- CAV/VVHD: Dialysed. Dose as in
- GFR<30 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**
- Dosage guidelines are from the company and have not been tested so adjust the dose according to virological response and monitor for side effects
- Has been associated with myopathy and myalgia
- 4 hours of haemodialysis removes 23% of the dose
Telithromycin

**CLINICAL USE**

Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**

800 mg daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>812</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>60–70</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>12</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1.9–3.9</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>2–3/14.64</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Dose as in GFR&lt;10 mL/min. (Give 800 mg dose after dialysis session)</th>
<th>Dialysed. Dose as in GFR&lt;10 mL/min. (Give 800 mg dose after dialysis session)</th>
<th>Dialysed. Dose as in GFR=10–20 mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>600 mg daily (given as 800 mg/400 mg alternating days)</td>
<td>800 mg daily (given as 800 mg/400 mg alternating days)</td>
<td>400 mg daily (given as 800 mg/400 mg alternating days)</td>
<td></td>
</tr>
<tr>
<td>10–30</td>
<td>600 mg daily (given as 800 mg/400 mg alternating days)</td>
<td>800 mg daily (given as 800 mg/400 mg alternating days)</td>
<td>400 mg daily (given as 800 mg/400 mg alternating days)</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>600 mg daily (given as 800 mg/400 mg alternating days)</td>
<td>800 mg daily (given as 800 mg/400 mg alternating days)</td>
<td>400 mg daily (given as 800 mg/400 mg alternating days)</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD:** Unknown dialysability. Dose as in GFR<10 mL/min
- **HD:** Dialysed. Dose as in GFR<10 mL/min. (Give 800 mg dose after dialysis session)
- **HDF/High flux:** Dialysed. Dose as in GFR<10 mL/min. (Give 800 mg dose after dialysis session)
- **CAV/VVHD:** Dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Antibacterials: concentration reduced by rifampicin – avoid during and for 2 weeks after rifampicin therapy
- Antidepressants: concentration reduced by St John’s wort – avoid during and for 2 weeks after St John’s wort therapy
- Anti-epileptics: concentration reduced by carbamazepine, phenytoin, phenobarbital and primidone – avoid during and for 2 weeks after treatment
- Antifungals: avoid in combination with ketoconazole in severe renal and hepatic impairment
- Antipsychotics: increased risk of ventricular arrhythmias with pimozide – avoid concomitant use
- Antivirals: avoid concomitant use with amprenavir, atazanavir, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir and tipranavir in severe renal and hepatic impairment
- Anxiolytics and hypnotics: inhibits metabolism of midazolam (increased sedation)
- Ciclosporin: possibly increased ciclosporin levels
- Diuretics: increased eplerenone concentration – avoid concomitant use
- Telithromycin and ergot derivatives should not be co-administered due to possibility of ergotism
- Ivabradine: possibly increased ivabradine concentration – avoid concomitant use
- Lipid-regulating drugs: increased risk of myopathy with atorvastatin and simvastatin – avoid concomitant use
- Sirolimus: increased sirolimus levels – avoid concomitant use
- Tacrolimus: possibly increased tacrolimus levels

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

**COMMENTS**

- Do not give to people at risk of QT interval prolongation due to its potential to prolong the QT interval
- Oral bioavailability is approximately 57% after a single dose of 800 mg
- In patients with renal and hepatic impairment the dose should be reduced to 400 mg daily
- Monitor for signs of liver toxicity
- AUC increased 2-fold if GFR<30 mL/min

RETURN TO CONTENTS
Telmisartan

**CLINICAL USE**
Angiotensin-II antagonist:
- Hypertension

**DOSE IN NORMAL RENAL FUNCTION**
20–80 mg daily

**PHARMACOKINETICS**
- Molecular weight: 514.6 daltons
- % Protein binding: >99.5
- % Excreted unchanged in urine: <1
- Volume of distribution (L/kg): 500 litres
- Half-life – norma/ESRF (hrs): 24/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Start with 20 mg and adjust according to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function

**IMPRESSIVE DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Analgesics: antagonism of hypotensive effect and increased risk of renal impairment with NSAIDs; hyperkalaemia with ketorolac and other NSAIDs
- Cardiac glycosides: concentration of digoxin increased
- Ciclosporin: increased risk of hyperkalaemia and nephrotoxicity
- Diuretics: enhanced hypotensive effect; hyperkalaemia with potassium-sparing diuretics
- Epoetin: increased risk of hyperkalaemia; antagonism of hypotensive effect
- Lithium: reduced excretion (possibility of enhanced lithium toxicity)
- Potassium salts: increased risk of hyperkalaemia
- Tacrolimus: increased risk of hyperkalaemia and nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**
- Hyperkalaemia and other side effects are more common in patients with impaired renal function
- Close monitoring of renal function required during therapy in patients with renal insufficiency
- Renal failure has been reported in association with angiotensin-II inhibitors in patients with renal artery stenosis, post renal transplant, and those with congestive heart failure
Temazepam

**CLINICAL USE**

Benzodiazepine:
- Insomnia (short-term use)
- Pre-med anxiolytic prior to minor procedures

**DOSE IN NORMAL RENAL FUNCTION**
- 10–40 mg at night
- Premedication: 20–40 mg, 60 minutes prior to procedure

**PHARMACOKINETICS**

Molecular weight (daltons) 300.7
% Protein binding 96
% Excreted unchanged in urine <2
Volume of distribution (L/kg) 1.3–1.5
Half-life – normal/ESRF (hrs) 7–11/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Antibacterials: metabolism possibly increased by rifampicin
- Antipsychotics: increased sedative effects
- Antivirals: concentration possibly increased by ritonavir
- Disulfiram: metabolism of temazepam inhibited (increased toxicity)
- Sodium oxybate: enhanced effects of sodium oxybate – avoid

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  -

**OTHER INFORMATION**

- Increased CNS sensitivity in renal impairment
- Long-term use may lead to dependence and withdrawal symptoms in certain patients
- 80% of metabolites excreted in the urine
**Temocillin**

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
1–2 g every 12 hours
Acute uncomplicated UTIs: 1 g daily in a single or divided doses

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>458.4 (as sodium salt)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>75–85</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>90</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.23</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>3.1–5.4/28.2</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose in normal renal function</th>
<th>30–50: Dose as in normal renal function</th>
<th>10–30: 1–2 g daily</th>
<th>&lt;10: 1–2 g every 48 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>Dose as in normal renal function</td>
<td>30–50: Dose as in normal renal function</td>
<td>10–30: 1–2 g daily</td>
<td>&lt;10: 1–2 g every 48 hours</td>
</tr>
<tr>
<td>10–30</td>
<td>1–2 g daily</td>
<td>10–30: 1–2 g daily</td>
<td>&lt;10: 1–2 g every 48 hours</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>1–2 g every 48 hours</td>
<td>&lt;10: 1–2 g every 48 hours</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy Type</th>
<th>Dose in renal function-method</th>
<th>CAPD: Not dialysed. Dose as in GFR&lt;10 mL/min</th>
<th>HD: Dialysed. Dose as in GFR&lt;10 mL/min</th>
<th>HDF/High flux: Dialysed. Dose as in GFR&lt;10 mL/min</th>
<th>CAV/VVHD: Dialysed. Dose as in GFR=10–30 mL/min</th>
</tr>
</thead>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Temocillin can reduce the excretion of methotrexate (increased risk of toxicity)

**ADMINISTRATION**

**RECONSTITUTION**
- IV: Dissolve in 20 mL water for injection
- IV infusion: Dilute in 50–100 mL sodium chloride 0.9%
- IM: Dissolve in 2 mL water for injection or lidocaine 0.5–1% (volume 2.7 mL)

**ROUTE**
- IV, IM

**RATE OF ADMINISTRATION**
- Slow IV bolus over 3–4 minutes
- Infusion over 30–40 minutes

**COMMENTS**
- Incompatible with proteins, blood products, lipid emulsions and aminoglycosides

**OTHER INFORMATION**
- Bleeding has occurred in some patients (more likely in those with renal impairment)
- 20% is removed by haemodialysis and 17–26% by peritoneal dialysis
Temozolomide

**CLINICAL USE**
Antineoplastic agent:
- Glioblastoma multiforme
- Malignant glioma

**DOSE IN NORMAL RENAL FUNCTION**
- 75 mg/m² daily for 42 days with radiotherapy
- Adjuvant phase/monotherapy: 150–200 mg/m² once daily for 5 days
- Or according to local policy

**PHARMACOKINETICS**
- Molecular weight (daltons): 194.2
- % Protein binding: 10–20
- % Excreted unchanged in urine: 5–10
- Volume of distribution (L/kg): 0.3–0.5 (IV) (15–18 L/m² oral)
- Half-life – normal/ESRF (hrs): 1.8/Unchanged

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR<10 mL/min
- HD: Unknown dialysability. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antipsychotics: avoid concomitant use with clozapine, increased risk of agranulocytosis

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
  - Do not administer with food

**OTHER INFORMATION**
- Nadir for white cell count usually occurs 21–28 days after a dose, with recovery within 1–2 weeks
- Rapidly and completely absorbed with 100% bioavailability and has extensive tissue distribution
- Major route of elimination is renal: approximately 5–10% is excreted unchanged and the remainder excreted as metabolites

RETURN TO CONTENTS
Tenecteplase

CLINICAL USE
Thrombolytic:
- Acute myocardial infarction

DOSE IN NORMAL RENAL FUNCTION
30–50 mg depending on patient weight (500–600 micrograms/kg)

PHARMACOKINETICS
Molecular weight 70,000 daltons
% Protein binding No data
% Excreted unchanged in urine Minimal
Volume of distribution 6.1–9.1 litres\(^1\) (weight and dose related)
Half-life – normal/ESRF (hrs) 90–130 minutes/Unchanged

DOSE IN RENAL IMPAIRMENT GFR (mL/Min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unlikely to be dialysed. Dose as in normal renal function
HD Unlikely to be dialysed. Dose as in normal renal function
HDF/High flux Unknown dialysability. Dose as in normal renal function
CAV/ VVHD Unknown dialysability. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Drugs that affect coagulation or platelet function: increased risk of bleeding

ADMINISTRATION
RECONSTITUTION
- Water for injection
ROUTE
- IV
RATE OF ADMINISTRATION
- Over 10 seconds
COMMENTS
- Incompatible with dextrose

OTHER INFORMATION
- It has an initial half-life of 20–24 minutes
- Cleared mainly by hepatic metabolism
- Re-administration is not recommended due to lack of experience

References:
Tenofovir disoproxil

**CLINICAL USE**
Nucleoside reverse transcriptase inhibitor:
- Treatment of HIV in combination with other antiretroviral drugs
- Treatment of hepatitis B in compensated liver disease

**DOSE IN NORMAL RENAL FUNCTION**
245 mg once daily

**PHARMACOKINETICS**
- Molecular weight: 635.5 (as disoproxil fumarate)
- % Protein binding: 0.7–7.2
- % Excreted unchanged in urine: IV: 70–80; Oral: 32
- Volume of distribution: 0.8 (L/kg)
- Half-life – normal/ESRF (hrs): 12–18/Increased

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 30–50: 245 mg every 48 hours
  - 10–30: 245 mg every 72–96 hours
  - <10: 245 mg every 7 days

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR<10mL/min
- HD: Dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10mL/min
- CAV/VVHD: Dialysed. Dose as in GFR=10–30mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antivirals: reduces concentration of atazanavir; concentration of both drugs may be increased with cidofovir; increased didanosine concentration resulting in increased toxicity (e.g. pancreatitis and lactic acidosis) – avoid concomitant use; concentration increased by lopinavir and atazanavir; monitor renal function with adefovir
- Co-administration with other drugs that are actively secreted via the tubular anionic transporter, e.g. cidofovir – increased concentrations of both drugs

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
- COMMENTS

**OTHER INFORMATION**
- Lactic acidosis, sometimes fatal, and usually associated with severe hepatomegaly and steatosis, has been reported in patients receiving nucleoside reverse transcriptase inhibitors
- Following a single 300mg dose of tenofovir, subjects with a calculated creatinine clearance <50 mL/min, and those with ERF requiring dialysis, had substantial reductions in renal elimination of tenofovir, resulting in high systemic exposures necessitating an adjustment in dose
- A 4 hour high-flux haemodialysis session was found to remove 10% of tenofovir from plasma
- Renal impairment, which may include hypophosphataemia, has been reported with the use of tenofovir. The majority of these cases occurred in patients with underlying systemic or renal disease, or in patients taking nephrotoxic agents – monitor creatinine clearance and phosphate levels
### Terazosin

#### CLINICAL USE

Alpha-adrenoceptor blocker:
- Hypertension
- Benign prostatic hyperplasia (BPH)

#### DOSE IN NORMAL RENAL FUNCTION

- Hypertension: 1–20 mg once daily
- BPH: 1–10 mg once daily

#### PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>459.9</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>90–94</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>10</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.5–0.9</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>9–12/Unchanged</td>
</tr>
</tbody>
</table>

#### DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

#### DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

### IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Antidepressants: enhanced hypotensive effect with MAOIs
- Beta-blockers: enhanced hypotensive effect; increased risk of first dose hypotensive effect
- Calcium-channel blockers: enhanced hypotensive effect; increased risk of first dose hypotensive effect
- Diuretics: enhanced hypotensive effect; increased risk of first dose hypotensive effect
- Moxisylyte: possibly severe postural hypotension when used in combination
- Vardenafil, sildenafil and tadalafil: enhanced hypotensive effect – avoid concomitant use

### ADMINISTRATION

#### RECONSTITUTION

- **ROUTE**
  - Oral

#### RATE OF ADMINISTRATION

#### COMMENTS

#### OTHER INFORMATION

- Therapy should be initiated with a single dose of 1 mg given at bedtime

RETURN TO CONTENTS
Terbinafine

**CLINICAL USE**
Antifungal agent:
- Fungal infections of the skin and nails

**DOSE IN NORMAL RENAL FUNCTION**
250 mg daily
Topical: apply once or twice daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>291.4; (327.9 as hydrochloride)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>99%</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>0%</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>6–11 1–2</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>17–36/Increased</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>100% on alternate days</td>
</tr>
<tr>
<td>10–20</td>
<td>100% on alternate days</td>
</tr>
<tr>
<td>&lt;10</td>
<td>100% on alternate days</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral, topical

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**

- Terbinafine is hepatically metabolised to two major metabolites, 80% of which are renally excreted
- Little information is available regarding the handling of terbinafine in renal failure but clearance is reduced by 50% if GFR<50 mL/min
- In CKD 5 use with caution and monitor for side effects

References:
Terbutaline sulphate

**CLINICAL USE**
Beta₂-adrenoceptor agonist:
- Reversible airways obstruction

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: 2.5–5 mg 3 times daily
- SC/IM/IV: 250–500 micrograms up to 4 times daily
- IV infusion: 90–300 micrograms/hour
- Turbohaler: 500 micrograms (1 inhalation) up to 4 times daily
- Nebulisation: 5–10 mg 2–4 times daily, or more frequently

**PHARMACOKINETICS**
- Molecular weight (daltons) 548.6
- % Protein binding 15–25
- % Excreted unchanged in urine 55–60
- Volume of distribution (L/kg) 0.9–1.5
- Half-life – normal/ESRF (hrs) 16–20

**DOSE IN RENAL IMPAIRMENT**
GFR (mL/min)
- 20–50 50% of normal parenteral dose. Other routes Dose as in normal renal function
- 10–20 50% of normal parenteral dose. Other routes. Dose as in normal renal function
- <10 Avoid parenteral dose. Other routes Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Likely dialysability. Dose as in GFR<10 mL/min
- HD Likely dialysability. Dose as in GFR<10 mL/min
- HDF/High flux Likely dialysability. Dose as in GFR<10 mL/min
- CAV/ Likely dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Effect may be diminished by beta-blockers
- Theophylline: increased risk of hypokalaemia

**ADMINISTRATION**
- **RECONSTITUTION**
- **ROUTE**
- IV, SC, IM, oral, inhaled, nebulised
- **RATE OF ADMINISTRATION**
- 1.5–5 mcg/minute
- **COMMENTS**
- For IV infusion, add 1.5–2.5 mg to 500 mL glucose 5% or sodium chloride 0.9% (3–5 micrograms/mL)
Terlipressin

CLINICAL USE
Treatment of bleeding oesophageal varices

DOSE IN NORMAL RENAL FUNCTION
2 mg stat dose followed by 1–2 mg every 4–6 hours when required (until bleeding is controlled) for up to 72 hours

PHARMACOKINETICS
Molecular weight (daltons) 1227.4 (1437.6 as acetate)
% Protein binding ≈30
% Excreted <2 unchanged in urine
Volume of distribution (L/kg) 0.6–0.9
Half-life – normal/ESRF (hrs) 50–70 minutes

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function. Use with caution
<10 Dose as in normal renal function. Use with caution

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unknown dialysability. Dose as in GFR<10mL/min
HD Unlikely to be dialysed. Dose as in GFR<10mL/min
HDF/High flux Unknown dialysability. Dose as in GFR<10mL/min
CAV/VVHD Unknown dialysability. Dose as in GFR<10mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● None known

ADMINISTRATION
RECONSTITUTION
● With solvent provided
ROUTE
● IV
RATE OF ADMINISTRATION
–
COMMENTS
● Store reconstituted solution in the fridge and discard after 12 hours

OTHER INFORMATION
● Maximum plasma levels are reached after 1–2 hours with a duration of action of 4–6 hours
● Initial response within 25–40 minutes, duration 2–10 hours
● Some studies have found it can be used to improve renal function in hepatorenal syndrome, in doses of about 3 mg per day for about 11 days
● May cause hypertension
● There is a case report of rhabdomyolysis
Tetracycline

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
250–500 mg 4 times a day
Acne: 500 mg twice daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>444.44</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>20–65</td>
</tr>
<tr>
<td>% Excreted</td>
<td>55–60</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>&gt;0.7</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>6–12/57–120</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
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</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>250 mg 4 times a day</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose in GFR&lt;10 mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in</td>
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<td>Unknown dialysability. Dose as in</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: possibly enhance anticoagulant effect of coumarins and phenindione
- Oestrogens: possibly reduce contraceptive effects of oestrogens (risk probably small)
- Retinoids: possible increased risk of benign intracranial hypertension with retinoids – avoid concomitant use

**ADMINISTRATION**

<table>
<thead>
<tr>
<th>RECONSTITUTION</th>
<th>–</th>
</tr>
</thead>
<tbody>
<tr>
<td>ROUTE</td>
<td>Oral</td>
</tr>
<tr>
<td>RATE OF ADMINISTRATION</td>
<td>–</td>
</tr>
</tbody>
</table>

**OTHER INFORMATION**

- 10% is removed by haemodialysis and 7% by peritoneal dialysis
- Avoid if possible in renal impairment due to its potential nephrotoxicity and increased risk of azotaemia, hyperphosphataemia and acidosis
- May cause an increase in blood urea which is dose related
- Avoid in SLE

**IMPORTANT DRUG INTERACTIONS**

- Anticoagulants: possibly enhance anticoagulant effect of coumarins and phenindione
- Oestrogens: possibly reduce contraceptive effects of oestrogens (risk probably small)
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- Avoid if possible in renal impairment due to its potential nephrotoxicity and increased risk of azotaemia, hyperphosphataemia and acidosis
- May cause an increase in blood urea which is dose related
- Avoid in SLE
Thalidomide

**CLINICAL USE**
- Untreated multiple myeloma in patients >65 or who are ineligible for high dose chemotherapy, in combination with either melphalan and prednisone, or cyclophosphamide and dexamethasone (Unlicensed indications):
  - Erythema nodosum leprosum
  - Lupus erythematosus, aphthous ulceration, stomatitis, graft-versus-host disease, AIDS-associated waste syndrome, rheumatoid arthritis and other acute inflammatory conditions

**DOSE IN NORMAL RENAL FUNCTION**
- 200 mg daily
- Unlicensed dose: 50–800 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 258.2
- % Protein binding: 55–66
- % Excreted unchanged in urine: <0.7
- Volume of distribution (L/kg): 166 litres
- Half-life – normal/ESRF (hrs): 5–7/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux: Not dialysed. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs:
  - Thalidomide enhances the effects of barbiturates, alcohol, chlorpromazine and reserpine
  - Use with caution with other drugs that can cause peripheral neuropathy

**ADMINISTRATION**

**RECONSTITUTION**
- –

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- –

**COMMENTS**
- –

**OTHER INFORMATION**
- Major route of elimination is non-renal (i.e. by spontaneous non-enzymatic hydrolytic cleavage) therefore normal doses may be given in renal failure
- Has been used to treat uroemic pruritus in haemodialysis patients unresponsive to other therapy. (Silva SR. Thalidomide for the treatment of uroemic pruritus: a crossover randomised double-blind trial. *Nephron*. 1994; 67(3): 270–3.)
Theophylline

**CLINICAL USE**
- Reversible airways obstruction
- Acute severe asthma

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: depends on preparation used
- IV: Deteriorating asthma not previously treated with theophylline: 5 mg/kg (250–500 mg) (as aminophylline) over at least 20 minutes
- Acute severe asthma: 500 mcg/kg/hour (as aminophylline) adjusted according to plasma-theophylline levels

**PHARMACOKINETICS**
- Molecular weight (daltons): 180.2
- % Protein binding: 35–60
- % Excreted unchanged in urine: 10
- Volume of distribution (L/kg): 0.3–0.7

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Antibacterials: increased concentration with azithromycin, clarithromycin, erythromycin, ciprofloxacin, norfloxacin and isoniazid; decreased plasma levels with erythromycin if erythromycin taken orally; increased risk of convulsions if given with quinolones; rifampicin accelerates metabolism of theophylline
  - Antidepressants: concentration increased by fluvoxamine – avoid concomitant use or halve theophylline dose and monitor levels; concentration reduced by St John’s wort – avoid concomitant use
  - Anti-epileptics: metabolism increased by carbamazepine and primidone; concentration of both drugs increased with phenytoin
  - Antifungals: concentration increased by fluconazole and ketoconazole
  - Antivirals: metabolism of theophylline increased by ritonavir
  - Calcium-channel blockers: concentration increased by diltiazem and verapamil and possibly other calcium-channel blockers
  - Tacrolimus: may increase tacrolimus levels
  - Ulcer-healing drugs: metabolism inhibited by cimetidine; absorption possibly reduced by sucralfate

**ADMINISTRATION**

**RECONSTITUTION**
- –

**ROUTE**
- Oral, IV

**RATE OF ADMINISTRATION**
- At least 20 minutes or 500 mcg/kg/hour depends on indication

**COMMENTS**
- –

**OTHER INFORMATION**
- Therapeutic levels should be in the range 10–20 mg/litre (55–110 micromols/litre)
- 50% of dose is removed by haemodialysis
- Studies have used it to protect against contrast nephropathy, with conflicting results
Thiotepa

**CLINICAL USE**
Alkylating antineoplastic agent

**DOSE IN NORMAL RENAL FUNCTION**
- IM, bladder and intracavitary instillations: 60 mg in single or divided doses
- Intrathecal: maximum 10 mg
- Other doses depend on indication or local protocol

**PHARMACOKINETICS**
- Molecular weight: 189.2 daltons
- % Protein binding: 10–40
- % Excreted unchanged in urine: <2
- Volume of distribution: 0.3–1.6 L/kg
- Half-life – normal/ESRF (hrs): 2.4

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50: IM: Use a reduced dose with caution
- 10–20: IM: Use a reduced dose with caution
- <10: IM: Use a reduced dose with caution

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR<10mL/min
- HD: Dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10mL/min
- CAV/VVHD: Dialysed. Dose as in GFR=10–20mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antipsychotics: avoid concomitant use with clozapine
- Avoid concomitant use with other myelosuppressive agents

**ADMINISTRATION**

**RECONSTITUTION**
- 1.5 mL water for injection

**ROUTE**
- IV, IM, intrathecal (can be administered directly into pleural, pericardial or peritoneal cavities and as a bladder instillation)

**RATE OF ADMINISTRATION**

**COMMENTS**

**OTHER INFORMATION**
- Haemorrhagic cystitis has occurred
- Metabolised in liver to triethylene phosphoramide (TEPA). Only traces of unchanged thiotepa and (TEPA) are excreted in the urine, together with a large proportion of metabolites (60% within 72 hours)
Tiagabine

**CLINICAL USE**
Anti-epileptic agent

**DOSE IN NORMAL RENAL FUNCTION**
15–45 mg daily in 3 divided doses if dose >30 mg

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>412</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>96</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;2</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>7–9 (2–3 in patients on enzyme inducing drugs)</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs

- Antidepressants: antagonism of anticonvulsant effect (convulsive threshold lowered)
- Anti-epileptics: concentration reduced by phenytoin, carbamazepine, phenobarbital and primidone
- Antimalarials: mefloquine antagonises anticonvulsant effect; chloroquine and hydroxychloroquine occasionally reduce convulsive threshold

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**
  -

**OTHER INFORMATION**
- Although there is no evidence of withdrawal seizures, it is recommended to taper off treatment over a period of 2–3 weeks
Tigecycline

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
Loading dose of 100 mg, then 50 mg twice daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>585.6</td>
</tr>
<tr>
<td>% Protein binding (%)</td>
<td>71–89</td>
</tr>
<tr>
<td>% Excreted unchanged in urine (%)</td>
<td>22</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>7–9</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>42/Probably unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapies</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs

- Anticoagulants: possibly enhanced anticoagulant effect of coumarins
- Oestrogens: possibly reduced contraceptive effects of oestrogens (risk probably small)

**ADMINISTRATION**

**RECONSTITUTION**

- 5.3 mL of sodium chloride 0.9% or glucose 5% (gently swirl to reconstitute)

**ROUTE**

- IV infusion

**RATE OF ADMINISTRATION**

- 30–60 minutes

**COMMENTS**

- Add required dose to 100 mL of sodium chloride 0.9% or glucose 5%

**OTHER INFORMATION**

- AUC increased by 30% in CKD 5
**Tiludronic acid**

**CLINICAL USE**
Paget’s disease of bone

**DOSE IN NORMAL RENAL FUNCTION**
400 mg daily for 12 weeks

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>318.6</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>91</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>60</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>No data</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>&gt;100/205</td>
</tr>
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</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>60–90</td>
<td>Use with caution</td>
</tr>
<tr>
<td>30–60</td>
<td>Use with caution</td>
</tr>
<tr>
<td>&lt;30</td>
<td>Avoid</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**  Unlikely to be dialysed. Avoid
- **HD**    Unlikely to be dialysed. Avoid
- **HDF/High flux**  Unknown dialysability. Avoid
- **CAV/VVHD**  Unlikely to be dialysed. Avoid

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Calcium salts: reduced absorption

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**

**OTHER INFORMATION**

- Take as a single dose with a glass of water at least 2 hours before or after meals, calcium supplements or aluminium or magnesium containing antacids
- Patients should ensure their calcium and vitamin D intake is adequate
- Calcium metabolism disorders should be corrected before starting therapy
- Bisphosphonates are mainly eliminated by excretion of unchanged drug in the urine
Timentin (ticarcillin/clavulanic acid)

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
3.2 g every 6–8 hours, increased to every 4 hours in severe infections

**PHARMACOKINETICS**
- **Molecular weight (daltons)**
  - Ticarcillin (as Na) 428.4, clavulanic acid 199.2
- **% Protein binding**
  - Ticarcillin 50, clavulanic acid 25
- **% Excreted unchanged in urine**
  - Ticarcillin 85–90, clavulanic acid 40
- **Volume of distribution (L/kg)**
  - Ticarcillin 0.14–0.21, clavulanic acid 0.3
- **Half-life – normal/ESRF (hrs)**
  - Ticarcillin 1.2/15, clavulanic acid 1/3–4

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/min)**
  - >30 3.2 g every 8 hours
  - 10–30 1.6 g every 8 hours
  - <10 1.6 g every 12 hours

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**
  - Not dialysed. Dose as in GFR<10mL/min
- **HD**
  - Dialysed. Dose as in GFR<10mL/min
- **HDF/High flux**
  - Dialysed. Dose as in GFR<10mL/min
- **CAV/VVHD**
  - Unknown dialysability. Dose as in GFR=10–30mL/min or 2.4 g every 6–8 hours
- **CVVHD/HDF**
  - Dialysed. 3.2 g every 6 hours

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: effects of coumarins are potentially enhanced
- Oral contraceptive: potentially reduced efficacy
- Methotrexate: reduced excretion thereby increasing risk of toxicity

**ADMINISTRATION**
- **RECONSTITUTION**
  - With 10 mL water for injection and add to 100 mL glucose 5%
- **ROUTE**
  - IV
- **RATE OF ADMINISTRATION**
  - 30–40 minutes

**COMMENTS**
- Each 3.2 g of ticarcillin/clavulanic acid contains 16 mmol of sodium and 1 mmol of potassium

**OTHER INFORMATION**
- CSM has advised that cholestatic jaundice may occur if treatment exceeds a period of 14 days and can present up to 6 weeks after treatment has been stopped. The incidence of cholestatic jaundice occurring with Timentin is higher in males than in females and is particularly prevalent in men over the age of 65 years

References:
Timolol maleate

**CLINICAL USE**

Beta-adrenoceptor blocker:
- Hypertension
- Angina
- Glaucoma
- Migraine prophylaxis

**DOSE IN NORMAL RENAL FUNCTION**

- Hypertension: 10–60 mg daily, doses >30 mg in divided doses
- Angina: 5–30 mg twice daily
- Post MI: 5–10 mg twice daily
- Migraine: 10–20 mg daily in 1–2 divided doses

**PHARMACOKINETICS**

- Molecular weight (daltons): 432.5
- % Protein binding: 10
- % Excreted unchanged in urine: 5
- Volume of distribution (L/kg): 1.7

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Dose as in normal renal function. Start with lowest dose and titrate according to response</th>
<th>Dose as in normal renal function. Start with lowest dose and titrate according to response</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**: Not dialysed. Dose as in GFR<10 mL/min
- **HD**: Not dialysed. Dose as in GFR<10 mL/min
- **HDF/High flux**: Unknown dialysability. Dose as in GFR<10 mL/min
- **CAV/VVHD**: Unknown dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Analgesics: NSAIDs antagonise hypotensive effect
- Anti-arrhythmics: increased risk of myocardial depression and bradycardia; increased risk of bradycardia, myocardial depression and AV block with amiodarone
- Antidepressants: enhanced hypotensive effect with MAOIs
- Antihypertensives: enhanced hypotensive effect; increased risk of withdrawal hypertension with clonidine; increased risk of first dose hypotensive effect with post-synaptic alpha-blockers such as prazosin
- Antimalarials: increased risk of bradycardia with mefloquine
- Antipsychotics enhanced hypotensive effect with phenothiazines
- Calcium-channel blockers: increased risk of bradycardia and AV block with diltiazem; hypotension and heart failure possible with nifedipine and nisoldipine; asystole, severe hypotension and heart failure with verapamil
- Diuretics: enhanced hypotensive effect
- Moxisylyte: possible severe postural hypotension
- Sympathomimetics: severe hypertension with adrenaline and noradrenaline and possibly with dobutamine
- Tropisetron: increased risk of ventricular arrhythmias – use with caution

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral, topical

**RATE OF ADMINISTRATION**

- **COMMENTS**

**OTHER INFORMATION**

- Timolol is more hydrophilic than lipophilic

RETURN TO CONTENTS
Tinidazole

CLINICAL USE
Antibacterial agent

DOSE IN NORMAL RENAL FUNCTION
1–2 g daily

PHARMACOKINETICS
Molecular weight (daltons) 247.3
% Protein binding 8–12\(^1\)
% Excreted unchanged in urine 20–25
Volume of distribution (L/kg) 0.61–0.67\(^1\)
Half-life – normal/ESRF (hrs) 12–14/Unchanged

DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose in Normal Renal Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Dialysis Modality</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability, but likely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Alcohol: disulfiram-like reaction

ADMINISTRATION

RECONSTITUTION
- ROUTE
  - Oral

RATE OF ADMINISTRATION
- COMMENTS
- OTHER INFORMATION
- Dosage adjustment in renal failure is not necessary as a decrease in renal clearance is compensated for by increased faecal excretion of tinidazole
- 43% can be removed during a 6 hour haemodialysis session.\(^1\)

References:
Tinzaparin sodium (LMWH)

CLINICAL USE
- Peri- and postoperative surgical thromboprophylaxis
- Treatment of DVT and pulmonary embolism
- Prevention of thrombus formation in extracorporeal circulation during HD

DOSE IN NORMAL RENAL FUNCTION
- General surgery: (low-moderate risk) 3500 IU daily
- Orthopaedic surgery: (high risk) 50 IU/kg or 4500 IU daily
- DVT and PE: 175 IU/kg bodyweight once daily for at least 6 days and until adequate oral anticoagulation is established

DOSE IN RENAL IMPAIRMENT

GFR (mL/min)
- 20–50: Dose as in normal renal function. See ‘Other Information’
- <20: See ‘Other Information’

PHARMACOKINETICS
- Molecular weight (daltons): 5500–7500 (average 6500)
- % Protein binding: 14
- % Excreted unchanged in urine: 80–90
- Volume of distribution (L/kg): 3.1–5 litres
- Half-life – normal/ESRF (hrs): 1.5/5.2 (detectable anti-Factor Xa activity persists for 24 hours)

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD: Not dialysed. Dose as in GFR<20mL/min
- HD: Not dialysed. Dose as in GFR<20mL/min
- HDF/High flux: Dialysed. Dose as in GFR<20mL/min
- CAV: Not dialysed. Dose as in GFR=20–50mL/min
- VVHD: Not dialysed. Dose as in GFR<20mL/min

IMPORTANT DRUG INTERACTIONS
- Potentially hazardous interactions with other drugs
  - Analgesics: increased risk of bleeding with NSAIDs – avoid concomitant use with IV diclofenac; increased risk of haemorrhage with ketorolac – avoid concomitant use
  - Nitrates: anticoagulant effect reduced by infusions of glyceryl trinitrate
  - Drotrecogin alfa: manufacturer advises to avoid use of high doses of heparin with drotrecogin alfa
  - Use with care in patients receiving oral anticoagulants, platelet aggregation inhibitors, aspirin or dextran

ADMINISTRATION
- RECONSTITUTION
- ROUTE
  - SC injection
  - IV bolus/infusion
- RATE OF ADMINISTRATION
- See ‘Other Information’

OTHER INFORMATION
- Tinzaparin is also indicated for prevention of clotting in the extracorporeal circulation during haemodialysis
  - Dose for >4 hr session: IV bolus (into arterial side of the dialyser or intravenously) of 3500–4500 IU
  - Dose for <4 hr session: IV bolus of 2500 IU
- Additional tinzaparin (500–1000 IU) may be given if concentrated RBCs or blood transfusions are given during dialysis, or additional treatment beyond the normal dialysis duration is employed
- Determination of plasma antifactor-Xa may be used to monitor the tinzaparin dose during haemodialysis; plasma antifactor-Xa, one hour after dosing should be within the range 0.4–0.5 IU/mL
Heparin can suppress adrenal secretion of aldosterone leading to hyperkalaemia particularly in patients with chronic renal impairment and diabetes mellitus.

Low molecular weight heparins are renally excreted and hence accumulate in severe renal impairment. While the doses recommended for prophylaxis against DVT and prevention of thrombus formation in extracorporeal circuits are well tolerated in patients with CKD 5, the doses recommended for treatment of DVT and PE have not yet been verified as safe. LMWHs have been associated with severe, sometimes fatal, bleeding episodes in such patients. Hence the use of unfractionated heparin would be preferable in these instances.

Information from Leo Pharma states that tinzaparin can safely be used in elderly patients with a GFR>20 mL/min for 10 days without any accumulation (Nagge J. Is impaired renal function a contraindication to the use of low-molecular weight heparin? Arch Intern Med. 2002; 162:2605–09.)

(Siguret V. Elderly patients treated with tinzaparin (Innohep) administered once daily (175 anti-Xa IU/kg): anti-Xa and anti-IIa activities over 10 days. Thromb Haemostat. 2000; 84: 800–04.)

Additional doses may be required if using LMWHs for anticoagulation in HDF.

Use 1 mg of protamine for every 100 anti-Xa IU to neutralise the effects of tinzaparin. If prothrombin time is still raised 2–4 hours later, give 0.5 mg/kg infusion of protamine.
Tioguanine

**CLINICAL USE**
Antineoplastic agent (antimetabolite):
- Acute leukaemia
- Chronic myeloid leukaemia

**DOSE IN NORMAL RENAL FUNCTION**
100–200 mg/m² in 1 or 2 divided doses

**PHARMACOKINETICS**
- Molecular weight: 167.2 daltons
- % Protein binding: Probably low
- % Excreted unchanged in urine: 40
- Volume of distribution: 0.148 L/kg
- Half-life – normal/ESRF (hrs): 80 minutes

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Reduce dose, use with care
  - 10–20: Reduce dose, use with care
  - <10: Reduce dose, use with care

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR<10 mL/min
- HD: Unknown dialysability. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV: Unknown dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antipsychotics: avoid concomitant use with clozapine (increased risk of agranulocytosis)

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
- Oral

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**
- Variable and incomplete oral absorption with 14–46% bioavailability. Extensive metabolism in the liver and other tissues to several active and inactive metabolites. 24–46% of the dose is excreted in the urine within 24 hours

RETURN TO CONTENTS
Tiotropium

**CLINICAL USE**
Maintenance treatment of chronic obstructive pulmonary disease

**DOSE IN NORMAL RENAL FUNCTION**
18 micrograms once daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>472.4 (as bromide)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>72</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>14 (of inhaled dose)</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>32</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>5–6 days/Increased</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function. Use with caution</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function. Use with caution</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
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</tr>
<tr>
<td>HD</td>
<td>Unknown dialysability. Dose as in normal renal function. Use with caution</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function. Use with caution</td>
</tr>
<tr>
<td>CAV/ VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function. Use with caution</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Avoid administration with other anticholinergic drugs

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Inhalation

**RATE OF ADMINISTRATION**
- COMMENTS
  -

**OTHER INFORMATION**
- Not to be used for acute episodes of bronchospasm
Tipranavir

**CLINICAL USE**

Protease inhibitor:
- Treatment of HIV infected patients in combination with ritonavir and other antiretroviral agents

**DOSE IN NORMAL RENAL FUNCTION**

500 mg twice daily in combination with ritonavir 200 mg twice daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight</td>
<td>602.7 daltons</td>
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<tr>
<td>% Protein binding</td>
<td>&gt;99.9</td>
</tr>
<tr>
<td>% Excreted</td>
<td>0.5, unchanged in urine</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>7.7–10.2 litres</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>5.5–6/ unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapeutic Modality</th>
<th>Dose as for GFR&lt;10mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability</td>
</tr>
<tr>
<td>CA V</td>
<td>Not dialysed</td>
</tr>
<tr>
<td>VVHD</td>
<td>GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Antacids: avoid giving for 2 hours after tipranavir administration
- Antibacterials: plasma concentration of clarithromycin and other macrolides increased – reduce dose of clarithromycin in renal impairment; concentration increased by clarithromycin; rifabutin concentration increased (risk of uveitis) – reduce dose; concentration reduced by rifampicin – avoid concomitant use; avoid concomitant use with telithromycin in severe renal and hepatic failure
- Antidepressants: concentration possibly reduced by St John’s wort – avoid concomitant use
- Antimalarials: possibly increased risk of ventricular arrhythmias with artemether/lumefantrine – avoid concomitant use
- Antivirals: reduces concentration of abacavir, amprenavir, didanosine, lopinavir, saquinavir and zidovudine; concentration increased by atazanavir
- Ciclosporin: levels possibly altered by tipranavir
- Sirolimus: levels possibly altered by tipranavir
- Tacrolimus: levels possibly altered by tipranavir

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**

- Administer with food; enhanced bioavailability with high fat meals
Tirofiban

**CLINICAL USE**

Antiplatelet agent:
- Prevention of early myocardial infarction in patients with unstable angina or non-ST segment elevation myocardial infarction, and with last episode of chest pain within 12 hours

**DOSE IN NORMAL RENAL FUNCTION**

Initially 0.4 mcg/kg/minute for 30 minutes then 0.1 mcg/kg/minute for at least 48 hours

**PHARMACOKINETICS**

- Molecular weight (daltons) 495.1
- % Protein binding 65
- % Excreted unchanged in urine 66
- Volume of distribution (L/kg) 22–42 litres
- Half-life – normal/ESRF (hrs) 1.5–2/increased

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in normal renal function</th>
<th>Dose in renal impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>0.1–0.4 mcg/kg/minute</td>
<td>50% of dose</td>
</tr>
<tr>
<td>10–30</td>
<td>0.1–0.4 mcg/kg/minute</td>
<td>50% of dose</td>
</tr>
<tr>
<td>&lt;10</td>
<td>0.1–0.4 mcg/kg/minute</td>
<td>50% of dose</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD** Unknown dialysability. Dose as in GFR<10mL/min
- **HD** Dialysed. Dose as in GFR<10mL/min
- **HDF/High flux** Dialysed. Dose as in GFR<10mL/min
- **CAV/VVHD** Unknown dialysability. Dose as in GFR=10–30mL/min

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Iloprost: increased risk of bleeding
- Heparin: increased risk of bleeding

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - IV infusion
- **RATE OF ADMINISTRATION**
  - 0.1–0.4 mcg/kg/minute
- **COMMENTS**
  - Add 50 mL of the concentrate (250 mcg/mL) to 250 mL sodium chloride 0.9% or glucose 5%, to give a final concentration of 50 mcg/mL. (remove 50 mL from bag first)

**OTHER INFORMATION**

- Antiplatelet effect lasts for about 4–8 hours after stopping infusion
- Main side effect is bleeding
- Increased risk of bleeding once renal function falls to a GFR<60 mL/min – monitor carefully
Tizanidine

CLINICAL USE
Spasticity associated with multiple sclerosis or spinal cord injury/disease

DOSE IN NORMAL RENAL FUNCTION
2–24 mg daily in up to 3–4 divided doses (depending on response)

PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight</td>
<td>290.2 (as hydrochloride)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>30%</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Volume of distribution</td>
<td>2.4 (L/kg)</td>
</tr>
<tr>
<td>Half-life – normal/ESRF</td>
<td>2–4/Increased (hrs)</td>
</tr>
</tbody>
</table>

DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Initial dose 2 mg once daily and slowly increase by 2 mg increments. Increase daily dose before increasing frequency of administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>25–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>&lt;25</td>
<td>Initial dose 2 mg once daily and slowly increase by 2 mg increments. Increase daily dose before increasing frequency of administration</td>
<td></td>
</tr>
</tbody>
</table>

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dialysability</th>
<th>Dose as in GFR</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown</td>
<td>GFR&lt;25 mL/min</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td>Unknown</td>
<td>GFR&lt;25 mL/min</td>
<td></td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown</td>
<td>GFR&lt;25 mL/min</td>
<td></td>
</tr>
<tr>
<td>CAV/</td>
<td>Unknown</td>
<td>GFR&lt;25 mL/min</td>
<td></td>
</tr>
<tr>
<td>VVHD</td>
<td>GFR=25–50 mL/min</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Anti-arrhythmics: enhanced muscle relaxant effect with procainamide
- Antibacterials: concentration increased by ciprofloxacin – avoid concomitant use
- Antihypertensives: enhanced hypotensive effect
- Oral contraceptives: clearance of tizanidine reduced by 50%

ADMINISTRATION

RECONSTITUTION

ROUTE
- Oral

RATE OF ADMINISTRATION

- COMMENTS

OTHER INFORMATION

- Pharmacokinetic data suggest that renal clearance in the elderly may be decreased by up to 3-fold
- May induce hypotension; therefore may potentiate the effect of antihypertensive drugs, including diuretics – exercise caution
- With beta-blockers or digoxin, may potentiate hypotension or bradycardia
- LFTs should be monitored monthly for the first 4 months
- Tizanidine undergoes rapid and extensive first pass metabolism. The metabolites (mainly inactive) constitute 70% of the administered dose and are excreted via the renal route

References:
1. Shellenberger MK. A controlled pharmacokinetic evaluation of tizanidine and baclofen at steady state. Drug Metab Dispos. 1999; 27(2): 201–4
Tobramycin

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
- IM/IV: 3 mg/kg/day in 3 divided doses; maximum 5 mg/kg/day in 3–4 divided doses
- Urinary tract infections: 2–3 mg/kg daily as a single dose (IM)

**PHARMACOKINETICS**
- Molecular weight (daltons): 467.5
- % Protein binding: <5
- % Excreted unchanged in urine: 90
- Volume of distribution (L/kg): 0.25
- Half-life – normal/ESRF (hrs): 2–3/5–70

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Give 1–2 mg/kg then dose according to serum levels
  - 10–20: Give 1 mg/kg then dose according to serum levels
  - <10: Give 1 mg/kg then dose according to serum levels

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Dialysed. Dose as in GFR<10mL/min
- HD: Dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10mL/min
- CAV/VVHD: Dialysed. 1.5–2 mg/kg every 24 hours and monitor levels

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Botulinum toxin: neuromuscular block enhanced – risk of toxicity
- Ciclosporin: increased risk of nephrotoxicity
- Cytotoxics: increased risk of nephrotoxicity and possibly of ototoxicity with platinum compounds
- Diuretics: increased risk of ototoxicity with loop diuretics
- Muscle relaxants: enhanced effect of non-depolarising muscle relaxants and suxamethonium
- Parasympathomimetics: antagonism of effect of neostigmine and pyridostigmine
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**
- **RECONSTITUTION**
  - Add to 50–100 mL sodium chloride 0.9% or glucose 5% for IV infusion
- **ROUTE**
  - IV, IM, IP, nebulised
- **RATE OF ADMINISTRATION**
  - 20–60 minutes
- **COMMENTS**
  - Plasma concentrations should be measured frequently; trough ≤2 mg/L, peak 60 minutes post dose ≤10 mg/L; avoid prolonged peaks above 12 mg/L

**OTHER INFORMATION**
- 25–70% can be removed by haemodialysis
- Used via nebuliser for chronic pulmonary *Pseudomonas aeruginosa* infection in cystic fibrosis: 300 mg every 12 hours for 28 days, repeat after 28 days
- Can be used for peritonitis at doses of 6 mg/L intraperitoneally

References:
1. Dose from CVVH Initial Drug Dosing Guidelines on [www.thedrugmonitor.com](http://www.thedrugmonitor.com)
Tolbutamide

**CLINICAL USE**
Hypoglycaemic agent for non-insulin dependent diabetes

**DOSE IN NORMAL RENAL FUNCTION**
0.5–2 g daily in divided doses

**PHARMACOKINETICS**
- Molecular weight (daltons): 270.3
- % Protein binding: 95–97
- % Excreted unchanged in urine: 0
- Volume of distribution (L/kg): 0.1–0.15

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function.</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Use with caution</td>
</tr>
<tr>
<td>10–20</td>
<td>Use with caution</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Use with caution</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Not dialysed. Dose as in GFR=10–20 mL/min</td>
</tr>
<tr>
<td>VVHD</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: effects enhanced by NSAIDs – avoid with azapropazone
- Antibacterials: effects enhanced by chloramphenicol, sulphonamides, and trimethoprim; effect reduced by rifamycins
- Anticoagulants: effect possibly enhanced by coumarins; also possibly changes to INR
- Antifungals: concentration increased by fluconazole and miconazole, and possibly voriconazole
- Sulfinpyrazone: enhanced effect of sulphonylureas

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

- **RATE OF ADMINISTRATION**
  - COMMENTS
    -

**OTHER INFORMATION**
- Tolbutamide is not removed by dialysis. It is contraindicated in severe renal impairment, and should be used with great caution in mild to moderate renal impairment because of risk of hypoglycaemia
Tolfenamic acid

**CLINICAL USE**

NSAID:
- Treatment of migraine

**DOSE IN NORMAL RENAL FUNCTION**

200 mg when first symptoms appear; repeat once after 1–2 hours if satisfactory response is not obtained

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>261.7</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>&gt;99</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>8 (90% as metabolites)</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.16</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>2.5</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/MIN)</th>
<th>Dose as in normal renal function</th>
<th>Use with caution and monitor renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Avoid</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Removal unlikely. Use with caution</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Use with caution</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Use with caution</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unlikely to be dialysed. Use with caution</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- ACE inhibitors and angiotensin-II antagonists: antagonism of hypotensive effect; increased risk of nephrotoxicity and hyperkalaemia
- Analgesics: avoid concomitant use of 2 or more NSAIDs, including aspirin (increased side effects); avoid with ketorolac (increased risk of side effects and haemorrhage)
- Antibacterials: possibly increased risk of convulsions with quinolones
- Anticoagulants: effects of coumarins enhanced; possibly increased risk of bleeding with heparins and coumarins
- Antidepressants: increased risk of bleeding with SSRIs and venlafaxine
- Antidiabetic agents: effects of sulphonylureas enhanced
- Anti-epileptics: possibly increased phenytoin concentration
- Antivirals: increased risk of haematological toxicity with zidovudine; concentration possibly increased by ritonavir
- Ciclosporin: may potentiate nephrotoxicity
- Cytotoxic agents: reduced excretion of methotrexate; increased risk of bleeding with erlotinib
- Diuretics: increased risk of nephrotoxicity; antagonism of diuretic effect; hyperkalaemia with potassium-sparing diuretics
- Lithium: excretion decreased
- Pentoxifylline: increased risk of bleeding
- Tacrolimus: increased risk of nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
- Oral
- RATE OF ADMINISTRATION
- COMMENTS
- OTHER INFORMATION

- Contraindicated in significantly impaired kidney or liver function
- The urine may become a little more lemon-coloured due to coloured metabolites
- Use only with extreme caution (or not at all) in haemodialysis patients with some degree of urine output, especially if other risk factors are present, e.g. nephrotic syndrome or diabetes mellitus or treatment with loop diuretics
- Use normal doses in patients with CKD 5 on dialysis as long as they no longer pass any urine
- Inhibition of renal prostaglandin synthesis by NSAIDs may interfere with renal function, especially in the presence of existing renal disease – avoid NSAIDs if
possible; if not, check serum creatinine 48–72 hours after starting NSAID — if increased, discontinue therapy

- Use with caution in renal transplant recipients as can reduce intrarenal autocoid synthesis
Tolterodine tartrate

**CLINICAL USE**
Treatment of urinary frequency, urgency and incontinence

**DOSE IN NORMAL RENAL FUNCTION**
1–2 mg twice daily
M/R: 4 mg daily

**PHARMACOKINETICS**
Molecular weight (daltons) 475.6
% Protein binding 96
% Excreted unchanged in urine <1
Volume of distribution (L/kg) 0.9–1.6
Half-life – normal/ESRF (hrs) 2–3 (10 hours in poor metabolisers)/–
                       MR: 6/–

**DOSE IN RENAL IMPAIRMENT**
GFR (mL/MIN)
30–50 Dose as in normal renal function. Use with caution
10–30 1 mg twice daily. Use with caution
<10 1 mg twice daily. Use with caution

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
CAPD Unlikely to be dialysed. Dose as in GFR<10mL/min
HD Unlikely to be dialysed. Dose as in GFR<10mL/min
HDF/High flux Unlikely to be dialysed. Dose as in GFR<10mL/min
CAV/ VVHD Unlikely to be dialysed. Dose as in GFR=10–30mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
● None known

**ADMINISTRATION**
RECONSTITUTION
–
ROUTE
● Oral
RATE OF ADMINISTRATION
–
COMMENTS
–

**OTHER INFORMATION**
● Active metabolites may accumulate in renal failure
● Modified release preparation is not suitable for renal patients
● Use with caution in patients at risk of QT elongation

RETURN TO CONTENTS
Topiramate

CLINICAL USE
- Anti-epileptic agent
- Prophylactic treatment of migraine

DOSE IN NORMAL RENAL FUNCTION
- Epilepsy: 50–400 mg twice daily
- Migraine: Initially, 25 mg at night. Maintenance, 25–50 mg twice daily

PHARMACOKINETICS
- Molecular weight (daltons): 339.4
- % Protein binding: 9–17
- % Excreted unchanged in urine: 70
- Volume of distribution (L/kg): 0.55–0.8

DOSE IN RENAL IMPAIRMENT
- GFR (mL/min)
  - 20–50 Migraine/epilepsy: Dose as in normal renal function
  - 10–20 Migraine: Dose as in normal renal function
    - Epilepsy: 50% of normal dose and increase according to response
  - <10 Migraine: Dose as in normal renal function
    - Epilepsy: 25–50% of normal dose and increase according to response

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD: Unknown dialysability. Dose as for GFR<10 mL/min
- HD: Dialysed. Dose as for GFR<10 mL/min
- HDF/High flux: Dialysed. Dose as for GFR<10 mL/min
- CAV/ VVHD: Unknown dialysability. Dose as for GFR=10–20 mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Antidepressants: antagonism of anticonvulsant effect
- Anti-epileptics: concentration reduced by phenytoin and carbamazepine; increases phenytoin concentration
- Antimalarials: mefloquine antagonises anticonvulsant effect; chloroquine and hydroxychloroquine occasionally reduces convulsive threshold
- Oestrogens and progestogens: reduced contraceptive effect

ADMINISTRATION

RECONSTITUTION
- ROUTE
  - Oral
  - RATE OF ADMINISTRATION
    - COMMENTS

OTHER INFORMATION
- Patients with moderate to severe renal impairment may take 10–15 days to reach steady state, compared to 4–8 days in patients with normal renal function
- A higher frequency of renal stones has been noted in topiramate treated patients, although the risk is not related to dose or duration of therapy. Adequate hydration is recommended to reduce this risk

RETURN TO CONTENTS
Topotecan

CLINICAL USE
Treatment of metastatic ovarian cancer

DOSE IN NORMAL RENAL FUNCTION
1.5 mg/m² for 5 days, repeated every 3 weeks

PHARMACOKINETICS
- Molecular weight: 457.9 (as hydrochloride)
- % Protein binding: 35
- % Excreted unchanged in urine: 51
- Volume of distribution (L/kg): 132 litres +/- 57

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
- 40–59: Dose as in normal renal function.
- 20–39: 0.75 mg/m²/day. See ‘Other Information’
- <20: Use with caution. See ‘Other Information’

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD: Unknown dialysability. Dose as in GFR<10mL/min
- HD: Dialysed. Dose as in GFR<10mL/min
- HDF/High flux: Dialysed. Dose as in GFR<10mL/min
- CAV/VVHD: Unknown dialysability. 0.5–0.75 mg/m²/day and monitor closely

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- None known

ADMINISTRATION
RECONSTITUTION
- Add 4 mL of water for injection to each 4 mg vial
ROUTE
- IV infusion
RATE OF ADMINISTRATION
- Over 30 minutes
COMMENTS
- Dilute further in sodium chloride 0.9% or glucose 5% to obtain a concentration of 25–50 mcg/mL
- Once reconstituted use within 12 hours if stored at room temperature, and 24 hours if stored at 2–8°C if made under aseptic conditions

OTHER INFORMATION
- Undergoes reversible, pH-dependent hydrolysis of the active lactone moiety to the inactive hydroxyacid (carboxylate) form. A relatively small amount of topotecan is metabolised by hepatic microsomal enzymes to an active metabolite, N-demethyltopotecan; the clinical significance of this metabolite is not known. Excretion is via biliary and renal routes with 20–60% excreted in the urine as topotecan or the open ring form
- If the patient has received extensive prior therapy it has been suggested that 1 mg/m²/day can be used in mild renal impairment and 0.5 mg/m²/day in moderate renal impairment. (Ormrod D, Spencer CM. Topotecan: a review of its efficacy in small cell lung cancer. Drugs. 1999, Sep; 58(3): 533–51.)
- In renal failure there is an increased risk of haematological toxicity (even at low doses, e.g. 0.5 mg/m²/day), therefore if it is to be used in severe renal failure, start at doses less than 0.5 mg/m²/day and monitor closely
  - CrCl 60 mL/min: 80% of dose
  - CrCl 45 mL/min: 75% of dose
  - CrCl 30 mL/min: 70% of dose
- Bennett suggests:
  - GFR>50 mL/min: 75% of dose
  - GFR=10–50 mL/min: 50% of dose
  - GFR<10 mL/min: 25% of dose
Torasemide

**CLINICAL USE**
Loop diuretic:
- Hypertension
- Oedema

**DOSE IN NORMAL RENAL FUNCTION**
2.5–40 mg once daily (varies according to indication)
Maximum dose: 200 mg daily

**PHARMACOKINETICS**
- Molecular weight: 348.4 daltons
- % Protein binding: >99
- % Excreted unchanged in urine: 25
- Volume of distribution (L/kg): 0.09–0.33

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as usual</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as usual</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
- Antibacterials: increased risk of ototoxicity with aminoglycosides, polymyxins and vancomycin; avoid concomitant use with lymecycline
- Antidepressants: increased risk of hypokalaemia with reboxetine; enhanced hypotensive effect with MAOIs; increased risk of postural hypotension with tricyclics
- Anti-epileptics: increased risk of hyponatraemia with carbamazepine
- Antifungals: increased risk of hypokalaemia with amphotericin
- Antihypertensives: enhanced hypotensive effect; increased risk of first dose hypotensive effect with alpha-blockers; increased risk of ventricular arrhythmias with sotalol if hypokalaemia occurs
- Antipsychotics: increased risk of ventricular arrhythmias with amisulpride, sertindole or pimozide (avoid with pimozide) if hypokalaemia occurs; enhanced hypotensive effect with phenothiazines
- Atomoxetine: hypokalaemia increases risk of ventricular arrhythmias
- Cardiac glycosides: increased toxicity if hypokalaemia occurs
- Lithium: risk of toxicity

**ADMINISTRATION**

**RECONSTITUTION**

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**

**COMMENTS**

**OTHER INFORMATION**

- Torasemide 10 mg is equivalent to furosemide 20–40 mg
- In patients with renal failure, the renal clearance is reduced but total plasma clearance is not significantly altered
- Approximately 80% of dose is excreted renally as parent drug and metabolites

References:
Toremifene

**CLINICAL USE**
Hormone dependent metastatic breast cancer in post-menopausal women

**DOSE IN NORMAL RENAL FUNCTION**
60 mg daily

**PHARMACOKINETICS**
- Molecular weight (daltons): 406
- % Protein binding: >99.5
- % Excreted unchanged in urine: 10%
- Volume of distribution (L/kg): 580 litres
- Half-life – normal/ESRF (hrs): 5 days/Unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function
  - <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. See ‘Other Information’
- HD: Unlikely to be dialysed. See ‘Other Information’
- HDF/High flux: Unknown dialysability. See ‘Other Information’
- CAV/VVHD: Unlikely to be dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: enhanced anticoagulant effect of coumarins

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - COMMENTS

**OTHER INFORMATION**
- As it is not renally excreted, it may be possible to prescribe the normal dose in dialysis patients, although it has not previously been used in this population
Tramadol hydrochloride

**CLINICAL USE**
Analgesic

**DOSE IN NORMAL RENAL FUNCTION**
Oral: 50–100 mg up to 4 hourly; maximum 400 mg daily
IM/IV: 50–100 mg every 4–6 hours; total daily dose 600 mg

**PHARMACOKINETICS**
Molecular weight (daltons) 299.8
% Protein binding 20
% Excreted unchanged in urine 90
Volume of distribution (L/kg) 163–243 litres
Half-life – normal/ESRF (hrs) 6/11

**DOSE IN RENAL IMPAIRMENT**
GFR (mL/min)
20–50 Dose as in normal renal function
10–20 50–100 mg every 8 hours initially and titrate dose as tolerated
<10 50 mg every 8 hours initially and titrate dose as tolerated

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
CAPD Unknown dialysability. Dose as in GFR<10 mL/min
HD Dialysed. Dose as in GFR<10 mL/min
HDF/High flux Dialysed. Dose as in GFR<10 mL/min
CAV/VVHD Dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: enhances effect of coumarins
- Antidepressants: possibly increased serotonergic effects with duloxetine; possible CNS excitation or depression with MAOIs and moclobemide – avoid concomitant use with MAOIs; increased risk of CNS toxicity with SSRIs or tricyclics
- Anti-epileptics: effect reduced by carbamazepine
- Antivirals: concentration possibly increased by ritonavir
- Atomoxetine: increased risk of convulsions
- Dopaminergics: use selegiline with caution
- Sodium oxybate: enhanced effect of sodium oxybate – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- –
- IV, IM, oral

**RATE OF ADMINISTRATION**
- Slow bolus or continuous IV infusion/PCA

**COMMENTS**
- –

**OTHER INFORMATION**
- Tramadol is a centrally acting opioid agonist which also acts on inhibitory pain pathways
Trandolapril

**CLINICAL USE**
Angiotensin converting enzyme inhibitor:
- Hypertension
- Heart failure
- After myocardial infarction

**DOSE IN NORMAL RENAL FUNCTION**
0.5–4 mg once daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>430.5</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>&gt;80 (as trandolaprilat)</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>10–15</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>18 litres</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>16–24/– (as trandolaprilat)</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Initial dose 500 mcg once daily, and increase according to response</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Analgesics: antagonism of hypotensive effect and increased risk of renal impairment with NSAIDs; hyperkalaemia with ketorolac and other NSAIDs
- Ciclosporin: increased risk of hyperkalaemia and nephrotoxicity
- Diuretics: enhanced hypotensive effect; hyperkalaemia with potassium-sparing diuretics
- Epoetin: increased risk of hyperkalaemia; antagonism of hypotensive effect
- Lithium: reduced excretion (possibility of enhanced lithium toxicity)
- Potassium salts: increased risk of hyperkalaemia
- Tacrolimus: increased risk of hyperkalaemia and nephrotoxicity

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS

**OTHER INFORMATION**

- Hyperkalaemia and other side effects are more common in patients with impaired renal function
- Close monitoring of renal function required during therapy in patients with renal insufficiency
- Renal failure has been reported in association with ACE inhibitors in patients with renal artery stenosis, post renal transplant, and those with congestive heart failure
- High incidence of anaphylactoid reactions has been reported in patients dialysed with high-flux polycrylonitrile membranes and treated concomitantly with an ACE inhibitor – this combination should therefore be avoided
- Normal doses can be used in CKD 5

RETURN TO CONTENTS
Tranexamic acid

**CLINICAL USE**
Haemostatic agent

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: 1–1.5 g every 8–12 hours (15–25 mg/kg every 8–12 hours)
- IV: 0.5–1 g every 8 hours (25–50 mg/kg daily in divided doses)
- Dose depends on indication

**PHARMACOKINETICS**
- Molecular weight: 157.2 (daltons)
- % Protein binding: 3
- % Excreted unchanged in urine: 90
- Volume of distribution: 1 (L/kg)
- Half-life – normal/ESRF (hrs): 2/–

**DOSE IN RENAL IMPAIRMENT GFR (mL/min)**
- 20–50: IV: 10 mg/kg 12 hourly; Oral: 25 mg/kg 12 hourly
- 10–20: IV: 10 mg/kg 12–24 hourly; Oral: 25 mg/kg 12–24 hourly
- <10: IV: 5 mg/kg 12–24 hourly; Oral: 12.5 mg/kg 12–24 hourly

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in GFR<10 mL/min
- HD: Unknown dialysability. Dose as in GFR<10 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min
- CAV: Unknown dialysability. Dose as in GFR=10–20 mL/min
- VVHD: Unknown dialysability.

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs:
- None known

**ADMINISTRATION**

**RECONSTITUTION**
- –

**ROUTE**
- IV, oral

**RATE OF ADMINISTRATION**
- Slow bolus = 100 mg/minute or continuous IV infusion in glucose 5% or sodium chloride 0.9%

**COMMENTS**
- –

**OTHER INFORMATION**
- A 5% topical solution can be made up using the IV preparation, mixed with water for injection. This can be used as a mouthwash to stop bleeding after dental surgery, or placed on a swab to reduce bleeding at fistula or other bleeding sites if conventional measures have not worked (anecdotal)

*It is not licensed for use by anyone else.*
Trastuzumab

**CLINICAL USE**
Antineoplastic agent:
- Main indication is for HER2-expressing breast cancer

**DOSE IN NORMAL RENAL FUNCTION**
- 4 mg/kg then 2 mg/kg weekly
- Or 8 mg/kg initially then 6 mg/kg every 3 weeks
- Or according to local policy

**PHARMACOKINETICS**
- Molecular weight: 148,000–185,000 daltons
- % Protein binding: No data
- % Excreted unchanged in urine: No data
- Volume of distribution: 0.044 L/kg
- Half-life – normal/ESRF (hrs): 1.7–28.5 days/Probably unchanged

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function. Use with caution
  - <10: Dose as in normal renal function. Use with caution

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HD: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- HDF/High flux: Unlikely to be dialysed. Dose as in GFR<10 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - None known

**ADMINISTRATION**
- **RECONSTITUTION**
  - 7.2 mL water for injection per 150 mg vial
- **ROUTE**
  - IV infusion
- **RATE OF ADMINISTRATION**
  - 4 mg/kg over 90 minutes
  - 2 mg/kg over 30 minutes
- **COMMENTS**
  - Allow to stand for 5 minutes after reconstitution
  - Dilute dose in 250 mL sodium chloride 0.9%

**OTHER INFORMATION**
- Distributes to normal cells, tumour cells and serum where HER2 antigens are found
- Remains in body for 24 weeks
- Doesn’t require hepatic or renal metabolism for elimination
- Nadir for bone-marrow depression is 4 weeks with recovery within 6 weeks
- Associated with cardiotoxicity
- May remain in circulation for up to 24 weeks
Trazodone hydrochloride

**CLINICAL USE**

Antidepressant

**DOSE IN NORMAL RENAL FUNCTION**

- Depression: 100–300 mg daily; maximum 600 mg daily in divided doses for hospital patients
- Anxiety: 75–300 mg daily

**PHARMACOKINETICS**

- Molecular weight: 408.3 daltons
- % Protein binding: 89–95
- % Excreted unchanged in urine: <5
- Volume of distribution: 1–2 (L/kg)
- Half-life: normal/ESRF (hrs) 5–13/

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function. Start with small doses and increase gradually</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Start with small doses and increase gradually</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed. Dose as in GFR &lt; 10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed. Dose as in GFR &lt; 10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR &lt; 10 mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in GFR = 10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs:
- Alcohol: increased sedative effects
- Antidepressants: avoid concomitant use with MAOIs and moclobemide
- Anti-epileptics: antagonism of anticonvulsant effect
- Antimalarials: manufacturer advises avoid concomitant use with artemether and lumefantrine
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**

- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**

- **OTHER INFORMATION**
  - Use lower doses in elderly patients
  - The majority of a dose (75%) is excreted by the kidney, mainly as metabolites
Treosulfan

**CLINICAL USE**
Alkylation agent for ovarian cancer

**DOSE IN NORMAL RENAL FUNCTION**
- IV: 3–8 g/m² every 1–3 weeks; doses >3 g/m² should be given as an infusion
- Doses up to 1.5 g/m² have been given IP
- Oral: 1 g daily in 4 divided doses for 2–4 weeks or 1.5 g daily in 3 divided doses for 1 week
- Or according to local protocol

**PHARMACOKINETICS**
- Molecular weight (daltons) 278.3
- % Protein binding No data
- % Excreted 22–30 unchanged in urine
- Volume of distribution (L/kg) 44–88 litres
- Half-life – normal/ESRF (hrs) 1.5–1.94

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Use a reduced dose</td>
</tr>
<tr>
<td>10–20</td>
<td>Use a reduced dose</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Use a reduced dose</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10 mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unknown dialysability. Dose as in GFR=10–20 mL/min</td>
</tr>
<tr>
<td>VVHD</td>
<td>GFR=10–20 mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

- **RECONSTITUTION**
  - 20 or 100 mL water for injection for 1 g and 5 g vials respectively

- **ROUTE**
  - Oral, IV, IP

- **RATE OF ADMINISTRATION**
  - 3 g/m² over 5–10 minutes (8 g/m² over 30 minutes)

- **COMMENTS**
  - Powder reconstitutes easier if water heated to 25–30°C

**OTHER INFORMATION**

- Treosulfan is a prodrug of a bifunctional alkylating agent; high and relatively constant bioavailability. Mean urinary excretion of the parent compound is ~15% over 24 hrs
- Haemorrhagic cystitis has occurred after intravesical or intravenous administration
# Triamcinolone

## CLINICAL USE
Corticosteroid

## DOSE IN NORMAL RENAL FUNCTION
**IM:** 40 mg of acetonide; maximum single dose 100 mg  
Intra-articular: 2.5–40 mg of acetonide

## PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>394.4 (434.5 as acetonide)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>Low</td>
</tr>
<tr>
<td>% Excreted in urine</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>1.4–2.1</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>2–5/Unchanged</td>
</tr>
</tbody>
</table>

## DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

## DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

## IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Antibacterials: metabolism accelerated by rifampicin; metabolism possibly inhibited by erythromycin
- Anticoagulants: efficacy of coumarins may be altered
- Anti-epileptics: metabolism accelerated by carbamazepine, barbiturates, phenytoin and primidone
- Antifungals: increased risk of hypokalaemia with amphotericin – avoid concomitant use; metabolism possibly inhibited by itraconazole and ketoconazole
- Antivirals: concentration possibly increased by ritonavir
- Ciclosporin: rare reports of convulsions in patients on ciclosporin and high-dose corticosteroids
- Cytotoxics: increased risk of haematological toxicity with methotrexate
- Diuretics: enhanced hypokalaemic effects of acetazolamide, loop diuretics and thiazide diuretics
- Vaccines: high dose corticosteroids can impair immune response to vaccines; avoid concomitant use with live vaccines

## ADMINISTRATION

### RECONSTITUTION
- **ROUTE**  
  - IM, intra-articular, topical, nasal spray, intradermal

### RATE OF ADMINISTRATION
- **COMMENTS**
  - 

## OTHER INFORMATION
- Use with caution in severe renal impairment as sodium and water retention may occur
- 4 mg is equivalent to 5 mg of prednisolone
Triamterene

**CLINICAL USE**
Diuretic (potassium-sparing)

**DOSE IN NORMAL RENAL FUNCTION**
150–250 mg daily in divided doses; reduce to alternate days after 1 week

**PHARMACOKINETICS**
- Molecular weight: 253 (daltons)
- % Protein binding: 60
- % Excreted unchanged in urine: 5–10
- Volume of distribution: 2.2–3.7 L/kg
- Half-life – normal/ESRF (hrs): 2/10

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/Min)**
  - 20–50: Dose as in normal renal function
  - 10–20: Avoid. See ‘Other Information’
  - <10: Avoid. See ‘Other Information’

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Avoid
- HD: Unknown dialysability. Avoid
- HDF/High flux: Unknown dialysability. Avoid
- CAV/VVHD: Unknown dialysability. Avoid

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs:
  - ACE inhibitors and angiotensin-II antagonists: enhanced hypotensive effect (risk of severe hyperkalaemia)
  - Analgesics: increased risk of nephrotoxicity with NSAIDs; increased risk of hyperkalaemia, especially with indometacin; antagonism of hypotensive effect
  - Antibacterials: avoid concomitant use with lymecycline
  - Antidepressants: enhanced hypotensive effect with MAOIs; increased risk of postural hypotension with tricyclics
  - Antipsychotics: enhanced hypotensive effect with phenothiazines
  - Antihypertensives: enhanced hypotensive effect; increased risk of first dose hypotensive effect of post-synaptic alpha-blockers, e.g. prazosin
  - Ciclosporin: increased risk of hyperkalaemia
  - Lithium: reduced excretion of lithium (risk of lithium toxicity)
  - Potassium salts: increased risk of hyperkalaemia
  - Tacrolimus: increased risk of hyperkalaemia

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- Hyperkalaemia is common when GFR<30 mL/min. May cause acute renal failure
- Potassium-sparing diuretics are weak diuretics and are ineffective in moderate to severe renal failure
Trifluoperazine

CLINICAL USE
- Schizophrenia and other psychoses
- Anxiety
- Severe nausea and vomiting

DOSE IN NORMAL RENAL FUNCTION
- Schizophrenia: initially 5 mg twice daily, increased by 5 mg after 1 week, then at intervals of 3 days according to response
- Anxiolytic and anti-emetic: 2–4 mg daily in divided doses; maximum 6 mg

PHARMACOKINETICS
- Molecular weight (daltons) 407.5
- % Protein binding >99
- % Excreted unchanged in urine <1
- Volume of distribution (L/kg) 160
- Half-life – normal/ESRF (hrs) 22/-

DOSE IN RENAL IMPAIRMENT
- GFR (mL/min)
  - 20–50 Dose as in normal renal function. Start with low dose
  - 10–20 Dose as in normal renal function. Start with low dose
  - <10 Dose as in normal renal function. Start with low dose

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD Not dialysed. Dose as in GFR<10 mL/min
- HD Not dialysed. Dose as in GFR<10 mL/min
- HDF/High flux Unknown dialysability. Dose as in GFR<10 mL/min
- CAV/ Unlikely to be dialysed. Dose as in GFR=10–20 mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Analgesics: increased risk of convulsions with tramadol; enhanced hypotensive and sedative effects with opioids
- Anti-arrhythmics: increased risk of ventricular arrhythmias with anti-arrhythmics that prolong the QT interval, e.g. procainamide, disopyramide and amiodarone – avoid concomitant use with amiodarone
- Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin – avoid concomitant use
- Antidepressants: increased level of tricyclics; possibly increased risk of antimuscarinic side effects
- Anti-epileptics: antagonism (convulsive threshold lowered)
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: increased risk of ventricular arrhythmias with pimozide – avoid concomitant use
- Antivirals: concentration possibly increased with ritonavir
- Anxiolytics and hypnotics: increased sedative effects
- Beta-blockers: enhanced hypotensive effect; increased risk of ventricular arrhythmias with sotalol
- Diuretics: enhanced hypotensive effect
- Lithium: increased risk of extrapyramidal side effects and possibly neurotoxicity
- Pentamidine: increased risk of ventricular arrhythmias
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use

ADMINISTRATION
- RECONSTITUTION
  - ROUTE Oral
  - RATE OF ADMINISTRATION
    - COMMENTS
- OTHER INFORMATION
  - Reduce starting dose in elderly or frail patients by at least half
Trimethoprim

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**

Treatment: 200 mg every 12 hours
Prophylaxis: 100 mg at night

**PHARMACOKINETICS**

Molecular weight (daltons) 290.3
% Protein binding 45
% Excreted unchanged in urine 40–60
Volume of distribution (L/kg) 1–2.2
Half-life – normal/ESRF (hrs) 8–10/20–49

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**

<table>
<thead>
<tr>
<th>GFR</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;25</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>15–25</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;15</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Probably dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Anti-arrhythmics: increased risk of ventricular arrhythmias with amiodarone — avoid concomitant use; concentration of procainamide increased
- Anti-epileptics: antifolate effect and concentration of phenytoin increased
- Antimalarials: increased risk of antifolate effect with pyrimethamine
- Ciclosporin: increased risk of nephrotoxicity
- Cytotoxics: increased risk of haematological toxicity with azathioprine and mercaptopurine; antifolate effect of methotrexate increased

**ADMINISTRATION**

**RECONSTITUTION**

- ROUTE
  - Oral
- RATE OF ADMINISTRATION
  - COMMENTS

**OTHER INFORMATION**

- Serum creatinine may rise due to competition for renal secretion
- Hyperkalaemia is common in CKD 5
- Short-term folic acid supplementation may be prescribed in patients with CKD 4-5 to cover antifolate effects of treatment dose
Trimipramine

**CLINICAL USE**
Tricyclic antidepressant

**DOSE IN NORMAL RENAL FUNCTION**
50–300 mg daily in divided doses
Elderly: 10–25 mg 3 times daily; half the dose should be sufficient for maintenance

**PHARMACOKINETICS**
- Molecular weight: 410.5 (as maleate)
- % Protein binding: 95
- % Excreted unchanged in urine: 0
- Volume of distribution: 31 (L/kg)

**DOSE IN RENAL IMPAIRMENT**
<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in normal renal function
- HD: Not dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Alcohol: increased sedative effect
- Analgesics: increased risk of CNS toxicity with tramadol; possibly increased risk of side effects with nefopam; possibly increased sedative effects with opioids
- Anti-arrhythmics: increased risk of ventricular arrhythmias with amiodarone – avoid concomitant use; increased risk of ventricular arrhythmias with drugs that prolong the QT interval; increased risk of arrhythmias with propafenone
- Antibacterials: increased risk of ventricular arrhythmias with moxifloxacin – avoid concomitant use; concentration reduced by rifampicin
- Anticoagulants: may alter anticoagulant effect of coumarins
- Antidepressants: enhanced CNS excitation and hypertension with MAOIs and moclobemide – avoid concomitant use; concentration possibly increased with SSRIs
- Anti-epileptics: convulsive threshold lowered; concentration reduced by carbamazepine, primidone, barbiturates and possibly phenytoin
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: increased risk of ventricular arrhythmias especially with pimozide; increased antimuscarnic effects with clozapine and phenothiazines; concentration increased by antipsychotics
- Antivirals: increased tricyclic side effects with amprenavir; concentration possibly increased with ritonavir
- Atomoxetine: increased risk of ventricular arrhythmias and possibly convulsions
- Beta-blockers: increased risk of ventricular arrhythmias with sotalol
- Clonidine: tricyclics antagonise hypotensive effect; increased risk of hypertension on clonidine withdrawal
- Dopaminergics: avoid use with entacapone; CNS toxicity reported with selegiline and rasagiline
- Pentamidine: increased risk of ventricular arrhythmias
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use
- Sympathomimetics: increased risk of hypertension and arrhythmias with adrenaline and noradrenaline; metabolism possibly inhibited by methylphenidate

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
  -
Triptorelin

CLINICAL USE
- Advanced prostate cancer
- Endometriosis
- Precocious puberty
- Uterine fibroids prior to surgery

DOSE IN NORMAL RENAL FUNCTION
- 3–3.75 mg every 4 weeks; depends on preparation
- 11.25 mg every 3 months

PHARMACOKINETICS
- Molecular weight: 1311.4 daltons
- % Protein binding: No data
- % Excreted unchanged in urine: 3–14
- Volume of distribution (L/kg): 92.4–115.8 litres

DOSE IN RENAL IMPAIRMENT
- GFR (mL/Min)
  - 20–50: Dose as in normal renal function
  - 10–20: Dose as in normal renal function, but monitor carefully
  - <10: Dose as in normal renal function, but monitor carefully

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD: Unlikely to be dialysed. Dose as in normal renal function, but monitor carefully
- HD: Unlikely to be dialysed. Dose as in normal renal function, but monitor carefully
- HDF/High flux: Unknown dialysability. Dose as in normal renal function, but monitor carefully
- CAV/VVHD: Unlikely to be dialysed. Dose as in normal renal function, but monitor carefully

IMPORTANT DRUG INTERACTIONS
- Potentially hazardous interactions with other drugs
  - None known

ADMINISTRATION
- RECONSTITUTION
  - With 2 mL diluent provided
- ROUTE
  - SC, IM
- RATE OF ADMINISTRATION
  - COMMENTS

RETURN TO CONTENTS
Tropisetron

**CLINICAL USE**

Anti-emetic:
- Cancer chemotherapy
- Postoperative nausea and vomiting (PONV)

**DOSE IN NORMAL RENAL FUNCTION**

- Chemotherapy: IV bolus or infusion of 5 mg before chemotherapy, then 5 mg every morning orally for 5 days
- PONV: IV bolus or infusion of 2 mg before induction of anaesthesia, then 2 mg within 2 hours of the end of surgery

**PHARMACOKINETICS**

- Molecular weight: 284.4 (320.8 as hydrochloride)
- % Protein binding: 71
- % Excreted unchanged in urine: 8 (70% as metabolites)
- Volume of distribution (L/kg): 400–600 litres
- Half-life – normal/ESRF (hrs): 8–45 (depends on metaboliser status)/Increased

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- CAPD: Unlikely to be dialysed. Dose as in normal renal function
- HD: Unlikely to be dialysed. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Anti-arrhythmics: increased risk of ventricular arrhythmias – use with caution; avoid with amiodarone, disopyramide, flecainide, lidocaine, mexiletine, procaainamide or propafenone
- Beta-blockers: increased risk of ventricular arrhythmias – use with caution; avoid with sotalol

**ADMINISTRATION**

**RECONSTITUTION**

- Route
  - Oral, IV bolus, IV infusion

**RATE OF ADMINISTRATION**

- Bolus: over at least 1 minute
- Infusion: over 15 minutes

**COMMENTS**

- Can be added to 100 mL sodium chloride 0.9%, glucose 5% or Ringer’s solution
- Give oral preparation at least an hour before food

**OTHER INFORMATION**

- In impaired kidney function, plasma concentrations of tropisetron may be increased by up to 50%, but no problem with short courses
Tryptophan

**CLINICAL USE**

Antidepressant

**DOSE IN NORMAL RENAL FUNCTION**

1–2 g 3 times daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight</td>
<td>204.2 daltons</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>80%</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>10–20%</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>0.34–0.7</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>1–3</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Dose as in normal renal function</th>
<th>Use lower doses initially</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt;10</td>
<td></td>
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</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unknown dialysability. Dose as in normal renal function</td>
</tr>
<tr>
<td>VVHD</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Antidepressants: possible increased serotonergic effects with duloxetine; CNS excitation and confusion with MAOIs – reduce dose of tryptophan; agitation and nausea with SSRIs
- Antimalarials: avoid concomitant administration with artemether/lumefantrine
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
- **OTHER INFORMATION**
  - Associated with eosinophilia-myalgia syndrome, therefore not first line therapy
Urokinase

CLINICAL USE
Fibrinolytic agent:
- Thrombosed arteriovenous shunts and intravenous cannulas
- Treatment of thromboembolic occlusive vascular disease, e.g. DVT, PE, peripheral vascular occlusion

DOSE IN NORMAL RENAL FUNCTION
- Lock: 5000–250 000 IU for 30 minutes – 2 hours
- Infusion: 5000–250 000 IU over 30 minutes – 48 hours, depending on local protocol

PHARMACOKINETICS
- Molecular weight (daltons): 33 000–54 000
- % Protein binding: No data
- % Excreted unchanged in urine: Low
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 20 minutes/Increased

DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
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<tr>
<td>10–20</td>
<td></td>
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<tr>
<td>&lt;10</td>
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</tbody>
</table>

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed.</td>
</tr>
<tr>
<td>HDF/HIF</td>
<td>Unknown dialysability.</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed.</td>
</tr>
</tbody>
</table>

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- None known

ADMINISTRATION

RECONSTITUTION
- 2 mL of sodium chloride 0.9%

ROUTE
- 

RATE OF ADMINISTRATION
- Various

COMMENTS
- 

OTHER INFORMATION
- Can also be given during dialysis
- Care in patients with uraemic coagulopathies or bleeding diatheses
- Some units mix 5000 IU with 1.5 mL heparin 1000 u/mL
Ursodeoxycholic acid

**CLINICAL USE**
- Dissolution of gallstones
- Primary biliary cirrhosis

**DOSE IN NORMAL RENAL FUNCTION**
- Dissolution of gallstones: 8–12 mg/kg/day in 1–2 divided doses
- Primary biliary cirrhosis: 10–15 mg/kg/day in 2–4 divided doses

**PHARMACOKINETICS**
- Molecular weight (daltons): 392.6
- % Protein binding: 96–98
- % Excreted unchanged in urine: 0
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): No data

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min): 20–50 Dose as in normal renal function
- 10–20 Dose as in normal renal function
- <10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Unknown dialysability. Dose as in normal renal function
- HD Unknown dialysability. Dose as in normal renal function
- HDF/High flux Unknown dialysability. Dose as in normal renal function
- CAV/VVHD Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Ciclosporin: unpredictably increases the absorption of ciclosporin in some patients

**ADMINISTRATION**
**RECONSTITUTION**
- **ROUTE**
- **RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- Completely metabolised in the liver and excreted via the faecal route
Valaciclovir

**CLINICAL USE**

Antiviral:
- Herpes zoster and simplex
- Prevention of cytomegalovirus (CMV) disease after renal transplantation

**DOSE IN NORMAL RENAL FUNCTION**

- Herpes simplex: 500 mg twice daily for 5–10 days
- Herpes zoster: 1 g 3 times a day for 7 days
- Herpes simplex suppression: 500 mg daily in 1–2 divided doses (500 mg twice daily in the immunocompromised)
- Prevention of CMV disease: 1 g 3 times a day for 90 days

**PHARMACOKINETICS**

Molecular weight (daltons) 360.8 (as hydrochloride)
% Protein binding 15
% Excreted unchanged in urine <1
Volume of distribution (L/kg) 0.7
Half-life – normal/ESRF (hrs) 3/14

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>Herpes simplex: Dose as in normal renal function</td>
</tr>
<tr>
<td></td>
<td>Herpes zoster: 1 g every 12 hours CMV prophylaxis: 1 g every 12 hours</td>
</tr>
<tr>
<td>15–30</td>
<td>Herpes simplex: 500 mg daily</td>
</tr>
<tr>
<td>&lt;15</td>
<td>Herpes zoster: 1 g every 24 hours CMV prophylaxis: 1 g every 24 hours</td>
</tr>
<tr>
<td></td>
<td>Herpes simplex suppression: Immunocompetent – 250 mg daily Immunocompromised – 500 mg daily</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

| CAPD | Likely dialysability. Dose as in GFR<15 mL/min |
| HD | Dialysed. Dose as in GFR<15 mL/min post dialysis |
| HDF/High flux | Dialysed. Dose as in GFR<15 mL/min post dialysis |
| CAV/ | Likely dialysability. Dose as in |
| VVHD | GFR=15–30 mL/min |

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Ciclosporin: may alter ciclosporin levels
- Mycophenolate: higher concentrations of both aciclovir and mycophenolic acid on concomitant administration

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral
- **RATE OF ADMINISTRATION**
  - **COMMENTS**
  -

**OTHER INFORMATION**

- Almost completely (80%) converted to aciclovir – see aciclovir monograph for further information
- Bioavailability of aciclovir from 1 g oral dose of valaciclovir is 54%
- Mean peak aciclovir concentrations occur 1.5 hours post dose; peak plasma concentrations of valaciclovir are 4% of aciclovir levels, occur at a median of 30–60 minutes post dose, and are at or below the limit of quantification 3 hours post dose
- The dose quoted in the literature for CMV prophylaxis in transplant recipients is 2 g 4 times a day. However, in practice this results in severe aciclovir toxicity, especially in patients with poorly functioning grafts
Valganciclovir

CLINICAL USE

• Induction and maintenance treatment of CMV retinitis in AIDS patients
• Treatment (unlicensed indication) and prophylaxis of CMV disease in transplant patients

DOSE IN NORMAL RENAL FUNCTION

• Induction/treatment: 900 mg twice daily for 21 days
• Maintenance/prophylaxis: 900 mg daily

PHARMACOKINETICS

Molecular weight (daltons) 390.8 (as hydrochloride)
% Protein binding <2 (as ganciclovir)
% Excreted unchanged in urine 84.6–94.6 (as ganciclovir)
Volume of distribution (L/kg) 0.519–0.841
Half-life – normal/ESRF (hrs) 4.1/67.5

DOSE IN RENAL IMPAIRMENT GFR (mL/min)

40–59 Induction/Treatment: 450 mg twice daily
         Maintenance/Prophylaxis: 450 mg daily
25–39 Induction/Treatment: 450 mg daily
         Maintenance/Prophylaxis: 450 mg every 48 hours
10–24 Induction/Treatment: 450 mg every 48 hours
         Maintenance/Prophylaxis: 450 mg twice weekly
<10 Treatment: 450 mg 2–3 times a week
         Prophylaxis: 450 mg 1–2 times a week
See ‘Other Information’

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

CAPD Dialysed. See ‘Other Information’
HD Dialysed. See ‘Other Information’
HDF/High flux Dialysed. See ‘Other Information’
CAV/ VVHD Likely dialysability. Dose as in GFR=10–24 mL/min

IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs
• Antibacterials: increased risk of convulsions with imipenem-cilastatin
• Antivirals: possibly increased didanosine concentration; profound myelosuppression with zidovudine – avoid if possible
• Mycophenolate: possibly increased concentrations of both mycophenolic acid and ganciclovir
• Increased risk of myelosuppression with other myelosuppressive drugs

ADMINISTRATION

RECONSTITUTION
–
ROUTE
• Oral
RATE OF ADMINISTRATION
–
COMMENTS
–

OTHER INFORMATION

• 900 mg valganciclovir twice daily is therapeutically equivalent to 5 mg/kg intravenous ganciclovir twice daily
• Valganciclovir is a prodrug of ganciclovir
• Take with food if possible
• Manufacturer advises to avoid in severe renal impairment due to increased risk of bone marrow suppression
• Doses of 450 mg once or twice a week have been used to treat CMV disease in patients with GFR<10 mL/min on dialysis
• Approximately 50% of ganciclovir is removed by haemodialysis
Valproic acid

**CLINICAL USE**
Treatment of manic episodes associated with bipolar disorder

**DOSE IN NORMAL RENAL FUNCTION**
1–2 g daily in 2–3 divided doses

**PHARMACOKINETICS**
- Molecular weight (daltons) 144.2
- % Protein binding 85–94
- % Excreted unchanged in urine <3
- Volume of distribution (L/kg) 0.1–0.4
- Half-life – normal/ESRF (hrs) 14/Increased

**DOSE IN RENAL IMPAIRMENT**
- GFR (mL/Min)
  - 20–50 Dose as in normal renal function
  - 10–20 Dose as in normal renal function
  - <10 Start with a low dose, adjust according to response

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Not dialysed. Dose as in GFR<10mL/min
- HD Dialysed. Dose as in GFR<10mL/min
- HDF/High flux Dialysed. Dose as in GFR<10mL/min
- CAV/ VVHD Dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anticoagulants: may increase anticoagulant effect of coumarins
- Anti-epileptics: concentration reduced by carbamazepine, phenytoin and primidone; concentration of active carbamazepine metabolite increased; concentration of lamotrigine, primidone, active metabolite of primidone, and possibly ethosuximide increased; sometimes reduces concentration of active metabolite of oxcarbazepine; alters phenytoin concentration; phenytoin and primidone reduce valproate concentration
- Antipsychotics: increased risk of neutropenia with olanzapine
- Antivirals: may increase zidovudine levels and resulting toxicity
- Ciclosporin: variable ciclosporin blood level response
- Cimetidine: valproate metabolism inhibited

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- May cause carnitine deficiency
- Dialysis removes about 20% of dose
Valsartan

CLINICAL USE
Angiotensin-II antagonist:
- Hypertension
- Left ventricular dysfunction
- Myocardial infarction with left ventricular failure

DOSE IN NORMAL RENAL FUNCTION
40–320 mg daily
Myocardial infarction: 20–160 mg twice daily

PHARMACOKINETICS
Molecular weight 435.5 (daltons)
% Protein binding 94–97
% Excreted unchanged in urine 13
Volume of distribution (L/kg) 17 litres
Half-life – normal/ESRF (hrs) 5–9/Unchanged

DOSE IN RENAL IMPAIRMENT
GFR (mL/MIN)
20–50 Dose as in normal renal function
10–20 Initial dose 40 mg; titrate according to response
<10 Initial dose 40 mg; titrate according to response

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Not dialysed. Dose as in GFR<10mL/min
HD Not dialysed. Dose as in GFR<10mL/min
HDF/High flux Unknown dialysability. Dose as in GFR<10mL/min
CAV/ VVHD Unlikely to be dialysed. Dose as in GFR=10–20mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effect
- Analgesics: antagonism of hypotensive effect and increased risk of renal impairment with NSAIDs; hyperkalaemia with ketorolac and other NSAIDs
- Ciclosporin: increased risk of hyperkalaemia and nephrotoxicity
- Diuretics: enhanced hypotensive effect; hyperkalaemia with potassium-sparing diuretics
- Epoetin: increased risk of hyperkalaemia; antagonism of hypotensive effect
- Lithium: reduced excretion (possibility of enhanced lithium toxicity)
- Potassium salts: increased risk of hyperkalaemia
- Tacrolimus: increased risk of hyperkalaemia and nephrotoxicity

ADMINISTRATION

SIDE EFFECTS
Side effects (e.g. hyperkalaemia, metabolic acidosis) are more common in patients with impaired renal function
Close monitoring of renal function during therapy is necessary in those with renal insufficiency
Renal failure has been reported in association with angiotensin-II antagonists in patients with renal artery stenosis, post renal transplant, and in those with severe congestive heart failure

RETURN TO CONTENTS
Vancomycin

**CLINICAL USE**
Antibacterial agent

**DOSE IN NORMAL RENAL FUNCTION**
IV: 1 g every 12 hours
Oral: 125 mg or 500 mg 4 times daily
(Higher dose for resistant cases of *Clostridium difficile*)

**PHARMACOKINETICS**
- Molecular weight: 1449.3; (1485.7 as hydrochloride)
- % Protein binding: 10–50 (19 CKD 5)
- % Excreted unchanged in urine: 80–90
- Volume of distribution (L/kg): 0.47–1.1 (0.88 CKD 5)

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/min)**
  - 20–50: IV: 0.5–1 g every 12–24 hours
  - Oral: dose as in normal renal function
  - 10–20: IV: 0.5–1 g every 24–48 hours
  - Oral: dose as in normal renal function
  - <10: IV: 0.5–1 g every 48–96 hours
  - Oral: dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD** Not dialysed. Dose as in GFR<10 mL/min
- **HD** Not dialysed. Dose as in GFR<10 mL/min
- **HDF/High flux** Dialysed. See ‘Other Information’
- **CAV/VVH/HD** Dialysed. 1 g every 48 hours
- **CVVHD/HDF** Dialysed. 1 g daily and see ‘Other Information’

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Ciclosporin: variable response; increased risk of nephrotoxicity
- Diuretics: increased risk of ototoxicity with loop diuretics
- Muscle relaxants: enhanced effects of suxamethonium
- Tacrolimus: possible increased risk of nephrotoxicity

**ADMINISTRATION**
**RECONSTITUTION**
- 10 mL water for injection per 500 mg vial, then dilute 1 g to 250 mL with sodium chloride 0.9% (50 mL if giving centrally)

**ROUTE**
- IV, oral

**RATE OF ADMINISTRATION**
- Not faster than 10 mg/minute

**COMMENTS**
- Usual dilution is 10–20 mg/mL. (UK Critical Care Group, Minimum Infusion Volumes for fluid restricted critically ill patients, 3rd Edition, 2006.)

**USE IN CAPD PERITONITIS:**
- 12.5–25 mg/L per bag (see local protocol.)
- Various other regimens used in PD ranging from IV dosing to high dose stat IP use
- Some units use the following:
  - Patient weight >60 kg: stat dose of 2 g IP on days 1, 7 and 14 in with a 6 hour dwell
  - Patient weight <60 kg: 1.5 g IP on days 1, 7 and 14

**OTHER INFORMATION**
- Second line to metronidazole in treatment of pseudomembranous colitis
- Not absorbed via oral route at low doses but monitor plasma levels at higher doses
- Injection solution may be given orally; however, oral capsules available
- Alternative Dosage Adjustment In Moderate And Severe Renal Impairment:
  - Give 1 g loading dose and monitor serum levels at 24 hour intervals.
  - When level <10 mg/L give another 1 g dose. Peak levels, 2 hours after dose, should be in range 18–26 mg/L. Some units use a 500 mg loading dose
- Anephric/dialysis patients usually need 1 g once or twice weekly
• In HDF higher doses are required; possible doses are 1 g initially followed by 500 mg every dialysis for 3 dialysis sessions. (Ariano RE, Fine A, Sitar DS. Adequacy of a vancomycin dosing regimen in patients receiving high-flux haemodialysis. *Am J Kidney Dis.* 2005; 46(4): 681–7.)


References:
Vardenafil

**CLINICAL USE**
Treatment of erectile dysfunction

**DOSE IN NORMAL RENAL FUNCTION**
5–20 mg approximately 25–60 minutes before sexual activity

**PHARMACOKINETICS**
- Molecular weight: 488.6 (daltons)
- % Protein binding: 95
- % Excreted unchanged in urine: 2–6
- Volume of distribution: 208 litres (L/kg)

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
Initial doses as for normal renal function, then maintenance doses of:
- 30–50 mL/Min: Dose as in normal renal function
- 10–30 mL/Min: Initial dose 5 mg and adjust accordingly
- <10 mL/Min: Initial dose 5 mg and adjust accordingly

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min. Use with caution
- HD: Not dialysed. Dose as in GFR<10 mL/min. Use with caution
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min. Use with caution
- CAV/VVHD: Not dialysed. Dose as in GFR=10–30 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Alpha-blockers: enhanced hypotensive effect – avoid for 6 hours after alpha-blockers (max dose 5 mg)
- Antifungals: concentration increased by ketoconazole, and itraconazole – avoid concomitant use
- Antivirals: concentration increased by amprenavir, indinavir, ritonavir, saquinavir – avoid with indinavir and ritonavir; reduce initial dose with saquinavir
- Grapefruit juice: concentration possibly increased – avoid concomitant use
- Nicorandil: possibly enhanced hypotensive effect – avoid concomitant use
- Nitrates: possibly enhanced hypotensive effect – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- Contraindicated in dialysis patients due to lack of information, therefore suggest use with caution and monitor patients closely
**Varenicline**

**CLINICAL USE**
Aid to smoking cessation

**DOSE IN NORMAL RENAL FUNCTION**
0.5 mg once daily for 3 days, 0.5 mg twice daily for 3 days, then 0.5–1 mg twice daily

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>361.3 (as tartrate)</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>&lt;20</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>92</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>415 litres</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>24/Increased</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–50</td>
<td>1 mg once or twice daily</td>
</tr>
<tr>
<td>10–30</td>
<td>1 mg once daily</td>
</tr>
<tr>
<td>&lt;10</td>
<td>0.5–1 mg once daily</td>
</tr>
</tbody>
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**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High Flux</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/</td>
<td>Dialysed. Dose as in GFR=10–30mL/min</td>
</tr>
<tr>
<td>VVHD</td>
<td>GFR=10–30mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**

<table>
<thead>
<tr>
<th>Reconstitution</th>
<th>Route</th>
<th>Rate of Administration</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Oral</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

RETURN TO CONTENTS
**Vecuronium bromide**

**CLINICAL USE**
Non-depolarising muscle relaxant

**DOSE IN NORMAL RENAL FUNCTION**
- Intubation: 80–100 micrograms/kg, with maintenance of 20–30 micrograms/kg
- IV infusion: 40–100 micrograms/kg bolus, followed by 48–84 micrograms/kg/hour

**PHARMACOKINETICS**
- Molecular weight (daltons) 637.7
- % Protein binding 30
- % Excreted 25
- Volume of distribution (L/kg) 0.18–0.27
- Half-life – normal/ESRF (hrs) 0.5–1.3/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
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</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unlikely to be dialysed.</td>
</tr>
<tr>
<td>HD</td>
<td>Unlikely to be dialysed.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability.</td>
</tr>
<tr>
<td>CAV/</td>
<td>Unknown dialysability.</td>
</tr>
<tr>
<td>VVHD</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced muscle relaxant effect
- Anti-arrhythmics: procainamide enhances muscle relaxant effect
- Antibacterials: effect enhanced by aminoglycosides, clindamycin, polymyxins and piperacillin
- Botulinum toxin: neuromuscular block enhanced (risk of toxicity)

**ADMINISTRATION**
- RECONSTITUTION
  - 5 mL water for injection to reconstitute 10 mg vial; up to 10 mL sodium chloride 0.9% or glucose 5% may be used
- ROUTE
  - IV
- RATE OF ADMINISTRATION
  - See dose
- COMMENTS
  - May be added to sodium chloride 0.9%, glucose 5% or Ringer’s solution to give a final concentration of 40 mg/L

**OTHER INFORMATION**
- Vecuronium is largely excreted via the liver. Use normal doses with caution in renal failure as has active metabolites which may accumulate
Venlafaxine

**CLINICAL USE**
Antidepressant:
- Depressive illness
- Generalised anxiety disorders

**DOSE IN NORMAL RENAL FUNCTION**
37.5–187.5 mg twice daily
XL: 75–225 mg daily
Generalised anxiety disorder: 75 mg once daily

**PHARMACOKINETICS**
Molecular weight 277; (313.9 as hydrochloride)
% Protein binding 27
% Excreted unchanged in urine 5
Volume of distribution (L/kg) 7.5
Half-life – normal/ESRF (hrs) 5/6–8

**DOSE IN RENAL IMPAIRMENT**
GFR (mL/ min)
30–50 Dose as in normal renal function
10–30 Reduce total dose by 50% and administer daily
<10 Reduce total dose by 50% and administer daily

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
CAPD Not dialysed. Dose as in GFR<10mL/min
HD Not dialysed. Dose as in GFR<10mL/min
HDF/High flux Unknown dialysability. Dose as in GFR<10mL/min
CAV/VVHD Not dialysed. Dose as in GFR=10–30mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: increased risk of bleeding with aspirin and NSAIDs
- Anticoagulants: effects of warfarin possibly enhanced
- Antidepressants: avoid concomitant use with MAOIs and moclobemide (increased risk of toxicity); possibly enhanced serotonergic effects with duloxetine
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: increases concentration of clozapine and haloperidol
- Dopaminergics: use entacapone with caution; increased risk of hypertension and CNS excitation with selegiline – avoid concomitant use
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
-

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
-

**COMMENTS**
-

**OTHER INFORMATION**
- Withhold dose until after haemodialysis to minimise nausea and any other side effects
- May be used to treat peripheral diabetic neuropathy in haemodialysis patients; dose is up to 75 mg daily [www.medscape.com/viewarticle/440202](http://www.medscape.com/viewarticle/440202)
- An ECG is required before treatment
Verapamil hydrochloride

**CLINICAL USE**
Calcium-channel blocker:
- Supraventricular arrhythmias
- Angina
- Hypertension

**DOSE IN NORMAL RENAL FUNCTION**
Oral:
- Supraventricular arrhythmias: 40–120 mg 3 times daily
- Angina: 80–120 mg 3 times daily
- Hypertension: 240–480 mg daily in 2–3 divided doses

IV:
- 5–10 mg followed by 5 mg, 5–10 minutes later if required

**PHARMACOKINETICS**
- Molecular weight (daltons): 491.1
- % Protein binding: 90
- % Excreted unchanged in urine: <4
- Volume of distribution (L/kg): 3–6
- Half-life – normal/ESRF (hrs): 4.5–12/Increased

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function. Monitor carefully</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD** Not dialysed. Dose as in GFR<10 mL/min
- **HD** Not dialysed. Dose as in GFR<10 mL/min
- **HDF/High flux** Unknown dialysability. Dose as in GFR<10 mL/min
- **CAV/** Dialysability minimal. Dose as in GFR=10–20 mL/min
- **VVHD** GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: increased hypotensive effect
- Anti-arrhythmics: increased risk of amiodarone-induced bradycardia, AV block and myocardial depression; increased risk of myocardial depression and asystole with disopyramide and flecainide
- Antibacterials: metabolism increased by rifampicin; metabolism possibly inhibited by erythromycin and clarithromycin (increased risk of toxicity)
- Anti-epileptics: effect probably reduced by barbiturates, phenytoin and primidone; enhanced effect of carbamazepine
- Antihypertensives: enhanced hypotensive effect, increased risk of first dose hypotensive effect of post-synaptic alpha-blockers
- Antivirals: concentration possibly increased by atazanavir and ritonavir
- Beta-blockers: enhanced hypotensive effect; risk of asystole, severe hypotension and heart failure if co-prescribed with beta-blockers
- Cardiac glycosides: increased levels of digoxin. Increased AV block and bradycardia
- Ciclosporin: variable reports of decreased nephrotoxicity and potentiated effect; may also increase ciclosporin levels
- Grapefruit juice: concentration increased – avoid concomitant use
- Ivabradine: avoid concomitant use
- Sirolimus: concentration of both drugs increased
- Statins: increased myopathy with simvastatin – do not exceed 20 mg of simvastatin.1
- Tacrolimus: may increase tacrolimus levels
- Theophylline: enhanced effect of theophylline
**ADMINISTRATION**

RECONSTITUTION –

ROUTE
● Oral, IV

RATE OF ADMINISTRATION
● Over 2 minutes (3 minutes in elderly)

COMMENTS –

**OTHER INFORMATION**

● Monitor BP and ECG
● Active metabolites may accumulate in renal impairment

References:
Vigabatrin

CLINICAL USE
Anti-epileptic agent

DOSE IN NORMAL RENAL FUNCTION
1–3 g daily in single or divided doses

PHARMACOKINETICS
Molecular weight (daltons) 129.2
% Protein binding Negligible
% Excreted unchanged in urine 60–80
Volume of distribution (L/kg) 0.8
Half-life – normal/ESRF (hrs) 5–8/13–15

DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)
20–50 Give 50% of normal dose and titrate to response
10–20 Give 50% of normal dose and titrate to response
<10 Give 25% of normal dose and titrate to response

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unknown dialysability. Dose as for GFR<10 mL/min
HD Dialysed. Dose as for GFR<10 mL/min
HDF/High flux Dialysed. Dose as for GFR<10 mL/min
CAV/VVHD Unknown dialysability. Dose as for GFR=10–20 mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Antidepressants: anticonvulsant effect antagonised, convulsive threshold lowered
- Anti-epileptics: concentration of phenytoin and possibly phenobarbital and primidone reduced
- Antimalarials: mefloquine antagonises anticonvulsant effect; chloroquine and hydroxychloroquine occasionally reduce convulsive threshold

ADMINISTRATION
RECONSTITUTION –
ROUTE – Oral
RATE OF ADMINISTRATION –
COMMENTS –
Vildagliptin

**CLINICAL USE**
Treatment of type 2 diabetes mellitus in combination with other antidiabetic drugs

**DOSE IN NORMAL RENAL FUNCTION**
With metformin or thiazolidinedione: 50 mg twice daily
With a sulphonylurea: 50 mg in the morning

**PHARMACOKINETICS**
- Molecular weight (daltons) 303.4
- % Protein binding 9.3
- % Excreted unchanged in urine 23
- Volume of distribution (L/kg) 71 litres
- Half-life – normal/ESRF (hrs) 3/Increased

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50 Avoid
- 10–20 Avoid
- <10 Avoid

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Not dialysed. Avoid
- HD Not dialysed. Avoid
- HDF/High flux Not dialysed. Avoid
- CAV/VVHD Not dialysed. Avoid

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- None known

**ADMINISTRATION**
- RECONSTITUTION
  - ROUTE Oral
  - RATE OF ADMINISTRATION
    - COMMENTS

**OTHER INFORMATION**
- Use is contraindicated in renal impairment due to lack of data
- Cases of hepatic dysfunction have occasionally been reported
- The main metabolite (LAY 151) is removed by haemodialysis
Vinblastine sulphate

**CLINICAL USE**
Antineoplastic agent

**DOSE IN NORMAL RENAL FUNCTION**
5.5–7.4 mg/m² (maximum of once a week)
Or consult relevant local protocol

**PHARMACOKINETICS**
Molecular weight (daltons) 909.1
% Protein binding 99
% Excreted unchanged in urine 14
Volume of distribution (L/kg) 13–40
Half-life – normal/ESRF (hrs) 25/–

**DOSE IN RENAL IMPAIRMENT**
GFR (mL/MIN)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
CAPD Unlikely to be dialysed. Dose as in normal renal function
HD Unlikely to be dialysed. Dose as in normal renal function
HDF/High flux Unknown dialysability. Dose as in normal renal function
CAV/VVHD Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: toxicity increased by erythromycin – avoid concomitant use
- Anti-epileptics: phenytoin levels may be reduced
- Antifungals: metabolism possibly inhibited by posaconazole (increased risk of neurotoxicity)
- Antipsychotics: avoid concomitant use with clozapine (increased risk of agranulocytosis)

**ADMINISTRATION**

**RECONSTITUTION**
Add 10 mL of diluent to 10 mg vial. May be administered into fast-running drip of sodium chloride 0.9%

**ROUTE**
- IV

**RATE OF ADMINISTRATION**
- 1 minute

**COMMENTS**
- Do not dilute with large volumes (e.g. 100–250 mL) or give over long periods (30–60 minutes) as thrombophlebitis and extravasation may occur

**OTHER INFORMATION**
- Vinblastine is extensively metabolised (primarily in the liver) to desacetylvinblastine, which is more active than the parent compound.
- 33% of the drug is slowly excreted in the urine and 21% in the faeces within 72 hours
Vincristine sulphate

**CLINICAL USE**
Antineoplastic agent

**DOSE IN NORMAL RENAL FUNCTION**
IV: 1.4–1.5 mg/m² weekly; maximum 2 mg
Consult relevant local protocol

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
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<td>Molecular weight (daltons)</td>
<td>923</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>75</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>10–20</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>5–11</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>15–155/Unchanged</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**

- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

- **CAPD**: Unlikely to be dialysed. Dose as in normal renal function
- **HD**: Unlikely to be dialysed. Dose as in normal renal function
- **HDF/High flux**: Unknown dialysability. Dose as in normal renal function
- **CAV/VVHD**: Unlikely to be dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs
- Anti-epileptics: phenytoin levels may be reduced
- Antifungals: metabolism possibly inhibited by itraconazole and posaconazole (increased risk of neurotoxicity)
- Antipsychotics: avoid concomitant use with clozapine (increased risk of agranulocytosis)

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - IV
- **RATE OF ADMINISTRATION**
  - Slow bolus
  - May be administered into fast running drip of sodium chloride 0.9% or glucose 5%

**OTHER INFORMATION**

- Most of an IV dose is excreted into the bile after rapid tissue binding
- Metabolised by cytochrome P450 (in the CYP 3A subfamily). Elimination is primarily biliary; excreted into bile and faeces (67% within 72 hours, 40–50% as metabolites), 10% excreted in urine in 24 hrs
Vindesine sulphate

CLINICAL USE
Antineoplastic agent

DOSE IN NORMAL RENAL FUNCTION
3–4 mg/m² weekly

PHARMACOKINETICS
Molecular weight 852 (daltons)
% Protein binding No data
% Excreted unchanged in urine 13
Volume of distribution 8 (L/kg)
Half-life – normal/ESRF (hrs) 20–24

DOSE IN RENAL IMPAIRMENT
GFR (mL/min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function
<10 Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unlikely to be dialysed. Dose as in normal renal function
HD Unlikely to be dialysed. Dose as in normal renal function
HDF/High flux Unknown dialysability. Dose as in normal renal function
CAV/VVHD Unlikely to be dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● None known

ADMINISTRATION
RECONSTITUTION
● 5 mL sodium chloride 0.9% per 5 mg vial
ROUTE
● IV
RATE OF ADMINISTRATION
● 1–3 minutes
COMMENTS
● Can be injected into the tubing of a fast running infusion of sodium chloride 0.9%, glucose 5% or glucose/saline solutions, or directly into a vein
● Reconstituted solution is stable for 24 hours if stored in a fridge

OTHER INFORMATION
● Nadir of the WCC occurs 3–5 days after dose with recovery after another 4–5 days
● Metabolised by cytochrome P450 (in the CYP 3A subfamily). Elimination is primarily biliary (13% excreted in urine in 24 hrs)
Vinorelbine

**CLINICAL USE**
- Treatment of advanced breast cancer (where other anthracyclines have failed)
- Non-small cell lung cancer

**DOSE IN NORMAL RENAL FUNCTION**
- Oral: 60–80 mg/m² once weekly for 3 weeks
- IV: 25–30 mg/m² once a week
- Maximum 60 mg per dose

**PHARMACOKINETICS**
- Molecular weight: 1079.1 (as tartrate)
- % Protein binding: 13.5 (78% bound to platelets)
- % Excreted unchanged in urine: 18.5
- Volume of distribution (L/kg): >40

**DOSE IN RENAL IMPAIRMENT**
- **GFR (mL/Min)**
  - 20–50: Dose as in normal renal function and monitor closely
  - 10–20: Dose as in normal renal function and monitor closely
  - <10: Dose as in normal renal function and monitor closely

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- **CAPD**: Unlikely to be dialysed. Dose as in normal renal function and monitor closely
- **HD**: Unlikely to be dialysed. Dose as in normal renal function and monitor closely
- **HDF/High flux**: Unknown dialysability. Dose as in normal renal function and monitor closely
- **CAV/VVHD**: Unknown dialysability. Dose as in normal renal function and monitor closely

**IMPORTANT DRUG INTERACTIONS**
- Potentially hazardous interactions with other drugs
  - Antipsychotics: avoid concomitant use with clozapine (increased risk of agranulocytosis)

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral, IV bolus, infusion

**RATE OF ADMINISTRATION**
- **Bolus**: 5–10 minutes
- **Infusion**: 20–30 minutes

**COMMENTS**
- Dilute bolus in 20–50 mL with sodium chloride 0.9%
- Dilute infusion in 125 mL with sodium chloride 0.9%
- Stable for 24 hours at 2–8°C

**OTHER INFORMATION**
- Widely distributed in the body, mostly in spleen, liver, kidneys, lungs, thymus; moderately in heart, muscles; minimally in fat, brain, bone marrow. High levels are found in both normal and malignant lung tissues, with slow diffusion out of tumour tissue
- Metabolism appears to be hepatic. Excretion is mainly by the biliary route (18.5% appears in the urine)
- Flush line with saline after infusion
- Dose-limiting toxicity is mainly neutropenia
- In patients where >75% of the liver volume has been replaced by metastases, it is empirically suggested that the dose be reduced by a third, with close haematological follow-up
Vitamin B and C preparations

CLINICAL USE
Vitamin B and C supplementation

DOSE IN NORMAL RENAL FUNCTION
- Vitamin B Compound Strong: 1–2 tablets 1 to 3 times daily
- Pabrinex: Ampoules No 1 and No 2 every 8–12 hours depending on indication
- Can be given post dialysis for vitamin supplementation

PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>N/A</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>N/A</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>N/A</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>N/A</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>N/A</td>
</tr>
</tbody>
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DOSE IN RENAL IMPAIRMENT

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DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

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</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

IMPORTANT DRUG INTERACTIONS

Potentially hazardous interactions with other drugs
- None known

ADMINISTRATION

RECONSTITUTION

ROUTE
- Oral, IV, IM

RATE OF ADMINISTRATION
- Bolus: Max volume of 10 mL over 10 minutes
- Infusion: 15–30 minutes

COMMENTS
- Dilute in 50–100 mL sodium chloride or glucose 5%

OTHER INFORMATION

- NOT PRESCRIBABLE ON FP10
- PRESCRIPTION
- Supplement in HD patients due to loss on dialysis and poor diet
- Available as Nephrovite® (Kimal) and Dialyvit® (Vitaline) – each tablet contains:
  - Vitamin B1 (thiamine) 1.5 mg
  - Vitamin B2 (riboflavin) 1.7 mg
  - Vitamin B3 (niacinamide) 20 mg
  - Vitamin B6 (pyridoxine) 10 mg
  - Vitamin B12 (cyanocobalamin) 6 mcg
  - Vitamin C 60 mg
  - Biotin 300 mcg
  - Pantothenic acid 10 mg
  - Folic acid 800 mcg
- Ketovite®, each tablet contains:
  - Vitamin B1 (thiamine) 1 mg
  - Vitamin B2 (riboflavin) 1 mg
  - Acetomenaphthone 500 mcg
  - Vitamin B6 (pyridoxine) 330 mcg
  - Nicotinamide 3.3 mg
  - Vitamin C 16.6 mg
  - Biotin 170 mcg
  - Pantothenic acid 1.16 mg
  - Alpha tocopheryl acetate 5 mg
  - Inositol 50 mg
  - Folic acid 250 mcg
- Pabrinex:
  - Vitamin B1 (thiamine) 250 mg
  - Vitamin B2 (riboflavin) 4 mg
  - Vitamin B6 (pyridoxine) 50 mg
  - Vitamin C 500 mg
  - Nicotinamide 160 mg
Voriconazole

**CLINICAL USE**

Antifungal:
- Invasive aspergillosis
- Fluconazole-resistant serious invasive fungal infections
- Immunocompromised patients with progressive, possibly life-threatening infections

**DOSE IN NORMAL RENAL FUNCTION**

**IV:**
- 6 mg/kg 12 hourly for 24 hours, then 3–4 mg/kg 12 hourly

**Oral:**
- <40 kg, 200 mg 12 hourly for 24 hours, then 100–150 mg twice daily
- >40 kg, 400 mg 12 hourly for 24 hours, then 200–300 mg twice daily

**PHARMACOKINETICS**

- Molecular weight: 349.3 daltons
- % Protein binding: 58
- % Excreted unchanged in urine: <2
- Volume of distribution: 4.6 L/kg
- Half-life: normal/ESRF (hrs) 6 (depends on dose)/Unchanged

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Dose as in normal renal function</th>
<th>Dose as in normal renal function. See ‘Other Information’</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt;10</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Type</th>
<th>Dose as in normal renal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Probably dialysed.</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed.</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed.</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Probably dialysed.</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**

Potentially hazardous interactions with other drugs

- Analgesics: methadone concentration increased
- Antibacterials: concentration reduced by rifabutin; increase dose of voriconazole from 200 to 350 mg and from 100 to 200 mg (depends on patient's weight), and increase IV dose to 5 mg/kg if used in combination – avoid concomitant use if possible; increased rifabutin levels – monitor for toxicity; avoid concomitant use with rifampicin
- Anticoagulants: enhanced effect of coumarins
- Antidepressants: avoid concomitant use with reboxetine
- Antidiabetics: possibly increased concentration of sulphonylureas
- Anti-epileptics: concentration reduced by carbamazepine, barbiturates and primidone – avoid concomitant use; phenytoin reduces voriconazole concentration and voriconazole increases phenytoin concentration – double oral voriconazole dose and increase IV to 5 mg/kg dose if using with phenytoin; avoid concomitant use if possible
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: increased risk of ventricular arrhythmias with pimozide and sertindole – avoid concomitant use; possibly increased quetiapine levels – reduce dose of quetiapine
- Antivirals: concentration reduced by efavirenz and ritonavir; also concentration of efavirenz increased – avoid concomitant use with ritonavir; with efavirenz reduce dose by 50% and increase dose of voriconazole to 400 mg twice daily; possibly increased saquinavir levels
- Benzodiazepines: may inhibit metabolism of midazolam
- Ciclosporin: AUC increased – reduce ciclosporin dose by 50% and monitor closely
- Ergot alkaloids: risk of ergotism – avoid concomitant use
- Lipid-lowering drugs: possibly increased risk of myopathy with atorvastatin or simvastatin
Sirolimus: increased sirolimus concentration – avoid concomitant use
Tacrolimus: AUC increased – reduce tacrolimus dose to a third and monitor closely
Ulcer-healing drugs: omeprazole concentration increased – reduce omeprazole dose by 50%

**ADMINISTRATION**

**RECONSTITUTION**
- 19 mL water for injection

**ROUTE**
- Oral, IV

**RATE OF ADMINISTRATION**
- 1–2 hours (3 mg/kg/hour)

**COMMENTS**
- Not compatible with sodium bicarbonate or TPN solutions
- Dilute to a concentration of 2–5 mg/mL with sodium chloride 0.9%, Hartmann's solution or glucose 5%

**OTHER INFORMATION**

- Haemodialysis clearance is 121 mL/min
- Oral bioavailability is 96%
- Only use IV in renal patients if patient is unable to tolerate oral, as intravenous vehicle (SBECED) accumulates in renal failure. The vehicle is dialysed at a rate of 55 mL/min
- Take oral dose 1 hour before or an hour after meals
- Monitor renal function as can enhance nephrotoxicity of other drugs and concurrent conditions
- Rare reports of acute renal failure and discoid lupus erythematosus occurring
- Also reports of haematuria, nephritis and tubular necrosis
- In clinical trials, 30% of patients had visual problems, usually with higher doses
Warfarin sodium

CLINICAL USE
Anticoagulant

DOSE IN NORMAL RENAL FUNCTION
Depends on INR

PHARMACOKINETICS
Molecular weight (daltons) 330.3
% Protein binding 99
% Excreted unchanged in urine 0
Volume of distribution (L/kg) 0.14
Half-life – normal/ESRF (hrs) 37/Unchanged

DOSE IN RENAL IMPAIRMENT

GFR (mL/MIN)

20–50  Dose as in normal renal function
10–20  Dose as in normal renal function
<10  Dose as in normal renal function

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

CAPD  Not dialysed. Dose as in normal renal function
HD  Not dialysed. Dose as in normal renal function
HDF/High flux  Unknown dialysability. Dose as in normal renal function
CAV/VVHD  Not dialysed. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- There Are Many Significant Interactions With Warfarin
Prescribe With Care With Regard To The Following:
- Anticoagulant effect enhanced by: alcohol, amiodarone, anabolic steroids, aspirin, azithromycin, aztreonam, bicalutamide, cephalexin, cimetidine, ciprofloxacin, clarithromycin, clonidogrel, cranberry juice, danazol, dapsone, dextropropoxyphene, diphenidol, disulfiram, entacapone, erythromycin, esomprazole, exenatide, ezetimibe, fumaric acid, fluconazole, flutamide, fluvastatin, glucosamine, grapefruit juice, itraconazole, ketoconazole, levamisole, levofloxacin, levothyroxine, macrolides, methylphenidate, metronidazole, miconazole, mitoxantrone, nalidixic acid, neomycin, norfloxacin, NSAIDs, ofloxacin, omeprazole, pantoprazole, paracetamol, penicillins, proguanil, propafenone, rosvuastatin, saquinavir, SSRIs, simvastatin, sitaxentan, sulfipyrazone, sulphonamides, tamoxifen, testosterone, tetracyclines, tigecycline, toremifene, tramadol, trimethoprim, valproate, venlafaxine, voriconazole

- Anticoagulant effect decreased by: acitretin, atorvastatin, azathioprine, barbiturates, carbamazepine, ginseng, griseofulvin, mercaptopurine, mitotane, oral contraceptives, phenytoin, primidone, rifampicin, St John's wort (avoid concomitant use), sucralfate, vitamin K

- Anticoagulant effects enhanced/reduced by: amprenavir, anion exchange resins, atazanavir, corticosteroids, dietary changes, nevirapine, ritonavir, tricyclics

- Analgesics: increased risk of bleeding with IV diclofenac and ketorolac – avoid concomitant use

- Antidiabetic agents: enhanced hypoglycaemic effect with sulphfonylureas

- Camomile: enhanced anticoagulation

- Ciclosporin: there have been a few reports of altered anticoagulant effect; decreased ciclosporin levels have been seen rarely

- Cytotoxics: increased risk of bleeding with erlotinib and imatinib; enhanced effect with etoposide, fluorouracil, ifosfamide and sorafenib

- Melatonin: possibly enhanced INR

ADMINISTRATION

RECONSTITUTION
-

ROUTE
- Oral

RATE OF ADMINISTRATION
- COMMENTS
-

OTHER INFORMATION

- Inactive metabolites renally excreted and may accumulate in renal impairment
- Reduced protein binding in renal impairment
Xipamide

**CLINICAL USE**
Thiazide diuretic:
- Hypertension
- Oedema

**DOSE IN NORMAL RENAL FUNCTION**
Oedema: 40–80 mg in the morning
Maintenance: 20 mg in the morning
Hypertension: 20 mg in the morning

**PHARMACOKINETICS**
- Molecular weight: 354.8 daltons
- % Protein binding: 99
- % Excreted unchanged in urine: 50
- Volume of distribution (L/kg): 10–21 litres

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Dialysed. Dose as in normal renal function
- HDF/High flux: Dialysed. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: increased risk of nephrotoxicity with NSAIDs; antagonism of diuretic effect
- Anti-arrhythmics: hypokalaemia leads to increased cardiac toxicity; effects of lidocaine and mexiletine antagonised
- Antibacterials: avoid administration with lymecycline
- Antidepressants: increased risk of hypokalaemia with reboxetine; enhanced hypotensive effect with MAOIs; increased risk of postural hypotension with tricyclics
- Anti-epileptics: increased risk of hyponatraemia with carbamazepine
- Antifungals: increased risk of hypokalaemia with amphotericin
- Antihypertensives: enhanced hypotensive effect; increased risk of first dose hypotension with post-synaptic alpha-blockers like prazosin; hypokalaemia increases risk of ventricular arrhythmias with sotalol
- Antipsychotics: hypokalaemia increases risk of ventricular arrhythmias with amisulpride or sertindole; enhanced hypotensive effect with phenothiazines; hypokalaemia increases risk of ventricular arrhythmias with pimozide – avoid concomitant use
- Atomoxetine: hypokalaemia increases risk of ventricular arrhythmias with amisulpride or sertindole; enhanced hypotensive effect with phenothiazines; hypokalaemia increases risk of ventricular arrhythmias with pimozide – avoid concomitant use
- Anti-arrhythmics: hypokalaemia leads to increased cardiac toxicity; effects of lidocaine and mexiletine antagonised
- Antibacterials: avoid administration with lymecycline
- Cardiac glycosides: increased toxicity if hypokalaemia occurs
- Ciclosporin: increased risk of nephrotoxicity and possibly hypomagnesaemia
- Lithium excretion reduced (increased toxicity)

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral
  - RATE OF ADMINISTRATION
  - COMMENTS

**OTHER INFORMATION**
- Monitor for hypokalaemia
- Diuresis starts within 1–2 hours, peaks at 4–6 hours and lasts for almost 24 hours
- Manufacturer advises to avoid in severe renal impairment due to reduced clearance
Zafirlukast

CLINICAL USE
Prophylaxis of asthma

DOSE IN NORMAL RENAL FUNCTION
20 mg twice daily

PHARMACOKINETICS
Molecular weight (daltons) 575.7
% Protein binding 99
% Excreted unchanged in urine 0 (10% as metabolites)
Volume of distribution (L/kg) 70 litres
Half-life – normal/ESRF (hrs) 10/Possibly unchanged

DOSE IN RENAL IMPAIRMENT
GFR (mL/Min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function, but use with care
<10 Dose as in normal renal function, but use with care

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Unlikely to be dialysed. Dose as in normal renal function, but use with care
HD Unlikely dialysability. Dose as in normal renal function, but use with care
HDF/High flux Unknown dialysability. Dose as in normal renal function, but use with care
CAV/VVHD Unknown dialysability. Dose as in normal renal function, but use with care

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
● Analgesics: concentration increased by aspirin
● Antibacterials: concentration reduced by erythromycin
● Anticoagulants: may enhance the effects of warfarin
● Theophylline: zafirlukast possibly increases theophylline concentration; zafirlukast concentration reduced

ADMINISTRATION
RECONSTITUTION
–
ROUTE
● Oral
RATE OF ADMINISTRATION
–
COMMENTS
–

OTHER INFORMATION
● Do not take with food as it reduces bioavailability
Zanamivir

CLINICAL USE
- Treatment of influenza A and B within 48 hours after onset of symptoms
- Post exposure prophylaxis

DOSE IN NORMAL RENAL FUNCTION
Treatment: 10 mg twice daily for 5 days
Prophylaxis: 10 mg once daily for 10 days

PHARMACOKINETICS
- Molecular weight (daltons): 332.3
- % Protein binding: <10
- % Excreted unchanged in urine: 100
- Volume of distribution (L/kg): No data
- Half-life – normal/ESRF (hrs): 2.6–5/Increased

DOSE IN RENAL IMPAIRMENT
<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Dose as in normal renal function</td>
</tr>
</tbody>
</table>

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Unknown dialysability. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

IMPORTANT DRUG INTERACTIONS
- Potentially hazardous interactions with other drugs
  - None known

ADMINISTRATION
- RECONSTITUTION
  - ROUTE
    - Inhalation
  - RATE OF ADMINISTRATION
  - COMMENTS

OTHER INFORMATION
- 10–20% of dose is systemically absorbed
Ziconotide

**CLINICAL USE**
Analgesia for intrathecal use

**DOSE IN NORMAL RENAL FUNCTION**
2.4–21.6 mcg daily; majority require <9.6 mcg/day

**PHARMACOKINETICS**
- Molecular weight: 2639.1 (2699.2 as acetate)
- % Protein binding: 53%
- % Excreted unchanged in urine: <1%
- Volume of distribution (L/kg): 30 litres

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose as in normal renal function</th>
<th>Dose as in normal renal function</th>
<th>Dose as in normal renal function. Use with caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>10–20</td>
<td></td>
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<tr>
<td>&lt;10</td>
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<td></td>
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</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>MODality</th>
<th>Unknown dialysability. Dose as in GFR&lt;10mL/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td></td>
</tr>
<tr>
<td>HD</td>
<td></td>
</tr>
<tr>
<td>HDF/High flux</td>
<td></td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td></td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Contraindicated with IT chemotherapy

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Intrathecal
- **RATE OF ADMINISTRATION**
- Over 24 hours
- **COMMENTS**
  - Dilute with preservative-free sodium chloride 0.9%; concentration should be no lower than 5 mcg/mL in an external pump and 25 mcg/mL in an internal pump

**OTHER INFORMATION**
- Use with caution in renal impairment due to lack of studies
- Has rarely caused rhabdomyolysis, myositis, acute renal failure and urinary retention
Zidovudine

**CLINICAL USE**
Nucleoside reverse transcriptase inhibitor:
- Treatment of HIV in combination with other antiretroviral drugs
- Prevention of maternal-foetal HIV transmission

**DOSE IN NORMAL RENAL FUNCTION**
Oral: 500–600 mg daily in 2–3 divided doses
IV: 1–2 mg/kg every 4 hours

**PHARMACOKINETICS**
- Molecular weight (daltons) 267.2
- % Protein binding 34–38
- % Excreted unchanged in urine 8–25
- Volume of distribution (L/kg) 1.6
- Half-life – normal/ESRF (hrs) 1.1/1.4–3

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose Instruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Give 100% of normal dose every 8 hours</td>
</tr>
<tr>
<td>10–20</td>
<td>Give 100% of normal dose every 8 hours</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Give 50% of normal dose every 8 hours</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Not dialysed. Dose as in GFR<10 mL/min
- HD: Not dialysed. Dose as in GFR<10 mL/min Give post dialysis
- HDF/High flux: Unknown dialysability. Dose as in GFR<10 mL/min Give post dialysis
- CAV/ VVHD: Not dialysed. Dose as in GFR=10–20 mL/min

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: absorption reduced by clarithromycin; avoid concomitant use with rifampicin
- Anti-epileptics: phenytoin levels may be raised or lowered; concentration possibly increased by valproate (increased risk of toxicity)
- Antifungals: concentration increased by fluconazole
- Antivirals: profound myelosuppression with ganciclovir – avoid if possible; extreme lethargy on administration of IV aciclovir; effects of stavudine inhibited – avoid concomitant use; concentration reduced by tipranavir

**ADMINISTRATION**

**RECONSTITUTION**
- IV, oral

**ROUTE**
- 1 hour

**RATE OF ADMINISTRATION**
- Dilute with glucose 5% infusion to give a final concentration of 2 mg/mL or 4 mg/mL

**COMMENTS**
- Dialysis has little effect on zidovudine, presumably because of rapid metabolism. The glucuronide metabolite (T½ =1 hour) has no antiviral activity and will be significantly removed by dialysis
- Patients with severe renal failure have 50% higher maximum plasma concentrations
- 90% of a dose is excreted renally, mostly as the glucuronide. There is substantial accumulation of this metabolite in renal failure
- Main risk in renal impairment is haematological toxicity

**REFERENCES**
Zoledronic acid

CLINICAL USE
- Hypercalcaemia of malignancy
- Reduction of bone damage in advanced malignancies
- Paget’s disease

DOSE IN NORMAL RENAL FUNCTION
- Hypercalcaemia of malignancy: 4 mg as a single dose
- Reduction of bone damage in advanced malignancies: 4 mg every 3–4 weeks
- Paget’s disease: 5 mg as a single dose

PHARMACOKINETICS
- Molecular weight (daltons): 272.1
- % Protein binding: 56
- % Excreted unchanged in urine: 39 +/- 16
- Volume of distribution (L/kg): 6.1–10.8 litres
- Half-life – normal/ESRF (hrs): 146/Increased

DOSE IN RENAL IMPAIRMENT

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;60</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>50–49</td>
<td>3.5 mg</td>
</tr>
<tr>
<td>30–29</td>
<td>3.3 mg</td>
</tr>
<tr>
<td>&lt;29</td>
<td>Use 3 mg with caution if benefit outweighs risk</td>
</tr>
</tbody>
</table>

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES

- CAPD: Unknown dialysability. Dose as in GFR<29 mL/min
- HD: Unknown dialysability. Dose as in GFR<29 mL/min
- HDF/High flux: Unknown dialysability. Dose as in GFR<29 mL/min
- CAV/VVHD: Unknown dialysability. Dose as in GFR=30–39 mL/min

IMPORTANT DRUG INTERACTIONS
- Potentially hazardous interactions with other drugs
- Other nephrotoxic drugs: use with caution as can enhance nephrotoxicity

ADMINISTRATION
RECONSTITUTION
- Add 5 mL of water for injection to each 4 mg vial

ROUTE
- IV

RATE OF ADMINISTRATION
- 15 minutes

COMMENTS
- Add to 100 mL sodium chloride 0.9% or glucose 5%
- Reconstituted solutions are stable for 24 hours at room temperature

OTHER INFORMATION
- Also administer a calcium supplement of 500 mg daily plus 400 IU of vitamin D daily
- Increased risk of renal deterioration if GFR<10 mL/min – measure creatinine while on zoledronic acid
- Increased risk of renal failure if use 8 mg
- May cause osteonecrosis of the jaw

RETURN TO CONTENTS
Zolmitriptan

**CLINICAL USE**
Acute treatment of migraine

**DOSE IN NORMAL RENAL FUNCTION**
2.5–5 mg, repeated after 2 hours if required; maximum 10 mg in 24 hours

**PHARMACOKINETICS**
- Molecular weight (daltons): 287.4
- % Protein binding: 25
- % Excreted unchanged in urine: 60 (as metabolites)
- Volume of distribution (L/kg): 2.4

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50: Dose as in normal renal function
- 10–20: Dose as in normal renal function
- <10: Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD: Unknown dialysability. Dose as in normal renal function
- HD: Unknown dialysability. Dose as in normal renal function
- HDF/High flux: Unknown dialysability. Dose as in normal renal function
- CAV/VVHD: Unknown dialysability. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: quinolones possibly inhibit metabolism – reduce dose of zolmitriptan
- Antidepressants: risk of CNS toxicity with MAOIs and moclobemide – reduce dose of zolmitriptan to max 7.5 mg;
- SSRIs inhibit metabolism of zolmitriptan; possibly increased serotonergic effects with duloxetine; increased serotonergic effects with St John's wort – avoid concomitant use
- Cimetidine: inhibits metabolism of zolmitriptan; maximum dose is 5 mg
- Ergot alkaloids: increased risk of vasospasm
- Linezolid: risk of CNS toxicity – reduce dose of zolmitriptan

**ADMINISTRATION**

**RECONSTITUTION**
- ROUTE
  - Oral

**RATE OF ADMINISTRATION**
- COMMENTS
  -
**Zolpidem tartrate**

**CLINICAL USE**
Insomnia (short-term treatment)

**DOSE IN NORMAL RENAL FUNCTION**
5–10 mg at night

**PHARMACOKINETICS**
- Molecular weight (daltons) 764.9
- % Protein binding 92.5
- % Excreted unchanged in urine Negligible (56% as active metabolites)
- Volume of distribution (L/kg) 0.34–0.54 (depends on age)
- Half-life – normal/ESRF (hrs) Average: 2.4/

**DOSE IN RENAL IMPAIRMENT GFR (mL/MIN)**
- 20–50 Dose as in normal renal function
- 10–20 Dose as in normal renal function
- <10 Dose as in normal renal function

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**
- CAPD Not dialysed. Dose as in normal renal function
- HD Not dialysed. Dose as in normal renal function
- HDF/High flux Unknown dialysability. Dose as in normal renal function
- CAV/VVHD Not dialysed. Dose as in normal renal function

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Antibacterials: metabolism accelerated by rifampicin
- Antipsychotics: enhanced sedative effects
- Antivirals: concentration increased by ritonavir (risk of extreme sedation and respiratory depression) – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- 

**ROUTE**
- Oral

**RATE OF ADMINISTRATION**
- 

**COMMENTS**
- 

**OTHER INFORMATION**
- First pass metabolism by liver is 35%
- Clearance is reduced in renal impairment
Zonisamide

CLINICAL USE
Anti-epileptic

DOSE IN NORMAL RENAL FUNCTION
Initially: 25 mg twice daily, increasing to maintenance dose of 300–500 mg daily in 1 or 2 divided doses

PHARMACOKINETICS
Molecular weight (daltons) 212.2
% Protein binding 40–60
% Excreted unchanged in urine 15–35
Volume of distribution (L/kg) 0.8–1.6
Half-life – normal/ESRF (hrs) 60–63/Increased

DOSE IN RENAL IMPAIRMENT
GFR (mL/Min)
20–50 Dose as in normal renal function
10–20 Dose as in normal renal function, titrate slowly. See ‘Other Information’
<10 Dose as in normal renal function, titrate slowly. See ‘Other Information’

DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES
CAPD Dialysed. Dose as in GFR<10 mL/min
HD Dialysed. Dose as in GFR<10 mL/min
HDF/High flux Dialysed. Dose as in GFR<10 mL/min
CAV/ VVHD Probably dialysed. Dose as in GFR=10–20 mL/min

IMPORTANT DRUG INTERACTIONS
Potentially hazardous interactions with other drugs
- Antidepressants: anticonvulsant effect antagonised by MAOIs, SSRIs and tricyclics
- Antimalarials: possibly increased risk of convulsions with chloroquine and hydroxychloroquine; anticonvulsant effect antagonised by mefloquine

ADMINISTRATION
RECONSTITUTION
- ROUTE
● Oral
RATE OF ADMINISTRATION
- COMMENTS
-

OTHER INFORMATION
- AUC is increased by 35% in patients with a GFR<20 mL/min
- Increase dose at 2 weekly intervals in people with renal impairment and monitor more frequently
# Zopiclone

## Clinical Use
Hypnotic

## Dosage in Normal Renal Function
3.75–7.5 mg at night

## Pharmacokinetics
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>388.8</td>
</tr>
<tr>
<td>% Protein binding (%)</td>
<td>45–80</td>
</tr>
<tr>
<td>% Excreted unchanged in urine (%)</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>91.8–104.6 litres</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>3.5–6.5/Unchanged</td>
</tr>
</tbody>
</table>

## Dosage in Renal Impairment

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dosage</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
<td>-</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
<td>-</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Start with lower dose</td>
<td></td>
</tr>
</tbody>
</table>

## Dosage in Patients Undergoing Renal Replacement Therapies

<table>
<thead>
<tr>
<th>Type</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

## Important Drug Interactions
Potentially hazardous interactions with other drugs
- Antibacterials: metabolism inhibited by erythromycin and quinupristin/dalfopristin; concentration significantly reduced by rifampicin
- Antipsychotics: enhanced sedative effects
- Antivirals: concentration possibly increased by ritonavir

## Administration

### Reconstitution
- 

### Route
- Oral

### Rate of Administration
- 

### Comments
- 

## Other Information
- It is recommended that elderly patients and those with severe renal disease should start treatment with 3.75 mg; however, accumulation has not been observed

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RETURN TO CONTENTS
Zotepine

**CLINICAL USE**
Treatment of schizophrenia

**DOSE IN NORMAL RENAL FUNCTION**
25–100 mg 3 times a day

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular weight (daltons)</td>
<td>331.9</td>
</tr>
<tr>
<td>% Protein binding</td>
<td>97</td>
</tr>
<tr>
<td>% Excreted unchanged in urine</td>
<td>&lt;0.1 (40% as metabolites)</td>
</tr>
<tr>
<td>Volume of distribution (L/kg)</td>
<td>50–168</td>
</tr>
<tr>
<td>Half-life – normal/ESRF (hrs)</td>
<td>14/Increased</td>
</tr>
</tbody>
</table>

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>25 mg twice daily increasing to 75 mg twice daily</td>
</tr>
<tr>
<td>10–20</td>
<td>25 mg twice daily increasing to 75 mg twice daily</td>
</tr>
<tr>
<td>&lt;10</td>
<td>25 mg twice daily increasing to 75 mg twice daily</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Modality</th>
<th>Dialysability and Dosing Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Unknown dialysability. Dose as GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Unknown dialysability. Dose as GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV</td>
<td>Unknown dialysability. Dose as GFR=10–20mL/min</td>
</tr>
<tr>
<td>VVHD</td>
<td>Unknown dialysability. Dose as GFR=10–20mL/min</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Analgesics: increased risk of convulsions with tramadol; enhanced hypotensive and sedative effects with opioids
- Antidepressants: concentration increased by fluoxetine; concentration of tricyclics possibly increased
- Anti-epileptics: antagonism, as convulsive threshold lowered
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antivirals: concentration possibly increased by ritonavir
- Anxiolytics and hypnotics: enhanced sedative effects; concentration increased by diazepam
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral

**RATE OF ADMINISTRATION**
- **COMMENTS**
- 

**OTHER INFORMATION**

- Do not use if there is a history of nephrolithiasis
- Occasionally can increase creatinine levels
- Undergoes extensive first pass metabolism
Zuclopenthixol

**CLINICAL USE**
Antipsychotic for schizophrenia and other psychoses

**DOSE IN NORMAL RENAL FUNCTION**
Schizophrenia and paranoid psychoses:
- Oral: 20–30 mg daily in divided doses; maximum 150 mg daily
- Maintenance: 20–50 mg daily
- Deep IM: 200–500 mg every 1–4 weeks
- Maximum: 600 mg weekly
Acute psychoses: (Clopixol Acuphase)
- Deep IM: 50–150 mg, repeated if required after 2–3 days
- Maximum 400 mg per course

**PHARMACOKINETICS**
- Molecular weight (daltons): 401 (443 as acetate), (473.9 as hydrochloride), (555.2 as decanoate)
- % Protein binding: 98%
- % Excreted unchanged in urine: Minimal (10–20% unchanged drug and metabolites)
- Volume of distribution (L/kg): 10–20
- Half-life – normal/ESRF (hrs): 20–24

**DOSE IN RENAL IMPAIRMENT**

<table>
<thead>
<tr>
<th>GFR (mL/Min)</th>
<th>Dose Advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–50</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>10–20</td>
<td>Dose as in normal renal function</td>
</tr>
<tr>
<td>&lt;10</td>
<td>Start with 50% of the dose and titrate slowly</td>
</tr>
</tbody>
</table>

**DOSE IN PATIENTS UNDERGOING RENAL REPLACEMENT THERAPIES**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Dosing Advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAPD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HD</td>
<td>Not dialysed. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>HDF/High flux</td>
<td>Unknown dialysability. Dose as in GFR&lt;10mL/min</td>
</tr>
<tr>
<td>CAV/VVHD</td>
<td>Not dialysed. Dose as in normal renal function</td>
</tr>
</tbody>
</table>

**IMPORTANT DRUG INTERACTIONS**
Potentially hazardous interactions with other drugs
- Anaesthetics: enhanced hypotensive effects
- Analgesics: increased risk of convulsions with tramadol; enhanced hypotensive and sedative effects with opioids
- Anti-arrhythmics: increased risk of ventricular arrhythmias with anti-arrhythmics that prolong the QT interval
- Antidepressants: increased level of tricyclics
- Anti-epileptics: anticonvulsant effect antagonised
- Antimalarials: avoid concomitant use with artemether/lumefantrine
- Antipsychotics: avoid concomitant use of clozapine with depot preparations in case of neutropenia
- Antivirals: concentration possibly increased with ritonavir
- Anxiolytics and hypnotics: increased sedative effects
- Sibutramine: increased risk of CNS toxicity – avoid concomitant use
- Avoid concomitant use with drugs that prolong the QT interval

**ADMINISTRATION**

**RECONSTITUTION**
- **ROUTE**
  - Oral, IM
**RATE OF ADMINISTRATION**
- **COMMENTS**

**OTHER INFORMATION**
- May cause hypotension and excessive sedation
- Increased CNS sensitivity in renally impaired patients – start with small doses as can accumulate
- Peak levels occur 3–6 hours after oral administration
Drugs for malaria prophylaxis

The malaria prophylaxis regimens below reflect the guidelines agreed by UK malaria specialists, and are aimed at residents of the UK who travel to endemic areas. Because the drug sensitivities of malaria parasites change with time and place, the most up-to-date information on prophylaxis should always be obtained from an appropriate travel clinic.

**MEFLOQUINE (LARIAM®)**
- 250 mg (ONE tablet) ONCE a WEEK, starting 1–3 weeks prior to travelling and continuing for 4 weeks after returning.
- NO dose changes are required for patients with any degree of renal impairment.

**DOXYCYCLINE**
- 100 mg (ONE capsule) ONCE a DAY starting 1–3 weeks prior to travelling and continuing for 4 weeks after returning.
- CAPD or HAEMODIALYSIS patients – No dose adjustment required.
- TRANSPLANT patients – Doxycycline can DOUBLE the blood levels of ciclosporin and tacrolimus. Avoid if at all possible. Alternatively, commence taking the doxycycline at least 2 weeks prior to travelling to enable ciclosporin or tacrolimus levels to be monitored and adjusted as necessary.

**CHLOROQUINE (AVLOCLOR® OR NIVAQUINE®) AND PROGUANIL (PALUDRINE®)**
- CHLOROQUINE 300 mg (TWO tablets) ONCE a WEEK, plus
- PROGUANIL 200 mg (TWO tablets) ONCE a DAY starting 1–3 weeks prior to travelling and continuing for 4 weeks after returning.

**Chloroquine:**
- Malaria prophylaxis: no dose adjustment necessary for renal impairment.
- Malaria treatment, i.e. full therapeutic dose: take the following into consideration:
  - Transplant patients: chloroquine increases plasma ciclosporin levels – monitor carefully.

**Patients with renal insufficiency:**

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>20–59</td>
<td>100% dose</td>
</tr>
<tr>
<td>10–19</td>
<td>100% dose</td>
</tr>
<tr>
<td>&lt; 10</td>
<td>50% dose</td>
</tr>
</tbody>
</table>

**Proguanil:**
- Transplant patients dose according to the level of function of the renal transplant.
- CAPD and haemodialysis patients half a tablet (50 mg) once a week.
- Patients with renal insufficiency:

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 60</td>
<td>200 mg OD</td>
</tr>
<tr>
<td>20–59</td>
<td>100 mg OD</td>
</tr>
<tr>
<td>10–19</td>
<td>50 mg alt days</td>
</tr>
<tr>
<td>&lt; 10</td>
<td>50 mg once a week</td>
</tr>
</tbody>
</table>

**ATOVAQUONE 250 MG + PROGUANIL 100 MG (MALARONE®)**
- One tablet daily starting 24–48 hours before travelling, and continuing for 7 days after returning.

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 30</td>
<td>Normal dose</td>
</tr>
<tr>
<td>&lt; 30</td>
<td>Malarone not recommended, because with the combined preparation it is not possible to reduce the dose of proguanil but take the full dose of atovaquone. Use alternative therapy.</td>
</tr>
</tbody>
</table>
Vaccines

Live vaccines should not be administered to immunosuppressed patients – this includes both transplant patients, and those on dialysis.

Inactivated vaccines can be administered to immunosuppressed patients, although the response may be reduced, and further booster doses may be required as dictated by measuring antibody titres.

VACCINES THAT ARE NOT RECOMMENDED:
- BCG (Bacillus Calmette-Guerin) vaccine
- MEASLES, MUMPS, RUBELLA vaccine (MMR®, Priorix®)
- POLIO Oral vaccine (Sabin) (OPV®), including household contacts of immunosuppressed patients as transmission of the live virus through faeces is possible.
- TYPHOID Oral vaccine (Vivotif®)
- VARICELLA-ZOSTER vaccine (Varilix®, Varivax®)
- YELLOW FEVER vaccine (Arilvax®, Stamaril®)

VACCINES THAT MAY BE ADMINISTERED:
- Adsorbed DIPHTHERIA (low dose), TETANUS and INACTIVATED POLIOMYELITIS vaccine (Revaxis®)
- ANTHRAX vaccine
- CHOLERA oral vaccine (Dukoral®)
- HAEMOPHILUS INFLUENZAE type b & MENINGOCOCCAL Group C conjugate vaccine (Menitorix®)
- HEPATITIS A vaccine (Avaxim®, Havrix Monodose®, Epaxal®)
- HEPATITIS B vaccine (Engerix B®, Fendrix®, HBvaxPRO®)
- HEPATITIS A & B vaccine (Twinrix®)
- HEPATITIS A & TYPHOID vaccine (Hepatyrix®, ViATIM®)
- POLIO Inactivated vaccine (Salk) (IPV®)
- INFLUENZA vaccine (Split Virion vaccines, and Surface Antigen vaccines)
- MENINGOCOCCAL Group C Conjugate vaccine (Meningitec®, Menjugate Kit®, NeisVac-C®)
- MENINGOCOCCAL Polysaccharide A, C, W135 and Y vaccine (ACWY Vax®)
- PNEUMOCOCCAL vaccine (Pneumovax II®)
- RABIES vaccine (Rab®, Rabipur®)
- TYPHOID Vi Capsular Polysaccharide vaccine (Typherix®, Typhim Vi®)
- TICK-BORNE ENCEPHALITIS vaccine (FSME-IMMUN®)