WELLINGTON ICU

DRUG MANUAL

third edition

2020

The following references were used in compiling these monographs:

Fink, Mitchell et al. http://www.criticalcaretext.com/content/drugdb/default.cfm Textbook of Critical Care. 5th edition 2005

Ashley, Caroline and Currie, Aileen. *The Renal Drug Handbook.* 2nd ed. United Kingdom: Radcliffe Medical Press Ltd, 2004

Shann, Frank. *Drug Doses.* 14th ed. Intensive Care Unit. Royal Children's Hospital, Parkville, Victoria 3052, Australia, 2008

McClintock, Alan et al. Notes on Injectable Drugs. 5th ed. New Zealand. New Zealand Healthcare Pharmacists' Association, 2004

Medsafe Drug Data sheets (New Zealand Medicine and Medical Devices Safety Authority): http://www.medsafe.govt.nz/profs/Datasheet/dsform.asp

MIMS Gateway: http://mimsgateway.co.nz/NewZealand/membership/index/

An online version of this drug manual, optimised for smartphone & tablet viewing, is available at:
https://drug.wellingtonicu.com/

An offline version is available for download (as a PDF) from:
https://forms.wellingtonicu.com/

The most up-to-date version of this drug manual will always be available online. Should any discrepancies exist between the printed & online versions, the latter should always take precedence.

Preface

The **first edition** of the Intensive Care Drug Manual was developed by Dr. Paul Young for use in the Intensive Care Unit in Wellington Regional Hospital in 2011.

This **third edition** has been updated for 2020 with revisions reflecting changes in our unit's Intensive Care practice and the ever-evolving critical care literature.

On occasion, doses, methods of administration and indications differ from those available given in the product information. In such cases, recommendations reflect common ICU practice both here and elsewhere.

All doses have been checked independently by two Intensive Care Specialists. However if you suspect an error, please check data with alternative sources and notify the editor.

Clinical responsibility for the choice, dose, route & frequency of any medication always remains with the prescribing doctor. This manual is for use in a monitored critical care environment only.

Specific changes for this third edition include:

- *New entries for levetiracetam, mannitol & tranexamic acid.*
- *Updated & expanded appendices providing more information on common drug-related queries.*
- *New appendices on drug cost by administration route, intravenous to oral antibiotic SWITCH, and local anaesthetic toxicity.*
- *Vancomycin dosage & monitoring has been changed extensively.*
- *All drug prices have been updated as of August 2017 and are quoted are in* ***New Zealand dollars.***

Prices have been included to inform prescribing choices where intravenous or enteral routes of administration are equivocal. *For example, the intravenous preparation of Acetazolamide costs* ***250 times*** *that of a single tablet (bioavailability >90%).*

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APPENDICES

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Acetazolamide [1 vial $43.00, 1 tablet 17 cents]

ADMINISTRATION ROUTES:
PO, NG, IV

ALTERNATIVE NAMES:
Diamox (Tab), Glaumox (Vial)

ICU INDICATIONS:
1. Diuretic (particularly in the presence of metabolic alkalosis)
2. Correction of severe metabolic alkalosis

PRESENTATION AND ADMINISTRATION:
PO / NG:
Diamox 250 mg tablets (white); for NG use, crush prior to administration.

IV:
Glaumox is supplied as a sterile powder requiring reconstitution. Each vial contains an amount of acetazolamide sodium equivalent to 500 mg of acetazolamide.
Each 500 mg vial containing acetazolamide should be reconstituted with at least 5 ml of sterile water for injection prior to use. Reconstituted solutions retain their physical and chemical properties for 24 hours under refrigeration at 2-8°C or 12 hours at room temperature

DOSAGE:
For diuresis, the dose is usually 250-375 mg stat. If, after an initial response, the patient fails to continue to diurese, do not increase the dose but allow for kidney recovery by skipping medication for a day. Acetazolamide yields best diuretic results when given on alternate days, or for 2 days alternating with a day of rest.

DOSAGE IN PAEDIATRICS:
The safety and effectiveness of acetazolamide in paediatric patients below the age of 12 years have not been established.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
No dose adjustment is required when administered for ICU indications (beware that acetazolamide is contraindicated in the presence of metabolic acidosis).
This drug is not indicated in patients on renal replacement therapy.

CLINICAL PHARMACOLOGY:
Acetazolamide is an enzyme inhibitor that acts on carbonic anhydrase, the enzyme that catalyzes the reversible reaction involving the hydration of carbon dioxide and the dehydration of carbonic acid.

CONTRAINDICATIONS:
1. Hypersensitivity to acetazolamide or other sulphonamides
2. Metabolic acidosis
3. Cirrhosis (risk of development of hepatic encephalopathy)

WARNINGS:
Fatalities have occurred, although rarely, due to severe reactions to acetazolamide including Stevens-Johnson syndrome, toxic epidermal necrolysis, fulminant hepatic necrosis, agranulocytosis, aplastic anaemia, and other blood dyscrasias.

PRECAUTIONS:
General
Increasing the dose does not increase the diuresis and may increase the incidence of drowsiness and/or paraesthesia. Increasing the dose often results in a decrease in diuresis.

Laboratory Tests
No tests are required in addition to routine ICU blood tests.

Drug/Laboratory Test Interactions
Acetazolamide interferes with the HPLC method of assay for theophylline. Interference with the theophylline assay by acetazolamide depends on the solvent used in the extraction; acetazolamide may not interfere with other assay methods for theophylline.

IMPORTANT DRUG INTERACTIONS FOR THE ICU:
Acetazolamide modifies phenytoin metabolism with increased serum levels of phenytoin.
Acetazolamide increases lithium excretion and the lithium levels may be decreased.
Acetazolamide and sodium bicarbonate used concurrently increases the risk of renal calculus formation.
Acetazolamide may elevate cyclosporin levels.

ADVERSE REACTIONS:
Body as a Whole:
Headache, malaise, fatigue, fever, pain at injection site, flushing, flaccid paralysis, anaphylaxis.
Digestive:
Gastrointestinal disturbances such as nausea, vomiting, diarrhoea.
Hepato-Biliary Disorders:
Abnormal liver function, cholestatic jaundice, hepatic insufficiency, fulminant hepatic necrosis.
Metabolic/Nutritional:
Metabolic acidosis, electrolyte imbalance, including hypokalaemia, hyponatraemia, loss of appetite, taste alteration, hyper/hypoglycaemia.
Nervous:
Drowsiness, paraesthesia (including numbness and tingling of extremities and face), depression, excitement, ataxia, confusion, convulsions, dizziness.
Skin:
Allergic skin reactions including urticaria, photosensitivity, Stevens-Johnson syndrome
Special Senses:
Hearing disturbances, tinnitus, transient myopia.
Urogenital:
Crystalluria, haematuria, glycosuria, renal failure polyuria.

Acetylcysteine [1 vial $25.53]

ADMINISTRATION ROUTES:
PO, NG, IV

ALTERNATIVE NAMES:
Acetadote, Parvolex

ICU INDICATIONS:
1. Paracetamol overdose
2. Non-paracetamol induced fulminant hepatic failure

It is not recommended for use as a preventative agent in contrast-induced nephropathy.

PRESENTATION AND ADMINISTRATION:
PO / NG:
Give IV solution orally
IV:
Acetadote and Parvolex are supplied as sterile solutions in 10ml vials containing 20% (200 mg/ml) acetylcysteine. Compatible with 5% dextrose. Prepare immediately before use and discard any solution not used within 24 hours.
Note: Section 29 drug when administered orally (requires specific notification to Director-General of Health as unapproved route of administration)

DOSAGE IN ADULTS
Paracetamol Overdose:
Guidelines changed in 2020 to a two .
First infusion: 200mg/kg IV in 500 mL of 5% dextrose over 4 hours
Second Infusion: 100mg/kg IV in 1000 mL of 5% dextrose over 16 hours
If ongoing infusion is required, continue to repeat the second infusion

	First acetylcysteine infusion	**Second acetylcysteine infusion**
	200mg/kg over 4 hours in 500 mL 5% dextrose	**100mg/kg over 16 hours in 1000 mL 5% dextrose**
Weight (kg)	**Dose acetylcysteine (g) = 0.2 x body weight (kg)**	**Dose acetylcysteine (g) = 0.1 x body weight (kg)**
50	**10g**. Add 50 mL 20% acetylcysteine to 450 mL 5% dextrose	**5g**. Add 25 mL 20% acetylcysteine to 975 mL 5% dextrose
60	**12g**. Add 60 mL 20% acetylcysteine to 440 mL 5% dextrose	**6g**. Add 30 mL 20% acetylcysteine to 970 mL 5% dextrose
70	**14g**. Add 70 mL 20% acetylcysteine to 430 mL 5% dextrose	**7g**. Add 35 mL 20% acetylcysteine to 965 mL 5% dextrose
80	**16g**. Add 80 mL 20% acetylcysteine to 420 mL 5% dextrose	**8g**. Add 40 mL 20% acetylcysteine to 960 mL 5% dextrose
90	**18g**. Add 90 mL 20% acetylcysteine to 410 mL 5% dextrose	**9g**. Add 45 mL 20% acetylcysteine to 955 mL 5% dextrose
100	**20g**. Add 100 mL 20% acetylcysteine to 400 mL 5% dextrose	**10g**. Add 50 mL 20% acetylcysteine to 950 mL 5% dextrose
110*	**22g**. Add 110 mL 20% acetylcysteine to 390 mL 5% dextrose	**11g**. Add 55 mL 20% acetylcysteine to 945 mL 5% dextrose

Run the first infusion at 125 mL/hour and the second at 62.5 mL/hour
*all patients weighing >110kg should be dosed according to a bodyweight of 110kg

DOSAGE IN PAEDIATRICS (less than 14 years of age)
Paracetamol Overdose
First infusion: 200 mg/kg IV in 7 mL/kg (up to 500 mL) of 0.9% saline over 4 hours
Second infusion: 100 mg/kg IV in 14 mL/kg (up to 1000 mL) of 0.9% saline over 16 hours

ADDITIONAL DOSAGE NOTES
Where there has been a massive overdose with initial paracetamol concentrations more than double the nomogram line, the second infusion should be 200 mg/kg and toxicology advice should be obtained. Weight-based dosing is the same for both adults & children; the volume of diluent fluid differs for children. Saline is used as the diluent for children due to the risk of hyponatraemia with 5% dextrose.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY
No dose adjustment is required.

CLINICAL PHARMACOLOGY
Paracetamol Overdose
Acetylcysteine likely protects the liver by maintaining or restoring the glutathione levels, or by acting as an alternate substrate for conjugation with, and thus detoxification of, the reactive metabolite.

CONTRAINDICATIONS
1. Hypersensitivity or previous anaphylactoid reactions to acetylcysteine

WARNINGS
Serious anaphylactoid reactions, including death in a patient with asthma, have been reported in patients administered acetylcysteine intravenously.

PRECAUTIONS
General
The total volume administered should be adjusted for patients less than 40 kg and for those requiring fluid restriction (use DOSAGE IN PAEDIATRICS regimen).

Laboratory Tests:
No tests are required in addition to routine ICU blood tests
Drug/Laboratory Test Interactions:
None reported

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None known

ADVERSE REACTIONS
Body as a Whole: Urticaria, vasodilatation, rash and itch
Cardiovascular System: Hypotension
Digestive System: Dyspepsia, nausea, vomiting
Nervous System: Abnormal thinking (dysphoria), Gait disturbances
Respiratory System: Bronchospasm, coughing, dyspnoea
Skin & Appendages: Angioedema, facial erythema, palmar erythema, pruritus, pruritus, rash, sweating

SEE **APPENDIX 3** FOR PARACETAMOL POISONING TREATMENT NOMOGRAM

Acyclovir [1 vial $2.87, 1 tablet 7 cents, 1 tube $13.47]

ADMINISTRATION ROUTES:
PO, NG, IV, TOP

ALTERNATIVE NAMES:
Zovirax, Acyclovir, Aciclovir

ICU INDICATIONS:
1. Herpes Simplex encephalitis
2. Prophylaxis in an allogeneic bone marrow transplant patient (at risk of CMV)
3. Varicella Pneumonia
4. Uncomplicated Herpes Simplex or Varicella Zoster infection in an immunocompromised patient.
5. Treatment of Shingles

PRESENTATION AND ADMINISTRATION:
PO / NG:
Acyclovir is available in 200mg, 400mg and 800mg tablets; 200mg dispersible tablets are also available.

IV:
Acyclovir sodium for IV administration comes in a vial containing 250mg in 10ml. It is a clear, colourless to pale yellow solution. Do not refrigerate. Stable in compatible IV fluid for 24 hours at room temperature. Do not use solution if it appears cloudy or visible crystals are present. Acyclovir solution is highly alkaline. It should not be administered by mouth.
Administer as:
EITHER: 25mg/ml solution via a controlled rate infusion pump over at least one hour (preferred method if administering via a central line)
OR: dilute 25mg/ml solution to make a solution of 5mg/ml using a compatible IV fluid (eg dilute 5ml into 25ml total) and then administer by controlled infusion over at least one hour (preferred method if administering via a peripheral line)
Compatible with the following IV fluids:
Saline, Hartmann's, Glucose and Sodium Chloride

TOP:
Each gram of Zovirax cream 5% contains 50 mg acyclovir in an aqueous cream base. It is supplied in 2 g tubes.

DOSAGE:
Herpes Simplex Encephalitis
Adults and Adolescents (12 years of age and older):
10 mg/kg IV infused at a constant rate over 1 hour, every 8 hours for 10 days.

Herpes Simplex Infections in Immunocompromised Patients
Adults and Adolescents (12 years of age and older):
5 mg/kg IV infused at a constant rate over 1 hour, every 8 hours for 7 days.

Varicella Zoster Infections including Varicella Pneumonia
Adults and Adolescents (12 years of age and older):
10 mg/kg IV infused at a constant rate over 1 hour, every 8 hours for 7 days.

OR (for uncomplicated Shingles in the non-immunocompromised patient):
800 mg five times daily for 10 days (There are no data on treatment initiated more than 72 hours after onset of the zoster rash.)
NOTE: IV therapy is indicated in the immunocompromised and in patients with Varicella pneumonia

Cold sores (in the non-immunocompromised)
Acyclovir cream should be applied 5 times per day for 4 days. Therapy should be initiated as early as possible following onset of signs and symptoms. Data indicating efficacy are poor and use in the critically ill has not been studied.

NOTE: Obese patients should be dosed at the recommended adult dose using ideal body weight.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	2.5-5mg/kg every 24 hours
10-25	5-10mg/kg every 12 hours
>25-50	5-10mg/kg every 12 hours

Dose in renal replacement therapy

CAPD	Dose as for GFR <10ml/min
HD	Dose as for GFR <10ml/min
CVVHDF	Dose as for GFR 10-25ml/min

DOSAGE IN PAEDIATRICS:
Herpes Simplex Encephalitis
Paediatrics (3 months to 12 years of age):
20 mg/kg IV infused at a constant rate over 1 hour, every 8 hours for 10 days.

Herpes Simplex Infections in Immunocompromised patients
Paediatrics (under 12 years of age):
10 mg/kg IV infused at a constant rate over 1 hour, every 8 hours for 7 days.

Varicella Zoster Infections including Varicella Pneumonia
Paediatrics (under 12 years of age):
20 mg/kg IV infused at a constant rate over 1 hour, every 8 hours for 7 days.

CLINICAL PHARMACOLOGY:
Acyclovir is a synthetic purine nucleoside analogue with in vitro and in vivo inhibitory activity against herpes simplex virus types 1 (HSV-1), 2 (HSV-2), and varicella-zoster virus (VZV).

CONTRAINDICATIONS:
1. hypersensitivity to acyclovir or valacyclovir

WARNINGS
Acyclovir for injection is intended for IV infusion only, and should not be administered topically, intramuscularly, orally, subcutaneously, or into the eye.
IV infusions must be given over a period of at least 1 hour to reduce the risk of renal tubular damage. Renal failure, in some cases resulting in death, has been observed with acyclovir therapy

Thrombotic thrombocytopenic purpura/haemolytic uremic syndrome (TTP/HUS), which has resulted in death, has occurred in immunocompromised patients receiving acyclovir therapy.

PRECAUTIONS

General

Precipitation of acyclovir crystals in renal tubules can occur if the drug is administered by bolus injection. Ensuing renal tubular damage can produce acute renal failure.

Abnormal renal function (decreased creatinine clearance) can occur as a result of acyclovir administration and depends on the state of the patient's hydration, other treatments, and the rate of drug administration. Concomitant use of other nephrotoxic drugs, pre-existing renal disease, and dehydration make further renal impairment with acyclovir more likely.

Approximately 1% of patients receiving IV acyclovir have manifested encephalopathic changes characterised by either lethargy, obtundation, tremors, confusion, hallucinations, agitation, seizures, or coma.

Laboratory Tests

No tests are required in addition to routine ICU blood tests.

Drug/Laboratory Test Interactions

None reported

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Coadministration with other nephrotoxic drugs increases the risk of renal toxicity

ADVERSE REACTIONS

Body as a Whole:

Anaphylaxis, fever, pain, peripheral oedema.

Cardiovascular System:

Hypotension.

Digestive System:

Diarrhoea, gastrointestinal distress, nausea.

Nervous System:

Aggressive behavior, agitation, ataxia, coma, confusion, delirium, dizziness, hallucinations, obtundation, paraesthesia, psychosis, seizure, somnolence. These symptoms may be marked, particularly in older adults

Haematologic and Lymphatic:

Disseminated intravascular coagulation, haemolysis, leukopaenia, lymphadenopathy.

Hepatobiliary Tract and Pancreas:

Elevated liver function tests, hepatitis, hyperbilirubinemia, jaundice.

Musculoskeletal:

Myalgia.

Skin:

Alopecia, erythema multiforme, photosensitive rash, pruritus, rash, Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria. Severe local inflammatory reactions, including tissue necrosis, have occurred following infusion of acyclovir into extravascular tissues.

Special Senses:

Visual abnormalities.

Urogenital:

Renal failure, elevated blood urea nitrogen, elevated creatinine.

Adenosine [1 vial $17.43]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Adenocor

ICU INDICATIONS:
1. Conversion to sinus rhythm of paroxysmal supraventricular tachycardia (PSVT), including that associated with accessory bypass tracts (Wolff-Parkinson-White Syndrome).

PRESENTATION AND ADMINISTRATION:
IV:
Adenosine comes in a vial containing 6mg in 2mls solution
Compatible with the following IV fluids:
Normal Saline
Store at room temperature
DO NOT REFRIGERATE as crystallisation may occur. The solution must be clear at the time of use.

DOSAGE:
Adenosine injection should be given as a rapid bolus by the peripheral IV route. It should be given as close to the patient as possible and followed by a rapid saline flush (this is best achieved by using a three-way tap system)
The recommended IV doses for adults are as follows:
Initial dose:
6 mg given as a rapid IV bolus (administered over a 1-2 second period).
Repeat administration:
If the first dose does not result in elimination of the supraventricular tachycardia within 1-2 minutes, 12 mg should be given as a rapid IV bolus. This 12 mg dose may be repeated a second time if required.
Central venous administration of adenosine has not been systematically studied; however, in the ICU setting this route of administration is acceptable.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
No dosage adjustment is required in renal failure or renal replacement therapy.

DOSAGE IN PAEDIATRICS:
Paediatric Patients with a Body Weight < 50 kg:
Initial dose:
Give 0.05 to 0.1 mg/kg as a rapid IV bolus given either centrally or peripherally. A saline flush should follow.
Repeat administration:
If conversion of PSVT does not occur within 1-2 minutes, additional bolus injections of adenosine can be administered at incrementally higher doses, increasing the amount given by 0.05 to 0.1 mg/kg. Follow each bolus with a saline flush. This process should continue until sinus rhythm is established or a maximum single dose of 0.3 mg/kg is used.

Paediatric Patients with a Body Weight > 50 kg:
Administer the adult dose.

CLINICAL PHARMACOLOGY:
Adenosine slows conduction time through the A-V node, can interrupt the reentry pathways through the AV node, and can restore normal sinus rhythm in patients with paroxysmal supraventricular tachycardia (PSVT), including PSVT associated with Wolff-Parkinson-White Syndrome.
Intravenously administered adenosine is rapidly cleared from the circulation via cellular uptake, primarily by erythrocytes and vascular endothelial cells. Adenosine has a half-life of less than 10 seconds in whole blood.

CONTRAINDICATIONS:
1. Second- or third-degree A-V block (except in patients with a functioning artificial pacemaker).
2. Sinus node disease, such as sick sinus syndrome or symptomatic bradycardia (except in patients with a functioning artificial pacemaker).
3. Known hypersensitivity to adenosine.

WARNINGS
Heart Block
Adenosine injection exerts its effect by decreasing conduction through the A-V node and may produce a short lasting first-, second- or third-degree heart block. Appropriate therapy should be instituted as needed. Patients who develop high-level block on one dose of adensoine should not be given additional doses. Because of the very short half-life of adenosine, these effects are generally self-limiting.
Asystole and VF
Transient or prolonged episodes of asystole have been reported with fatal outcomes in some cases. Rarely, ventricular fibrillation has been reported following adenosine administration, including both resuscitated and fatal events. In most instances, these cases were associated with the concomitant use of digoxin and, less frequently with digoxin and verapamil. Although no causal relationship or drug-drug interaction has been established, adenosine should be used with caution in patients receiving digoxin or digoxin and verapamil in combination.
Arrhythmias at Time of Conversion
At the time of conversion to normal sinus rhythm, a variety of new rhythms may appear on the electrocardiogram. They generally last only a few seconds without intervention, and may take the form of premature ventricular contractions, atrial premature contractions, sinus bradycardia, sinus tachycardia, skipped beats, and varying degrees of A-V nodal block. Such findings are seen in 55% of patients.
Bronchoconstriction
Adenosine has been administered to a limited number of patients with asthma and mild to moderate exacerbation of their symptoms has been reported. Adenosine should be used with caution in patients with obstructive lung disease or asthma. Adenosine should be discontinued in any patient who develops severe respiratory difficulties.

PRECAUTIONS
General
See CONTRAINDICATIONS and WARNINGS

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Digoxin with or without verapamil use may be rarely associated with ventricular fibrillation when combined with adenosine (see WARNINGS).

The effects of adenosine are antagonised by methylxanthines such as caffeine and theophylline. In the presence of these methylxanthines, larger doses of adenosine may be required or adenosine may not be effective.

Adenosine effects are potentiated by dipyridamole (persantin). Thus, smaller doses of adenosine may be effective in the presence of dipyridamole.

Carbamazepine has been reported to increase the degree of heart block produced by adenosine.

ADVERSE REACTIONS
The half-life of adenosine is less than 10 seconds. Thus, adverse effects are generally rapidly self-limiting.
Body as a Whole:
Apprehension
Cardiovascular System:
Facial flushing, headache, sweating, palpitations, chest pain, hypotension
Respiratory System:
Bronchospasm, shortness of breath/dyspnea, chest pressure
Digestive System:
Nausea, metallic taste, tightness in throat, pressure in groin.
Nervous System:
Lightheadedness, dizziness, tingling in arms, numbness, blurred vision, burning sensation

Adrenaline [1 vial $1.05]

ADMINISTRATION ROUTES:
IV, IM, SC, NEBULISED

ALTERNATIVE NAMES:
Adrenaline mini-jet, EpiPen, Anapen

ICU INDICATIONS:
1. Cardiac arrest
2. Anaphylaxis
3. Upper airway obstruction
4. Inotrope / vasopressor

PRESENTATION AND ADMINISTRATION:
IV:
Adrenaline comes in vials containing 1mg in 1ml (1:1000) and vials containing 1mg in 10ml (1:10000). Mini-jets that contain 1mg in 10ml are also available.
The standard dilution for adrenaline by infusion in the ICU is 10mg in 100ml of compatible IV fluid
Compatible with the following IV fluids:
Normal saline, D5W, Glucose and Sodium Chloride, Hartmann's
Store at room temperature. Protect from light. Do not refrigerate. Solutions that are discoloured pink or brown should not be used.
IM:
Although IM use is said to be preferred in anaphylaxis and other emergencies, the IV route is generally more appropriate in the ICU setting. Use 1:1000 solution undiluted for administration by the IM route.
Nebulised
Use 1:1000 solution and (if required) make up to a total of 5ml using normal saline prior to administration

DOSAGE:
Cardiac arrest:
10ml of 1:10000 (i.e 1mg) IV
OR
3-10mg of 1:1000 via ETT can be used if IV access cannot be obtained
NOTE: in cardiac arrest after cardiac surgery, consideration should be given to immediate sternotomy. If adrenaline is administered in this setting, a standard 1mg dosage is inappropriate due to the risk of rebound hypertension leading to fatal haemorrhage. Give bolus doses of 1ml of 1:10000 and uptitrate gently if circulation is not restored.
Anaphylaxis:
0.05ml/kg of 1:10000 IV with dose titrated to effect followed by IV infusion if required.
OR
0.01ml/kg of 1:1000 IM (avoid administration in the buttocks)
Post-extubation stridor or other upper airway obtruction:
Use the 1:1000 vials up to max. dose 5ml and administer via a nebuliser (if giving less than 4mg, make up to at least 4ml with 0.9% saline).
IV Infusion:
10mg in 100ml of D5W or normal saline at up to 20ml/hr titrated to effect

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
No dosage adjustment is required in renal failure or renal replacement therapy.

DOSAGE IN PAEDIATRICS:
Cardiac arrest:
0.1ml/kg of 1:10000 IV
0.1ml/kg of 1:1000 via ETT
Anaphylaxis:
0.05ml/kg of 1:10000 IV
OR
0.01ml/kg of 1:1000 IM
Severe Croup:
Use the 1:1000 vials at a dose of 0.5ml/kg/dose, max. dose 5ml and administer via a nebuliser (make up to at least 4ml with 0.9% saline).
IV Infusion:
0.3mg/kg in 50ml D5W at 0.5-10ml/hr (equates to 0.05-1mcg/kg/min)

CLINICAL PHARMACOLOGY:
Adrenaline is a sympathomimetic drug. It activates an adrenergic receptive mechanism on effector cells and imitates all actions of the sympathetic nervous system except those on the arteries of the face and sweat glands. Adrenaline acts on both alpha and beta receptors.

CONTRAINDICATIONS:
There are no absolute contraindications to the use of adrenaline in a life-threatening situation.

WARNINGS
Adrenaline by infusion commonly leads to hyperlactataemia and hyperglycaemia.
Adrenaline by infusion may worsen dynamic outflow tract obstruction and paradoxically reduce cardiac output (particularly if used in the setting of hypovolaemia)

PRECAUTIONS
General
Some patients may be at greater risk of developing adverse reactions after adrenaline administration. These include: hyperthyroid individuals, individuals with cardiovascular disease, hypertension, or diabetes, and the elderly.

Laboratory Tests:
Adrenaline infusion commonly leads to increased lactate. It may be necessary to measure lactate levels if there are clinical concerns.

Drug/Laboratory Test Interactions
None reported

IMPORTANT DRUG INTERACTIONS FOR THE ICU
The effects of adrenaline may be potentiated by tricyclic antidepressants and monoamine oxidase inhibitors.

ADVERSE REACTIONS
Body as a Whole:
Apprehension, nervousness, anxiety and sweating.
Cardiovascular System:
Palpitations, tachycardia, pallor.
Respiratory System:
Hyperventilation, pulmonary oedema
Digestive System:
Nausea and vomiting,
Nervous System:
Headache, tremor, dizziness, weakness, cerebrovascular haemorrhage

Allopurinol [100mg tablets 2 cents, 200mg tablets 2 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Progout, Allohexal, Apo-Allopurinol

ICU INDICATIONS:
1. Prophylaxis against gout
2. The management of patients with leukaemia, lymphoma and malignancies who are receiving cancer therapy which causes elevations of serum and urinary uric acid levels.

PRESENTATION AND ADMINISTRATION:
PO / NG
100mg and 300mg tablets (white); tablets may be crushed and administered via the nasogastric tube.

DOSAGE:
Gout:
The minimal effective dosage is 100-200 mg daily and the maximal recommended dosage is 800 mg daily. The appropriate dosage may be administered in divided doses or as a single equivalent dose with the 300 mg tablet. Dosage requirements in excess of 300 mg should be administered in divided doses.

Prevention of hyperuricaemia in patients at risk of tumour lysis syndrome:
For the prevention of uric acid nephropathy during the vigorous therapy of neoplastic disease, treatment with 600-800 mg daily for 2-3 days is advisable together with a high fluid intake.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	100mg daily / alternate days
10-20	100-200mg daily
>20-50	200-300mg/daily

Dose in renal replacement therapy

CAPD	Dose as for GFR <10ml/min
HD	Dose as for GFR <10ml/min
CVVHDF	Dose as for GFR 10-20ml/min

Note – with all grades of renal impairment, commence with 100mg/day and increase if serum urate response is unsatisfactory. Doses of less than 100mg/day may be required in some patients.

DOSAGE IN PAEDIATRICS:
Prevention of hyperuricaemia in patients at risk of tumour lysis syndrome
Children, 6-10 years of age, with secondary hyperuricaemia associated with malignancies may be given 300 mg allopurinol daily while those under 6 years are generally given 150 mg daily. The response is evaluated after approximately 48 hours

of therapy and a dosage adjustment is made if necessary. Weight-based dosage is 10mg/kg 12-24 hrly.

CLINICAL PHARMACOLOGY:
Allopurinol is a structural analogue of the natural purine base, hypoxanthine. It is an inhibitor of xanthine oxidase, the enzyme responsible for the conversion of hypoxanthine to xanthine and of xanthine to uric acid, the end product of purine metabolism in man.
Allopurinol is approximately 90% absorbed from the gastrointestinal tract.

CONTRAINDICATIONS:
1. Hypersensitivity to allopurinol

WARNINGS
The most frequent adverse reaction to allopurinol is skin rash. Skin reactions can be severe and sometimes fatal. Therefore, treatment with allopurinol should be discontinued immediately if a rash develops.

PRECAUTIONS
General
An increase in acute attacks of gout has been reported during the early stages of allopurinol administration, even when normal or subnormal serum uric acid levels have been attained.

Some patients with pre-existing renal disease or poor urate clearance have shown a rise in creatinine during allopurinol administration. In patients with hyperuricaemia due to malignancy, the vast majority of changes in renal function are attributable to the underlying malignancy rather than to therapy with allopurinol. Although the mechanism responsible for this has not been established, patients with impaired renal function should be carefully observed during the early stages of allopurinol administration so that the dosage can be appropriately adjusted for renal function.

Bone marrow depression has been reported in patients receiving allopurinol, most of whom received concomitant drugs with the potential for causing this reaction. This has occurred as early as 6 weeks to as long as 6 years after the initiation of allopurinol therapy.

Laboratory Tests:
The correct dosage and schedule for maintaining the serum uric acid within the normal range is best determined by using the serum uric acid as an index. It may, on occasion be appropriate to measure a uric acid level in a patient on allopurinol in the intensive care unit.

Drug/Laboratory Test Interactions
Allopurinol is not known to alter the accuracy of laboratory tests.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Mercaptopurine/Azathioprine:
Allopurinol inhibits the enzymatic oxidation of mercaptopurine and azathioprine to 6-thiouric acid.

In patients receiving mercaptopurine or azathioprine, the concomitant administration of 300-600 mg/day of allopurinol will require a reduction in dose to approximately one third to one fourth of the usual dose of mercaptopurine or azathioprine. Subsequent adjustment of doses of mercaptopurine or azathioprine should be made on the basis of therapeutic response and the appearance of toxic effects.

Warfarin:

Allopurinol prolongs the half-life of warfarin.

Thiazide Diuretics:

Renal function may be more likely to deteriorate with the combination of allopurinol and thiazide diuretics and, in patients on thiazide diuretics, allopurinol dosage levels should be more conservative.

Amoxicillin:

An increase in the frequency of skin rash has been reported among patients receiving amoxicillin concurrently with allopurinol compared to patients who are not receiving both drugs. The cause of the reported association has not been established.

Cyclosporin:

Cyclosporin levels may be increased during concomitant treatment with allopurinol. Monitoring of cyclosporin levels and possible adjustment of cyclosporin dosage should be considered when these drugs are co-administered.

ADVERSE REACTIONS

Body as a Whole:

Skin rash, fever, chills,

Cardiovascular System:

Vasculitis

Respiratory System:

Bronchospasm, asthma, pharyngitis, rhinitis.

Digestive System:

Cholestatic jaundice, diarrhoea, nausea, LFT derangement, gastritis, dyspepsia

Nervous System:

Peripheral neuropathy, neuritis, paraesthesia, somnolence.

Musculoskeletal System:

Exacerbation of gout during initial treatment, arthralgias

Haematological System:

Eosinophilia and mild leukocytosis or leukopaenia

Aminophylline [1 vial $5.38]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Aminophylline (DBL)

ICU INDICATIONS:
1. Management of acute life threatening asthma (particularly in children)

PRESENTATION AND ADMINISTRATION:
IV:
250mg/10ml (solution). For adult administration dilute 500mg in 500ml of compatible IV fluid to make a concentration of 1mg/ml.
Store at room temperature 15-30°C; protect from light
Compatible with: normal saline, D5W, D10W, Glucose and Sodium chloride, Hartmann's.
Do not mix with other medications – many medications with precipitate if mixed with aminophylline.

DOSAGE:
Asthma and COPD:
IV aminophylline is very rarely used for treatment in asthma or COPD in adults in our Intensive Care Unit. The dilution when used for adults is 500mg in 500ml of compatible IV fluid (ie 1mg/ml) at 0.5-1mg/kg/hr (usually 0-40ml/hr).
Dose adjustment for obesity
Theophylline does not distribute into fatty tissue. Dosage should be calculated on the basis of lean (ideal) body weight.
Note: Do not use standard dosing for IV infusion if the patient is already on oral theophylline; dosage should be worked out after determining the serum concentration.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
While dose adjustment in renal failure is possible, dosage is complex and the risk of toxicity is high. Aminophylline should be ceased if the patient develops significant renal impairment.

DOSAGE IN PAEDIATRICS:
Aminophylline Infusion in Life threatening asthma
Dose if patient aged 1 – 9 years:
• 1.1 mg/kg/hour
• Add 55 mg/kg of IV aminophylline solution (25 mg/ml) to a 50 ml syringe and make up to 50ml with 5% dextrose
• Then infuse at 1 ml/hr
Dose if patient aged 10 – 15 years and weight < 35 kg:
• 0.7 mg/kg/hour
• Add 35 mg/kg of IV aminophylline solution (25 mg/ml) to a 50 ml syringe and make up to 50ml with 5% dextrose
• Then infuse at 1 ml/hr

Dose if patient aged 10 – 15 years and weight > 35 kg
• 0.7 mg/kg/hour
• Draw up neat IV Aminophylline solution (25 mg/ml) into a 50 ml syringe
• Then infuse at 0.028 ml/kg/hr
For example if you have a 40 kg child then infusion rate will be 40 x 0.028 = 1.12 ml/hr
Dose adjustment for obesity
Theophylline does not distribute into fatty tissue. Dosage should be calculated on the basis of lean (ideal) body weight. Use the 50th percentile of expected weight for age
Note: Do not use standard dosing for IV infusion if the patient is already on oral theophylline; dosage should be worked out after determining the serum concentration.

CLINICAL PHARMACOLOGY:
Aminophylline is a 2:1 complex of theophylline and ethylenediamine. The activity is of theophylline alone. Theophylline directly relaxes the smooth muscle of the bronchial airway and pulmonary blood vessels, thus acting mainly as a bronchodilator and smooth muscle relaxant. It has also been demonstrated that aminophylline has a potent effect on diaphragmatic contractility in normal persons and may then be capable of reducing fatigability and therapy improve contractility in patients with chronic obstructive airway disease. The exact mode of action remains unsettled.

CONTRAINDICATIONS:
1. Hypersensitivity to either aminophylline or ethylenediamine.
2. Active peptic ulcer disease
3. Underlying seizure disorders (unless receiving appropriate anticonvulsant medications).

WARNINGS
In individuals in whom theophylline plasma clearance is reduced for any reason, even conventional doses may result in increased serum levels and potential toxicity. Reduced theophylline clearance has been documented in the following readily identifiable groups:
(1) patients with impaired liver function;
(2) patients over 55 years of age, particularly males and those with chronic lung disease;
(3) those with cardiac failure from any cause;
(4) patients with sustained high fever;
(5) neonates and infants under 1 year of age; and
(6) those patients taking certain drugs (see DRUG INTERACTIONS).

Serious side effects such as ventricular arrhythmias, convulsions or even death may appear as the first sign of toxicity without any previous warning. A serum concentration measurement is the only reliable method of predicting potentially life-threatening toxicity. Theophylline products may cause or worsen arrhythmias and any significant change in rate and/or rhythm warrants measurement of a serum level and consideration of cessation of the drug.

PRECAUTIONS
General
See WARNINGS

Laboratory Tests:
Spec Collection: SST (Yellow) or Plain (Red); Paediatric and Neonatal only: 0.4 mL green microtainer
Therapeutic Range: 55-110 umol/L Neonates: 35-70 umol/L.
Sampling Time:
IV infusion: anytime after 12 hours on infusion.

Drug/Laboratory Test Interactions
Acetazolamide interferes with the HPLC method of assay for theophylline. Interference with the theophylline assay by acetazolamide depends on the solvent used in the extraction; acetazolamide may not interfere with other assay methods for theophylline

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Aminophylline With:

Allopurinol (high-dose):	Increased serum theophylline levels
Ciprofloxacin:	Increased serum theophylline levels
Erythromycin:	Increased serum theophylline levels
Lithium carbonate:	Increased renal excretion of lithium
Oral contraceptives:	Increased serum theophylline levels
Phenytoin:	Decreased theophylline and phenytoin serum levels
Propranolol:	Increased serum theophylline levels
Rifampin:	Decreased serum theophylline levels

Increased toxicity may be seen with combinations of high dose beta agonists and aminophylline.

ADVERSE REACTIONS
Body as a Whole:
Irritability, restlessness, insomnia
Cardiovascular System:
Palpitation, tachycardia, extrasystoles, flushing, hypotension, circulatory failure, ventricular arrhythmias.
Respiratory System:
Tachypnoea.
Digestive System:
Nausea, vomiting, epigastric pain, haematemesis, diarrhoea.
Nervous System:
Headaches, reflex hyperexcitability, muscle twitching, clonic and tonic generalized convulsions.

Amiodarone

[1 vial $6.08, 1 tablet 100mg 62 cents, 1 tablet 200mg $1.02]

ADMINISTRATION ROUTES:
PO, NG, IV

ALTERNATIVE NAMES:
Cordarone-X

ICU INDICATIONS:
1. VT, VF
2. Atrial tachycardias

PRESENTATION AND ADMINISTRATION:
PO / NG
200mg tablets; tablets may be crushed for NG administration
IV
150mg in 3ml vials. Cordarone IV is a sterile clear, pale-yellow solution visually free from particulate matter.
Compatible with D5W only
Do not use PVC infusion bags for infusion as adsorption may occur. When mixing for infusion use only EXCEL container 250ml bags of 5% dextrose Injection USP. Add 450mg amiodarone.
For stat dose (usually 300mg) add to a standard 100ml plastic bag of D5W.
Administration via a central line is preferred
Store at room temperature; do not refrigerate.

DOSAGE:
Tachydysrhythmias:
IV load 300-450mg in 100ml D5W over 20 minutes to two hours
Ongoing infusion:
450mg in 250ml glucose 5% over 12 hours x 2 i.e. 900mg over 24 hours Dilute in glucose 5% only using Excel Container 250ml 5% Dextrose Injection USP.
Note - 300mg stat may be considered for VT/VF (this should be added to 10-20ml of D5W and administered by slow IV push over 3 minutes or more)

Transition from IV to oral therapy:
200mg PO 8 hourly for 1 week followed by 200mg PO 12 hourly for one week followed by 200mg PO 12-24 hourly thereafter
Note – higher oral dosages (up to 1600mg per day can be used in patients who have not received a full IV load). An overlap of intravenous and oral medication of up to two days is recommended.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
The safety and efficacy of amiodarone in the paediatric population have not been established; therefore, its use in paediatric patients is not recommended.

CLINICAL PHARMACOLOGY: Amiodarone is generally considered a Class III antiarrhythmic drug, but it possesses electrophysiologic characteristics of all four Vaughan Williams classes.

CONTRAINDICATIONS:

1. Known hypersensitivity to any of the components of amiodarone, including iodine.
2. Second- or third-degree AV block unless a functioning pacemaker is available.

WARNINGS

Hypotension

Hypotension is the most common adverse effect seen with amiodarone. Hypotension should be treated by vasopressor drugs, positive inotropic agents, and volume expansion. Slowing the rate of infusion may also be effective.

Bradycardia and AV Block

Drug-related bradycardia should be treated by discontinuing amiodarone. Additional measures including drug therapy and/or temporary pacing may be required if bradycardia does not resolve.

PRECAUTIONS

General

Liver enzyme elevations in patients on amiodarone are not uncommon; however, baseline abnormalities in hepatic enzymes are not a contraindication to treatment. Rare cases of fatal hepatocellular necrosis after treatment with amiodarone have been reported.

Like all antiarrhythmic agents, amiodarone may cause a worsening of existing arrhythmias or precipitate a new arrhythmia.

There have been reports of acute-onset (days to weeks) pulmonary injury in patients treated with amiodarone. Findings have included pulmonary infiltrates on X-ray, bronchospasm, wheezing, fever, dyspnea, cough, haemoptysis, and hypoxia. Some cases have progressed to respiratory failure and/or death.

Laboratory Tests:

Consider measurement of thyroid function as a baseline (if not measured previously).

Drug/Laboratory Test Interactions

Amiodarone alters the results of thyroid-function tests, causing an increase in serum T4 and serum reverse T3, and a decline in serum T3 levels. Despite these biochemical changes, most patients remain clinically euthyroid.

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Amiodarone with:

Cyclosporin:	increased cyclosporin levels; dosage reduction of cyclosporin required
Digoxin:	increased digoxin levels; dosage reduction of digoxin required.
Antiarrhythmics:	in general, any added antiarrhythmic drug should be initiated at a lower than usual dose with careful monitoring.
Antihypertensives:	beta blockers and calcium channel blockers may lead to increased risk of bradycardia when combined with amiodarone
Warfarin:	dose of warfarin should be reduced by 1/2 to 1/3rd and INR should be closely monitored
Rifampin:	decreases in serum concentrations of amiodarone.
Fluoroquinolones:	increased risk of QTc prolongation when combined with amiodarone

Macrolides: increased risk of QTc prolongation when combined with amiodarone

ADVERSE REACTIONS
Body as a Whole:
Fever
Cardiovascular System:
Bradycardia, congestive heart failure, hypotension, ventricular tachycardia
Respiratory System:
Dyspnea, cough, haemoptysis, wheezing, hypoxia, pulmonary infiltrates
Digestive System:
Nausea, deranged LFTs
Nervous System:
Hallucinations, confusional state, pseudotumour cerebri
Endocrine System:
Hypothyroidism, hyperthyroidism, SIADH
Skin:
Toxic epidermal necrolysis

Amitriptyline [1 tablet 10mg 6 cents, 1 tablets 25mg 2 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Amirol, Amitrip

ICU INDICATIONS:
1. Neurogenic pain (eg GBS)
2. Nocturnal sedation

PRESENTATION AND ADMINISTRATION:
PO / NG:
Amirol 10mg (light blue), 25mg (yellow); Amitrip 10mg (blue), 25mg (yellow), 50mg (orange). Tablets may be crushed for nasogastric administration

DOSAGE:
Neurogenic pain and nocturnal sedation in the ICU:
Commence at 10mg at night; increase to 25mg to 50mg as tolerated
Note – the usual dose for treatment of depression is up to 75-300mg per day (this dose is rarely appropriate in ICU patients)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
In view of the lack of experience with the use of this drug in paediatric patients, it is not recommended for patients under 12 years of age.
Quoted paediatric dosing for enuresis is 1-1.5mg/kg at night.

CLINICAL PHARMACOLOGY:
Amitriptyline is an antidepressant with sedative effects. It is also used in treatment of neurogenic and chronic pain. Its mechanism of action is unclear.

CONTRAINDICATIONS:
1. Hypersensitivity to amitriptyline
2. Should not be given concomitantly with monoamine oxidase inhibitors.
3. This drug is not recommended for use during the acute recovery phase following myocardial infarction.

WARNINGS:
Amitriptyline should be used with caution in patients with a history of seizures and, because of its atropine-like action.
Amitriptyline has been reported to produce arrhythmias, sinus tachycardia, and prolongation of the conduction time. Myocardial infarction and stroke have been reported with drugs of this class.

PRECAUTIONS:
General
See WARNINGS

Laboratory Tests:
No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:
None known.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Increased sedation when combined with other sedative drugs.

ADVERSE REACTIONS
Body as a Whole:
Hyperpyrexia; Lupus-like syndrome (migratory arthritis, positive ANA and rheumatoid factor).
Cardiovascular System:
Myocardial infarction; stroke; nonspecific ECG changes and changes in AV conduction; heart block; arrhythmias; hypotension, particularly orthostatic hypotension; syncope; hypertension; tachycardia; palpitation.
Digestive System:
Paralytic ileus; constipation; dry mouth; rarely hepatitis.
Nervous System:
Seizures; hallucinations; ataxia; tremors; peripheral neuropathy; numbness, tingling, and paraesthesias of the extremities; extrapyramidal symptoms; drowsiness.
Skin:
Rash, itch

Amlodipine [1 tablet 5mg 7 cents, 1 tablet 10mg 12 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Apo-amlodipine, Calvasc, Norvasc

ICU INDICATIONS:
1. Hypertension
2. Afterload reduction
3. Angina (can be used for treatment of angina but is rarely used for this indication in the ICU setting)

PRESENTATION AND ADMINISTRATION:
PO / NG
Apo-amlodipine 5mg and 10mg (white), Calvasc 5mg and 10mg (white), Norvasc 5mg and 10mg (white). Tablets may be crushed for NG administration.

DOSAGE:
Hypertension & afterload reduction:
Usual dosage 5mg daily; increasing to maximum 10mg daily

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
0.05-0.2mg/kg daily oral. Has not been adequately studied for use in children under 6.

CLINICAL PHARMACOLOGY:
Amlodipine is a dihydropyridine calcium channel blocker. Amlodipine is a peripheral arterial vasodilator that acts directly on vascular smooth muscle to cause a reduction in peripheral vascular resistance and reduction in blood pressure. It does not cause significant negative inotropy. Peak plasma concentrations between 6 and 12 hours after oral administration.

CONTRAINDICATIONS:
1. Known hypersensitivity to amlodipine

WARNINGS
Increased Angina and/or Myocardial Infarction
Rarely, patients, particularly those with severe obstructive coronary artery disease, have developed documented increased frequency, duration and/or severity of angina or acute myocardial infarction on starting calcium channel blocker therapy or at the time of dosage increase. The mechanism of this effect has not been elucidated.

PRECAUTIONS

General

Caution should be exercised when administering amlodipine as with any other peripheral vasodilator particularly in patients with severe aortic stenosis.

Since amlodipine besylate is extensively metabolized by the liver and the plasma elimination half-life (T½) is 56 hours in patients with impaired hepatic function, caution should be exercised when administering amlodipine besylate to patients with severe hepatic impairment.

Laboratory Tests:

No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions:

None known.

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Synergistic with other antihypertensives

ADVERSE REACTIONS

Body as a Whole:

Allergic reaction, back pain, hot flushes, malaise, pain, rigors, weight gain, weight decrease.

Cardiovascular System:

Arrhythmia (including ventricular tachycardia and atrial fibrillation), bradycardia, chest pain, hypotension, peripheral ischemia, syncope, tachycardia, postural dizziness, postural hypotension, vasculitis.

Digestive System:

Anorexia, constipation, dyspepsia, dysphagia, diarrhoea, flatulence, pancreatitis, vomiting, gingival hyperplasia.

Nervous System:

Hypoesthesia, neuropathy peripheral, paraesthesia, tremor, vertigo.

Skin:

Angioedema, erythema multiforme, pruritus, rash.

Respiratory System:

Dyspnea, epistaxis.

Musculoskeletal System:

Arthralgia, arthrosis, muscle cramps, myalgia.

Skin and Appendages:

Haemopoietic:

Leukopaenia, purpura, thrombocytopaenia.

Amoxicillin / Amoxycillin [1 vial $1.30, 1 tablet 6 cents]

ADMINISTRATION ROUTES:
PO, NG, IV

ALTERNATIVE NAMES:
Apo-Amoxi , Ospamox, Ranbaxy-Amoxi, Ibiamox

ICU INDICATIONS:
1. Treatment of infections caused by susceptible organisms
2. Empirical treatment to cover enterococcus

PRESENTATION AND ADMINISTRATION:
IV:
1gm vial (powder). Dilute to total of 5ml if part dose is required (making concentration of 200mg/ml). Inject slowly over 3-4 minutes or in 100ml of compatible fluid over 30-60 minutes.
Compatible for 6 hours with normal saline, 3 hours with Hartmanns, 1 hour with D5W and glucose and sodium. (note that amoxicillin is less stable in solutions that contain glucose so it is preferable to avoid these solutions). Store at room temperature
PO / NG:
Apo-Amoxi 250mg tablets & 500mg tablets (red/gold, marked APO and strength), Ospamox capsules 500mg capules (yellow), Ospamox suspension (125mg/5ml and 250mg/ml), Ranbaxy-Amoxi (125mg/5ml and 250mg/5ml), Amoxil paediatric drops (125mg/1.25ml), Ospamox paediatric drops (100mg/ml). Liquid is preferred for NG administration.

DOSAGE:
IV:
1-2gm IV Q6hrly
PO:
500mg-1gm Q8hrly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	500mg every 8 hours
10-20	dose as in normal renal function
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	500mg every 8 hours
HD	500mg every 8 hours
CVVHDF	dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
Severe infections: 1st week of life 50mg/kg 12hrly; otherwise 50mg/kg 6hrly

CLINICAL PHARMACOLOGY:
Amoxicillin is bactericidal against susceptible organisms during the stage of active multiplication. It acts through the inhibition of biosynthesis of cell wall mucopeptide. Amoxicillin has been shown to be active against most strains of the following microorganisms:

Aerobic Gram-Positive Microorganisms:
Enterococcus faecalis.
Staphylococcus spp*. (beta-lactamase-negative strains only).
Streptococcus pneumoniae.
*Staphylococci which are susceptible to amoxicillin but resistant to methicillin/oxacillin should be considered as resistant to amoxicillin.
Aerobic Gram-Negative Microorganisms:
Escherichia coli (beta-lactamase-negative strains only).
Haemophilus influenzae (beta-lactamase-negative strains only).
Neisseria gonorrhoeae (beta-lactamase-negative strains only).
Proteus mirabilis (beta-lactamase-negative strains only).
Amoxicillin diffuses readily into most body tissues and fluids, with the exception of brain and spinal fluid, except when meninges are inflamed.

CONTRAINDICATIONS:

1. A history of allergic reaction to any of the penicillins is a contraindication.

WARNINGS
Anaphylaxis
Penicillins are a common cause of anaphylactic reactions
Pseudomembranous colitis
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including amoxicillin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents.

PRECAUTIONS
General
Prescribing Amoxicillin in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug resistant bacteria.

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions
None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of significance

ADVERSE REACTIONS
Body as a Whole:
Serum sickness like reactions, Anaphylaxis
Digestive System:
Nausea, vomiting, diarrhoea, and haemorrhagic/pseudomembranous colitis. Hepatic dysfunction including cholestatic jaundice, hepatic cholestasis and acute cytolytic hepatitis have been reported.

Nervous System:
Reversible hyperactivity, agitation, anxiety, insomnia, confusion, convulsions, behavioral changes, and/or dizziness have been reported rarely.

Skin:
Stevens-Johnson Syndrome, exfoliative dermatitus, toxic epidermal necrolysis, acute generalized exanthematous pustulosis, hypersensitivity vasculitis and urticaria have been reported
Haematological System:
Anaemia, including haemolytic anaemia, thrombocytopaenia, thrombocytopenic purpura, eosinophilia, leukopaenia, and agranulocytosis have been reported during therapy with penicillins.

Amoxicillin-Clavulanic Acid [1 vial 1.2gm $2.82, one tablet 32 cents]

ADMINISTRATION ROUTES:
PO, NG, IV

ALTERNATIVE NAMES:
Alpha-amoxyclav, augmentin, synermox.

ICU INDICATIONS:
1. Treatment of infections caused by susceptible organisms

PRESENTATION AND ADMINISTRATION:
IV:
600mg and 1.2gm vials (powder). Contain 500mg or 1gm amoxicillin and 100mg or 200mg clavulanic acid. Reconstitute by adding 10ml of water for injection to 600mg vial (final volume 10.5ml) or 20ml to 1.2gm vial (final volume 20.9 ml) and agitating until dissolved.
If less than 600mg is required, add 11.5ml of diluent to 600mg dial to give a solution with a concentration of 50mg/ml. Inject slowly over 3-4 minutes or in 100ml of compatible fluid over 30-40 minutes.
Compatible for 4 hours with normal saline, 3 hours with Hartmanns.
Note that amoxicillin and clavulanic acid is less stable in solutions that contain glucose so these solutions should be avoided for intermittent infusions.
Store at room temperature
PO / NG:
Alpha-amoxyclav 625mg (500mg amoxicillin, 125mg clavulanic acid) white tablets, augmentin 500 (500mg amoxicillin, 125mg clavulanic acid) white tablets, synermox (500mg amoxicillin, 125mg clavulanic acid) white tablets, alpha-amoxyclav 125mg/5ml suspension (125mg amoxicillin, 31.25mg clavulanic acid), alpha-amoxyclav 250mg/5ml (250mg amoxicillin, 62.5mg clavulanic acid), augmentin forte syrup 250 (250mg amoxicillin, 62.5mg clavulanic acid), augmentin forte syrup 125 (125mg amoxicillin, 31.25mg clavulanic acid). Amoxicillin and clavulanate potassium are well absorbed from the gastrointestinal tract after oral administration of Augmentin. Augmentin can be given without regard to meals. Liquid is available for NG administration.

DOSAGE:
IV:
1.2gm IV q8hrly
PO:
500mg/125mg PO Q8hrly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY (for IV dosing):
Dose in renal impairment [GFR (ml/min)]

<10	600mg every 8 hours
10-20	dose as in normal renal function
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	600mg every 8 hours
HD	600mg every 8 hours
CVVHDF	dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV
Severe infections: 1st week of life 50mg/kg amoxicillin and 12.5mg/kg clavulanic acid 12hrly; otherwise 50mg/kg amoxicillin and 12.5mg/kg clavulanic acid 6hrly.

CLINICAL PHARMACOLOGY:
Augmentin is an oral antibacterial combination consisting of the semisynthetic antibiotic amoxicillin and the lactamase inhibitor, clavulanate potassium. Clavulanic acid is active against the clinically important plasmid mediated beta-lactamases frequently responsible for transferred drug resistance to penicillins and cephalosporins. Amoxicillin is bactericidal against susceptible organisms during the stage of active multiplication. It acts through the inhibition of biosynthesis of cell wall mucopeptide. Amoxicillin/ clavulanic acid has been shown to be active against most strains of the following microorganisms, both in vitro and in clinical infections:
Gram-Positive Aerobes:
Staphylococcus aureus (beta-lactamase and non-beta-lactamase producing).*
*Staphylococci which are resistant to methicillin/oxacillin must be considered resistant to amoxicillin/clavulanic acid.
Gram-Negative Aerobes:
Enterobacter species. (Although most strains of Enterobacter species are resistant in vitro, clinical efficacy has been demonstrated with Augmentin in urinary tract infections caused by these organisms.)
Escherichia coli (beta-lactamase and non-beta-lactamase producing).
Haemophilus influenzae (beta-lactamase and non-beta-lactamase producing).
Klebsiella species (all known strains are beta-lactamase producing).
Moraxella catarrhalis (beta-lactamase and non-beta-lactamase producing).
Amoxicillin diffuses readily into most body tissues and fluids with the exception of the brain and spinal fluid. The results of experiments involving the administration of clavulanic acid to animals suggest that this compound, like amoxicillin, is well distributed in body tissues.
Note: additional organisms (not outline above) which are adequately treated with amoxicillin alone should be treated with amoxicillin rather than augmentin.

CONTRAINDICATIONS:
1. History of allergic reaction to any of the penicillins.
2. Previous history of cholestatic jaundice/hepatic dysfunction associated with augmentin

WARNINGS
Anaphylaxis
Penicillins are a common cause of anaphylactic reactions
Pseudomembranous colitis
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including amoxicillin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents.

PRECAUTIONS
General
Prescribing Amoxicillin in the absence of a proven or strongly suspected bacterial

infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug resistant bacteria.

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions
None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of significance

ADVERSE REACTIONS
Body as a Whole:
Serum sickness like reactions, Anaphylaxis
Digestive System:
Nausea, vomiting, diarrhoea, and haemorrhagic/pseudomembranous colitis. Hepatic dysfunction including cholestatic jaundice, hepatic cholestasis and acute cytolytic hepatitis have been reported.
Nervous System:
Reversible hyperactivity, agitation, anxiety, insomnia, confusion, convulsions, behavioral changes, and/or dizziness have been reported rarely.
Skin:
Stevens-Johnson Syndrome, exfoliative dermatitus, toxic epidermal necrolysis, acute generalized exanthematous pustulosis, hypersensitivity vasculitis and urticaria have been reported
Haematological System:
Anaemia, including haemolytic anaemia, thrombocytopaenia, thrombocytopaenic purpura, eosinophilia, leukopaenia, and agranulocytosis have been reported during therapy with penicillins.

Amphotericin B (Liposomal) [1 vial $345]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
AmBisome

ICU INDICATIONS:
1. Suspected or proven fungal infection (particularly after bone marrow transplant or in the setting of febrile neutropaenia)
2. Aspergillus infection
3. Cryptococcal meningitis

PRESENTATION AND ADMINISTRATION:
IV:
AmBisome for injection is a sterile, nonpyrogenic lyophilized product for IV infusion. Each vial contains 50 mg of amphotericin B, intercalated into a liposomal membrane. Following reconstitution with sterile water for injection, the resulting pH of the suspension is between 5-6. Add 12ml of water for injection ONLY to vial. Immediately shake vial vigorously for 30 seconds to completely disperse powder (concentration = 4mg/ml). Inspect for particulate matter and continue shaking until completely dispersed. Add required volume of reconstituted solution using 5-micron filter provided to D5W giving a concentration of 2mg/ml (i.e. dilute one part reconstituted solution with one part D5W by volume). Infuse over 120 minutes (infusion time may be reduced to 60 minutes if the medication is well tolerated)
Store refrigerated at 2-8 degrees. Do not freeze. Reconstituted solution contains no preservative and should be refrigerated at 2-8 degrees celcius and discarded 24 hours after preparation.
Compatible with D5W ONLY. Do not mix with other medications or IV fluids.
Aseptic technique must be strictly observed in all handling since no preservative or bacteriostatic agent is present in AmBisome or in the materials specified for reconstitution and dilution.

DOSAGE:
IV:
Empirical therapy 3.0 mg/kg/day
Systemic fungal infections due to Aspergillus, Candida, or Cryptococcus: 3-5 mg/kg/day
Always commence at 3.0mg/kg/day and increase dose as required.
When this drug is administered for the first time an initial infusion of 10% of the total dose over 30 minutes should be given as a ‘test dose’. The remainder of the dose can then be administered over a further 120 minutes.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
Empirical therapy 3.0 mg/kg/day
Systemic fungal infections due to Aspergillus, Candida, or Cryptococcus: 3-5 mg/kg/day
Safety and effectiveness in paediatric patients below the age of 1 month have not been established.

CLINICAL PHARMACOLOGY:
Amphotericin B, the active ingredient of AmBisome, acts by binding to the sterol component of a cell membrane leading to alterations in cell permeability and cell death in susceptible fungi.
AmBisome has activity against the following organisms:
Aspergillus species (A. fumigatus, A. flavus), Candida species (C. albicans, C. krusei, C. lusitaniae, C. parapsilosis, C. tropicalis), Cryptococcus neoformans, and Blastomyces dermatitidis.

CONTRAINDICATIONS:
1. Known hypersensitivity to liposomal amphotericin

WARNINGS
Anaphylaxis
Anaphylaxis has been reported with amphotericin. If a severe anaphylactic reaction occurs, the infusion should be immediately discontinued and the patient should not receive further infusions of AmBisome.

PRECAUTIONS
General
A test dose is recommended (see DOSAGE)

Laboratory Tests:
No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions
None known.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
The following drugs are known to interact with amphotericin B and may interact with AmBisome:
Corticosteroids:
Concurrent use of corticosteroids may potentiate hypokalaemia
Digitalis Glycosides:
Concurrent use may induce hypokalaemia and may potentiate digitalis toxicity.
Flucytosine:
Concurrent use of flucytosine may increase the toxicity of flucytosine by possibly increasing its cellular uptake and/or impairing its renal excretion.
Azoles:
In vitro and in vivo animal studies of the combination of amphotericin B and imidazoles suggest that imidazoles may induce fungal resistance to amphotericin B. Combination therapy should be administered with caution, especially in immunocompromised patients.
Leukocyte Transfusions:
Acute pulmonary toxicity has been reported in patients simultaneously receiving IV amphotericin B and leukocyte transfusions.

ADVERSE REACTIONS
Body as a Whole:
Abdominal pain, Back pain, Chills, Pain, Rigors.
Cardiovascular System:
Chest pain, Hypertension, Hypotension, Tachycardia

Respiratory System:
Cough increased, Dyspnea, Epistaxis, Hypoxia
Digestive System:
Diarrhoea, Gastrointestinal haemorrhage, Nausea, Vomiting, Hepatitis, Cholestasis
Nervous System:
Anxiety, Confusion, Headache, Insomnia
Skin:
Pruritus, Rash
Urogenital System:
Renal impairment, haematuria
Metabolic:
Hypokalaemia, Hypomagnesaemia

Aspirin [1 tablet 100 mg enteric coated 4 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Aspec, Aspro, Cartia, Cardiprin, Disprin, Solprin

ICU INDICATIONS:
1. Antiplatelet therapy for cardiovascular and cerebrovascular disease

PRESENTATION AND ADMINISTRATION:
PO:
Disprin 300mg tablets (non-enteric coated) or Aspirin Ethics 100mg (enteric coated) .Store at room temperature.

DOSAGE:
PO:
For intubated patients use ½ a 300mg Disprin tablet daily crushed and administered via NG; for non-intubated patients use Aspirin Ethics 100mg (enteric coated) daily.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO
Analgesia / antipyrexia: 10-15 mg/kg 4-6 hrly;
Kawasaki: 10 mg/kg 6hrly (low dose) OR 25 mg/kg 6 hrly (high dose) for 2 weeks then 3-5 mg/kg daily

CLINICAL PHARMACOLOGY:
Aspirin is a salicylate that has demonstrated antiplatelet, antiinflammatory, analgesic and antipyretic activity.

CONTRAINDICATIONS:
1. Hypersensitivity to aspirin.
2. Gastrointestinal bleeding.

WARNINGS
Subclinical GI blood loss is common; frank GI bleeding may occur

PRECAUTIONS
General
Aspirin tablets should be administered with caution to patients with asthma, nasal polyps, or nasal allergies.

Laboratory Tests:
No tests in addition to routine ICU tests are indicated.

Drug/Laboratory Test Interactions
Salicylates can produce changes in thyroid function tests.

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Oral hypoglycaemics:

Large doses of salicylates have a hypoglycaemic action and may enhance the effect of the oral hypoglycaemics.

Phenytoin:

Serum phenytoin levels may be increased by aspirin.

Anticoagulants:

Combination with other anticoagulants increases the risk of bleeding

ADVERSE REACTIONS

Body as a Whole:

Headache and fever, anaphylaxis.

Digestive System:

Dyspepsia, thirst, nausea, vomiting, diarrhoea, acute reversible hepatotoxicity, gastrointestinal bleeding, and/or ulceration.

Nervous System:

Mental confusion, drowsiness, and dizziness

Skin:

Urticaria, angioedema, and pruritus.

Haematological System:

Prolongation of bleeding time, leukopaenia, thrombocytopaenia, purpura, decreased plasma iron concentration and shortened erythrocyte survival time.

Special Senses:

Tinnitus, vertigo, reversible hearing loss, and dimness of vision.

Atenolol [1 tablet 1 cent]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Noten

ICU INDICATIONS:
1. Hypertension
2. Acute myocardial infarction
3. Secondary prevention in patients with coronary artery disease
4. Angina
5. Rate control

PRESENTATION AND ADMINISTRATION:
PO / NG:
Pacific atenolol: orange 50mg and 100mg tablets. Tablets may be crushed and administered via nasogastric tube.

DOSAGE:
PO:
Commence at 50mg daily; increase to 100mg daily as tolerated.
[Note: Metoprolol is the preferred as 1st line beta blocker rather than atenolol in our ICU]

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	50mg once daily
10-20	dose as in normal renal function
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	50mg once daily
HD	50mg once daily
CVVHDF	dose as in normal renal function

DOSAGE IN PAEDIATRICS:
Safety and effectiveness in paediatric patients have not been established
1-2mg/kg PO 12-24hrly.

CLINICAL PHARMACOLOGY:
Atenolol is a beta1-selective (cardioselective) beta-adrenergic receptor blocking agent without membrane stabilizing or intrinsic sympathomimetic (partial agonist) activities. This preferential effect is not absolute, however, and at higher doses, atenolol inhibits beta2-adrenoreceptors, chiefly located in the bronchial and vascular musculature. Absorption of an oral dose of atenolol is rapid and consistent but incomplete. Approximately 50% of an oral dose is absorbed from the gastrointestinal tract, the remainder being excreted unchanged in the faeces. Peak blood levels are reached between 2 and 4 hours after ingestion.

CONTRAINDICATIONS:

1. sinus bradycardia,
2. heart block greater than first degree
3. cardiogenic shock,
4. overt cardiac failure
5. asthma

WARNINGS

Cardiac Failure

Sympathetic stimulation is necessary in supporting circulatory function in congestive heart failure, and beta blockade carries the potential hazard of further depressing myocardial contractility and precipitating more severe failure.

Discontinuation of therapy

Discontinuation of therapy in a patient with coronary artery disease may lead to rebound angina, arrhythmia or myocardial infarction.

Diabetes and Hypoglycaemia

Beta blockers may mask tachycardia occurring with hypoglycaemia.

Thyrotoxicosis

Beta-adrenergic blockade may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism. Abrupt withdrawal of beta blockade might precipitate a thyroid storm.

PRECAUTIONS

General

Atenolol may aggravate peripheral arterial circulatory disorders.

Laboratory Tests:

No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions :

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Beta blockers may exacerbate the rebound hypertension which can follow the withdrawal of clonidine

ADVERSE REACTIONS

Body as a Whole:

Tiredness, Fatigue

Cardiovascular System:

Bradycardia , Cold extremities, Hypotension, Leg pain

Respiratory System:

Wheeziness, Dyspnoea

Digestive System:

Diarrhoea, Nausea

Nervous System:

Dizziness, Vertigo, Light-headedness

Atorvastatin [1 tablet 10mg 61 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Lipitor

ICU INDICATIONS:
1. Secondary prevention in patients with coronary artery disease
2. Treatment of hypercholesterolaemia

PRESENTATION AND ADMINISTRATION:
PO / NG:
10mg, 20mg, 40mg and 80mg strengths (white). Tablets may be crushed for administration via NG tube.

DOSAGE:
PO:
Commence at 10-20mg daily at night; slowly increase to a maximum of 80mg if required.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO
Familial hypercholesterolaemia:
0.2mg/kg daily, increased every 4 weeks to a maximum of 1.6mg/kg daily.

CLINICAL PHARMACOLOGY:
Atorvastatin is a selective, competitive inhibitor of HMG-CoA reductase. Atorvastatin is rapidly absorbed after oral administration; maximum plasma concentrations occur within 1-2 hours. It can be taken with or without food.

CONTRAINDICATIONS:
1. Active liver disease or unexplained persistent elevations of serum transaminases.
2. Hypersensitivity to any component of this medication.

WARNINGS
Liver Dysfunction
HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function.
Skeletal Muscle
Rare cases of rhabdomyolysis with acute renal failure secondary to myoglobinuria have been reported with atorvastatin and with other drugs in this class.

PRECAUTIONS
General
Patients should be advised to report promptly unexplained muscle pain, tenderness, or weakness, particularly if accompanied by malaise or fever.

Laboratory Tests:
CK should be measured if there is concern about development of myopathy due to statins.

Drug/Laboratory Test Interactions
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
The risk of myopathy during treatment with other drugs of this class is increased with concurrent administration of cyclosporin, fibric acid derivatives, niacin (nicotinic acid), erythromycin, and azole antifungals
When multiple doses of atorvastatin and digoxin were coadministered, steady-state plasma digoxin concentrations increased by approximately 20%. Patients taking digoxin should be monitored appropriately.

ADVERSE REACTIONS
Body as a Whole:
Malaise
Digestive System:
Constipation, derangement of LFTs, flatulence, dyspepsia, and abdominal pain
Nervous System:
Insomnia, dizziness, paraesthesia, somnolence
Skin:
Pruritus
Musculoskeletal:
Myalgia, myopathy

Atracurium [1 vial 25mg $2.51]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Tracrium, tracurium

ICU INDICATIONS:
1. Muscle Relaxant

PRESENTATION AND ADMINISTRATION:
IV:
50mg in 5ml solution
Administer neat for IV injection or infusion
Compatible with the following IV fluids:
Normal saline 5% dextrose dextrose and sodium chloride Hartmanns
[NOTE: only compatible in Hartmanns for 4 hours therefore do not use by infusion]
Tracrium is a sterile, non-pyrogenic aqueous solution. Each ml contains 10 mg atracurium besylate. Atracurium besylate slowly loses potency with time at the rate of approximately 6%/year under refrigeration. Atracurium besylate should be refrigerated at 2-8°C to preserve potency. Rate of loss in potency increases to approximately 5%/month at 25°C. Upon removal from refrigeration to room temperature storage conditions, use atracurium besylate within 14 days even if re-refrigerated.

DOSAGE:
IV:
0.3-0.6mg/kg stat (usually give 50mg) then 0.1-0.2mg/kg when required or
5-9mcg/kg/min

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
0.3-0.6mg/kg stat then 0.1-0.2mg/kg when required or 5-10mcg/kg/min

CLINICAL PHARMACOLOGY:
Atracurium besylate is an intermediate-duration, nondepolarizing, skeletal muscle relaxant. Elimination of atracurium is not dependent on renal clearance mechanisms and no dose adjustment is required in renal impairment

CONTRAINDICATIONS:
1. Hypersensitivity to atracurium

WARNINGS
Although atracurium besylate is a less potent histamine releaser than d-tubocurarine or metocurine, the possibility of substantial histamine release in sensitive individuals must be considered. Special caution should be exercised in administering atracurium besylate to patients in whom substantial histamine release would be especially

hazardous (e.g., patients with clinically significant cardiovascular disease) and in patients with any history (e.g., severe anaphylactoid reactions or asthma) suggesting a greater risk of histamine release.

PRECAUTIONS

General

Atracurium besylate may have profound effects in patients with myasthenia gravis, Eaton-Lambert syndrome, or other neuromuscular diseases in which potentiation of nondepolarizing agents has been noted. The use of a peripheral nerve stimulator is especially important for assessing neuromuscular block in these patients.

When there is a need for long-term mechanical ventilation, the benefits-to-risk ratio of neuromuscular block must be considered. Little information is available on the plasma levels and clinical consequences of atracurium metabolites that may accumulate during days to weeks of atracurium administration in ICU patients. Laudanosine, a major biologically active metabolite of atracurium without neuromuscular blocking activity, produces transient hypotension and, in higher doses, cerebral excitatory effects (generalized muscle twitching and seizures) when administered to several species of animals. There have been rare spontaneous reports of seizures in ICU patients who have received atracurium or other agents.

Laboratory Tests:

No tests additional to routine ICU tests are required

Drug/Laboratory Test Interactions

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Drugs which may enhance the neuromuscular blocking action of atracurium besylate include: certain antibiotics, especially the aminoglycosides and polymyxins; lithium; magnesium salts; procainamide; and quinidine.

The prior administration of succinylcholine does not enhance the duration, but quickens the onset and may increase the depth, of neuromuscular block induced by atracurium besylate.

ADVERSE REACTIONS

General:

Allergic reactions (anaphylactic or anaphylactoid responses) which, in rare instances, were severe (e.g., cardiac arrest).

Musculoskeletal:

Inadequate block, prolonged block.

Cardiovascular:

Hypotension, vasodilatation (flushing), tachycardia, bradycardia.

Respiratory:

Dyspnea, bronchospasm, laryngospasm.

Integumentary:

Rash, urticaria, reaction at injection site.

Atropine [1 vial $1.42, 1 minijet $16.25]

ADMINISTRATION ROUTES:
IV, IM, SC, ENDOTRACHEAL

ALTERNATIVE NAMES:
Atropine

ICU INDICATIONS:
1. To temporarily increase heart rate or decrease AV-block until definitive intervention can take place
2. As an antidote for inadvertent overdose of cholinergic drugs or for cholinesterase poisoning such as from organophosphorus insecticides

PRESENTATION AND ADMINISTRATION:
Atropine vials contain 600mcg in 1ml or 1200mcg in 1ml
Atropine mini-jets contain 1mg in 10ml (i.e. 100mcg/ml)
Compatible with the following IV fluids:
Dilution in IV fluids is not recommended
Atropine sulphate is stated to be compatible, when mixed in a syringe immediately before use, with the following:

Chlorpromazine	Droperidol	Fentanyl	Glycopyrrolate
Metoclopramide	Midazolam	Morphine	Pethidine
Prochlorperazine	Promethazine	Ranitidine	

If the solution is cloudy, do not use.
Store at room temperature below 25°C

DOSAGE:
IV:
Bradycardia: 0.6mg IV
Organophosphate poisoning: 2mg IV then 2mg every 15 minutes until atropinised, then 0.02-0.08mg/kg/hr for several days
Endotracheal route(only if IV access cannot be obtained)
The recommended adult dose of atropine for endotracheal administration is 1 to 2 mg diluted to a total not to exceed 10 ml of sterile water or normal saline.
Note: The administration of less than 0.5 mg can produce a paradoxical bradycardia because of the central or peripheral parasympathomimatic effects of low dose in adults.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
Bradycardia: 0.02mg/kg

CLINICAL PHARMACOLOGY:
Atropine is commonly classified as an anticholinergic or antiparasympathetic (parasympatholytic) drug. More precisely, however, it is termed an antimuscarinic agent since it antagonizes the muscarine-like actions of acetylcholine and other choline esters.

CONTRAINDICATIONS:
There are no absolute contraindications to atropine. However, atropine is relatively contraindicated in:

1. pyloric stenosis
2. glaucoma
3. prostatic hypertrophy

See WARNINGS.

WARNINGS
In adults, the administration of less than 0.5 mg can produce a paradoxical bradycardia because of the central or peripheral parasympathomimatic effects of low dose in adults.
Conventional systemic doses may precipitate acute glaucoma in susceptible patients, convert partial organic pyloric stenosis into complete obstruction, lead to complete urinary retention in patients with prostatic hypertrophy or cause inspissation of bronchial secretions and formation of dangerous viscid plugs in patients with chronic lung disease.

PRECAUTIONS
General
See WARNINGS above

Laboratory Tests:
No laboratory tests in addition to routine tests are required.

Drug/Laboratory Test Interactions
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note.

ADVERSE REACTIONS
Body as a Whole:
Thirst,
Cardiovascular System:
Tachycardia
Gastrointestinal System:
Dryness of the mouth, constipation
Neurological System:
Blurred vision, dilated pupils, difficulty in swallowing, tremor,
Urological System:
Difficulty in micturition

Azathioprine [1 vial $60, 1 tablet 18 cents]

ADMINISTRATION ROUTES:
PO, IV

ALTERNATIVE NAMES:
Imuran, Azamun

ICU INDICATIONS:
1. Prevention of rejection in renal transplantation.
2. Management of severe, active rheumatoid arthritis
3. Management of Crohns disease
4. Management of various autoimmune conditions

In patients in the ICU the benefits of continuing immunosuppressive therapy with azathioprine needs to be weighed up against the risks of such therapy. Dose reduction may be appropriate.

PRESENTATION AND ADMINISTRATION:
IV:
50 mg vials of powder. Reconstitute in 5-15ml of water for Injection ONLY and swirl vial gently until solution is clear. Dilute the reconstituted solution to 20-200ml in compatible IV fluid and administer over 30-60 minutes
Compatible with the following IV fluids:
0.45% sodium chloride normal saline Glucose and Sodium chloride
D5W
Store at room temperature. Reconstituted solution is stable for 24 hrs at room temperature. When diluted in compatible IV fluid, resultant solution is stable for 24 hours at room temperature.
Administration via a central line is preferred if a central line is present

PO / NG:
Azamun 50mg tablets (pale yellow), Imuran 50mg tablets (yellow)
Note: crushing tablets is NOT recommended. See Pharmacist for advice.

DOSAGE:
IV and Oral:
Transplant survival:
5mg/kg on the 1st day; maintenance 1-4mg/kg/day; continue indefinitely
Other indications:
Initially 1-3mg/kg/day until response evident then reduce to the lowest effective dose.
Note: the IV route should only be used when the oral route is not available.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	50-75% of usual dose
10-20	75-100% of usual dose
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	50-75% of usual dose
HD	dose as in normal renal function
CVVHDF	75-100% of usual dose

DOSAGE IN PAEDIATRICS:
Safety and efficacy of azathioprine in children have not been established.

CLINICAL PHARMACOLOGY:
Azathioprine is an immunosuppressive antimetabolite. Azathioprine is well absorbed following oral administration.

CONTRAINDICATIONS:
1. Hypersensitivity to Azathioprine.

WARNINGS
Cytotoxicity:
Azathioprine is cytotoxic and therefore presents a potential occupational hazard to personnel handling the drug. It should be handled accordingly.
Leukopaenia and thrombocytopaenia:
Severe leukopaenia and/or thrombocytopaenia may occur in patients on azathioprine. Macrocytic anaemia and severe bone marrow depression may also occur. Haematologic toxicities are dose related and may be more severe in renal transplant patients whose homograft is undergoing rejection.
Serious Infections
Serious infections are a constant hazard for patients receiving chronic immunosuppression, especially for homograft recipients. Fungal, viral, bacterial and protozoal infections may be fatal and should be treated vigorously. Reduction of azathioprine dosage and/or use of other drugs should be considered.
Risk of Neoplasia
Renal transplant patients receiving azathioprine are known to have an increased risk of malignancy, predominantly skin cancer and reticulum cell or lymphomatous tumours.

PRECAUTIONS
General
A gastrointestinal hypersensitivity reaction characterised by severe nausea and vomiting has been reported. These symptoms may also be accompanied by diarrhoea, rash, fever, malaise, myalgias, elevations in liver enzymes, and occasionally, hypotension.

Laboratory Tests:
No tests additional to routine ICU tests are required.

Drug/Laboratory Test Interactions
None known.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Use with Allopurinol:
The principal pathway for detoxification of azathioprine is inhibited by allopurinol. Patients receiving azathioprine and allopurinol concomitantly should have a dose reduction of azathioprine, to approximately 1/3 to 1/4 the usual dose.
Use with Other Agents Effecting Myelopoiesis:
Drugs which may affect leukocyte production, including co-trimoxazole, may lead to exaggerated leukopaenia, especially in renal transplant recipients.
Use with Angiotensin Converting Enzyme Inhibitors:
The use of angiotensin converting enzyme inhibitors to control hypertension in patients on azathioprine has been reported to induce severe leukopaenia.

Use with Warfarin:
Azathioprine may inhibit the anticoagulant effect of warfarin.

ADVERSE REACTIONS
Body as a Whole:
Fever, neoplasia, infections
Respiratory System:
Reversible interstitial pneumonitis
Digestive System:
Nausea and vomiting, diarrhoea, hepatic veno-occlusive disease, pancreatitis.
Musculoskeletal Systemc:
Myalgias, arthralgias
Haematological system:
Leukopaenia and/or thrombocytopaenia, anaemia, bone marrow suppression.

Bendrofluazide [1 tablet 3 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Neo-naclex

ICU INDICATIONS:
1. Second line diuretic
2. Hypertension (usually in patients already on this medication)

PRESENTATION AND ADMINISTRATION:
PO / NG:
2.5mg and 5mg tablets (white)
Store below 25°C. Protect from light. Tablets can be crushed for NG administration.

DOSAGE:
PO:
2.5-10mg daily

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
When given in ICU patients, dose as in normal renal function.

DOSAGE IN PAEDIATRICS:
0.1-0.2mg/kg daily

CLINICAL PHARMACOLOGY:
Inhibits the renal tubular absorption of salt and water. Sodium and chloride ions are excreted in equivalent proportions, and there is little or no disturbance of the acid/base equilibrium. Initiates diuresis in about 2 hours and maintains a steady diuresis lasting for about 12 hours. The mechanism whereby the thiazides exert their antihypertensive effect has not been clearly established. In non-oedematous patients there may be little noticeable diuretic effect.

CONTRAINDICATIONS:
1. Severe renal or hepatic failure,
2. Hypersensitivity to bendrofluazide or other sulphonamide-like medicines,
3. Addison's disease
4. Treatment with lithium

WARNINGS
In cirrhosis of the liver, thiazides may precipitate hepatic encephalopathy.
Thiazides may aggravate existing diabetes mellitus and cause symptoms in patients with latent disease.
Bendrofluazide may impair control of diabetes in patients receiving sulphonylureas.
Serum uric acid levels may be raised in some patients, with or without gout.

PRECAUTIONS
General
Thiazide diuretics may precipitate hypokalaemia

Laboratory Tests:
No tests additional to standard ICU tests are indicated.

Drug/Laboratory Test Interactions
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
The renal clearance of lithium carbonate is reduced. Bendrofluazide should not be administered concurrently with lithium carbonate.
Bendrofluazide may impair control of diabetes in patients receiving sulphonylureas
The use of allopurinol and thiazides in patients with renal dysfunction should be avoided: severe hypersensitivity vasculitis has been reported.

ADVERSE REACTIONS
Body as a Whole:
Anaphylaxis
Digestive System:
gastric irritation, diarrhoea or constipation, pancreatitis, hepatic encephalopathy
Musculoskeletal Systemc:
precipitation of gout, muscle cramps
Haematological system:
Thrombocytopaenia
Metabolic:
Hypokalaemia, hyponatraemia

Benzylpenicillin / Penicillin G [1 vial $1.15]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Penicillin G, BenPen

ICU INDICATIONS:
1. Treatment of infections caused by susceptible organisms

PRESENTATION AND ADMINISTRATION:
IV:
ICU stocks 600mg (=1 mega unit) vials of Pencillin G Sodium (Novartis).
Add 1.6ml of water for injection to each 600mg vial (using 1.6ml of water for injection in a vial will give a concentration of 300mg/ml)
Store at room temperature. Protect from light.
Benzylpenicillin is not stable in glucose and glucose/saline combination IV fluids.
Compatible with: water for injection normal saline
Administer by either IV injection or intermittent infusion.
To administer by IV injection dilute to 10ml with water for injection and inject slowly at a rate not greater than 300mg/min
To administer by intermittent infusion add to 50-100ml of compatible IV fluid and infuse over 30-60 minutes.
The dry powder is relatively stable and may be stored at room temperature without significant loss of potency. Sterile solutions may be kept in the refrigerator one week without significant loss of potency. Solutions prepared for intravenous infusion are stable at room temperature for at least 24 hours.

DOSAGE:
IV:
In ICU patients higher dose penicillin is usually preferred.
Use 1.2gm-2.4gm Q4-6hrly.
In patients with meningitis use 2.4gm 4hrly.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	20-50% of normal dose
10-20	75% of normal dose
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	20-50% of normal dose
HD	20-50% of normal dose
CVVHDF	75% of normal dose

DOSAGE IN PAEDIATRICS:
30-50 mg/kg 6hrly
Note that reduced dosage may be required in neonates.

CLINICAL PHARMACOLOGY:
Penicillin G is bactericidal against penicillin-susceptible microorganisms during the stage of active multiplication. It acts by inhibiting biosynthesis of cell-wall mucopeptide. It is not active against the penicillinase-producing bacteria, which include many strains of staphylococci.
Penicillin G is highly active in vitro against:

- staphylococci (except penicillinase-producing strains),
- streptococci (groups A, C, G, H, L, and M) and
- pneumococci.

Other organisms susceptible in vitro to penicillin G are:

- Neisseria gonorrhoea,
- Corynebacterium diphtheriae,
- Bacillus anthracis,
- Clostridia,
- Actinomyces bovis,
- Streptobacillus moniliformis,
- Listeria monocytogenes, and
- Leptospira;
- Treponema pallidum is extremely susceptible.

Some species of gram-negative bacilli are susceptible to moderate to high concentrations of penicillin G obtained with intravenous administration. These include:

- most strains of Escherichia coli;
- all strains of Proteus mirabilis, Salmonella, and Shigella;
- Some strains of Enterobacter aerogenes and
- Alcaligenes faecalis.

CONTRAINDICATIONS:

1. Hypersensitivity to any penicillin

WARNINGS
Anaphylaxis
Serious and occasional fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy.
Pseudomembranous colitis
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including penicillin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents.

PRECAUTIONS
General
Penicillin should be used with caution in individuals with histories of significant allergies and/or asthma.
Haemolytic anaemia, leukopaenia, thrombocytopaenia, neuropathy, and nephropathy are rarely observed adverse reactions and are usually associated with high intravenous dosage.
High dosage of penicillin G sodium may result in congestive heart failure due to high sodium intake

Laboratory Tests:
No tests in addition to routine ICU tests are required

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Fusidic Acid: May diminish the therapeutic effect of Penicillins.
Methotrexate: Penicillins may decrease the excretion of Methotrexate. Mycophenolate: Penicillins may decrease serum concentrations of the active metabolite(s) of Mycophenolate. This effect appears to be the result of impaired enterohepatic recirculation.
Tetracycline Derivatives: May diminish the therapeutic effect of Penicillins.

ADVERSE REACTIONS
Body as a Whole:
Anaphylaxis, serum sickness
Nervous System:
Coma (high doses), hyperreflexia (high doses), seizures (high doses)
Digestive System:
Pseudomembranous colitis, hepatitis
Haematological system:
Neutropaenia, haemolytic anaemia (rare, high doses)
Metabolic:
Hypernatraemia
Renal System:
Acute interstitial nephritis (high doses), renal tubular damage (high doses)
Skin:
Rash

Caffeine [1 vial $11.15]

ADMINISTRATION ROUTES:
PO, NG, IV

ALTERNATIVE NAMES:
Caffeine Citrate (Biomed)

ICU INDICATIONS:
1. Apnoea of prematurity

PRESENTATION AND ADMINISTRATION:
IV
10mg/mL (caffeine base) clear colourless solution in a glass vial [2.5mL vial]
Prepare immediately before use.
1. Ensure solution in the vial is clear and free of any particulate matter.
2. Open the vial and withdraw the required dose using a filter needle.
3. Administer via IV infusion or push no further dilutions are required but dilution preferred with 0.9% sodium chloride (undiluted can cause discomfort for infant). The solution can be diluted to 1mg/ml.

Loading dose to be given via a 30-minute infusion using a syringe pump
Maintenance dose can be given as a slow push over 5 minutes
Compatible with:
0.9% sodium chloride, D5W, D10W, D50W
PO
10mg/mL (caffeine base) clear colourless solution in an amber bottle [25mL bottle]
Give dose with feeds closest to dose time. Administer prescribed dose by mouth using an oral syringe / teat.

DOSAGE:
See DOSAGE IN PAEDIATRICS

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
No data available. See PRECAUTIONS.

DOSAGE IN PAEDIATRICS:
IV and Oral:
Loading Dose:
10mg/kg as a single dose
Maintenance Dose:
5mg/kg as a single dose at 1300hrs to start 24 hours after loading dose. For babies >28 days old the dose may have to be increased to 5mg/kg/dose q12H.
In babies with a post natal/gestational age of more than 52 weeks who require treatment it is often necessary to give a maintenance dose of 5mg/kg four times a day.
Doses should be reviewed weekly with respect to changes in weight
Note: 0.5mg of caffeine base = 1mg of caffeine citrate. (all dosing in this monograph is for citrate)

CLINICAL PHARMACOLOGY:
Caffeine is widely used to manage recurrent central or “mixed” apnoea when other causes such as subtle seizures, sepsis, hypoglycaemia or respiratory exhaustion have been excluded. Caffeine citrate is a general stimulant of the central nervous system,

which increases metabolic rate, central chemoreceptor sensitivity to CO2, and inspiratory drive. Caffeine is well absorbed by mouth, and IV treatment is seldom necessary. It is mostly excreted, unchanged, in the urine in the first month of life. Clearance rises, as a result of increased liver metabolism, and approaches the rate found in adults and in infants more than 4 months old.

CONTRAINDICATIONS:

1. Hypersensitivity to caffeine

WARNINGS

Necrotising enterocolitis

Reports in the published literature have raised a question regarding the possible association between the use of caffeine and the risk of developing necrotising enterocolitis. Although a causal relationship between methylxanthine use and necrotizing enterocolitis has not been established, patients being treated with caffeine citrate should be carefully monitored for the development of necrotising enterocolitis.

PRECAUTIONS

General

Studies examining the pharmacokinetics of caffeine in neonates with hepatic or renal insufficiency have not been conducted. Caffeine citrate should be administered with caution in preterm neonates with impaired renal or hepatic function.

Apnea of prematurity is a diagnosis of exclusion. Other causes of apnea (e.g., central nervous system disorders, primary lung disease, anaemia, sepsis, metabolic disturbances, cardiovascular abnormalities, or obstructive apnoea) should be ruled out or properly treated prior to initiation of caffeine citrate.

Caffeine citrate should be used with caution in infants with seizure disorders.

Laboratory Tests:

Prior to initiation of caffeine citrate, baseline serum levels of caffeine should be measured in infants previously treated with theophylline, since preterm infants metabolize theophylline to caffeine.

Paediatric Use

See DOSAGE IN PAEDIATRICS

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Theophylline is metabolised to caffeine; therefore, these drugs should not be co-administered due to the potential for additive toxicity. See *Laboratory Tests*.

ADVERSE REACTIONS

Nervous System:

Agitation & restlessness

Digestive System:

Feeding intolerance

Cardiovascular System:

Tachycardia

Renal System:

Renal failure

Skin:

Rash

Calcitriol [1 capsule 13 cents, liquid $3.94/ml]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Rocaltrol

ICU INDICATIONS:
1. Post-menopausal osteoporosis
2. Renal osteodystrophy
3. Secondary hyperparathyroidism
4. Hypoparathyroidism
5. Prevention of corticosteroid-induced osteoporosis

Note: initiation of calcitriol in ICU is rarely indicated and this therapy is often withheld while patients are critically ill (see PRECAUTIONS).

PRESENTATION AND ADMINISTRATION:
PO / NG
Calcitriol-AFT 0.25mcg capsules (orange)
Rocaltrol solution 1mcg/ml (colourless to slightly yellowish oily solution). Mix with a drink (eg orange juice). Liquid is available if NG administration is deemed necessary.

DOSAGE:
The optimal daily dose of calcitriol must be carefully determined for each patient. Calcitriol can be administered orally either as a capsule or as an oral solution.
Calcitriol therapy should always be started at the lowest possible dose and should not be increased without careful monitoring of serum calcium.
PO:
0.25mcg per day; increasing to up to 0.5mcg twice daily if required.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO:
0.02mcg/kg daily oral, increase by 0.02mcg/kg every 4-8 weeks according to serum calcium (usual maximum 0.1mcg/kg)

CLINICAL PHARMACOLOGY:
Calcitriol is a synthetic vitamin D analog which is active in the regulation of the absorption of calcium from the gastrointestinal tract and its utilization in the body.

CONTRAINDICATIONS:
1. Hypercalcaemia
2. Evidence of vitamin D toxicity
3. Known hypersensitivity to calcitriol

WARNINGS
Calcitriol is the most potent metabolite of vitamin D available. Excessive dosing can cause hypercalcaemia, hypercalciuria, and hyperphosphataemia.

Calcitriol increases inorganic phosphate levels in serum. While this is desirable in patients with hypophosphataemia, caution is called for in patients with renal failure because of the danger of ectopic calcification. A non-aluminum phosphate-binding compound and a low-phosphate diet should be used to control serum phosphorus levels in patients undergoing dialysis.

PRECAUTIONS

General

Excessive dosage of calcitriol induces hypercalcaemia. Should hypercalcaemia develop, treatment with calcitriol should be stopped immediately. Immobilised patients, e.g., the critically ill, are particularly exposed to the risk of hypercalcaemia which is why this medication is often withheld in ICU.

Laboratory Tests:

No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions:

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Thiazides:

Thiazides are known to induce hypercalcaemia by the reduction of calcium excretion in urine. Some reports have shown that the concomitant administration of thiazides with calcitriol causes hypercalcaemia. Therefore, precaution should be taken when coadministration is necessary.

Digitalis:

Calcitriol dosage must be determined with care in patients undergoing treatment with digitalis, as hypercalcaemia in such patients may precipitate cardiac arrhythmias.

ADVERSE REACTIONS

Since calcitriol is believed to be the active hormone which exerts vitamin D activity in the body, adverse effects are, in general, similar to those encountered with excessive vitamin D intake, i.e., hypercalcaemia syndrome or calcium intoxication (depending on the severity and duration of hypercalcaemia) (see WARNINGS). The early and late signs and symptoms of vitamin D intoxication associated with hypercalcaemia include:

Early:

Weakness, headache, somnolence, nausea, vomiting, dry mouth, constipation, muscle pain, bone pain, metallic taste, and anorexia.

Late:

Polyuria, polydipsia, anorexia, weight loss, nocturia, conjunctivitis (calcific), pancreatitis, photophobia, rhinorrhea, pruritus, hyperthermia, decreased libido, elevated Cr, albuminuria, hypercholesterolemia, elevated AST and ALT, ectopic calcification, nephrocalcinosis, hypertension, cardiac arrhythmias, dystrophy, sensory disturbances, dehydration, apathy, arrested growth, urinary tract infections, and, rarely, overt psychosis.

Calcium Carbonate [1 tablet 5 cents]

ADMINISTRATION ROUTES:
PO

ALTERNATIVE NAMES:
Calci-Tab, Caltrate, Calcium-Sandoz

ICU INDICATIONS:
1. Calcium supplementation

PRESENTATION AND ADMINISTRATION:
PO:
Calci-Tab 500 (500mg elemental calcium), Calci-Tab 600 (600mg elemental calcium), Caltrate tablets (600mg elemental calcium), Calci-Tab Effervescent (1gm elemental calcium), Calcium Sandoz (5.23gm of calcium lactate-gluconate, 0.8gm of calcium carbonate)

DOSAGE:
PO:
500mg-1800mg of elemental calcium per day

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
Not applicable

CLINICAL PHARMACOLOGY:
Calcium.

CONTRAINDICATIONS:
1. Hypercalcaemia,
2. Digitalis toxicity.
3. Hyperphosphataemia (do not administer calcium if the Calcium + Phosphate is >5.5; this is an indication for dialysis)

WARNINGS
Nil

PRECAUTIONS
General
Elderly, fluid restriction, decreased GI motility, GI obstruction, dehydration.

Laboratory Tests:
No tests in addition to standard ICU tests are required.

Drug/Laboratory Test Interactions:
False Increase:
Chloride, benzodiazepine (false positive).
False Decrease:
Magnesium, lipase.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Calcium channel blockers:
Calcium administration may inhibit calcium channel blocker activity.
Doxycycline, tetracycline:
Co-therapy with a tetracycline and calcium carbonate can reduce the serum concentrations and efficacy of tetracyclines.
Quinolones:
Reduced bioavailability of quinolone antibiotics.
Thiazides:
Large doses of calcium with thiazides may lead to milk-alkali syndrome.

ADVERSE REACTIONS
Cardiovascular:
Bradycardia, cardiac arrest, dysrhythmias, heart block, haemorrhage, hypotension, rebound hypertension, shortened QT interval.
Gastrointestinal:
Anorexia, constipation, diarrhoea, flatulence, nausea, obstruction, rebound hyperacidity, vomiting.
Genitourinary:
Renal dysfunction, renal failure, renal stones.
Metabolic:
Hypercalcaemia (drowsiness, lethargy, muscle weakness, headache, constipation, coma, anorexia, nausea, vomiting, polyuria, thirst); metabolic alkalosis; milk-alkali syndrome (nausea, vomiting, disorientation, headache).

Calcium Chloride [1 vial $7.80]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Calcium Chloride

ICU INDICATIONS:
1. Hypocalaemia (particular if there is refractory shock or bleeding)
2. ECG abnormalities caused by hyperkalaemia (acts as a membrane stabiliser)
3. Magnesium toxicity

PRESENTATION AND ADMINISTRATION:
IV:
Preferably give via a central line (if this is present)
Injection undiluted solution. 1gm calcium chloride/10ml (i.e. 10% solution). 6.8mmol of calcium per 10ml. Calcium chloride is a clear colourless solution
For direct IV injection, inject undiluted solution at a rate not exceeding 0.5-1ml/min (0.35 – 0.7 mmol of calcium per minute).
For intermittent infusion, add 1gm of calcium chloride to 50ml of compatible IV fluid. Administer at a rate not exceeding 0.35-0.7mmol of calcium per minute (50-100mg/min). That is, for a 2% solution the maximum rate range is 2.5-5ml/min
Compatible with the following IV fluids:
D5W normal saline glucose and sodium chloride Hartmanns
Room temperature below 30°C

DOSAGE:
IV:
Usually give one vial and repeat as necessary.
(Note 1 vial of calcium chloride contains approximately three times the amount of calcium that is present in a vial of calcium gluconate.)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
0.2ml/kg (max 10ml)

CLINICAL PHARMACOLOGY:
Calcium.

CONTRAINDICATIONS:
1. Hypercalcaemia,
2. Digitalis toxicity.
3. Hyperphosphataemia (do not administer calcium if the Calcium + Phosphate is >5.5; this is an indication for dialysis)

WARNINGS
Calcium chloride should be injected into a large vein very slowly, as it may cause peripheral vasodilatation and a cutaneous burning sensation (it is preferable to

administer it centrally if the patient has a central line)

Avoid IV calcium in patients on digoxin where possible due to the risk of inducing digoxin toxicity.

PRECAUTIONS

General

Calcium chloride injection, 10% is irritating to veins and must not be injected into tissues, since severe necrosis and sloughing may occur. Great care should be taken to avoid extravasation or accidental injection into perivascular tissues.

Laboratory Tests:

An arterial or venous blood gas should be repeated after administration of calcium chloride to check the ionised calcium.

Drug/Laboratory Test Interactions:

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Hypercalcaemia increases the risk of digitalis toxicity. Because of the danger involved in the simultaneous use of calcium salts and drugs of the digitalis group, a digitalized patient should not receive intravenous injections of calcium unless the indications are clearly defined.

ADVERSE REACTIONS

The major side effects are those due to hypercalcaemia as a result of inadvertent over dosing.

Early:

Weakness, headache, somnolence, nausea, vomiting, dry mouth, constipation, muscle pain, bone pain, metallic taste, and anorexia.

Late:

Polyuria, polydipsia, anorexia, weight loss, nocturia, conjunctivitis (calcific), pancreatitis, photophobia, rhinorrhea, pruritus, hyperthermia, decreased libido, elevated Cr, albuminuria, hypercholesterolemia, elevated AST and ALT, ectopic calcification, nephrocalcinosis, hypertension, cardiac arrhythmias, dystrophy, sensory disturbances, dehydration, apathy, arrested growth, urinary tract infections, and, rarely, overt psychosis.

Calcium Gluconate [1 vial $2.14]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Calcium gluconate

ICU INDICATIONS:
1. Hypocalaemia (particular if there is refractory shock or bleeding)
2. ECG abnormalities caused by hyperkalaemia (acts as a membrane stabiliser)
3. Magnesium toxicity

PRESENTATION AND ADMINISTRATION:
IV:
Preferably give via a central line (if this is present)
Injection undiluted solution. 1gm calcium gluconate/10ml (i.e. 10% solution). 2.2mmol of calcium per 10ml. Calcium gluconate is a clear colourless solution
For direct IV injection, inject undiluted solution at a rate not exceeding 2ml/min
For intermittent infusion, add 1gm of calcium gluconate to 50ml of compatible IV fluid and administer over 10 to 20 minutes. Compatible with the following IV fluids:
D5W normal saline glucose and sodium chloride Hartmanns
Store at room temperature below 30°C

DOSAGE:
IV:
Usually give one vial and repeat as necessary.
(Note 1 vial of calcium gluconate contains approximately one third the amount of calcium that is present in a vial of calcium chloride.)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
0.5ml/kg (max 20ml)

CLINICAL PHARMACOLOGY:
Calcium.

CONTRAINDICATIONS:
1. Hypercalcaemia,
2. Digitalis toxicity.

WARNINGS
Calcium gluconate should be injected into a large vein very slowly, as it may cause peripheral vasodilatation and a cutaneous burning sensation (it is preferable to administer it centrally if the patient has a central line)
Avoid IV calcium in patients on digoxin where possible due to the risk of inducing digoxin toxicity.

PRECAUTIONS

General

Calcium gluconate injection, 10% is irritating to veins and must not be injected into tissues, since severe necrosis and sloughing may occur. Great care should be taken to avoid extravasation or accidental injection into perivascular tissues.

Laboratory Tests:

An arterial or venous blood gas should be repeated after administration of calcium chloride to check the ionised calcium.

Drug/Laboratory Test Interactions:

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Hypercalcaemia increases the risk of digitalis toxicity. Because of the danger involved in the simultaneous use of calcium salts and drugs of the digitalis group, a digitalized patient should not receive intravenous injections of calcium unless the indications are clearly defined.

ADVERSE REACTIONS

The major side effects are those due to hypercalcaemia as a result of inadvertent over dosing.

Early:

Weakness, headache, somnolence, nausea, vomiting, dry mouth, constipation, muscle pain, bone pain, metallic taste, and anorexia.

Late:

Polyuria, polydipsia, anorexia, weight loss, nocturia, conjunctivitis (calcific), pancreatitis, photophobia, rhinorrhea, pruritus, hyperthermia, decreased libido, elevated Cr, albuminuria, hypercholesterolemia, elevated AST and ALT, ectopic calcification, nephrocalcinosis, hypertension, cardiac arrhythmias, dystrophy, sensory disturbances, dehydration, apathy, arrested growth, urinary tract infections, and, rarely, overt psychosis.

Candesartan [1 tablet 8mg 40 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Atacand

ICU INDICATIONS:
1. Hypertension
2. Congestive heart failure (Note: Candesartin cilexetil is indicated for the treatment of heart failure (NYHA class II-IV) in patients with left ventricular systolic dysfunction (ejection fraction <40%) to reduce cardiovascular death and to reduce heart failure hospitalizations. Candesartin cilexetil also has an added effect on these outcomes when used with an ACE inhibitor.)

PRESENTATION AND ADMINISTRATION:
PO / NG:
Atacand 4mg (white), 8mg (light pink), 16mg (pink), 32mg (pink)
Crush tablets for NG administration

DOSAGE:
PO:
Initially 4mg once daily, increasing gradually to 32mg once daily

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	initial dose 2mg and increase dose according to response
10-20	initial dose 2mg and increase dose according to response
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	initial dose 2mg and increase dose according to response
HD	initial dose 2mg and increase dose according to response
CVVHDF	initial dose 2mg and increase dose according to response

DOSAGE IN PAEDIATRICS:
0.1-0.3mg/kg daily
Note: Safety and effectiveness in paediatric patients have not been established.

CLINICAL PHARMACOLOGY:
Candesartan cilexetil (atacand) is a prodrug which is hydrolysed to candesartan during absorption from the gastrointestinal tract. Candesartan is a selective AT1 subtype angiotensin II receptor antagonist.

CONTRAINDICATIONS:
1. Hypersensitivity to candesartan (atacand)
2. Cardiogenic shock

WARNINGS
Hypotension in Heart Failure Patients
Caution should be observed when initiating therapy in patients with heart failure. Patients with heart failure given candesartin cilexetil commonly have some reduction in blood pressure. In patients with symptomatic hypotension this may require temporarily reducing the dose of candesartin cilexetil, or diuretic, or both, and volume repletion
Impaired Hepatic Function
A lower initiating dose should be considered for patients with moderate hepatic impairment.
Hyperkalaemia
In heart failure patients treated with candesartin cilexetil, hyperkalaemia may occur, especially when taken concomitantly with ACE inhibitors and potassium-sparing diuretics such as spironolactone.

PRECAUTIONS
General
See WARNINGS

Laboratory Tests:
No tests additional to standard ICU investigations are required

Drug/Laboratory Test Interactions :
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
An increase in serum lithium concentration has been reported during concomitant administration of lithium with candesartan cilexetil, so careful monitoring of serum lithium levels is recommended during concomitant use.

ADVERSE REACTIONS
Body as a Whole:
Asthenia, fever.
Nervous System:
Paraesthesia, vertigo.
Gastrointestinal System:
Dyspepsia, gastroenteritis.
Cardiovascular System:
Tachycardia, palpitation, hypotension.
Metabolic and Nutritional System:
Creatine phosphokinase increased, hyperglycaemia, hypertriglyceridaemia, hyperuricaemia.
Musculoskeletal System:
Myalgia.
Respiratory System:
Dyspnea.
Urinary System:
Haematuria.

Captopril [1 tablet 12.5mg 2 cents, syrup $1 per ml]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Capoten

ICU INDICATIONS:
1. Hypertension
2. Congestive heart failure or left ventricular dysfunction after myocardial infarction
3. Diabetic nephropathy

PRESENTATION AND ADMINISTRATION:
PO / NG:
Apo-captopril & capoten tablets (12.5mg, 25mg, 50mg white tablets)
Capoten solution (5mg/ml) – clear and colourless
Tablets can be crushed for NG administration and liquid is also available.

DOSAGE:
PO/NG:
6.25mg PO TDS increased to maximum of 50mg PO TDS.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	start with 6.25mg or less and increase gradually
10-20	start with 6.25mg or less and increase gradually
>20-50	start with 6.25mg or less and increase gradually

Dose in renal replacement therapy

CAPD	start with 6.25mg or less and increase gradually
HD	start with 6.25mg or less and increase gradually
CVVHDF	start with 6.25mg or less and increase gradually

Note: Recent clinical observations have shown an association of hypersensitivity-like (anaphylactoid) reactions during haemodialysis with high-flux dialysis membranes (e.g. AN69) in patients receiving ACE inhibitors.

DOSAGE IN PAEDIATRICS:
0.1mg/kg 8hrly; increased if required to a maximum of 2mg/kg 8hrly.

CLINICAL PHARMACOLOGY:
Captopril is a specific competitive inhibitor of angiotensin I-converting enzyme (ACE), the enzyme responsible for the conversion of angiotensin I to angiotensin II.

CONTRAINDICATIONS:
1. Hypersensitivity to captopril or any other angiotensin-converting enzyme inhibitor (e.g. a patient who has experienced angioedema during therapy with any other ACE inhibitor).
2. Cardiogenic shock

WARNINGS

Anaphylactoid and Possibly Related Reactions

Captopril can cause anaphylactoid reactions

Head and Neck Angioedema

Angioedema involving the extremities, face, lips, mucous membranes, tongue, glottis or larynx has been seen in patients treated with ACE inhibitors, including captopril. If angioedema involves the tongue, glottis or larynx, airway obstruction may occur and be fatal. Swelling confined to the face, mucous membranes of the mouth, lips and extremities has usually resolved with discontinuation of captopril; some cases required medical therapy.

Intestinal Angioedema

Intestinal angioedema has been reported in patients treated with ACE inhibitors. These patients presented with abdominal pain (with or without nausea or vomiting); in some cases there was no prior history of facial angioedema and C-1 esterase levels were normal.

Neutropaenia/Agranulocytosis

Neutropaenia (<1000/mm3) with myeloid hypoplasia has resulted from use of captopril.

Hypotension in Heart Failure Patients

Caution should be observed when initiating therapy in patients with heart failure. Patients with heart failure given captopril commonly have some reduction in blood pressure. In patients with symptomatic hypotension this may require temporarily reducing the dose of captopril, or diuretic, or both, and volume repletion

Hepatic Failure

Rarely, ACE inhibitors have been associated with a syndrome that starts with cholestatic jaundice and progresses to fulminant hepatic necrosis and (sometimes) death. The mechanism of this syndrome is not understood. Patients receiving ACE inhibitors who develop jaundice or marked elevations of hepatic enzymes should discontinue the ACE inhibitor.

PRECAUTIONS

General

Some patients with renal disease, particularly those with severe renal artery stenosis, have developed increases in serum creatinine after reduction of blood pressure with captopril. Captopril dosage reduction and/or discontinuation of diuretic may be required.

Elevations in serum potassium have been observed in some patients treated with ACE inhibitors, including captopril.

Presumably due to the inhibition of the degradation of endogenous bradykinin, persistent nonproductive cough has been reported with all ACE inhibitors, always resolving after discontinuation of therapy. ACE inhibitor-induced cough should be considered in the differential diagnosis of cough.

Laboratory Tests:

No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions:

Captopril may cause a false-positive urine test for acetone.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Increased serum lithium levels and symptoms of lithium toxicity have been reported in patients receiving concomitant lithium and ACE inhibitor therapy.
The risk of hypotension increases if captopril is coadministered with other antihypertensives

ADVERSE REACTIONS:
Body as a Whole:
Gynaecomastia, anaphylactoid reactions, angioedema
Cardiovascular:
Cardiac arrest, cerebrovascular accident / insufficiency, rhythm disturbances, orthostatic hypotension, syncope
Dermatological:
Bullous pemphigus, erythema multiforme (Stevens Johnson syndrome), exfoliatice dermatitis
Gastrointestinal:
Pancreatitis, glossitis, dyspepsia, jaundice, hepatitis, rare causes of hepatic necrosis, cholestasis
Haematological:
Anaemia (including cases of haemolytic anaemia), thrombocytopaenia, neutropaenia
Metabolic:
Hyponatraemia
Musculoskeletal:
Myalgia, myasthenia
Nervous system:
Ataxia, confusion, depression, nervousness, somnolence
Respiratory system;
Bronchospasm, eosinophilic pneumonia, angioedema
Urogenital system;
Renal failure, proteinuria

Carbamazepine [1 tablet 200mg 15 cents, syrup 10c per ml]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Tegretol

ICU INDICATIONS:
1. Epilepsy
2. Trigeminal neuralgia and other neuropathic pain

(Note: this medication is usually prescribed in ICU patients who were taking it for a pre-existing indication prior to admission; it may occasionally be commenced de novo in patients with new seizures or neurogenic pain but is not first line therapy for either of these conditions)

PRESENTATION AND ADMINISTRATION:
PO / NG:
Tegretol 200mg and 400mg tablets (white); tegretol CR tablets 200mg (beige/orange) and 400mg (brown/orange); tegretol syrup 100mg/5ml (white)
Tegretol liquid is available for NG administration – it should be diluted in equal parts with water to prevent possible adsorption.

DOSAGE:
PO/NG:
Epilepsy
Initial:
Either 200 mg BD for tablets and extended-release tablets or 100mg QID for suspension. Increase at weekly intervals by adding up to 200 mg/day using a BD regimen of extended-release or TDS or QID regimen of the other formulations until the optimal response is obtained. Dosage generally should not exceed 1200 mg daily. Doses up to 1600 mg daily have been used in adults in rare instances.
Maintenance:
Adjust dosage to the minimum effective level, usually 800-1200 mg daily.

Trigeminal neuralgia and other neuropathic pain
Initial:
On the first day, either 100 mg BD for tablets or extended-release tablets or 50mg QID for suspension for a total daily dose of 200 mg. This daily dose may be increased by up to 200mg/day using increments of 100 mg every 12 hours for tablets or extended-release tablets or 50 mg QID for suspension, only as needed to achieve freedom from pain. Do not exceed 1200 mg/daily.
Maintenance:
Control of pain can be maintained in most patients with 400-800 mg daily. However, some patients may be maintained on as little as 200 mg daily, while others may require as much as 1200 mg daily. At least once every 3 months throughout the treatment period, attempts should be made to reduce the dose to the minimum effective level or even to discontinue the drug.

Carbamazepine suspension produces higher peak levels than the same dose given as the tablet, therefore it is recommended that patients given the suspension be dosed in

lower doses more given more frequently. For conversion of patients from oral carbamazepine tablets to carbamazepine suspension, administer the same number of mg/day in smaller, more frequent doses (eg change dosing from twice daily to three times daily). When converting patients from carbamazepine conventional tablets to carbamazepine extended-release tablets, the same total daily mg dose of carbamazepine extended-release should be administered.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
2mg/kg 8 hourly may increase over 2-4 weeks to 5-10mg/kg 8 hourly

CLINICAL PHARMACOLOGY:
Carbamazepine is an anticonvulsant and mood-stabiliser. It stabilises the inactivated state of voltage-gated sodium channels, meaning less are subsequently available to open. The affected cells are then less excitable until the drug dissociates.

CONTRAINDICATIONS:

1. History of previous bone marrow depression,
2. Hypersensitivity to the drug, or known sensitivity to any of the tricyclic compounds such as amitriptyline, desipramine, imipramine, protriptyline, nortriptyline, etc.

WARNINGS
The most serious complications of carbamazepine are those of bone marrow depression including aplastic anaemia, agranulocytosis, & pancytopaenia. Patients with a history of adverse haematologic reaction to any drug may be particularly at risk.
Severe dermatologic reactions including toxic epidermal necrolysis and Stevens-Johnson syndrome, have been reported with carbamazepine.
Because of the relationship of the drug to other tricyclic compounds, the possibility of activation of a latent psychosis and, in elderly patients, of confusion or agitation should be borne in mind.

PRECAUTIONS
General
Carbamazepine suspension produces higher peak levels than the same dose given as the tablet, therefore it is recommended that patients given the suspension be dosed in lower doses more given more frequently

Hyponatraemia has been reported in association with carbamazepine use, either alone or in combination with other drugs.
Cessation of carbamazepine may lead to seizures.

Laboratory Tests:
Carbamazepine levels (collect in red or yellow tube):
Measure levels if:

(i) there is concern about possible non-compliance
(ii) there is concern about possible toxicity

Induces its own metabolism so that following the initiation of therapy, it takes 2 - 4 weeks to obtain a steady state.
Measure levels pre-dose (i.e. trough)

Therapeutic range is 16-50µmol/L
Potentially toxic levels and associated clinical features:

>50 µmol/L	nystagmus
>85 µmol/L	CNS and anticholinergic effects
>170 µmol/L	Coma, seizures and cardiac conduction abnormalities

Drug/Laboratory Test Interactions :
Interference with some pregnancy tests has been reported.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Carbamazepine may be used alone or with other anticonvulsants. When added to existing anticonvulsant therapy, the drug should be added gradually while the other anticonvulsants are maintained or gradually decreased, except phenytoin, which may have to be increased.

Clinically meaningful drug interactions have occurred with concomitant medications and include, but are not limited to, the following:
CYP 3A4 inhibitors inhibit carbamazepine metabolism and can thus increase plasma carbamazepine levels. Drugs that have been shown, or would be expected, to increase plasma carbamazepine levels include:
Diltiazem, erythromycin, clarithromycin, fluoxetine, loratadine, terfenadine, isoniazid, verapamil, & valproate.
CYP 3A4 inducers can increase the rate of carbamazepine metabolism. Drugs that have been shown, or that would be expected, to decrease plasma carbamazepine levels include:
Cisplatin, doxorubicin, rifampin, phenobarbital, phenytoin, & theophylline.

ADVERSE REACTIONS
The most frequently observed adverse reactions, particularly during the initial phases of therapy, are dizziness, drowsiness, unsteadiness, nausea, and vomiting. To minimise the possibility of such reactions, therapy should be initiated at the low dosage recommended.
Body as a whole:
Multi-organ hypersensitivity reactions occurring days to weeks or months after initiating treatment have been reported in rare cases. Signs or symptoms may include, but are not limited to fever, skin rashes, vasculitis, lymphadenopathy, disorders mimicking lymphoma, arthralgia, leukopaenia, eosinophilia, hepato-splenomegaly and abnormal liver function tests.
Haemopoietic System:
Aplastic anaemia, agranulocytosis, pancytopaenia, bone marrow depression, thrombocytopaenia, leukopaenia, leukocytosis, eosinophilia, acute intermittent porphyria.
Skin:
Pruritic and erythematous rashes, urticaria, toxic epidermal necrolysis, Stevens-Johnson syndrome, photosensitivity reactions, alterations in skin pigmentation, exfoliative dermatitis, erythema multiforme and nodosum, purpura, aggravation of disseminated lupus erythematosus, alopecia, and diaphoresis.
Cardiovascular System:
Congestive heart failure, edema, aggravation of hypertension, hypotension, syncope and collapse, aggravation of coronary artery disease, arrhythmias and AV block, thrombophlebitis, thromboembolism, and adenopathy or lymphadenopathy.

Gastrointestinal System:
Abnormalities in liver function tests, cholestatic and hepatocellular jaundice, hepatitis; very rare cases of hepatic failure, pancreatitis, nausea, vomiting, gastric distress and abdominal pain, diarrhoea, constipation, anorexia, and dryness of the mouth and pharynx, including glossitis and stomatitis.
Musculoskeletal System:
Aching joints and muscles, and leg cramps.
Respiratory System:
Pulmonary hypersensitivity characterised by fever, dyspnea, pneumonitis or pneumonia.
Genitourinary System:
Renal failure
Nervous System:
Dizziness, drowsiness, disturbances of coordination, confusion, headache, fatigue, blurred vision, visual hallucinations, transient diplopia, oculomotor disturbances, nystagmus, speech disturbances, abnormal involuntary movements, peripheral neuritis and paraesthesias, depression with agitation, talkativeness, tinnitus, and hyperacusis.

Carvedilol [1 tablet 12.5mg 90 cents]

ADMINISTRATION ROUTES:
PO / NG

ALTERNATIVE NAMES:
Dilatrend

ICU INDICATIONS:
1. Hypertension
2. Acute myocardial infarction
3. Secondary prevention in patients with coronary artery disease
4. Angina
5. Rate control

PRESENTATION AND ADMINISTRATION:
PO/NG:
Dilatrend tablets 6.25mg (yellow), 12.5mg (light brown), 25mg (white to pale yellowish beige)
When administered with food, the rate of absorption is slowed. Carvedilol should be taken with food to minimize the risk of hypotension.

DOSAGE:
PO/NG:
Commence at 3.125mg BD and increase gradually as required

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
0.08mg/kg 12 hrly; if tolerated, increase gradually to a maximum of 0.5-0.75mg/kg 12 hourly

CLINICAL PHARMACOLOGY:
Non selective beta blocker and alpha-1 blocker. Carvedilol is rapidly absorbed following oral administration. Following oral administration, the apparent mean terminal elimination half-life of carvedilol generally ranges from 7-10 hours.

CONTRAINDICATIONS:
1. Bronchial asthma (two cases of death from status asthmaticus have been reported in patients receiving single doses of carvedilol)
2. Second- or third-degree AV block, sick sinus syndrome or severe bradycardia (unless a permanent pacemaker is in place),
3. Cardiogenic shock
4. Clinically manifest hepatic impairment
5. Hypersensitivity to any component of the product.

WARNINGS

Cardiac Failure

Sympathetic stimulation is necessary in supporting circulatory function in congestive heart failure, and beta blockade carries the potential hazard of further depressing myocardial contractility and precipitating more severe failure.

Discontinuation of therapy

Discontinuation of therapy in a patient with coronary artery disease may lead to rebound angina, arrhythmia or myocardial infarction.

Diabetes and Hypoglycaemia

Beta blockers may mask tachycardia occurring with hypoglycaemia.

Thyrotoxicosis

Beta-adrenergic blockade may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism. Abrupt withdrawal of beta blockade might precipitate a thyroid storm.

PRECAUTIONS

General

Carvedilol may aggravate peripheral arterial circulatory disorders.

Nonallergic Bronchospasm (e.g., chronic bronchitis and emphysema)

Patients with bronchospastic disease should, in general, not receive beta-blockers. Carvedilol may be used with caution, however, in patients who do not respond to, or cannot tolerate, other antihypertensive agents. It is prudent, if carvedilol is used, to use the smallest effective dose. In clinical trials of patients with congestive heart failure, patients with bronchospastic disease were enrolled if they did not require oral or inhaled medication to treat their bronchospastic disease.

Laboratory Tests:

No tests additional to standard ICU tests are required

Drug/Laboratory Test Interactions:

None known.

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Clonidine:

Concomitant administration of clonidine with carvedilol agents may potentiate blood-pressure- and heart-rate-lowering effects due to both agents possessing alpha²-blocking properties.

Cyclosporin:

On the average, the required dose of cyclosporin reduces by about 20% after initiation of carvedilol therapy. Close monitoring of cyclosporin levels is warranted.

Digoxin:

Digoxin concentrations are increased by about 15% when digoxin and carvedilol are administered concomitantly. Both digoxin and carvedilol slow AV conduction. Therefore, increased monitoring of digoxin is recommended when initiating, adjusting or discontinuing carvedilol.

Rifampin:

Rifampin reduces plasma concentrations of carvedilol by about 70%.

ADVERSE REACTIONS
Body as a whole:
Fatigue
Cardiovascular System:
Bradycardia, Hypotension, Syncope, Angina
Gastrointestinal System:
Diarrhoea, Nausea, Vomiting
Musculoskeletal System:
Arthralgia
Respiratory System:
Cough
Nervous System:
Dizziness, Headache

Caspofungin [1 vial 50mg $577.27, 1 vial 70mg $862.50]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Cacidas

ICU INDICATIONS:

1. invasive of oesophageal candidiasis:
   Treatment of candidaemia and the following Candida infections: intra-abdominal abscesses, peritonitis and pleural space infections. Caspofungin acetate has not been studied in endocarditis, osteomyelitis, and meningitis due to Candida.
2. Aspergillus infection
   Caspofungin is indicated for treatment of invasive aspergillosis in patients who are refractory to or intolerant of other therapies (i.e., amphotericin B, lipid formulations of amphotericin B, and/or itraconazole); however, it has not been studied as initial therapy for invasive aspergillosis.
3. Empirical therapy for presumed fungal infections in febrile, neutropaenic patients.

PRESENTATION AND ADMINISTRATION:
IV
50mg and 70mg vials of white powder
Refrigerate at 2-8°C. Do not freeze.
Bring vial to room temperature and reconstitute by adding 10.5ml of water for injection. Mix gently until completely dissolved producing a clear solution. Concentrations of reconstituted vials are 7mg/ml (70mg vial) or 5mg/ml (50mg vial).
Add required volume of reconstituted solution to 250ml of compatible IV fluid and administer slowly over approximately 1 hour. A reduced volume of 100ml may be used for 50mg or 35mg doses only.
Reconstituted solution and diluted infusion solution are stable for 24 hours at or below 25°C
Compatible with:
Normal saline Hartmanns

DOSAGE:
IV:
Loading dose of 70mg followed by 50mg daily
See also IMPORTANT DRUG INTERACTIONS FOR THE INTENSIVE CARE UNIT as dosage adjustment is required when coadministered with particular medicines.
Note: dosage adjustment is required in liver failure:
Patients with mild hepatic insufficiency (Child-Pugh score 5-6) do not need a dosage adjustment. For patients moderate hepatic insufficiency (Child-Pugh score 7-9), caspofungin acetate 35 mg daily is recommended. However, where recommended, a 70-mg loading dose should still be administered on Day 1. There is no clinical experience in patients with severe hepatic insufficiency (Child-Pugh score >9).

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
70mg/m^2 day 1, then 50mg/m^2 daily IV
Note: The safety and efficacy of Caspofungin in the paediatric population is not established.

CLINICAL PHARMACOLOGY:
Caspogunfin is the first of a new class of antifungal drugs (echinocandins) that inhibit the synthesis of an integral component of the fungal cell wall.

Caspofungin exhibits in vitro activity against Aspergillus species (Aspergillus fumigatus, Aspergillus flavus, and Aspergillus terreus) and Candida species (Candida albicans, Candida glabrata, Candida guilliermondii, Candida krusei, Candida parapsilosis, and Candida tropicalis).

Based on available evidence from clinical studies, it appears that caspofungin is as effective as amphotericin B in empirical therapy of persistent febrile neutropaenia and in patients with invasive Candidiasis.

CONTRAINDICATIONS:
1. Hypersensitivity to caspofungin.

WARNINGS
Concomitant use of caspofungin acetate with cyclosporin is not recommended unless the potential benefit outweighs the potential risk to the patient due to an increased risk of liver toxicity.

PRECAUTIONS
General
The efficacy of a 70-mg dose regimen in patients with invasive aspergillosis who are not clinically responding to the 50-mg daily dose is not known. Limited safety data suggest that an increase in dose to 70 mg daily is well tolerated.
Laboratory abnormalities in liver function tests have been seen in healthy volunteers and patients treated with caspofungin acetate. In some patients with serious underlying conditions who were receiving multiple concomitant medications along with caspofungin acetate, clinical hepatic abnormalities have also occurred. Isolated cases of significant hepatic dysfunction, hepatitis, or worsening hepatic failure have been reported in patients; a causal relationship to caspofungin acetate has not been established.

Laboratory Tests:
No tests in addition to standard tests are indicated.

Drug/Laboratory Test Interactions:
None known.

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Caspofungin with:

Tacrolimus	Caspofungin acetate reduces the blood levels of tacrolimus. For patients receiving both therapies, standard monitoring of tacrolimus blood concentrations and appropriate tacrolimus dosage adjustments are recommended.
Cyclosporin	See WARNINGS.
Rifampicin	A drug-drug interaction study with rifampin in healthy volunteers has shown a 30% decrease in caspofungin trough concentrations. Patients on rifampin should receive 70 mg of caspofungin acetate daily.
Dexamethasone	Increases clearance of caspofungin; use 70mg daily of caspofungin
Phenytoin	Increases clearance of caspofungin; use 70mg daily of caspofungin
Carbamazepine	Increases clearance of caspofungin; use 70mg daily of caspofungin

ADVERSE REACTIONS

Body as a whole:
Chills, Fever, Flushing, Perspiration/diaphoresis
Cardiovascular System:
Hypertension, Tachycardia
Gastrointestinal System:
Abdominal pain, Diarrhoea, Nausea, Vomiting
Musculoskeletal System:
Back pain
Respiratory System:
Dyspnoea, Tachypnoea
Nervous System:
Headache
Metabolic:
Hypokalaemia
Skin:
Rash

Cefaclor [1 tablet 250mg 25 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Ranbaxy-cefaclor

ICU INDICATIONS:
1. Treatment of infections caused by susceptible organisms

Note 1: used on occasion as de-escalation from IV therapy in patients recovering from serious infections in the ICU.
Note 2: beta-lactamase-negative, ampicillin-resistant (BLNAR) strains of Haemophilus influenzae should be considered resistant to cefaclor despite apparent in vitro susceptibility of some BLNAR strains.

PRESENTATION AND ADMINISTRATION:
PO/NG:
Ranbaxy-cefaclor capsules 250mg (purple/white) and Ranbaxy Cefaclor oral suspension 125mg/5ml (white to off white)
Store at room temperature, 15-30°C
Suspension may block nasogastric tubes. Check with Pharmacist.

DOSAGE:
PO:
250-500mg 8 hourly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	250mg every 8 hours
10-20	dose as in normal renal function
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	250mg every 8 hours
HD	500mg every 8 hours
CVVHDF	dose as in normal renal function

DOSAGE IN PAEDIATRICS:
10-15mg/kg 8 hourly

CLINICAL PHARMACOLOGY:
Cefaclor is a semisynthetic cephalosporin antibiotic for oral administration. Cefaclor is well absorbed after oral administration to fasting subjects. Total absorption is the same whether the drug is given with or without food.

In vitro tests demonstrate that the bactericidal action of the cephalosporins results from inhibition of cell-wall synthesis. Cefaclor is shown to be active against most strains of the following microorgansims, both in vitro and in clinical infections:
Aerobes, Gram-Positive:
Staphylococci, including coagulase-positive, coagulase-negative, and penicillinase-producing strains.

Streptococcus pneumoniae, streptococcus pyogenes
Aerobes, Gram-Negative:
Escherichia coli, Haemophilus influenza, excluding beta-lactamase-negative ampicillin-resistant strains, Klebsiella spp., Proteus mirabilis.

Note: Pseudomonas sp, Acinetobacter and most strains of enterococci (Enterococcus faecalis), Enterobacter spp, indole-positive Proteus, and Serratia spp are resistant to cefaclor.

CONTRAINDICATIONS:
1. Hypersensivity to cephalosporins

WARNINGS
Anaphylaxis
Cephalosporins are a common cause of anaphylactic reactions and cross reactivity with penicillins may occur
Pseudomembranous colitis
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including cefaclor, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents.

PRECAUTIONS
General
Prescribing Ceclor in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.
Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. It should be recognized that a positive Coombs' test may be due to the drug.

Laboratory Tests:
No tests additional to usual ICU tests are required

Drug/Laboratory Test Interactions :
May cause a positive Coombs’ test and may cause false positive on some urinary glucose tests

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note.

ADVERSE REACTIONS
Body as a whole:
Hypersensitivity reactions, serum-sickness-like reactions, anaphylaxis
Haemopoietic System:
Positive Coombs' tests, eosinophilia, thrombocytopaenia
Skin:
Pruritus, urticaria, Stevens-Johnson syndrome, toxic epidermal necrolysis
Cardiovascular System:
Syncope, or vasodilation

Gastrointestinal System:
Transient hepatitis and cholestatic jaundice, nausea and vomiting, pseudomembranous colitis, diarrhoea
Respiratory System:
Angioedema, dyspnea
Genitourinary System:
Genital pruritus and vaginitis, reversible interstitial nephritis.
Nervous System:
Paraesthesias

Cephalosporin-Class Adverse Reactions
In addition to the adverse reactions listed above that have been observed in patients treated with cefaclor, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics: fever, abdominal pain, superinfection, renal dysfunction, toxic nephropathy, haemorrhage, false positive test for urinary glucose, elevated bilirubin, elevated LDH, and pancytopaenia.
Several cephalosporins have been implicated in triggering seizures, paticularly in patients with renal impairment when the dosage was not reduced. If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated

Cefazolin / Cephazolin [1 vial 1gm $3.99]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Cefazolin, cephazolin

ICU INDICATIONS:
1. Prophylaxis around surgery
2. Treatment of infections caused by susceptible organisms

PRESENTATION AND ADMINISTRATION:
IV:
1gm vials of powder
Reconstitute with 2.5ml of water for injection ONLY to make a total of 3ml of final solution in a concentration of 330mg/ml then shake well until all powder is dissolved.
Store at room temperature
Compatible with:
Normal saline Glucose and sodium chloride Glucose 5% Glucose 10% Hartmanns

DOSAGE:
IV:
1-2gm IV 6-8 hourly
Note: for prophylaxis after cardiac surgery, patients should be given 1gm 3 hours after ICU admission and 1gm 8 hours later

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	1gm daily
10-20	1gm 12 hourly
>20-50	1gm 8 hourly

Dose in renal replacement therapy

CAPD	1gm daily
HD	1gm after dialysis
CVVHDF	1gm 12 hourly

DOSAGE IN PAEDIATRICS:
25-50mg/kg IV 6-8 hourly

CLINICAL PHARMACOLOGY:
Cefazolin for injection is a 1st generation cephalosporin for parenteral administration. It has a bactericidal action resulting from inhibition of cell wall synthesis.
When organisms are susceptible, Cefazolin sodium is active against the following organisms in vitro and in clinical infections:
Staphylococcus aureus (including penicillinase-producing strains).
Staphylococcus epidermidis
Group A beta-haemolytic streptococci and other strains of streptococci (many strains of enterococci are resistant).

Streptococcus pneumoniae.
Escherichia coli.
Proteus mirabilis.
Klebsiella species.
Enterobacter aerogenes.
Haemophilus influenzae.

Most strains of indole positive Proteus (Proteus vulgaris), Enterobacter cloacae, Morganella morganii and Providencia rettgeri are resistant. Serratia, Pseudomonas, Mima, Herellea species are almost uniformly resistant to cefazolin.

CONTRAINDICATIONS:

1. Hypersensivity to cephalosporins

WARNINGS

Anaphylaxis

Cephalosporins are a common cause of anaphylactic reactions and cross reactivity with penicillins may occur

Pseudomembranous colitis

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including cefazolin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents.

PRECAUTIONS

General

Prescribing cefazolin in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. It should be recognized that a positive Coombs' test may be due to the drug.

Laboratory Tests:

No tests additional to usual ICU tests are required

Drug/Laboratory Test Interactions :

A false positive reaction for glucose in the urine may occur with Benedict's solution, Fehling's solution or with Clinitest tablets, but not with enzyme-based tests such as Clinistix.

Positive direct and indirect antiglobulin (Coombs) tests have occurred; these may also occur in neonates whose mothers received cephalosporins before delivery.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note.

ADVERSE REACTIONS
Body as a whole:
Anaphylaxis, itching, drug fever, Stevens-Johnson syndrome.
Haemopoietic System:
Neutropaenia, leukopaenia, thrombocytopaenia, thrombocythaemia, eosinophilia.
Skin:
Skin rash
Gastrointestinal System:
Diarrhoea, oral candidiasis (oral thrush), vomiting, nausea, stomach cramps, anorexia and pseudomembranous colitis. Transient rises in ALT, AST, and alkaline phosphatase levels has been observed. As with other cephalosporins, reports of hepatitis have been received.

Cephalosporin-Class Adverse Reactions
In addition to the adverse reactions listed above that have been observed in patients treated with cefazolin, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics: fever, abdominal pain, superinfection, renal dysfunction, toxic nephropathy, haemorrhage, false positive test for urinary glucose, elevated bilirubin, elevated LDH, and pancytopaenia.
Several cephalosporins have been implicated in triggering seizures, paticularly in patients with renal impairment when the dosage was not reduced. If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated

Cefotaxime [1 vial 500mg $1.90]

ADMINISTRATION ROUTES:
IV, IM

ALTERNATIVE NAMES:
Cefotaxime, Claforan

ICU INDICATIONS:
1. Treatment of infections caused by susceptible organisms

PRESENTATION AND ADMINISTRATION:
IV:
500mg, 1gm and 2gm vials of powder
Add at least 2ml of water for injection to a 500mg vial, at least 4ml of water for injection to a 1gm vial or 10ml of water for injection to a 2gm vial then shake well until all powder is dissolved.
For doses not equalling vial size, prepare the solutions as follows:

Vial size	500mg	1gm	2gm
Volume of diluent	10ml	10ml	10ml
Volume of final solution	10.2ml	10.4ml	11ml
Approximate concentration	50mg/ml	95mg/ml	180mg/ml

Inject slowly over 3-5 minutes
Store at room temperature
Compatible with:
Normal saline Glucose and sodium chloride glucose 5%
Hartmanns

IM:
Reconstitute with 0.5% lignocaine adding 2ml to a 500mg vial, 3ml to a 1gm vial, and 5ml to a 2gm vial. Inject no more than 4ml of solution into either buttock. If the daily dose exceeds 2gm this route is not recommended

DOSAGE:
IV:
2gm 8 hourly (may increase to maximum of 12gm daily in severe infections)
Note: during postmarketing surveillance, a potentially life-threatening arrhythmia was reported in each of 6 patients who received a rapid (less than 60 seconds) bolus injection of cefotaxime through a central venous catheter. Therefore, cefotaxime should only be administered as instructed in PRESENTATION AND ADMINISTRATION.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]
<10 0.5-1gm 8-12 hourly
10-20 dose as in normal renal function
>20-50 dose as in normal renal function
Dose in renal replacement therapy
CAPD 0.5-1gm 8-12 hourly
HD 0.5-1gm 8-12 hourly
CVVHDF 1gm 12 hourly

DOSAGE IN PAEDIATRICS:
25-50mg/kg/day 6-12hrly; for bacterial meningitis load 100 mg/kg then give 50 mg/kg/dose (max. 2000 mg/dose) 6 hourly

CLINICAL PHARMACOLOGY:
Cefotaxime is a 3rd generation cephalosporin. It has a bactericidal action resulting from inhibition of cell wall synthesis. Cefotaxime sodium has a high degree of stability in the presence of beta-lactamases, both penicillinases and cephalosporinases, of gram-negative and gram-positive bacteria. Cefotaxime has been shown to be active against most strains of the following microorganisms both in vitro and in clinical infections:
Aerobes, Gram-Positive:
Enterococcus spp., Staphylococcus aureus,* including beta-lactamase-positive and negative strains, Staphylococcus epidermidis, Streptococcus pneumoniae, Streptococcus pyogenes (Group A beta-haemolytic streptococci), Streptococcus spp.
*Staphylococci which are resistant to methicillin/oxacillin must be considered resistant to cefotaxime sodium.
Aerobes, Gram-Negative:
Acinetobacter spp., Citrobacter spp., Enterobacter spp., Escherichia coli, Haemophilus influenzae (including ampicillin-resistant strains), Haemophilus parainfluenzae, Klebsiella spp. (including Klebsiella pneumoniae), Morganella morganii, Neisseria gonorrhoeae (including beta-lactamase-positive and negative strains), Neisseria meningitidis, Proteus mirabilis, Proteus vulgaris, Providencia rettgeri, Providencia stuartii, Serratia marcescens.
NOTE:
Many strains of the above organisms that are multiply resistant to other antibiotics, e.g., penicillins, cephalosporins, and aminoglycosides, are susceptible to cefotaxime sodium. Cefotaxime sodium is active against some strains of Pseudomonas aeruginosa.
Anaerobes:
Bacteroides spp., including some strains of Bacteroides fragilis, Clostridium spp. (Note: Most strains of Clostridium difficile are resistant.) Fusobacterium spp. (Including Fusobacterium nucleatum). Peptococcus spp., Peptostreptococcus spp.

CONTRAINDICATIONS:
1. Hypersensivity to cephalosporins

WARNINGS
Anaphylaxis
Cephalosporins are a common cause of anaphylactic reactions and cross reactivity with penicillins may occur
Pseudomembranous colitis
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including cefotaxime, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents.
Agranulocytosis
As with other beta-lactam antibiotics, granulocytopaenia and, more rarely, agranulocytosis may develop during treatment with cefotaxime sodium, particularly if given over long periods.

PRECAUTIONS
General
Prescribing cefotaxime in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.
Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. It should be recognized that a positive Coombs' test may be due to the drug.

Laboratory Tests:
No tests additional to usual ICU tests are required

Drug/Laboratory Test Interactions:
None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note.

ADVERSE REACTIONS
Cardiovascular System:
Potentially life-threatening arrhymias following rapid (less than 60 seconds) bolus administration via central venous catheter have been observed.
Haematologic System:
Neutropaenia, transient leukopaenia, eosinophilia, thrombocytopaenia and agranulocytosis have been reported. Some individuals have developed positive direct Coombs Tests during treatment with cefotaxime sodium and other cephalosporin antibiotics. Rare cases of haemolytic anaemia have been reported.
Genitourinary System:
Moniliasis, vaginitis.
Central Nervous System:
Headache.
Liver:
Transient elevations in AST, ALT, serum LDH, and serum ALP levels have been reported.
Kidney:
As with some other cephalosporins, interstitial nephritis and transient elevations of creatinine have been occasionally observed with cefotaxime sodium.
Cutaneous:
As with other cephalosporins, isolated cases of erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported.

Cephalosporin-Class Adverse Reactions
In addition to the adverse reactions listed above that have been observed in patients treated with cefotaxime, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics: fever, abdominal pain, superinfection, renal dysfunction, toxic nephropathy, haemorrhage, false positive test for urinary glucose, elevated bilirubin, elevated LDH, and pancytopaenia.
Several cephalosporins have been implicated in triggering seizures, paticularly in patients with renal impairment when the dosage was not reduced. If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated

Ceftazidime [1 vial 1gm $9.00]

ADMINISTRATION ROUTES:
IV, IM

ALTERNATIVE NAMES:
Fortum

ICU INDICATIONS:
1. Treatment of infections caused by susceptible organisms (esp Pseudomonas)
2. Empiric treatment of hospital acquired pneumonia

PRESENTATION AND ADMINISTRATION:
IV:
500mg, 1gm and 2gm vials of powder
Add appropriate volume of water for injection to a vial then shake well until all powder is dissolved. Prepare the solutions as follows:

Vial size	500mg	1gm	2gm
Volume of diluent	5ml	10ml	10ml
Approximate concentration	90mg/ml	90mg/ml	170mg/ml

Inject slowly over 3-5 minutes
Store at room temperature
Compatible with:
Normal saline Glucose and sodium chloride Glucose 5%
Hartmanns

IM:
Reconstitute with 0.5% lignocaine adding 1.5ml to a 500mg vial, or 3ml to a 1gm vial. Do not give single doses of more than 1gm via this route.

DOSAGE:
IV:
1-2gm 8hrly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]
<10 0.5-1gm every 24 hours
10-20 1gm every 24 hours
>20-50 1gm every 12 hours
Dose in renal replacement therapy
CAPD 0.5-1gm 24 hourly
HD 0.5-1gm 24-48 hourly
CVVHDF 1gm 12 hourly

DOSAGE IN PAEDIATRICS:
25-50mg/kg 8 hourly

CLINICAL PHARMACOLOGY:
Ceftazidime is a 3rd generation cephalosporin. It has a bactericidal action resulting from inhibition of cell wall synthesis.

A wide range of gram-negative organisms is susceptible to ceftazidime in vitro, including strains resistant to gentamicin and other aminoglycosides. In addition, ceftazidime has been shown to be active against gram-positive organisms (although it is not 1st line for these infections). Ceftazidime has been shown to be active against the following organisms both in vitro and in clinical infections:
Gram-Negative Aerobes:
Citrobacter spp., including Citrobacter freundii and Citrobacter diversus.
Enterobacter spp., including Enterobacter cloacae and Enterobacter aerogenes.
Escherichia coli.
Haemophilus influenzae, including ampicillin-resistant strains.
Klebsiella spp. (including Klebsiella pneumoniae).
Neisseria meningitidis.
Proteus mirabilis.
Proteus vulgaris.
Pseudomonas spp. (including Pseudomonas aeruginosa).
Serratia spp.
Gram-Positive Aerobes:
Staphylococcus aureus, including penicillinase- and non-penicillinase-producing strains.
Streptococcus agalactiae (group B streptococci).
Streptococcus pneumoniae.
Streptococcus pyogenes (group A beta-haemolytic streptococci).
Anaerobes:
Bacteroides spp. (Note:Many strains of Bacteroides fragilis are resistant).
Ceftazidime and the aminoglycosides have been shown to be synergistic in vitro against Pseudomonas aeruginosa and the enterobacteriaceae. Ceftazidime is not active in vitro against methicillin-resistant staphylococci, Streptococcus faecalis and many other enterococci, Listeria monocytogenes, Campylobacter spp., or Clostridium difficile.

CONTRAINDICATIONS:
1. Hypersensivity to cephalosporins

WARNINGS
Anaphylaxis
Cephalosporins are a common cause of anaphylactic reactions and cross reactivity with penicillins may occur
Pseudomembranous colitis
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including cefotaxime, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents.
Risk of seizures in patients with renal failure
Elevated levels of ceftazidime in patients with renal insufficiency can lead to seizures, encephalopathy, coma, asterixis, neuromuscular excitability, and myoclonia (see PRECAUTIONS).

PRECAUTIONS
General
Prescribing ceftazidime in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. It should be recognised that a positive Coombs' test may be due to the drug.
High and prolonged serum ceftazidime concentrations can occur from usual dosages in patients with transient or persistent reduction of urinary output because of renal insufficiency. The total daily dosage should be reduced when ceftazidime is administered to patients with renal insufficiency. Elevated levels of ceftazidime in these patients can lead to seizures, encephalopathy, coma, asterixis, neuromuscular excitability, and myoclonia.
If patients fail to respond to monotherapy, an aminoglycoside or similar agent should be considered.

Laboratory Tests:
No tests additional to usual ICU tests are required

Drug/Laboratory Test Interactions:
None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note.

ADVERSE REACTIONS
Body as a Whole:
Fever, candidiasis (including oral thrush), angioedema and anaphylaxis
Haematological System:
haemolytic anaemia, eosinophilia, positive Coombs test, thrombocytosis, leukopaenia, neutropaenia, agranulocytosis, thrombocytopaenia, and lymphocytosis.
Urogenital System:
increased creatinine
Digestive System:
Diarrhoea, nausea, vomiting, and abdominal pain, slight elevations in one or more of the hepatic enzymes
Nervous System:
Seizures encephalopathy, coma, asterixis, neuromuscular excitability, myoclonia, headache, dizziness, and paraesthesia
Skin:
pruritus, rash, Toxic epidermal necrolysis, Stevens-Johnson syndrome, and erythema multiforme

Cephalosporin-Class Adverse Reactions
In addition to the adverse reactions listed above that have been observed in patients treated with ceftazidime, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics: fever, abdominal pain, superinfection, renal dysfunction, toxic nephropathy, haemorrhage, false positive test for urinary glucose, elevated bilirubin, elevated LDH, and pancytopaenia.
Several cephalosporins have been implicated in triggering seizures, paticularly in patients with renal impairment when the dosage was not reduced. If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated

Ceftriaxone [1 vial 1gm $3.80]

ADMINISTRATION ROUTES:
IV or IM

ALTERNATIVE NAMES:
Rocephin

ICU INDICATIONS:
1. Treatment of infections caused by susceptible organisms
2. Empirical treatment of bacterial meningitis

PRESENTATION AND ADMINISTRATION:
IV
500mg, 1gm and 2gm vials of powder
Add appropriate volume of water for injection to a vial then shake well until all powder is dissolved. Prepare the solutions as follows:

Vial size	250mg	500mg	1gm
Volume of diluent	2.3ml	4.6ml	9.25ml
Approximate concentration	100mg/ml	100mg/ml	100mg/ml

Inject slowly over 3-5 minutes
Store at room temperature
Compatible with:
Normal saline Glucose and sodium chloride Glucose 5%
IM
Reconstitute with 0.5% lignocaine as follows:

Vial size	250mg	500mg	1gm
Volume of diluent	0.8ml	1.6ml	3.25ml
Approximate concentration	250mg/ml	250mg/ml	250mg/ml

DOSAGE:
IV:
1-2gm daily; for bacterial meningitis 4gm daily is required and is often administered as 2gm 12 hrly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
50mg/kg daily
IM:
Note: for treatment of bacterial meningitis where IV access is not obtained use an IM load of 80-100 mg/kg, then 80-100 mg/kg/dose IM (max. 2000 mg/dose) every 24 hours starting 12 hrs after load.

CLINICAL PHARMACOLOGY:
Ceftriaxone is excreted via both biliary and renal excretion. The bactericidal activity of ceftriaxone results from inhibition of cell wall synthesis. Ceftriaxone has a high degree

of stability in the presence of beta lactamases, both penicillinases and cephalosporinases, of gram-negative and gram-positive bacteria.
Ceftriaxone has been shown to be active against most strains of the following microorganisms, both in vitro and in clinical infections:
Aerobic Gram-Negative Microorganisms:
Acinetobacter calcoaceticus
Enterobacter aerogenes
Enterobacter cloacae
Escherichia coli
Haemophilus influenzae (including ampicillin-resistant and beta-lactamase producing strains)
Haemophilus parainfluenzae
Klebsiella oxytoca
Klebsiella pneumoniae
Moraxella catarrhalis (including beta-lactamase producing strains)
Morganella morganii
Neisseria gonorrhoeae (including penicillinase- and nonpenicillinase-producing strains)
Neisseria meningitidis
Proteus mirabilis
Proteus vulgaris
Serratia marcescens
Note:
Many strains of the above organisms that are multiply resistant to other antibiotics, e.g., penicillins, cephalosporins, and aminoglycosides, are susceptible to ceftriaxone.

Aerobic Gram-Positive Microorganisms:
Staphylococcus aureus (including penicillinase-producing strains)
Staphylococcus epidermidis
Streptococcus pneumoniae
Streptococcus pyogenes
Viridans group streptococci
Note:
Methicillin-resistant staphylococci are resistant to cephalosporins, including ceftriaxone. Most strains of Group D streptococci and enterococci, e.g., Enterococcus (Streptococcus) faecalis are resistant.

Anaerobic Microorganisms:
Bacteroides fragilis
Clostridium species
Peptostreptococcus species
Note:
Most strains of Clostridium difficile are resistant.

CONTRAINDICATIONS:
1. Hypersensivity to cephalosporins

WARNINGS
Anaphylaxis
Cephalosporins are a common cause of anaphylactic reactions and cross reactivity with penicillins may occur.

Pseudomembranous colitis
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including cefotaxime, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents.

PRECAUTIONS
General
Prescribing Ceftriaxone in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.
Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. It should be recognised that a positive Coombs' test may be due to the drug.

Laboratory Tests:
No tests additional to usual ICU tests are required

Drug/Laboratory Test Interactions:
None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note.

ADVERSE REACTIONS
Body as a Whole:
serum sickness, diaphoresis and flushing
Haematological System:
Agranulocytosis, leukocytosis, leukopaenia, lymphocytosis, thrombocytopaenia, monocytosis, eosinophilia
Urogenital System:
Elevated creatinine
Digestive System:
Diarrhoea, abdominal pain, nausea or vomiting, increased ALP and bilirubin
Nervous System:
Headache, dizziness
Skin:
Rash

Cephalosporin-Class Adverse Reactions
In addition to the adverse reactions listed above that have been observed in patients treated with ceftriaxone, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics: fever, abdominal pain, superinfection, renal dysfunction, toxic nephropathy, haemorrhage, false positive test for urinary glucose, elevated bilirubin, elevated LDH, and pancytopaenia.
Several cephalosporins have been implicated in triggering seizures, paticularly in patients with renal impairment when the dosage was not reduced. If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated

Cefuroxime [1 vial 1gm $4.04]

ADMINISTRATION ROUTES:
PO, IV or IM

ALTERNATIVE NAMES:
Zinacef, Zinnat

ICU INDICATIONS:
1. Treatment of infections caused by susceptible organisms

PRESENTATION AND ADMINISTRATION:
IV
750mg and 1.5gm vials of powder
Add at least 6ml of water to 750mg vial or 15ml water to 1.5gm vial. Shake gently until all powder is dissolved. Inject slowly over 3-5 minutes
If dose does not equal vial size, prepare as follows to obtain desired dose:

Vial size	Volume of diluent	Final volume	Concentration
750mg	4.5ml	5ml	150mg/ml

Store at room temperature
Compatible with:
Normal saline Glucose and sodium chloride Glucose 5%
Hartmanns
Do NOT mix with sodium bicarbonate; however, if required, can be given into the tubing of a sodium bicarbonate infusion.

IM
Reconstitute with 3ml of 1% lignocaine or 3ml water to make an opaque suspension. Inject into a large muscle mass. Single doses of more than 750mg must not be given at one site.

PO
Zinnat 250mg tablets (white)

DOSAGE:
IV:
750mg-1.5gm 8 hourly

PO:
Pneumonia: 500mg PO twice daily (not appropriate initial therapy in intensive care)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]
<10 750mg - 1.5gm 24 hourly
10-20 750mg – 1.5gm 12 hourly
>20-50 750mg – 1.5gm 8 hourly

Dose in renal replacement therapy

CAPD	750mg - 1.5gm 24 hourly
HD	750mg - 1.5gm 24 hourly
CVVHDF	750mg – 1.5gm 12 hourly

Note: oral cefuroxime should be dosed as in normal renal function

DOSAGE IN PAEDIATRICS:

IV:

Severe infection: 50mg/kg (max 2gm) 12 hrly (1st week of life), 8hrly (2nd week of life), 6 hrly (>2nd week of life)

PO:

10-15mg/kg 12hrly

CLINICAL PHARMACOLOGY:

Cefuroxime is a second generation cephalosporin with in vitro activity against a wide range of gram-positive and gram-negative organisms. The bactericidal action of cefuroxime results from inhibition of cell-wall synthesis.

Cefuroxime is usually active against the following organisms in vitro:

Aerobes, Gram-Positive:

Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pneumoniae, and Streptococcus pyogenes (and other streptococci).

NOTE: Most strains of enterococci, e.g., Enterococcus faecalis (formerly Streptococcus faecalis), are resistant to cefuroxime. Methicillin-resistant staphylococci and Listeria monocytogenes are resistant to cefuroxime.

Aerobes, Gram-Negative:

Citrobacter spp., Enterobacter spp., Escherichia coli, Haemophilus influenzae (including ampicillin-resistant strains), Haemophilus parainfluenzae, Klebsiella spp. (including Klebsiella pneumoniae), Moraxella (Branhamella) catarrhalis (including ampicillin- and cephalothin-resistant strains), Morganella morganii (formerly Proteus morganii), Neisseria gonorrhoeae (including penicillinase- and non-penicillinase-producing strains), Neisseria meningitidis, Proteus mirabilis, Providencia rettgeri (formerly Proteus rettgeri), Salmonella spp., and Shigella spp.

NOTE: Some strains of Morganella morganii, Enterobacter cloacae, and Citrobacter spp. have been shown by in vitro tests to be resistant to cefuroxime and other cephalosporins. Pseudomonas and Campylobacter spp., Acinetobacter calcoaceticus, and most strains of Serratia spp. and Proteus vulgaris are resistant to most first- and second-generation cephalosporins.

Anaerobes:

Gram-positive and gram-negative cocci (including Peptococcus and Peptostreptococcus spp.), gram-positive bacilli (including Clostridium spp.), and gram-negative bacilli (including Bacteroides and Fusobacterium spp.).

NOTE: Clostridium difficile and most strains of Bacteroides fragilis are resistant to cefuroxime.

CONTRAINDICATIONS:

1. Hypersensivity to cephalosporins

WARNINGS
Anaphylaxis
Cephalosporins are a common cause of anaphylactic reactions and cross reactivity with penicillins may occur

Pseudomembranous colitis
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including cefotaxime, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents.

PRECAUTIONS
General
Prescribing Cefuroxime in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.
Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. It should be recognised that a positive Coombs' test may be due to the drug.

Laboratory Tests:
No tests additional to usual ICU tests are required

Drug/Laboratory Test Interactions:
A false-positive reaction for glucose in the urine may occur with copper reduction tests (Benedict's or Fehling's solution or with CLINITEST tablets) but not with enzyme-based tests for glycosuria. As a false-negative result may occur in the ferricyanide test, it is recommended that either the glucose oxidase or hexokinase method be used to determine blood plasma glucose levels in patients receiving Cefuroxime

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note

ADVERSE REACTIONS
Body as a Whole:
Drug fever
Haematological System:
positive Coombs' test, thrombocytopaenia
Urogenital System:
interstitial nephritis
Digestive System:
diarrhoea, nausea, hepatitis, cholestasis
Nervous System:
seizure
Skin:
Thrombophlebitis, rash, Stevens-Johnson syndrome, toxic epidermal necrolysis

Cephalosporin-Class Adverse Reactions
In addition to the adverse reactions listed above that have been observed in patients treated with cefuroxime, the following adverse reactions and altered laboratory tests have been reported for cephalosporin-class antibiotics: fever, abdominal pain, superinfection, renal dysfunction, toxic nephropathy, haemorrhage, false positive test for urinary glucose, elevated bilirubin, elevated LDH, and pancytopaenia.
Several cephalosporins have been implicated in triggering seizures, paticularly in patients with renal impairment when the dosage was not reduced. If seizures associated with drug therapy occur, the drug should be discontinued. Anticonvulsant therapy can be given if clinically indicated

Celiprolol [1 tablet 11 cents]

ADMINISTRATION ROUTES:
PO

ALTERNATIVE NAMES:
Celol, Selectol

ICU INDICATIONS:
1. Hypertension
2. Acute myocardial infarction
3. Secondary prevention in patients with coronary artery disease
4. Angina
5. Rate control

Note: celiprolol may be used with caution in patients with asthma or COPD (see WARNINGS)

PRESENTATION AND ADMINISTRATION:
PO:
Celol 200mg tablets (yellow)
Should be taken on an empty stomach. Absorption is significantly affected by food. Unknown effects with NG feed – consider alternatives.

DOSAGE:
PO:
Initially 200mg daily; increasing to up to 600mg daily

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	150-300mg daily
10-20	Dose as in normal renal function
>20-50	Dose as in normal renal function

Dose in renal replacement therapy

CAPD	150-300mg daily
HD	150-300mg daily
CVVHDF	Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO:
5-10mg/kg daily

CLINICAL PHARMACOLOGY:
Celiprolol is a cardioselective beta-blocker, whose beta-blocking action results from a selective competitive blockade at the level of the beta-1 receptors; it is a partial agonist at beta-2 receptors. The vasodilative effect of Celiprolol probably results in part from its partial agonist properties at the level of the beta-2 receptors. Celiprolol lacks a membrane stabilising effect. It is devoid of any cardiodepressive effect at the doses used in clinical practice. It does not appear to have bronchoconstrictive effect at therapeutic doses.

CONTRAINDICATIONS:

1. Sinus bradycardia,
2. Heart block greater than first degree,
3. Cardiogenic shock,
4. Overt cardiac failure

WARNINGS

Cardiac Failure

Sympathetic stimulation is necessary in supporting circulatory function in congestive heart failure, and beta blockade carries the potential hazard of further depressing myocardial contractility and precipitating more severe failure.

Discontinuation of therapy

Discontinuation of therapy in a patient with coronary artery disease may lead to rebound angina, arrhythmia or myocardial infarction.

Diabetes and Hypoglycaemia

Beta blockers may mask tachycardia occurring with hypoglycaemia.

Thyrotoxicosis

Beta-adrenergic blockade may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism. Abrupt withdrawal of beta blockade might precipitate a thyroid storm.

Asthma

Due to its beta-1 selective blocking and beta-2 agonist properties, celiprolol may be used with caution in asthmatics out of acute episodes and in patients with compensated chronic obstructive pulmonary disease (see CLINICAL PHARMACOLOGY). It may still precipitate bronchospasm in these patients and should be used with caution.

PRECAUTIONS

General

Celiprolol may aggravate peripheral arterial circulatory disorders.

Laboratory Tests:

No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions :

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Beta blockers may exacerbate the rebound hypertension which can follow the withdrawal of clonidine

ADVERSE REACTIONS

Body as a Whole:

Tiredness, Fatigue

Cardiovascular System:

Bradycardia , Cold extremities, Hypotension, Leg pain

Respiratory System:

Wheeziness, Dyspnoea

Digestive System:

Diarrhoea, Nausea

Nervous System:

Dizziness, Vertigo, Light-headedness

Charcoal (Activated) [1 packet 50gm $43.50]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Carbosorb X (does not contain sorbitol), carbosorb XS (contains sorbitol)

ICU INDICATIONS:

1. Single dose activated charcoal is indicated where it is likely that toxin remains in the gastrointestinal tract (i.e. within one hour of ingestion for most agents) and where the potential benefits outweigh the potential risk
2. Multiple dose activated charcoal may be indicated for agents that undergo enterohepatic recirculation and are adsorbed by activated charcoal. Such agents are:

(i) carbamazepine
(ii) dapsone
(iii) phenobarbitone
(iv) quinine
(v) theophylline

PRESENTATION AND ADMINISTRATION:
PO / NG:
Carbosorb XS contains 50gm activated charcoal and 99.8g of sorbitol in 250ml
Carbosorb X contains 50gm activated charcoal in 250ml
Give to the patient in a cup for self administration
Note: there are no data to support the use of activated charcoal in sorbitol or other cathartic over activated charcoal in water (generally, therefore, carbosorb X is preferred)

DOSAGE:
PO:
Single dose: 50gm
Multiple dose: give an initial dose of activated charcoal 50gm and follow with repeated doses of 25gm every 2 hours (check for bowel sounds prior to administration of each dose and cease administration if bowel sounds are absent). Reconsider the indication every 6 hours.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO:
Single dose: children greater than one month 1gm/kg (max 50g)
Multiple dose: give an initial dose of activated charcoal 1gm/kg and follow with repeated doses of 0.5gm/kg every 2 hours (check for bowel sounds prior to administration of each dose and cease administration if bowel sounds are absent). Reconsider the indication every 6 hours.

CLINICAL PHARMACOLOGY:
Carbosorb X (does not contain sorbitol), carbosorb XS (contains sorbitol). Charcoal is an adsorbent. Sorbitol is a cathartic.

Activated charcoal is produced by super-heating of distilled wood pulp. The resulting fine porous particles are suspended in water (or sorbitol). The particles have a very large surface area and readily absorb most ingested toxins in the gastrointestinal tract.

CONTRAINDICATIONS:
1. Decreased level of consciousness without airway protection
2. Bowel obstruction
3. Intoxication due to a substance that is not adsorbed by charcoal (i.e hydrocarbons, alcohols, metals and corrosives)
4. Non-toxic ingestion or sub-toxic dose

Note: if mental status precludes self-administration, activated charcoal should be withheld until the patient is intubated if and when this becomes clinically necessary. Only in very rare circumstances does the risk assessment justify intubation specifically to administer charcoal.

WARNINGS
Do not use activated charcoal if risk assessment suggests the potential for imminent onset of seizures or the potential for a rapid decrease in conscious state.

PRECAUTIONS
General
Activated charcoal may lead to impaired absorption of medications administered via the oral route.

Laboratory Tests:
No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions:
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Activated charcoal may lead to impaired absorption of medications administered via the oral route.

ADVERSE REACTIONS
Respiratory System:
Pulmonary aspiration of charcoal (esp if decreased conscious state or seizures)
Digestive System:
Vomiting, constipation, charcoal bezoar formation, perforation, obstruction

Chloral Hydrate [9 cents per ml]

ADMINISTRATION ROUTES:
PO

ALTERNATIVE NAMES:
Chloral hydrate

ICU INDICATIONS:
1. Paediatric sedation

PRESENTATION AND ADMINISTRATION:
PO:
100mg/ml liquid in 200ml bottle
Note: Section 29 drug (requires specific notification to Director-General of Health)

DOSAGE:
Not used in adults

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	do not use
10-20	10mg/kg PRN 4-6 hrly
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	do not use
HD	do not use
CVVHDF	10mg/kg PRN 4-6 hrly

DOSAGE IN PAEDIATRICS:
PO:
25mg/kg/dose PRN 4-6hrly (do not chart higher regular doses than this; additional stat doses may be given if required)
Often an initial loading dose of 50mg/kg may be needed

CLINICAL PHARMACOLOGY:
The mechanism of action of chloral hydrate is not known, but the CNS depressant effects are believed to be due to its active metabolite trichloroethanol.

CONTRAINDICATIONS:
1. Patients with marked hepatic or renal impairment
2. Patients with severe cardiac disease.
3. The presence of gastritis.
4. Patients with a known hypersensitivity to the drug.

WARNINGS
Chloral hydrate is genotoxic and may be carcinogenic in mice. Chloral hydrate should not be used when less potentially dangerous agents would be effective.

PRECAUTIONS

General

Chloral hydrate has been reported to precipitate attacks of acute intermittent porphyria and should be used with caution in susceptible patients.

Laboratory Tests:

No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:

Chloral hydrate may interfere with copper sulfate tests for glycosuria (suspected glycosuria should be confirmed by a glucose oxidase test when the patient is receiving chloral hydrate), fluorometric tests for urine catecholamines (it is recommended that the medication not be administered for 48 hours preceding the test), or urinary 17-hydroxycorticosteroid determinations.

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Chloral hydrate may cause hypoprothrombinaemic effects in patients taking oral anticoagulants

Administration of chloral hydrate followed by intravenous furosemide may result in sweating, hot flashes, and variable blood pressure including hypertension due to a hypermetabolic state caused by displacement of thyroid hormone from its bound state.

CNS depressants are additive in effect and the dosage should be reduced when combinations of sedatives are given concurrently.

ADVERSE REACTIONS

Central Nervous System:

Excitement, tolerance, addiction, delirium, drowsiness, staggering gait, ataxia, lightheadedness, vertigo, dizziness, nightmares, malaise, mental confusion, and hallucinations.

Haematological:

Leukopaenia and eosinophilia.

Dermatological:

Allergic skin rashes including hives, erythema, eczematoid dermatitis, urticaria, and scarlatiniform exanthems.

Gastrointestinal:

Gastric irritation and occasionally nausea and vomiting, flatulence, diarrhoea, and unpleasant taste.

Miscellaneous:

Headache, hangover, idiosyncratic syndrome, and ketonuria have been reported.

Chlorpromazine [1 vial $2.56]

ADMINISTRATION ROUTES:
PO, IV, IM

ALTERNATIVE NAMES:
Largactil

ICU INDICATIONS:
1. Nausea and vomiting
2. Intractable hiccups
3. Psychosis

PRESENTATION AND ADMINISTRATION:
IV:
50mg/2ml vial
Dilute required dose in 500-1000ml of normal saline to a concentration of no greater than 1mg/ml and administer at 1mg/min in adults or 0.5mg/min in children
Dilute with normal saline only. Do not mix with other medications in the syringe or in IV fluids
Solutions that develop a pink or yellow colouration on exposure to light should be discarded.
Store at room temperature. Protect from light

PO:
10mg, 25mg, 100mg tablets (white or off white)
Note: swallow whole; do not break, crush or chew. Not suitable for nasogastric administration.

DOSAGE:
PO:
Large doses (up to 300mg per day) may be required to treat adults with Schizophrenia; however, such doses are not appropriate in the critically ill. The usual starting dose in the intensive care unit is **10mg 8 hourly**.

IV/IM:
The usual starting dose in the critically ill is **12.5mg IV 8 hourly**. 50mg via continuous infusion over 24hrs may be used in patients with intractable hiccups.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	use a small dose
10-20	dose as in normal renal function
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	dose as in normal renal function
HD	dose as in normal renal function
CVVHDF	dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO:
0.5-2mg/kg 8 hourly

IV/IM:
0.25-1mg/kg 8 hourly

Note: Chlorpromazine should generally not be used in children under 6 months of age except where potentially lifesaving. It should not be used in conditions for which specific children's dosages have not been established.

CLINICAL PHARMACOLOGY:
The precise mechanism whereby the therapeutic effects of chlorpromazine are produced is not known. Chlorpromazine has actions at all levels of the central nervous system as well as on multiple organ systems. Chlorpromazine has strong antiadrenergic and weaker peripheral anticholinergic activity; ganglionic blocking action is relatively slight. It also possesses slight antihistaminic and antiserotonin activity.

CONTRAINDICATIONS:
1. Hypersensitivity to phenothiazines.
2. Depressed conscious state (unless the airway is protected)
3. Hypotension or requiring vasopressor or inotropic support

WARNINGS
The extrapyramidal symptoms which can occur secondary to chlorpromazine may be confused with the CNS signs of an undiagnosed primary disease responsible for the vomiting

PRECAUTIONS
General
Given the likelihood that some patients exposed chronically to antipsychotics will develop tardive dyskinesia, it is advised that all patients in whom chronic use is contemplated be given, if possible, full information about this risk. The decision to inform patients and/or their guardians must obviously take into account the clinical circumstances and the competency of the patient to understand the information provided.
Chlorpromazine should be administered cautiously to persons with cardiovascular, liver or renal disease. There is evidence that patients with a history of hepatic encephalopathy due to cirrhosis have increased sensitivity to the CNS effects of chlorpromazine (i.e., impaired cerebration and abnormal slowing of the EEG).
Because of its CNS depressant effect, chlorpromazine should be used with caution in patients with chronic respiratory disorders such as severe asthma, emphysema, and acute respiratory infections, particularly in children (1-12 years of age).

Laboratory Tests:
No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:
Chlorpromazine may cause false positive urinary pregnancy tests

Pregnancy
Safety for the use of chlorpromazine during pregnancy has not been established. Reproductive studies in rodents have demonstrated potential for embryotoxicity, increased neonatal mortality, and nursing transfer of the drug. Tests in the offspring of the drug-treated rodents demonstrate decreased performance. The possibility of permanent neurological damage cannot be excluded.

Nursing Mothers
There is evidence that chlorpromazine is excreted in the breast milk of nursing mothers. Because of the potential for serious adverse reactions in nursing infants from chlorpromazine, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Paediatric Use
Chlorpromazine should generally not be used in children under 6 months of age except where potentially lifesaving. It should not be used in conditions for which specific children's dosages have not been established.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Chlorpromazine prolongs and intensifies the action of CNS depressants
Chlorpromazine diminishes the effect of oral anticoagulants.
Phenothiazines can produce alpha-adrenergic blockade.
Chlorpromazine may lower the convulsive threshold; dosage adjustments of anticonvulsants may be necessary. Potentiation of anticonvulsant effects does not occur. However, it has been reported that chlorpromazine may interfere with the metabolism of phenytoin and thus precipitate phenytoin toxicity.
Concomitant administration with propranolol results in increased plasma levels of both drugs.

ADVERSE REACTIONS
Body as a whole:
Neuroleptic malignant syndrome
Central nervous system:
Drowsiness, seizures, dystonias, motor restlessness, pseudo-parkinsonism, and tardive dyskinesia
Cardiovascular system:
Hypotension, tachycardia, non-specific T wave changes
Gastrointestinal system:
Jaundice, nausea, constipation, dry mouth
Haematological system:
agranulocytosis, eosinophilia, leukopaenia, haemolytic anaemia, aplastic anaemia, thrombocytopenic purpura, and pancytopaenia

Cilazapril [1 tablet 15 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Inhibace

ICU INDICATIONS:
1. Hypertension
2. Congestive heart failure or left ventricular dysfunction after myocardial infarction
3. Diabetic nephropathy

PRESENTATION AND ADMINISTRATION:
PO:
Inhibace 0.5mg (white), 2.5mg (pink), 5mg (reddish-brown)

DOSAGE:
PO:
0.5-5mg daily

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	Dose as in normal renal function
10-40	Initially 0.5mg once daily (usual maximum 2.5mg daily)
>40-50	1mg once daily

Dose in renal replacement therapy

CAPD	0.25-0.5mg once daily
HD	0.25-0.5mg once daily
CVVHDF	Initially 0.5mg once daily (usual maximum 2.5mg daily)

Note: Recent clinical observations have shown an association of hypersensitivity-like (anaphylactoid) reactions during haemodialysis with high-flux dialysis membranes (e.g., AN69) in patients receiving ACE inhibitors.

DOSAGE IN PAEDIATRICS:
PO:
0.02-0.1mg/kg daily

CLINICAL PHARMACOLOGY:
Cilazapril is an angiotensin I-converting enzyme (ACE) inhibitor

CONTRAINDICATIONS:
1. Hypersensitivity to cilazapril or any other angiotensin-converting enzyme inhibitor (e.g. a patient who has experienced angioedema during therapy with any other ACE inhibitor).
2. Cardiogenic shock

WARNINGS

Anaphylactoid and Possibly Related Reactions

Cilazapril can cause anaphylactoid reactions

Head and Neck Angioedema

Angioedema involving the extremities, face, lips, mucous membranes, tongue, glottis or larynx has been seen in patients treated with ACE inhibitors, including cilazapril. If angioedema involves the tongue, glottis or larynx, airway obstruction may occur and be fatal. Swelling confined to the face, mucous membranes of the mouth, lips and extremities has usually resolved with discontinuation of cilazapril; some cases required medical therapy.

Intestinal Angioedema

Intestinal angioedema has been reported in patients treated with ACE inhibitors. These patients presented with abdominal pain (with or without nausea or vomiting); in some cases there was no prior history of facial angioedema and C-1 esterase levels were normal.

Neutropaenia/Agranulocytosis

Neutropaenia (<1000/mm3) with myeloid hypoplasia has resulted from use of cilazapril.

Hypotension in Heart Failure Patients

Caution should be observed when initiating therapy in patients with heart failure. Patients with heart failure given cilazapril commonly have some reduction in blood pressure. In patients with symptomatic hypotension this may require temporarily reducing the dose of cilazapril, or diuretic, or both, and volume repletion

Hepatic Failure

Rarely, ACE inhibitors have been associated with a syndrome that starts with cholestatic jaundice and progresses to fulminant hepatic necrosis and (sometimes) death. The mechanism of this syndrome is not understood. Patients receiving ACE inhibitors who develop jaundice or marked elevations of hepatic enzymes should discontinue the ACE inhibitor.

PRECAUTIONS

General

Some patients with renal disease, particularly those with severe renal artery stenosis, have developed increases in serum creatinine after reduction of blood pressure with cilazapril. Cilazapril dosage reduction and/or discontinuation of diuretic may be required. Elevations in serum potassium have been observed in some patients treated with ACE inhibitors, including cilazapril.

Presumably due to the inhibition of the degradation of endogenous bradykinin, persistent nonproductive cough has been reported with all ACE inhibitors, always resolving after discontinuation of therapy. ACE inhibitor-induced cough should be considered in the differential diagnosis of cough.

Laboratory Tests:

No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions :

None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Increased serum lithium levels and symptoms of lithium toxicity have been reported in patients receiving concomitant lithium and ACE inhibitor therapy.
The risk of hypotension increases if cilazapril is coadministered with other antihypertensives

ADVERSE REACTIONS:
Body as a Whole:
Gynaecomastia, anaphylactoid reactions, angioedema
Cardiovascular:
Cardiac arrest, cerebrovascular accident / insufficiency, rhythm disturbances, orthostatic hypotension, syncope
Dermatological:
Bullous pemphigus, erythema multiforme (Stevens Johnson syndrome), exfoliatice dermatitis
Gastrointestinal:
Pancreatitis, glossitis, dyspepsia, jaundice, hepatitis, rare causes of hepatic necrosis, cholestasis
Haematological:
Anaemia (including cases of haemolytic anaemia), thrombocytopaenia, neutropaenia
Metabolic:
Hyponatraemia
Musculoskeletal:
Myalgia, myasthenia
Nervous system:
Ataxia, confusion, depression, nervousness, somnolence
Respiratory system;
Bronchospasm, eosinophilic pneumonia, angioedema
Urogenital system;
Renal failure, proteinuria

Ciprofloxacin [1 vial $4.10, 1 tablet 11 cents]

ADMINISTRATION ROUTES:
IV, PO, NG

ALTERNATIVE NAMES:
Ciproxin

ICU INDICATIONS:
1. Treatment of infections caused by susceptible organisms

PRESENTATION AND ADMINISTRATION:
IV:
200mg / 100ml (solution in normal saline)
Store at room temperature
Administer required dose over not less than 60 minutes. Solution is usually infused undiluted but can be mixed with other compatible IV fluids.
Compatible with the following IV fluids;
Normal saline 5% Dextrose 10% Dextrose Hartmann's
Glucose and sodium chloride
Do not mix with any infusion solution or medicines.

PO/NG:
250mg, 500mg and 750mg tablets
250mg/5ml and 500mg/100ml suspension
Tablets can be crushed and dispersed in water for NG administration (check brand with pharmacist)

DOSAGE:
IV:
400mg 8-12hrly

PO:
500mg 12hrly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	50% of normal dose
10-20	50% of normal dose
>20-50	Dose as in normal renal function

Dose in renal replacement therapy

CAPD	Oral: 250mg-500mg every 12hrs; IV: 100mg every 12 hrs
HD	Oral: 250mg-500mg every 12hrs; IV 100-200mg every 12 hrs
CVVHDF	Oral: 500mg-750mg every 12hrs; IV 200-400mg every 12 hrs

DOSAGE IN PAEDIATRICS:
IV:
4-7mg/kg 12 hourly

PO:
5-10mg/kg 12 hourly

Note: Ciprofloxacin is indicated in paediatric patients for inhalational anthrax (postexposure). The risk-benefit assessment indicates that administration of ciprofloxacin to paediatric patients is appropriate in this setting. Although effective in clinical trials, ciprofloxacin is not a drug of first choice in the paediatric population for other indications due to an increased incidence of adverse events compared to other agents.

CLINICAL PHARMACOLOGY:
Ciprofloxacin is a quinolone antibiotic which has a bactericidal action through inhibition of the enzymes topoisomerase II (DNA gyrase) and topoisomerase IV, which are required for bacterial DNA replication, transcription, repair, and recombination.

Ciprofloxacin has in vitro activity against a wide range of gram-negative and gram-positive microorganisms and has been shown to be active against most strains of the following microorganisms, both in vitro and in clinical infections.
Aerobic Gram-Positive Microorganisms
Enterococcus faecalis (many strains are only moderately susceptible),
Staphylococcus aureus (methicillin-susceptible strains only),
Staphylococcus epidermidis (methicillin-susceptible strains only),
Staphylococcus saprophyticus,
Streptococcus pneumoniae (penicillin-susceptible strains only),
Streptococcus pyogenes.

Aerobic Gram-Negative Microorganisms
Campylobacter jejuni,
Citrobacter diversus, Citrobacter freundii,
Enterobacter cloacae,
Escherichia coli,
Haemophilus influenzae,
Haemophilus parainfluenzae,
Klebsiella pneumoniae,
Moraxella catarrhalis,
Morganella morganii,
Neisseria gonorrhoeae,
Proteus mirabilis, Proteus vulgaris,
Providencia rettgeri, Providencia stuartii,
Pseudomonas aeruginosa,
Salmonella typhi,
Serratia marcescens,
Shigella boydii, Shigella dysenteriae, Shigella flexneri, Shigella sonnei.

Most strains of Burkholderia cepacia and some strains of Stenotrophomonas maltophilia are resistant to ciprofloxacin as are most anaerobic bacteria, including Bacteroides fragilis and Clostridium difficile.

CONTRAINDICATIONS:
1. Hypersensitivity to ciprofloxacin or any member of the quinolone class of antimicrobials

WARNINGS

Central Nervous System Disorders

Convulsions, increased intracranial pressure, and toxic psychosis have been reported in patients receiving quinolones, including ciprofloxacin.

Hypersensitivity Reactions

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions, some following the first dose, have been reported in patients receiving quinolone therapy. Severe hypersensitivity reactions characterised by rash, fever, eosinophilia, jaundice, and hepatic necrosis with fatal outcome have also been rarely reported in patients receiving ciprofloxacin along with other drugs.

Pseudomembranous Colitis

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including ciprofloxacin, and may range in severity from mild to life-threatening.

Peripheral Neuropathy

Rare cases of sensory or sensorimotor axonal polyneuropathy affecting small and/or large axons resulting in paraesthesias, hypoesthesias, dysesthesias and weakness have been reported in patients receiving quinolones, including ciprofloxacin.

Tendon Effects

Ruptures of the shoulder, hand, achilles tendon or other tendons that required surgical repair or resulted in prolonged disability have been reported in patients receiving quinolones, including ciprofloxacin.

PRECAUTIONS

General

Prescribing ciprofloxacin tablets and oral suspension in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Laboratory Tests:

No tests in addition to usual ICU tests are indicated

Drug/Laboratory Test Interactions:

None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU

SERIOUS AND FATAL REACTIONS HAVE BEEN REPORTED IN PATIENTS RECEIVING CONCURRENT ADMINISTRATION OF CIPROFLOXACIN AND THEOPHYLLINE. These reactions have included cardiac arrest, seizure, status epilepticus, and respiratory failure. Although similar serious adverse effects have been reported in patients receiving theophylline alone, the possibility that these reactions may be potentiated by ciprofloxacin cannot be eliminated. If concomitant use cannot be avoided, serum levels of theophylline should be monitored and dosage adjustments made as appropriate.

Concurrent administration of a quinolone, including ciprofloxacin, with oral multivalent cation-containing products such as magnesium/aluminum antacids, sucralfate, didanosine chewable/buffered tablets or paediatric powder, other highly buffered drugs, or products containing calcium, iron, or zinc may substantially decrease its absorption, resulting in serum and urine levels considerably lower than desired.
Altered serum levels of phenytoin (increased and decreased) have been reported in patients receiving concomitant ciprofloxacin.
The concomitant administration of ciprofloxacin with the sulfonylurea glyburide has, on rare occasions, resulted in severe hypoglycaemia.
Some quinolones, including ciprofloxacin, have been associated with transient elevations in serum creatinine in patients receiving cyclosporin concomitantly.
Quinolones, including ciprofloxacin, have been reported to enhance the effects of the oral anticoagulant warfarin or its derivatives.
Renal tubular transport of methotrexate may be inhibited by concomitant administration of ciprofloxacin potentially leading to increased plasma levels of methotrexate. This might increase risk of methotrexate associated toxic reactions. Therefore, patients under methotrexate therapy should be carefully monitored when concomitant ciprofloxacin therapy is indicated.
Non-steroidal antiinflammatory drugs (but not aspirin) in combination of very high doses of quinolones have been shown to provoke convulsions in preclinical studies.

ADVERSE REACTIONS
Body as a Whole:
Headache, abdominal pain/discomfort, foot pain, pain, pain in extremities, injection site reaction
Cardiovascular System:
Palpitation, atrial flutter, ventricular ectopy, syncope, hypertension, angina pectoris, myocardial infarction, cardiopulmonary arrest, cerebral thrombosis, phlebitis, tachycardia, migraine, hypotension.
Respiratory:
Dyspnea, epistaxis, laryngeal or pulmonary edema, hiccough, haemoptysis, bronchospasm, pulmonary embolism.
Central Nervous System:
Restlessness, dizziness, lightheadedness, insomnia, nightmares, hallucinations, manic reaction, irritability, tremor, ataxia, convulsive seizures, lethargy, drowsiness, weakness, malaise, anorexia, phobia, depersonalization, depression, paraesthesia, abnormal gait, grand mal convulsion.
Digestive System:
Painful oral mucosa, oral candidiasis, dysphagia, intestinal perforation, gastrointestinal bleeding, cholestatic jaundice, hepatitis.
Haematological System:
Lymphadenopathy, petechia.
Renal/Urogenital:
Interstitial nephritis, nephritis, renal failure, polyuria, urinary retention, urethral bleeding, vaginitis, acidosis, breast pain.
Skin:
Allergic reaction, pruritus, urticaria, photosensitivity, flushing, fever, chills, angioedema, edema of the face, neck, lips, conjunctivae or hands, cutaneous candidiasis, hyperpigmentation, erythema nodosum, sweating.

Citalopram [1 tablet 20mg 5 cents]

ADMINISTRATION ROUTES:
PO

ALTERNATIVE NAMES:
Celapram, Cipramil

ICU INDICATIONS:
1. Treatment of depression

Note: citalopram is usually used in ICU patients with a pre-existing diagnosis of depression who are already taking the medication at admission. Anti-depressants are rarely, if ever, indicated in patients who become depressed whilst in ICU. In these patients, depression is usually situational and the risks of medications outweigh the benefits. It is often appropriate to withhold Citalopram in the critically ill (see WARNINGS)

PRESENTATION AND ADMINISTRATION:
PO:
Celapram 20mg tablets (white), Cipramil 20mg tablets (white), Citalopram 20mg tablets (white)

DOSAGE:
PO:
Initially 20mg daily (10mg in the elderly); increasing to maximum of 60mg daily (40mg in the elderly' 30mg in hepatic impairment)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	Dose as in normal renal function (use with caution)
10-20	Dose as in normal renal function
>20-50	Dose as in normal renal function

Dose in renal replacement therapy

CAPD	Dose as in normal renal function (use with caution)
HD	Dose as in normal renal function (use with caution)
CVVHDF	Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO:
0.4mg/kg daily (see PRECAUTIONS: *Paediatric use*)

CLINICAL PHARMACOLOGY:
Citalopram is an orally administered selective serotonin reuptake inhibitor (SSRI).

CONTRAINDICATIONS:
1. Concomitant use in patients taking monoamine oxidase inhibitors (MAOI's)
2. Hypersensitivity to citalopram

WARNINGS
Use in Patients With Concomitant Illness

Clinical experience with Citalopram in patients with severe systemic illnesses is limited. Caution is advisable in using Citalopram in patients with diseases or conditions that produce altered metabolism or haemodynamic responses.

Clinical Worsening and Suicide Risk

Patients with major depressive disorder (MDD), both adult and paediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs

PRECAUTIONS

General

Abnormal Bleeding

Epidemiological studies, both of the case-control and cohort design, have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.

Hyponatraemia

Cases of hyponatraemia and SIADH (syndrome of inappropriate antidiuretic hormone secretion) have been reported. All patients with these events have recovered with discontinuation of citalopram and/or medical intervention.

Seizures

Although anticonvulsant effects of citalopram have been observed in animal studies, citalopram has not been systematically evaluated in patients with a seizure disorder. Citalopram should be introduced with care in patients with a history of seizure disorder.

Laboratory Tests:

No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions:

None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU

CNS Drugs:

Given the primary CNS effects of citalopram, caution should be used when it is taken in combination with other centrally acting drugs.

Monoamine Oxidase Inhibitors (MAOI's):

See CONTRAINDICATIONS

Drugs That Interfere With Haemostasis (NSAIDs, aspirin, warfarin, etc.):

Serotonin release by platelets plays an important role in haemostasis. Epidemiological studies of the case-control and cohort design that have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding have also shown that concurrent use of an NSAID or aspirin potentiated the risk of bleeding. Thus, patients should be cautioned about the use of such drugs concurrently with citalopram.

ADVERSE REACTIONS

Body as a Whole:

Increased sweating, serotonin syndrome

Central Nervous System:

Insomnia, somnolence, agitation, tremor

Digestive System:

Nausea, dry mouth, vomiting, dyspepsia

Clarithromycin [1 vial $30]

ADMINISTRATION ROUTES:
IV, PO

ALTERNATIVE NAMES:
Klacid, Klamycin, Clarac

ICU INDICATIONS:
1. Treatment of infections caused by susceptible organisms

PRESENTATION AND ADMINISTRATION:
PO:
Clarac 250mg tablets (yellow), Klacid 250mg tablets (yellow), Klamycin 250mg tablets (yellow), Klacid suspension 125mg/5ml

IV:
For initial reconstitution add 10ml of Water for Injection ONLY to a 500mg vial. Dilute the reconstituted solution (500mg/10ml) in at least 250ml of compatible IV fluid. Infuse over 60 minutes.
The initial reconstituted solution is stable for 24 hours when stored at room temperature or refrigerated. The final diluted solution should be used within 6 hours when stored at room temperature or with 24 hours if refrigerated.
Compatible with the following IV fluids:
Normal saline 5% Dextrose Glucose and sodium chloride
Hartmann's
Do not mix with other medications or IV fluids

DOSAGE:
PO:
250mg-500mg 12hrly

IV:
500mg 12hrly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	Oral: 250mg every 12 hours; IV: 250mg every 12 hours
10-20	Oral: 250mg every 12 hrs; IV: 250-500mg every 12 hrs
>20-50	Dose as in normal renal function

Dose in renal replacement therapy

CAPD	Oral: 250mg every 12-24 hours; IV: 250mg every 12 hours
HD	Oral: 250mg every 12-24 hours; IV: 250mg every 12 hours
CVVHDF	Oral: 250mg every 12 hrs; IV: 250-500mg every 12 hrs

DOSAGE IN PAEDIATRICS:
PO/IV:
7.5-15mg/kg 12 hourly

CLINICAL PHARMACOLOGY:
Clarithromycin is a semi-synthetic macrolide antibiotic. Clarithromycin exerts its antibacterial action by binding to the 50S ribosomal subunit of susceptible microorganisms resulting in inhibition of protein synthesis.

Clarithromycin has been shown to be active against most strains of the following microorganisms both in vitro and in clinical infections:
Aerobic Gram-Positive Microorganisms:
Staphylococcus aureus
Streptococcus pneumoniae
Streptococcus pyogenes

Aerobic Gram-Negative Microorganisms:
Haemophilus influenzae
Haemophilus parainfluenzae
Moraxella catarrhalis

Other Microorganisms:
Mycoplasma pneumoniae
Chlamydia pneumoniae (TWAR)
Mycobacterium avium complex (MAC) consisting of:
Mycobacterium avium
Mycobacterium intracellulare

CONTRAINDICATIONS:
1. Hypersensitivity to clarithromycin

WARNINGS
Pseudomembranous colitis
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including clarithromycin, and may range in severity from mild to life threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents.

PRECAUTIONS
General
Prescribing clarithromycin in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Laboratory Tests:
No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions:
None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Clarithromycin use in patients who are receiving theophylline may be associated with an increase of serum theophylline concentrations. Monitoring of serum theophylline concentrations should be considered for patients receiving high doses of theophylline or with baseline concentrations in the upper therapeutic range.

Spontaneous reports in the postmarketing period suggest that concomitant administration of clarithromycin and oral anticoagulants may potentiate the effects of warfarin.

Elevated digoxin serum concentrations in patients receiving clarithromycin and digoxin concomitantly have also been reported in postmarketing surveillance. Some patients have shown clinical signs consistent with digoxin toxicity, including potentially fatal arrhythmias. Serum digoxin concentrations should be carefully monitored while patients are receiving digoxin and clarithromycin simultaneously.

There have been postmarketing reports of colchicine toxicity with concomitant use of clarithromycin and colchicine, especially in the elderly, some of which occurred in patients with renal insufficiency.

As with other macrolides, clarithromycin has been reported to increase concentrations of HMG-CoA reductase inhibitors (e.g., lovastatin and simvastatin). Rare reports of rhabdomyolysis have been reported in patients taking these drugs concomitantly.
Erythromycin has been reported to increase the systemic exposure (AUC) of sildenafil. A similar interaction may occur with clarithromycin; reduction of sildenafil dosage should be considered.

ADVERSE REACTIONS
Body as a whole:
Anaphylaxis
Gastrointestinal system:
Diarrhoea, nausea, abnormal taste, dyspepsia, abdominal pain/discomfort, cholestasis, hepatitis
Haematological system:
Thrombocytopaenia, leukopaenia, neutropaenia

Clindamycin [1 vial $16.00, 1 tablet 150mg 62 cents]

ADMINISTRATION ROUTES:
IV, PO, NG

ALTERNATIVE NAMES:
Dalacin, Clinda

ICU INDICATIONS:
1. Treatment of infections caused by susceptible organisms (particularly Streptococcal or Staphylococcal toxic shock syndrome)

PRESENTATION AND ADMINISTRATION:
IV:
Vial of 600mg in 4 ml solution
Add required dose to compatible IV fluid as shown in the table and administer over the stated time:

Dose	Volume of IV fluid	Time for administration
300mg	50ml	10 minutes
600mg	50ml	20 minutes
900mg	100ml	30 minutes
1200mg	100ml	40 minutes

Infusion rate not to exceed 30mg/min
Administration of more than 1200mg in one hour is not recommended
Stable at room temperature for 24 hours after dilution in compatible IV fluid
Compatible with the following IV fluids:
Normal saline 5% and 10% dextrose Glucose and Sodium chloride Hartmanns

IM:
Not used by this route in ICU patients

PO:
Dalacin C 150mg tablets
To avoid oesophageal irritation, should be taken with a full glass of water

DOSAGE:
IV:
600mg 6 hourly

PO:
300-450mg 6 hourly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
10-20mg/kg 8 hourly

PO:
5-8mg/kg 8 hourly

CLINICAL PHARMACOLOGY:
Clindamycin inhibits bacterial protein synthesis by binding to the 50S subunit of the ribosome. It has activity against Gram-positive aerobes and anaerobes as well as the Gram-negative anaerobes. Clindamycin is bacteriostatic. Clindamycin has been shown to be active against most of the isolates of the following microorganisms, both in vitro and in clinical infections
Gram-Positive Aerobes
Staphylococcus aureus (methicillin-susceptible strains)
Streptococcus pneumoniae (penicillin-susceptible strains)
Streptococcus pyogenes

Anaerobes
Prevotella melaninogenica
Fusobacterium necrophorum
Fusobacterium nucleatum
Peptostreptococcus anaerobius
Clostridium perfringens

CONTRAINDICATIONS:
1. Hypersensitivity to preparations containing clindamycin or lincomycin.

WARNINGS
Anaphylaxis
Clindamycin may cause serious allergic reactions including anaphylaxis

Pseudomembranous colitis
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including clindamycin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents. Because clindamycin therapy has been associated with severe colitis which may end fatally, it should be reserved for serious infections where less toxic antimicrobial agents are inappropriate

Usage in Meningitis:
Since clindamycin does not diffuse adequately into the cerebrospinal fluid, the drug should not be used in the treatment of meningitis.

PRECAUTIONS
General
Prescribing clindamycin in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Laboratory Tests:
No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:
None noted

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Clindamycin has been shown to have neuromuscular blocking properties that may enhance the action of other neuromuscular blocking agents. Therefore, it should be used with caution in patients receiving such agents.

Antagonism has been demonstrated between clindamycin and erythromycin in vitro. Because of possible clinical significance, the two drugs should not be administered concurrently.

Clindamycin

ADVERSE REACTIONS

Body as a whole:

Anaphylaxis

Gastrointestinal system:

Metallic taste, jaundice and abnormalities in liver function tests, oesophageal irritation, diarrhoea

Haematological system:

Transient neutropaenia (leukopaenia), eosinophilia, agranulocytosis and thrombocytopaenia

Cardiovascular system:

Rare instances of cardiopulmonary arrest and hypotension have been reported following too rapid intravenous administration

Clonazepam [1 vial $3.80, 1 tablet 7 cents]

ADMINISTRATION ROUTES:
IV, IM, PO

ALTERNATIVE NAMES:
Rivotril, Paxam

ICU INDICATIONS:
1. Treatment of seizures / status epilepticus

PRESENTATION AND ADMINISTRATION:
IV:
Direct IV injection is the preferred route of administration. Immediately before use, mix the clonazepam with contents of the diluent vial. Concentration is 1mg/2ml. Administer at a rate not exceeding 0.5ml/min of prepared solution.
Can be given by IV infusion by mixing 1 vial in at least 85ml of compatible IV fluid and infusing slowly over 3-4 hours.
Compatible with the following IV fluids;
Normal saline Glucose and sodium chloride 5% Dextrose
10% Dextrose

IM:
Efficacy by IM route has not been demonstrated. May be given by this route only in exceptional cases or if IV administration is not feasible. Immediately before use, mix the clonazepam solution thoroughly with contents of the diluent vial. Concentration is 1mg/2ml

PO:
Paxam 0.5mg tablets (peach), 2mg tablet (white)
Rivotril drops 2.5mg/ml

DOSAGE:
IV:
For status epilepticus 1mg IV; total maximum dose 10mg

PO:
0.5mg 12hrly; slowly increasing to up to 2mg 6 hrly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
For status epilepticus dosage NOT dosed per kg:
Neonate 0.25mg (if ventilated)
Child 0.5mg

PO:
0.01mg/kg (max 0.5mg) 12 hourly; increasing slowly to a maximum of 0.05mg/kg (max 2mg) 6-12 hrly

CLINICAL PHARMACOLOGY:
Clonazepam is a benzodiazepine. The precise mechanism by which clonazepam exerts its antiseizure effect is unknown, although it is believed to be related to its ability to enhance the activity of gamma aminobutyric acid (GABA), the major inhibitory neurotransmitter in the central nervous system. Clonazepam is rapidly and completely absorbed after oral administration. The absolute bioavailability of clonazepam is about 90%. Maximum plasma concentrations of clonazepam are reached within 1-4 hours after oral administration.

CONTRAINDICATIONS:
1. Hypersensitivity to benzodiazepines

WARNINGS
Withdrawal Symptoms
Withdrawal symptoms of the barbiturate type have occurred after the discontinuation of benzodiazepines including clonazepam

PRECAUTIONS
General
Worsening of Seizures
When used in patients in whom several different types of seizure disorders coexist, clonazepam may increase the incidence or precipitate the onset of generalized tonic-clonic seizures (grand mal). This may require the addition of appropriate anticonvulsants or an increase in their dosages.
Hypersalivation
Clonazepam may produce an increase in salivation. This should be considered before giving the drug to patients who have difficulty handling secretions.

Laboratory Tests:
No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:
None noted

IMPORTANT DRUG INTERACTIONS FOR THE ICU
The CNS-depressant action of the benzodiazepine class of drugs may be potentiated by alcohol, narcotics, barbiturates, nonbarbiturate hypnotics, antianxiety agents, the phenothiazines, thioxanthene and butyrophenone classes of antipsychotic agents, monoamine oxidase inhibitors and the tricyclic antidepressants, and by other anticonvulsant drugs.

ADVERSE REACTIONS
Neurologic:
Abnormal eye movements, aphonia, choreiform movements, coma, diplopia, dysarthria, dysdiadochokinesis, 'glassy-eyed' appearance, headache, hypotonia, nystagmus, respiratory depression, slurred speech, tremor, vertigo.

Psychiatric:
Confusion, depression, amnesia, hallucinations, hysteria, increased libido, insomnia, psychosis, suicidal attempt (the behavior effects are more likely to occur in patients with a history of psychiatric disturbances). The following paradoxical reactions have been observed: Excitability, irritability, aggressive behavior, agitation, nervousness, hostility, anxiety, sleep disturbances, nightmares and vivid dreams.
Respiratory:
Chest congestion, rhinorrhea, shortness of breath, hypersecretion in upper respiratory passages.
Cardiovascular:
Palpitations.
Dermatologic:
Hair loss, hirsutism, skin rash, ankle and facial edema.
Gastrointestinal:
Anorexia, coated tongue, constipation, diarrhoea, dry mouth, encopresis, gastritis, increased appetite, nausea, sore gums.
Genitourinary:
Dysuria, enuresis, nocturia, urinary retention.
Musculoskeletal:
Muscle weakness, pains.
Miscellaneous:
Dehydration, general deterioration, fever, lymphadenopathy, weight loss or gain.
Hematopoietic:
Anaemia, leukopaenia, thrombocytopaenia, eosinophilia.
Hepatic:
Hepatomegaly, transient elevations of serum transaminases and alkaline phosphatase.

Clonidine [1 vial $3.21, patch 100mcg $5.82]

ADMINISTRATION ROUTES:
IV, IM, PO, transdermal

ALTERNATIVE NAMES:
Catapres, Dixarit

ICU INDICATIONS:
1. Agitated delirium
2. Analgesia
3. Hypertension

PRESENTATION AND ADMINISTRATION:
IV:
Catapress injection 150mcg in 1ml vial.
Dilute with 10ml of normal saline and give by slow injection over 5-10 minutes
Compatible with normal saline only
Dilute immediately before use and discard any unused solution after opening
Store at room temperature

IM:
Administer neat (not preferred route of administration in ICU)

PO:
Dixarit 25mcg tablets (blue)
Catapress 150mcg tablets (white)

Transdermal:
Catapress TTS-1 (0.1mg/24hrs), catapress TTS-2 (0.2mg/24hrs), catapress TTS-3 (0.3mg/24hrs)
Apply to an area of hairless skin on the upper arm or chest. Use a new site for each patch. One patch lasts for a week.

DOSAGE:
IV:
15mcg IV PRN up to maximum of 150mcg or more if tolerated

PO:
75mcg daily increased as required to up to 900mcg/day.
Note: rarely indicated by this route in ICU patients.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO / IV:
1-5mcg/kg/dose up to 8 hourly
see PRECAUTIONS *Paediatric use*

CLINICAL PHARMACOLOGY:
Clonidine is a centrally acting alpha-2 agonist.

CONTRAINDICATIONS:
1. Hypersensitivity to clonidine.
2. Bradycardia

WARNINGS
Hypotension
Because severe hypotension may follow the administration of clonidine, it should be used with caution in all patients. It is not recommended in most patients with severe cardiovascular disease or in those who are otherwise haemodynamically unstable. The benefit of its administration in these patients should be carefully balanced against the potential risks resulting from hypotension.

PRECAUTIONS
General
Withdrawal of clonidine may lead to rebound hypertension. If this occurs, clonidine should be reinstituted and withdrawn more slowly.

Laboratory Tests:
No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:
None noted

IMPORTANT DRUG INTERACTIONS FOR THE ICU
If a patient receiving clonidine is also taking tricyclic antidepressants, the effect of clonidine may be reduced, thus necessitating an increase in dosage. Clonidine may enhance the CNS-depressive effects of alcohol, barbiturates or other sedatives.

ADVERSE REACTIONS
Nervous system:
Excessive sedation, confusion, hallucinations
Cardiovascular system:
Hypotension, bradycardia, heart block
Dermatological
Rash, local skin reaction (transdermal)
Gastrointestinal:
Constipation

Clopidogrel [1 tablet 18 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Plavix

ICU INDICATIONS:
1. Treatment of acute coronary syndromes (especially post angioplasty when stents are deployed)
2. Prophylaxis of vascular ischaemic events (mainly in patients with coronary stents)

PRESENTATION AND ADMINISTRATION:
PO:
Apo-clopidogrel 75mg tablets (reddish brown)
Plavix 75mg tablets (pink)

DOSAGE:
PO/NG:
300mg loading dose followed by 75mg daily
Plavix brand clopidogrel can be crushed, mixed with water and administered via a nasogastric tube.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO:
1.5mg/kg daily
See PRECAUTIONS *Paediatric Use*

CLINICAL PHARMACOLOGY:
Clopidogrel is a platelet aggregation inhibitor. It selectively inhibits the binding of adenosine diphosphate (ADP) to its platelet receptor and the subsequent ADP-mediated activation of the glycoprotein GPIIb/IIIa complex, thereby inhibiting platelet aggregation.

CONTRAINDICATIONS:
1. Hypersensitivity to clopidogrel
2. Active bleeding

WARNINGS
Thrombotic Thrombocytopenic Purpura (TTP)
TTP has been reported rarely following use of clopidogrel bisulfate, sometimes after a short exposure (<2 weeks). TTP is a serious condition that can be fatal and requires urgent treatment including plasmapheresis (plasma exchange). It is characterised by thrombocytopaenia, microangiopathic haemolytic anaemia (schistocytes [fragmented RBCs] seen on peripheral smear), neurological findings, renal dysfunction, and fever

PRECAUTIONS

General

Clopidogrel bisulfate prolongs the bleeding time and therefore should be used with caution in patients who may be at risk of increased bleeding from trauma, surgery, or other pathological conditions (particularly gastrointestinal and intraocular). If a patient is to undergo elective surgery and an antiplatelet effect is not desired, clopidogrel bisulfate should be discontinued 5 days prior to surgery.

In patients with recent TIA or stroke who are at high risk for recurrent ischemic events, the combination of aspirin and clopidogrel has not been shown to be more effective than clopidogrel alone, but the combination has been shown to increase major bleeding.

In CAPRIE, clopidogrel bisulfate was associated with a rate of gastrointestinal bleeding of 2.0% vs 2.7% on aspirin. In CURE, the incidence of major gastrointestinal bleeding was 1.3% vs 0.7% (clopidogrel bisulfate + aspirin versus placebo + aspirin, respectively). Clopidogrel bisulfate should be used with caution in patients who have lesions with a propensity to bleed (such as ulcers).

Laboratory Tests:

No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:

None noted

IMPORTANT DRUG INTERACTIONS FOR THE ICU

The risk of bleeding increases when clopidogrel is combined with other anticoagulants. Omeprazole and other PPIs decrease the antiplatelet effect of clopidogrel. It may be more appropriate to use Ranitidine as ulcer prophylaxis in patients on clopidogrel. If clopidogrel is used concomitantly with a PPI the dosages should be separated by 12 hours.

ADVERSE REACTIONS

Body as a Whole:

Bleeding, anaphylaxis, angioedema, serum sickness, fatigue

Haematological:

TTP, leucopenia, eosinophilia

Gastrointestinal System:

Pancreatitis, stomatitis, colitis

Respiratory System:

Interstitial pneumonitis, bronchospasm

Skin:

Rash

Clozapine [1 tablet 27 cents]

ADMINISTRATION ROUTES:
PO

ALTERNATIVE NAMES:
Clopine, Clozaril

ICU INDICATIONS:
1. Treatment of Schizophrenia in patients intolerant or unresponsive to at least 2 classic antipsychotics

Note: Clozapine should rarely, if ever, be commenced in patients in the Intensive Care Unit. Any patient who is taking clozapine who is admitted to the Intensive Care Unit for any reason should be discussed with Psychiatry. Clozapine can only be prescribed by a Psychiatrist or a Psychiatry Registrar (this is a Legal Requirement)

PRESENTATION AND ADMINISTRATION:
PO:
Clopine 25mg, 50mg, 100mg and 200mg tablets (yellow)
Clozaril 25mg and 100mg tablets (lightish yellow)
Clopine oral suspension 50mg/ml (yellow)

DOSAGE:
PO:
Usual dose range is 25mg-300mg daily. Starting dose is usually 12.5mg daily.
Seek advice of a Psychiatrist (see ICU INDICATIONS)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Seek the advice of a Psychiatrist

DOSAGE IN PAEDIATRICS:
PO:
Seek the advice of a Psychiatrist

CLINICAL PHARMACOLOGY:
Clozapine is an 'atypical' antipsychotic drug

CONTRAINDICATIONS:
1. Previous hypersensitivity to clozapine
2. Myeloproliferative disorders
3. Uncontrolled epilepsy
4. hHstory of clozapine induced agranulocytosis or severe granulocytopaenia.
5. Clozapine should not be used simultaneously with other agents having a well-known potential to cause agranulocytosis or otherwise suppress bone marrow function.

WARNINGS
Agranulocytosis
Clozapine can cause life threatening agranulocytosis

Eosinophilia

In clinical trials, 1% of patients developed eosinophilia, which, in rare cases, can be substantial.

Seizures

Seizure has been estimated to occur in association with clozapine use at a cumulative incidence at 1 year of approximately 5%. Caution should be used in administering clozapine to patients having a history of seizures or other predisposing factors.

Myocarditis

Clozapine may cause myocarditis which can be fatal. Prompt discontinuation of clozapine treatment is warranted upon suspicion of myocarditis.

Other Adverse Cardiovascular and Respiratory Effects

Orthostatic hypotension with or without syncope can occur with clozapine treatment and may represent a continuing risk in some patients. Rarely (approximately 1 case per 3000 patients), collapse can be profound and be accompanied by respiratory and/or cardiac arrest.

Hyperglycaemia and Diabetes Mellitus

Hyperglycaemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics including clozapine.

Neuroleptic Malignant Syndrome (NMS)

A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs including clozapine.

PRECAUTIONS

General

Fever

During clozapine therapy, patients may experience transient temperature elevations above 38°C, with the peak incidence within the first 3 weeks of treatment. While this fever is generally benign and self limiting, it may necessitate discontinuing patients from treatment.

Pulmonary Embolism and Deep Vein Thrombosus

The possibility of pulmonary embolism should be considered in patients receiving clozapine who present with deep vein thrombosis, acute dyspnea, chest pain or with other respiratory signs and symptoms. As of December 31, 1993, there were 18 cases of fatal pulmonary embolism in association with clozapine therapy in users 10-54 years of age. Based upon the extent of use observed in the Clozaril National Registry, the mortality rate associated with pulmonary embolus was 1 death per 3450 person-years of use. This rate was about 27.5 times higher than that in the general population of a similar age and gender (95% Confidence Interval; 17.1, 42.2). Deep vein thrombosis has also been observed in association with clozapine therapy.

Hepatitis

Caution is advised in patients using clozapine who have concurrent hepatic disease. Hepatitis has been reported in both patients with normal and pre-existing liver function abnormalities. In patients who develop nausea, vomiting, and/or anorexia during clozapine treatment, liver function tests should be performed immediately. If the elevation of these values is clinically relevant or if symptoms of jaundice occur, treatment with clozapine should be discontinued.

Anticholinergic Toxicity

Clozapine has potent anticholinergic effects and care should be exercised in using this drug in the presence of narrow angle glaucoma. Clozapine use has been associated with varying degrees of impairment of intestinal peristalsis, ranging from constipation to intestinal obstruction, faecal impaction and paralytic ileus.

Laboratory Tests:
No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:
None noted

IMPORTANT DRUG INTERACTIONS FOR THE ICU
The risks of using clozapine in combination with other drugs have not been systematically evaluated.

The mechanism of clozapine induced agranulocytosis is unknown; nonetheless, the possibility that causative factors may interact synergistically to increase the risk and/or severity of bone marrow suppression warrants consideration. Therefore, clozapine should not be used with other agents having a well-known potential to suppress bone marrow function.

Orthostatic hypotension in patients taking clozapine can, in rare cases (approximately 1 case per 3000 patients), be accompanied by profound collapse and respiratory and/or cardiac arrest. Some of the cases of collapse/respiratory arrest/cardiac arrest during initial treatment occurred in patients who were being administered benzodiazepines; similar events have been reported in patients taking other psychotropic drugs or even clozapine by itself. Although it has not been established that there is an interaction between clozapine and benzodiazepines or other psychotropics, caution is advised when clozapine is initiated in patients taking a benzodiazepine or any other psychotropic drug. Clozapine may potentiate the hypotensive effects of antihypertensive drugs and the anticholinergic effects of atropine-type drugs.

Concomitant administration of drugs known to induce cytochrome P450 enzymes may decrease the plasma levels of clozapine. Phenytoin, nicotine, and rifampin may decrease clozapine plasma levels, resulting in a decrease in effectiveness of a previously effective clozapine dose.
Concomitant administration of drugs known to inhibit the activity of cytochrome P450 isozymes may increase the plasma levels of clozapine. Cimetidine, caffeine, and erythromycin may increase plasma levels of clozapine, potentially resulting in adverse effects.

ADVERSE REACTIONS
Central Nervous System
Drowsiness/sedation, Dizziness/vertigo, Headache, Tremor, Syncope, Disturbed sleep/nightmares, Restlessness, Hypokinesia/akinesia, Agitation, Seizures (convulsions), Rigidity, Akathisia.
Cardiovascular System
Tachycardia, Hypotension, Hypertension, Chest pain/angina, ECG changes, Myocarditis
Gastrointestinal System
Salivation, Constipation, Nausea, Abdominal discomfort/heartburn, Nausea/vomiting.
Skin
Rash
Haematological System
Leukopaenia, neutropaenia, agranulocytosis, eosinophilia

Codeine Phosphate [1 tablet 5 cents]

ADMINISTRATION ROUTES:
PO, IM

ALTERNATIVE NAMES:
Codeine

ICU INDICATIONS:
1. Relief of mild to moderate pain.

PRESENTATION AND ADMINISTRATION:
PO:
15mg and 30mg tablets (white)

IM:
50mg/1ml vials. Inject undiluted via IM route.
This route of administration is rarely used
NOT FOR IV USE

DOSAGE:
PO / IM:
15-60mg 4 hourly (max 300mg per day)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	50-100% of normal dose
10-20	75-100% of normal dose
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	50-100% of normal dose
HD	50-100% of normal dose
CVVHDF	75-100% of normal dose

DOSAGE IN PAEDIATRICS:
PO:
0.5-1mg/kg 4 hourly

CLINICAL PHARMACOLOGY:
Codeine phosphate is a centrally active analgesic

CONTRAINDICATIONS:
1. Hypersensitivity to codeine.

WARNINGS
Approximately 10% of Caucasian patients do not produce the enzyme required to convert codeine from its pro-drug form. These patients will derive no benefit from codeine

PRECAUTIONS
General
The respiratory depressant effects of narcotics and their capacity to depress consciousness may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a pre-existing increase in intracranial pressure.

Laboratory Tests:
No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:
None noted

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Codeine in combination with other narcotic analgesics, general anaesthetics, phenothiazines, tranquilisers, sedative-hypnotics, or other CNS depressants (including alcohol) has additive depressant effects.

ADVERSE REACTIONS
Central Nervous System:
lightheadedness, dizziness, sedation.
Gastrointestinal System:
Constipation, nausea, and vomiting.

Colchicine [1 tablet 10 cents]

ADMINISTRATION ROUTES:
PO

ALTERNATIVE NAMES:
Colgout

ICU INDICATIONS:
1. Acute gout

PRESENTATION AND ADMINISTRATION:
PO:
Colgout 500mcg tablets (white)

DOSAGE:
PO:
Acute Gout
1mg then 500mcg every 6 hours until pain relief achieved or diarrhoea occurs (maximum 6mg per course and 2500mcg/24 hours; do not repeat course within 3 days)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	50% of normal dose
10-20	50% of normal dose
>20-50	50% of normal dose

Dose in renal replacement therapy

CAPD	50% of normal dose
HD	50% of normal dose
CVVHDF	dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO:
Acute Gout
0.02mg/kg 2 hourly (maximum 3 doses per day)
Chronic Use
0.01-0.04mg/kg daily

CLINICAL PHARMACOLOGY:
The mechanism of the relief afforded by colchicine in acute attacks of gouty arthritis is not completely known

CONTRAINDICATIONS:
1. Diarrhoea
2. Combined renal and hepatic impairment

WARNINGS
Overdose can result in irreversible multiple organ failure and death

PRECAUTIONS
General
Reduction in dosage is indicated if weakness, anorexia, nausea, vomiting or diarrhoea occurs.

Laboratory Tests:
No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:
None noted

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Colchicine has been shown to induce reversible malabsorption of vitamin B12, apparently by altering the function of ileal mucosa. The possibility that colchicine may increase response to central nervous system (CNS) depressants and to sympathomimetic agents is suggested by the results of experiments on animals.

ADVERSE REACTIONS
Central Nervous System:
Peripheral neuritis.
Musculoskeletal System:
Muscular weakness.
Gastrointestinal System:
Nausea, vomiting, abdominal pain or diarrhoea may be particularly troublesome in the presence of peptic ulcer or spastic colon.
Haematologic System:
Aplastic anaemia, agranulocytosis, or thrombocytopaenia.
Skin:
Dermatitis, purpura, alopecia.

Coloxyl with Senna [1 tablet 11 cents]

ADMINISTRATION ROUTES:
PO

ALTERNATIVE NAMES:
Coloxyl with Senna, Docusate sodium & Total Sennosides, Laxsol

ICU INDICATIONS:
1. Constipation

PRESENTATION AND ADMINISTRATION:
PO:
Coloyxl with Senna tablets (brown) -each contains 50mg of Docusate sodium and 8mg of sennoside

DOSAGE:
*PO:*Usual ICU dosage two tablets twice a day

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
Not recommended in children, consider other agents

CLINICAL PHARMACOLOGY:
Faecal softener with peristaltic stimulant

CONTRAINDICATIONS
1. Mechanical intestinal obstruction

WARNINGS
See CONTRAINDICATIONS

PRECAUTIONS
General:
Maintain adequate fluid intake

Laboratory Tests:
No tests in addition to standard ICU tests are required

Drug/Laboratory Test Interactions:
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note

ADVERSE REACTIONS
Gastrointestinal System:
Cramps, diarrhoea, atonic colon (with chronic use)
Electrolytes:
Hypokalaemia

Co-trimoxazole [1 vial $6.70, 1 tablet 4 cents]

ADMINISTRATION ROUTES:
PO, IV

ALTERNATIVE NAMES:
Trisul, Deprim

ICU INDICATIONS:
1. Treatment and prophylaxis of pneumocystis pneumonia
2. Stenotrophomonas and other multidrug resistant infections
3. Nocardiosis
4. Toxoplasmosis
5. Treatment of infections caused by other susceptible organisms

PRESENTATION AND ADMINISTRATION:
PO:
Trisul tablets - Sulfamethoxazole 400mg / Trimethoprim 80mg (white)
Deprim and Trisul suspension – Sulfamethoxazole 200mg / Trimethoprim 40mg per 5ml

IV:
Each 5ml vial contains 480mg (80mg trimethoprim and 400mg sulfamethoxazole)
Normal dilution:
1 vial (5ml) diluted with 125ml of compatible IV fluid
2 vials (10ml) diluted with 250ml of compatible IV fluid
3 vials (15ml) diluted with 500ml of compatible IV fluid
Inspect for signs of turbidity or precipitation – if present, discard. Infuse over 60 to 90 minutes
Fluid restriction or high dose infusion:
1 vial (5ml) diluted with 75ml of 5% glucose
6 vials (30ml) diluted with 500ml of 5% glucose
More than 6 vials diluted with 1000ml of 5% glucose
Inspect for signs of turbidity or precipitation – if present, discard. Infuse over a period not exceeding 60 minutes and flush line thoroughly after drug administration.

Compatible with the following IV fluids:
0.45% sodium chloride 0.9% sodium chloride glucose and sodium chloride 5% glucose 10% glucose Hartmann's
If fluid restriction or high dose infusion is used, dilute ONLY with 5% glucose
Do not mix with any other drugs
Precipitation may occur if solutions are stored at low temperatures. If necessary, infusion solutions may be stored at room temperature. Solutions not used within 24 hours of preparation must be discarded. When diluted in Hartmann's, the prepared solution is stable for 8 hours at a 1 in 25 dilution and for 24 hours at a 1 in 35 dilution.
DO NOT use any solution that is cloudy or which has a visible precipitate.

DOSAGE:
IV:
Usual dosage 960-1440mg per day in divided doses;
For PCP treatment use 120mg/kg in divided doses administered every 6 hours for 14 days

PO:
PCP prophylaxis: 960-1920mg on alternate days.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<15	30mg/kg twice daily (PJP); or 50% of dose
15-30	60mg/kg for 3 days then 30mg/kg twice daily (PJP); or 50% of dose
>30-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	30mg/kg twice daily (PJP); or 50% of dose
HD	30mg/kg twice daily (PJP); or 50% of dose
CVVHDF	60mg/kg for 3 days then 30mg/kg twice daily (PJP) or 50% of dose

DOSAGE IN PAEDIATRICS:
IV/ PO:
6mg/kg trimethoprim and 30mg/kg sulfamethoxazole per day in equal divided doses

CLINICAL PHARMACOLOGY:
Sulfamethoxazole inhibits bacterial synthesis of dihydrofolic acid by competing with para-aminobenzoic acid (PABA). Trimethoprim blocks the production of tetrahydrofolic acid from dihydrofolic acid by binding to and reversibly inhibiting the required enzyme, dihydrofolate reductase. Thus, sulfamethoxazole; trimethoprim blocks two consecutive steps in the biosynthesis of nucleic acids and proteins essential to many bacteria.

The following organisms are usually susceptible: Escherichia coli, Klebsiella species, Enterobacter species, Morganella morganii, Proteus mirabilis, indole-positive Proteus species including Proteus vulgaris, Haemophilus influenzae (including ampicillin-resistant strains), Streptococcus pneumoniae, Shigella flexneri and Shigella sonnei. It should be noted, however, that there are little clinical data on the use of sulfamethoxazole; trimethoprim IV infusion in serious systemic infections due to Haemophilus influenzae and Streptococcus pneumoniae.

CONTRAINDICATIONS:
1. Known hypersensitivity to trimethoprim or sulfonamides
2. Megaloblastic anaemia due to folate deficiency

WARNINGS
FATALITIES ASSOCIATED WITH THE ADMINISTRATION OF SULFONAMIDES, ALTHOUGH RARE, HAVE OCCURRED DUE TO SEVERE REACTIONS, INCLUDING STEVENS-JOHNSON SYNDROME, TOXIC EPIDERMAL NECROLYSIS, FULMINANT HEPATIC NECROSIS, AGRANULOCYTOSIS, APLASTIC Anaemia AND OTHER BLOOD DYSCRASIAS. SULFAMETHOXAZOLE; TRIMETHOPRIM SHOULD BE DISCONTINUED AT THE FIRST APPEARANCE OF SKIN RASH
Sulfamethoxazole; trimethoprim IV infusion contains sodium metabisulfite, a sulfite that may cause allergic-type reactions, including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

PRECAUTIONS

General

Sulfamethoxazole; trimethoprim should be given with caution to patients with impaired renal or hepatic function, to those with possible folate deficiency (e.g., the elderly, chronic alcoholics, patients receiving anticonvulsant therapy, patients with malabsorption syndrome, and patients in malnutrition states) and to those with severe allergies or bronchial asthma.

In glucose-6-phosphate dehydrogenase deficient individuals, haemolysis may occur. This reaction is frequently dose-related.

Laboratory Tests:

No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:

None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU

In elderly patients concurrently receiving certain diuretics, primarily thiazides, an increased incidence of thrombocytopaenia with purpura has been reported.

It has been reported that sulfamethoxazole; trimethoprim may prolong the prothrombin time in patients who are receiving the anticoagulant warfarin. This interaction should be kept in mind when sulfamethoxazole; trimethoprim is given to patients already on anticoagulant therapy, and the coagulation time should be reassessed.

Sulfamethoxazole; trimethoprim may inhibit the hepatic metabolism of phenytoin.

ADVERSE REACTIONS

Haematologic:

Agranulocytosis, aplastic anaemia, thrombocytopaenia, leukopaenia, neutropaenia, haemolytic anaemia, megaloblastic anaemia, hypoprothrombinemia, methaemoglobinaemia, eosinophilia.

Allergic Reactions:

Stevens-Johnson syndrome, toxic epidermal necrolysis, anaphylaxis, allergic myocarditis, erythema multiforme, exfoliative dermatitis, angioedema, drug fever, chills. Henoch-Schoenlein purpura, serum sickness-like syndrome, generalized allergic reactions, generalized skin eruptions, conjunctival and scleral injection, photosensitivity, pruritus, urticaria and rash. In addition, periarteritis nodosa and systemic lupus erythematosus have been reported.

Gastrointestinal:

Hepatitis (including cholestatic jaundice and hepatic necrosis), elevation of serum transaminase and bilirubin, pseudomembranous enterocolitis, pancreatitis, stomatitis, glossitis, nausea, emesis, abdominal pain, diarrhoea, anorexia.

Genitourinary:

Renal failure, interstitial nephritis, BUN and serum creatinine elevation, toxic nephrosis with oliguria and anuria, and crystalluria.

Neurologic:

Aseptic meningitis, convulsions, peripheral neuritis, ataxia, vertigo, tinnitus, headache.

Psychiatric:

Hallucinations, depression, apathy, nervousness.

Endocrine:
The sulfonamides bear certain chemical similarities to some goitrogens, diuretics (acetazolamide and the thiazides) and oral hypoglycaemic agents. Cross-sensitivity may exist with these agents. Diuresis and hypoglycaemia have occurred rarely in patients receiving sulfonamides.
Musculoskeletal:
Arthralgia and myalgia.
Respiratory:
Pulmonary infiltrates.
Miscellaneous:
Weakness, fatigue, insomnia.

Cyclizine [1 vial $2.99]

ADMINISTRATION ROUTES:
PO, IM, IV

ALTERNATIVE NAMES:
Valoid, Nausicalm

ICU INDICATIONS:
1. Treatment of nausea and vomiting

PRESENTATION AND ADMINISTRATION:
PO:
Nausicalm 50mg tablets (white)

IV:
50mg per ml solution
Store at room temperature. Protect from light.
Cyclizine may be mixed with morphine in a syringe immediately before use
If cyclizine must be diluted in a syringe, either water for injection or 5% dextrose is recommended as the diluent rather than normal saline. This reduces the risk of crystallisation.

IM:
Inject undiluted solution

DOSAGE:
IV:
25-50mg up to three times daily

PO:
25-50mg 8 hourly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV / PO:
1mg/kg 8 hourly

CLINICAL PHARMACOLOGY:
The active ingredient cyclizine is a piperazine derivative with the general properties of H_1-blocking drugs but is used as an anti-emetic in a variety of clinical situations including drug-induced and motion sickness, vertigo, post-operative vomiting and radiation sickness. Cyclizine also possesses anticholinergic activity.

CONTRAINDICATIONS:
1. Hypersensitivity to cyclizine.

WARNINGS
In the critically ill, cyclizine often causes significant sedation.

PRECAUTIONS

General

As with other anticholinergic agents, cyclizine should be used with caution and appropriate monitoring in patients with glaucoma, obstructive disease of the gastrointestinal tract and in males with possible prostatic hypertrophy.

Cyclizine should be used with caution in patients with severe heart failure. In such patients, cyclizine may cause a fall in cardiac output associated with increases in heart rate, mean arterial pressure and pulmonary wedge pressure.

Laboratory Tests:

No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:

None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Cyclizine may have additive effects with alcohol and other central nervous system depressants e.g. hypnotics, tranquillisers. Because of its anticholinergic activity cyclizine may enhance the side-effects of other anticholinergic drugs.

ADVERSE REACTIONS

Central Nervous System:

Restlessness, nervousness, insomnia and auditory and visual hallucinations, drowsiness, blurred vision, dystonia, dyskinesia, extrapyramidal motor disturbances, tremor, twitching, muscle spasms, convulsions, disorientation, dizziness, decreased consciousness and transient speech disorders.

Respiratory System:

dryness of the mouth, nose and throat

Cardiovascular System:

tachycardia

Gastrointestinal System:

Cholestatic jaundice, constipation, hypersensitivity hepatitis

Haematological System:

agranulocytosis

Urogenital System:

Urinary retention,

Skin:

Urticaria, drug rash

Cyclosporin [1 vial $27.60, 1 capsule 25mg $1.19]

ADMINISTRATION ROUTES:
PO, IV

ALTERNATIVE NAMES:
Neoral, Sandimmun

ICU INDICATIONS:
It is unusual for this medication to be commenced in the ICU. Patients admitted to the intensive care unit may be on cyclosporin at the time of admission for the following indications:

1. Solid organ transplant rejection prophylaxis
2. Bone marrow transplant rejection prophylaxis
3. inflammatory disorders such as rheumatoid arthritis, uveitis and psoriasis

Note: decisions about indications and dosage of cyclosporin in ICU patients should be made in consultation with the relevant specialty team (Renal, Haematology etc)

PRESENTATION AND ADMINISTRATION:
IV:
Cyclosporin injection is a concentrate that must be diluted prior to IV infusion. It is an oily, faintly yellow coloured solution that contains polyoxyethylated castor oil 65% w/v, ethanol 33% v/v and with air in vials replaced by nitrogen
Dilute the concentrate 1:20 to 1:100 by volume (eg 50mg in 20-100ml) with compatible IV fluid. Ensure concentrate is well mixed in diluent fluid to reduce risk of an initial bolus of heavier non-solubilised polyoxyethylated castor oil, which carries an increased risk of anaphylactoid reactions. Diluted solution for infusion is clear and oily. Visually inspect infusion concentrated and infusion solution for particulate matter and / or discolouration.
Administer diluted infusion solution over 2-6 hours
Compatible with normal saline and 5% glucose
Use glass containers or 5% glucose in EXCEL containers (non PVC)
Do not mix with other fluids or medications
Discard any remaining concentrate after preparation of required dose
Discard any diluted fluid not used within 24 hours of preparation
Store at room temperature. Protect from light.

PO:
Neoral 25mg, 50mg and 100mg capsules
Neoral oral solution (100mg/ml)

DOSAGE:
Dosing should be titrated based on clinical assessments of rejection and tolerability and is generally directed by the primary team responsible for the transplant (eg haematology, renal etc)

IV:
Dose varies according to indication but is generally in the range of 1-5mg/kg/day

PO:
Dosage varies according to indication but is generally in the range of 3-15mg/kg/day

Note: Recommended IV dosage is approximately 1/3rd oral dosage

See *Laboratory Tests* for information about therapeutic drug monitoring which is mandatory

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose reduction is generally required and is based on therapeutic drug monitoring (see *Laboratory Tests* for information about therapeutic drug monitoring)

DOSAGE IN PAEDIATRICS:
Seek specialist paediatric advice

CLINICAL PHARMACOLOGY:
Cyclosporin is a potent immunosuppressive agent that prolongs survival of allogeneic transplants involving kidney, liver, heart, pancreas, bone marrow, small intestine, and lung.

CONTRAINDICATIONS:
1. Hypersensitivity to cyclosporin
2. Uncontrolled hypertension
3. Malignancy

WARNINGS
Increased susceptibility to infection and the possible development of lymphoma and other neoplasms may result from the degree of immunosuppression in patients treated with cyclosporin.

Cyclosporin can cause systemic hypertension and nephrotoxicity. The risk increases with increasing dose and duration of cyclosporin therapy.

Cyclosporin can cause nephrotoxicity and hepatotoxicity. The risk increases with increasing doses.

PRECAUTIONS
General
During treatment with cyclosporin, vaccination may be less effective; and the use of live attenuated vaccines should be avoided.

Laboratory Tests:
Cyclosporin has a narrow therapeutic index and variable pharmacokinetics and so monitoring of therapy is mandatory in the critically ill. It is usually appropriate to monitor levels twice weekly.

Two strategies are used for monitoring, one based on trough sampling, i.e. the concentration of drug found within 1 hour before the next dose (termed C0), and the other on the concentration of drug found 2 hours after the dose is given (termed C2).

C0 sampling has been widely used although it appears that C0 is only a weak indicator of absorption of drug. Moreover, the results are assay-dependent as samples of this type contain a large proportion of metabolite that may interfere.

C2 sampling is advantageous in that C2 is an acceptable surrogate for absorption (measured as the area under the concentration-time curve). Moreover, most of the measured drug found at this time is parent drug, making the measurement relatively free of interference from metabolites. A disadvantage of C2 is the need for samples to be taken close to the 2-hour time-point (+ or -15 minutes).

Factors affecting the target ranges for treatment include time of sampling (C0 or C2), organ transplanted, time since transplantation, and other medications. More specific recommended target concentrations for transplant patients are as follows. They may vary in individual cases on the basis of age, gender, renal function, number of episodes of rejection, and concomitant immunosuppressive medication.

Target trough (C0) ranges are as follows:

Liver:	
Induction	225-300 ng/mL
Maintenance	100-150 ng/mL
Heart:	
Induction	250-325 ng/mL
Maintenance	125-175 ng/mL
Kidney:	
Induction	150-225 ng/mL
Maintenance	100-180 ng/mL
Bone Marrow:	
Induction	95-205 ng/mL
Maintenance	95-205 ng/mL
Autoimmune indications:	
Induction	150-200 ng/mL
Maintenance	100-150 ng/mL

Target C2 ranges are as follows:

Liver:	
0-3 months post transplant	800-1200 ng/mL
3-6 months post transplant	640-960 ng/mL
>6 months post transplant	480-720 ng/mL
Renal:	
1 months post transplant	1360-2040 ng/mL
2 months post transplant	1200-1800 ng/mL
3 months post transplant	1040-1560 ng/mL
4-6 months post transplant	880-1320 ng/mL
7-12 months post transplant	720-1080 ng/mL
>12 months post transplant	640-960 ng/mL
Lung:	
0-2 days post transplant	>800
1-7 days post transplant	1200
1-4 weeks post transplant	1200-1700
2 months post transplant	1000-1500
3 months post transplant	800-1200
4-6 months post transplant	700-1000
7-12 months post transplant	600-900
>12 months post transplant	600-800

Note: samples for trough (C0) therapeutic monitoring should be collected in an EDTA (Purple tube) taken one hour before the next dose is due; samples for C2 monitoring should be taken 2 hours +/-15 minutes after the most recent dose

Drug/Laboratory Test Interactions:
Nil of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU
All of the individual drugs cited below are well substantiated to interact with cyclosporin

Drugs That May Potentiate Renal Dysfunction
Antibiotics:
Gentamicin, tobramycin, vancomycin, trimethoprim with sulfamethoxazole.
Antineoplastics:
Melphalan.
Antifungals:
Amphotericin B, ketoconazole.
Anti-Inflammatory Drugs:
Azapropazon, diclofenac, naproxen, sulindac, colchicine.
Gastrointestinal Agents:
Cimetidine, ranitidine.
Immunosuppressives:
Tacrolimus.

Drugs That Alter Cyclosporin Concentrations
Cyclosporin is extensively metabolized cytochrome P-450 3A. Substances that inhibit this enzyme could decrease metabolism and increase cyclosporin concentrations. Substances that are inducers of cytochrome P-450 activity could increase metabolism and decrease cyclosporin concentrations. Monitoring of circulating cyclosporin concentrations and appropriate dosage adjustment are essential when these drugs are used concomitantly.
Drugs That Increase Cyclosporin Concentrations
Calcium Channel Blockers:
Diltiazem, nicardipine, verapamil.
Antifungals:
Fluconazole, itraconazole, ketoconazole.
Antibiotics:
Clarithromycin, erythromycin, quinupristin/daldopristin.
Glucocorticoids:
Methylprednisolone.
Other Drugs:
Allopurinol, bromocriptine, danazol, metoclopramide, colchicine, amiodarone.

The HIV protease inhibitors (e.g., indinavir, nelfinavir, ritonavir, and saquinavir) are known to inhibit cytochrome P-450 3A and thus could potentially increase the concentrations of cyclosporin, however no formal studies of the interaction are available. Care should be exercised when these drugs are administered concomitantly.

Drugs/Dietary Supplements That Decrease Cyclosporin Concentrations
Antibiotics:
Nafcillin, rifampin.
Anticonvulsants:
Carbamazepine, phenobarbital, phenytoin.
Other Drugs:
Octreotide, ticlopidine, orlistat, St. John's Wort.

Other Drug Interactions
Cyclosporin may reduce the clearance of digoxin, colchicine, prednisolone and HMG-CoA reductase inhibitors (statins). Severe digitalis toxicity has been seen within days of starting cyclosporin in several patients taking digoxin. There are also reports on the potential of cyclosporin to enhance the toxic effects of colchicine such as myopathy and neuropathy, especially in patients with renal dysfunction.
Cyclosporin should not be used with potassium-sparing diuretics because hyperkalaemia can occur.

ADVERSE REACTIONS
Central nervous system:
Tremor, convulsions, headache, paraesthesia
Cardiovascular system:
Hypertension, arrhythmia
Gastrointestinal system:
Stomatitis, gum hyperplasia, diarrhoea, nausea/vomiting, hepatotoxicity, abdominal discomfort
Haematological system:
Leukopaenia, Lymphoma
Urogenital system:
Renal failure
Endocrine system
Hirsutism, Gynecomastia
Musculoskeletal system:
Cramps
Metabolic system:
Hypomagnesaemia

Dantrolene [1 vial $133, 1 tablet 25mg 65 cents]

ADMINISTRATION ROUTES:
IV, PO

ALTERNATIVE NAMES:
Dantrium

ICU INDICATIONS:
1. Malignant hyperthermia (IV therapy only)
2. Control of chronic spasticity (PO therapy)

PRESENTATION AND ADMINISTRATION:
IV:
Reconstitute each 20mg vial with 60ml of Water for Injection and shake vigorously until solution is clear (concentration is 0.333mg/ml). A large bore, vented needle (as found in the malignant hyperthermia box in theatre) will hasten the transfer of diluent and reconstituted solution. Inspect carefully for cloudiness or precipitation before administration. Compatible only with Water from Injection. Do not mix with other fluid or drugs. Reconstituted solution should be stored at room temperature and must be protected from direct light. Use solution within 6 hours of reconstitution.

PO:
Dantrolene 25mg and 50mg capsules (orange / tan)

DOSAGE:
IV:
Administer solution by continuous IV push beginning at 1mg/kg and continuing until response is achieved or a maximum cumulative dose of 10mg/kg is reached. May repeat if required.

PO:
Oral therapy is not appropriate for treatment of malignant hyperthermia. The usual dose for chronic spasticity is between 25mg daily and 50mg four times a day.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
Administer solution by continuous IV push beginning at 1mg/kg and continuing until response is achieved or a maximum cumulative dose of 10mg/kg is reached. May repeat if required.

PO:
For spasticity: 0.5mg/kg-3mg/kg 6 hourly

CLINICAL PHARMACOLOGY:
In skeletal muscle, dantrolene dissociates the excitation-contraction coupling, probably by interfering with the release of Ca++ from the sarcoplasmic reticulum. It is hypothesized that addition of dantrolene to the "triggered" malignant hyperthermic muscle cell

reestablishes a normal level of ionized calcium in the myoplasm. Inhibition of calcium release from the sarcoplasmic reticulum by dantrolene re-establishes the myoplasmic calcium equilibrium, increasing the percentage of bound calcium.

CONTRAINDICATIONS:
None.

WARNINGS
The use of dantrolene IV in the management of malignant hyperthermia crisis is not a substitute for previously known supportive measures. These measures must be individualized, but it will usually be necessary to discontinue the suspect triggering agents, attend to increased oxygen requirements, manage the metabolic acidosis, institute cooling when necessary, monitor urinary output, and monitor for electrolyte imbalance.

PRECAUTIONS
General
Care must be taken to prevent extravasation of dantrolene solution into the surrounding tissues due to the high pH of the intravenous formulation.
Fatal and non-fatal liver disorders of an idiosyncratic or hypersensitivity type may occur with dantrolene therapy.

Laboratory Tests:
No tests in addition to routine ICU test are indicated

Drug/Laboratory Test Interactions:
None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU
The combination of therapeutic doses of IV dantrolene sodium and verapamil in anaesthetised pigs has resulted in ventricular fibrillation and cardiovascular collapse in association with marked hyperkalaemia. It is recommended that the combination of IV dantrolene sodium and calcium channel blockers, such as verapamil, not be used together during the management of malignant hyperthermia crisis until the relevance of these findings to humans is established.
Administration of dantrolene may potentiate vecuronium-induced neuromuscular block.

ADVERSE REACTIONS
Body as a whole:
Erythematous rash, anaphylaxis
Central nervous system:
Weakness
Cardiovascular system:
Pulmonary oedema

None of the serious reactions occasionally reported with long-term oral dantrolene use, such as hepatitis, seizures, and pleural effusion with pericarditis, have been reasonably associated with short-term dantrolene IV therapy.
The following events have been reported in patients receiving oral dantrolene:
Hepatitis, seizures, pericarditis, aplastic anaemia, leukopaenia, lymphocytic lymphoma, and heart failure.

Desmopressin / DDAVP [1 vial $6.72]

ADMINISTRATION ROUTES:
IV, IM, SC, Intranasal

ALTERNATIVE NAMES:
Minirin, Octostim

ICU INDICATIONS:
1. Treatment of central diabetes insipidus
2. Prevention and control of bleeding (primarily when there are thought to be platelet function defects especially uraemia, clopidogrel or cardiopulmonary bypass-related)

PRESENTATION AND ADMINISTRATION:
IV:
Minirin 4mcg/ml injection
Octostim 15mcg/ml injection
Doses of 4mcg or less should be administered undiluted by direct IV injection. For small doses (eg 0.4mcg), 4mcg can be diluted in 10 ml of normal saline.
For doses of greater than 4mcg in adults or children weighing more than 10kg, dilute with 50ml of normal saline and infuse the first 5ml slowly over 5 minutes. For children weighing less than 10kg, dilute in 10ml of normal saline and infuse the first 1-2ml over 5 minutes. If no marked tachycardia or other adverse effects are observed, give the remainder slowly over 15 minutes

PO:
Minirin 0.1mg tablets (white)

Nasal Spray:
Desmopressin spray (10mcg/dose), Minirin spray (10mcg/dose), Octostim (150mcg/dose)

DOSAGE:
*IV (*preferred route*):*
Central diabetes insipidus:
0.4mcg repeated as required (may increase the dose if there is an adequate response)
Prevention and control of bleeding:
0.3mcg/kg (max 24mcg) over 30 minutes (once only)

PO:
0.1mg -1.2mg daily depending on indication (rarely used by this route in ICU)

Nasal Spray:
Not generally administered by this route in ICU

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
Prevention and control of bleeding:
>3 months old: 0.3mcg/kg (once only)

CLINICAL PHARMACOLOGY:
Desmopressin is a synthetic analogue of the natural pituitary hormone arginine vasopressin (ADH), an antidiuretic hormone affecting renal water conservation.

CONTRAINDICATIONS:
1. Hypersensitivity to desmopressin
2. Hyponatraemia

WARNINGS
When desmopressin acetate injection is administered to patients who do not have need of antidiuretic hormone for its antidiuretic effect, in particular in paediatric and geriatric patients, fluid intake should be adjusted downward to decrease the potential occurrence of water intoxication and hyponatraemia.
Particular attention should be paid to the possibility of the rare occurrence of an extreme decrease in plasma osmolality that may result in seizures which could lead to coma.

PRECAUTIONS
General
Desmopressin acetate injection has infrequently produced changes in blood pressure causing either a slight elevation in blood pressure or a transient fall in blood pressure and a compensatory increase in heart rate. The drug should be used with caution in patients with coronary artery insufficiency and/or hypertensive cardiovascular disease.
There have been rare reports of thrombotic events following desmopressin acetate
Severe allergic reactions have been reported rarely. Anaphylaxis has been reported rarely with desmopressin.

Laboratory Tests:
Laboratory tests for monitoring the patient include urine volume and osmolality. In some cases, plasma osmolality may be required.

Drug/Laboratory Test Interactions:
None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU
DDAVP may cause minor increases in blood pressure requiring changes in levels of vasopressor support.

ADVERSE REACTIONS
Central Nervous System:
transient headache, ischaemic stroke
Cardiovascular System:
changes in blood pressure causing either a slight elevation or a transient fall and a compensatory increase in heart rate, myocardial infarction
Gastrointestinal System:
nausea, mild abdominal cramps
Metabolic and Endocrine System:
water intoxication and hyponatraemia.
Skin:
Local irritation at site of injection

Dexamethasone Sodium Phosphate [1 vial $4.30]

ADMINISTRATION ROUTES:
IV, PO

ALTERNATIVE NAMES:
Dexamethasone

ICU INDICATIONS:
1. Cerebral oedema
2. Upper airway oedema
3. Nausea and vomiting
4. Croup
5. Other inflammatory conditions

PRESENTATION AND ADMINISTRATION:
IV:
4mg/1ml vial and 8mg/2ml vial
Inject undiluted over 3-5 minutes
Compatible with the following IV fluids:
0.9% Sodium chloride Glucose and Sodium Chloride 5% Dextrose
Store at room temperature.
Protect from light and freezing.

PO:
1mg and 4mg tablets (white)

DOSAGE:
IV/PO:
Cerebral oedema:
8-16mg stat, then 4-8mg 4 hourly reducing over 3-5 days to 2mg 8 to 12 hourly
Nausea:
4-8mg IV stat
Adult airway oedema:
8-16mg 1hr pre-extubation (may be repeated 8 hourly)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV / PO:
Cerebral oedema:
0.25-1mg/kg stat then 0.1-0.2mg/kg 4 hourly reducing over 3-5 days to 0.05mg/kg 8-12 hourly
Severe croup or extubation stridor:
0.6mg/kg stat IV, then 1mg/kg prednisilone 8-12 hourly

CLINICAL PHARMACOLOGY:
Dexamethasone is a glucorticoid which is 25 times more potent than hydrocortisone with respect to its glucocorticoid activity; it has no mineralocorticoid effect. Naturally occurring glucocorticoids (hydrocortisone and cortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. Their

synthetic analogs, including dexamethasone, are primarily used for their potent anti-inflammatory effects in disorders of many organ systems.

CONTRAINDICATIONS:

1. Systemic fungal infections
2. Hypersensitivity to dexamethasone or any component of the product

WARNINGS

Anaphylaxis:

Anaphylactoid and hypersensitivity reactions have been reported for dexamethasone sodium phosphate injection

Dexamethasone sodium phosphate injection contains sodium bisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

Exacerbation of fungal infections:

Corticosteroids may exacerbate systemic fungal infections and therefore should not be used in the presence of such infections unless they are needed to control drug reactions due to amphotericin B.

Relative steroid deficiency:

In patients on corticosteroid therapy subjected to any unusual stress, increased dosage of rapidly acting corticosteroids before, during, and after the stressful situation is indicated. Drug-induced secondary adrenocortical insufficiency may result from too rapid withdrawal of corticosteroids and may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstituted.

Masking of signs of infection:

Corticosteroids may mask some signs of infection, and new infections may appear during their use.

PRECAUTIONS

General

Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes, and severe depression to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Laboratory Tests:

No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Phenytoin, phenobarbital, ephedrine, and rifampin may enhance the metabolic clearance of corticosteroids resulting in decreased blood levels and lessened physiologic activity, thus requiring adjustment in corticosteroid dosage.

ADVERSE REACTIONS

Fluid and electrolyte disturbances:

Sodium retention, fluid retention, congestive heart failure in susceptible patients, potassium loss, hypokalemic alkalosis, hypertension.

Musculoskeletal:

Muscle weakness, steroid myopathy, loss of muscle mass, osteoporosis, vertebral compression fractures, aseptic necrosis of femoral and humeral heads, pathologic fracture of long bones, tendon rupture.

Gastrointestinal:

Peptic ulcer with possible subsequent perforation and haemorrhage, perforation of the small and large bowel, particularly in patients with inflammatory bowel disease, pancreatitis, abdominal distention, ulcerative oesophagitis.

Dermatologic:

Impaired wound healing, thin fragile skin, petechiae and ecchymoses, erythema, increased sweating, may suppress reactions to skin tests, burning or tingling, especially in the perineal area (after IV injection), other cutaneous reactions, such as allergic dermatitis, urticaria, angioneurotic edema.

Neurologic:

Convulsions, increased intracranial pressure with papilloedema (pseudotumour cerebri) usually after treatment, vertigo, headache, psychic disturbances.

Endocrine:

Menstrual irregularities, development of Cushingoid state, suppression of growth in children, secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery, or illness, decreased carbohydrate tolerance, manifestations of latent diabetes mellitus, increased requirements for insulin or oral hypoglycaemic agents in diabetics, hirsutism.

Metabolic:

Negative nitrogen balance due to protein catabolism.

Cardiovascular:

Myocardial rupture following recent myocardial infarction

Other:

Anaphylactoid or hypersensitivity reactions, thromboembolism, weight gain, increased appetite, nausea, malaise, hiccups.

Dexmedetomidine [1 vial $71.40]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Precedex

ICU INDICATIONS:
1. Agitation or delirium

Note: Dexmedetomidine is an expensive drug; it should only be administered with ICU Consultant authorisation.

PRESENTATION AND ADMINISTRATION:
IV:
200 micrograms/2ml vial

Dexmedetomidine must be diluted in 0.9% sodium chloride solution prior to administration. Dilute 400 micrograms (4 mL) of dexmedetomidine with 46 ml of 0.9% sodium chloride to total volume of 50 mL giving a concentration of 8 micrograms / mL

Dexmedetomidine has been shown to be compatible when administered with the following intravenous fluids and drugs:
Hartmanns, 5% Dextrose, 0.9% Sodium chloride

Handling Procedures: store at room temperature

DOSAGE:
Dose range 0.2 - 1.0 micrograms/kg/hr.

Dexmedetomidine should be administered using a controlled infusion device with dosing individualised and titrated to the desired clinical effect, measured using the Richmond Agitation-Sedation Scale (RASS).

Initially, the infusion should be commenced at 1 microgram/kg/hr of dexmedetomidine.
No loading dose is required.
The infusion rate should then be reduced by 0.2 micrograms/kg/hr every 30 minutes until the desired effect is achieved (generally, a target RASS of between -2 and +1).

Dexmedetomidine is usually co-administered with propofol at the lowest rate required to achieve target sedation (for propofol, this may be 10-70 mg/hr = 1-7 ml/hr). The usual maximal dose of dexmedetomidine is 1.0 micrograms/kg/hr but this can be increased up to 1.5 micrograms/kg/hr if the patient remains agitated. If this maximal dose is then inadequate, further sedation with other agents (including increased propofol sedation) is required.

Since dexmedetomidine clearance decreases with severity of hepatic impairment, dose reduction should be considered in patients with impaired hepatic function

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
There have been no clinical studies to establish the safety and efficacy of dexmedetomidine in paediatric patients below 18 years of age. Therefore, dexmedetomidine is not recommended for use in this population.

CLINICAL PHARMACOLOGY:
Dexmedetomidine is a relatively selective alpha2-adrenoceptor agonist with sedative properties.

CONTRAINDICATIONS:
1. Severe bradycardia
2. Second or third-degree AV block (unless paced)

WARNINGS
Clinically significant episodes of bradycardia and sinus arrest have been associated with dexmedetomidine administration

PRECAUTIONS
General
Some patients receiving dexmedetomidine have been observed to be rousable and alert when stimulated. This alone should not be considered an evidence of lack of efficacy in the absence of other clinical signs and symptoms.
Caution should be exercised when administering dexmedetomidine to patients with advanced heart block and/or severe ventricular dysfunction. Because dexmedetomidine decreases sympathetic nervous system activity, hypotension and/or bradycardia may be expected to be more pronounced in hypovolaemic patients and in those with diabetes mellitus or chronic hypertension and in the elderly.
In situations where other vasodilators or negative chronotropic agents are administered, co-administration of dexmedetomidine could have an additive pharmacodynamic effect and should be administered with caution.
Transient hypertension has been observed in association with the initial peripheral vasoconstrictive effects of dexmedetomidine. Treatment of the transient hypertension has generally not been necessary, although reduction of the infusion rate may be required.

Laboratory Tests:
No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:
None known.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Co-administration of dexmedetomidine with anaesthetics, sedatives, hypnotics, and opioids is likely to lead to an enhancement of effects.

ADVERSE REACTIONS
Body as a Whole:
Fever, rigors
Cardiovascular system:
Hypotension, hypertension, bradycardia, tachycardia, atrial fibrillation
Gastrointestinal system:
Nausea,Vomiting

Respiratory system:
Hypoxia, dry mouth
Metabolic and endocrine system:
Hyperglycaemia, acidosis
Haematological system:
Anaemia

Diazepam [1 vial $1.84, 1 tablet 2 cents, 1 rectal tube $5.01]

ADMINISTRATION ROUTES:
IV, IM, PO, PR

ALTERNATIVE NAMES:
Diazepam, Propam, Stesolid

ICU INDICATIONS:
1. Agitation
2. Alcohol and benzodiazepine withdrawal
3. Seizures

PRESENTATION AND ADMINISTRATION:
PO:
Propam 2mg (white), 5mg (yellow), 10mg (blue)
Diazepam elixir 10mg/10ml
Stesolid (rectal tube) 5mg/2.5ml and 10mg/2.5ml

IV:
10mg/2ml vial
Inject undiluted solution slowly at a rate not exceeding 5mg/min (avoid injecting into small veins)
In general, diazepam should not be mixed or diluted with other drugs or added to IV fluids. However, if IV infusion is required, diazepam in doses up to 20mg can be added to at least 250ml of 5% dextrose or normal saline. Do not use any solution that is cloudy.
Store at room temperature and protect from light.

IM:
Injection by this route is painful and absorption is slow and erratic. This route should be avoided where possible. If the *IM* route is used, inject undiluted.

DOSAGE:
IV, PO or PR:
Usual dose 2-20mg 8-12 hourly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	use small doses and titrate to response
10-20	use small doses and titrate to response
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	use small doses and titrate to response
HD	use small doses and titrate to response
CVVHDF	use small doses and titrate to response

DOSAGE IN PAEDIATRICS:
IV or PR:
0.1-0.4mg/kg
PO:
0.04-0.2mg/kg 8-12 hourly; pre-med 0.2-0.4mg/kg oral

CLINICAL PHARMACOLOGY:
Diazepam is a benzodiazepine. As with other benzodiazepines it has anticonvulsant, anxiolytic, sedative and muscle relaxant properties.

CONTRAINDICATIONS:
1. Hypersensitivity to diazepam

WARNINGS
Extreme care must be used in administering diazepam by the IV route to the elderly, to very ill patients and to those with limited pulmonary reserve because of the possibility that apnoea and/or cardiac arrest may occur. Concomitant use of barbiturates, alcohol or other central nervous system depressants increases depression with increased risk of apnoea.
Tonic status epilepticus has been precipitated in patients treated with IV diazepam for petit mal status or petit mal variant status.

PRECAUTIONS
General
Although seizures may be brought under control promptly, a significant proportion of patients experience a return to seizure activity, presumably due to the short-lived effect of diazepam after IV administration. Diazepam is not recommended for maintenance, and once seizures are brought under control, consideration should be given to the administration of agents useful in longer term control of seizures.

Withdrawal may precipitate seizures.

Laboratory Tests:
No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:
None known.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Increased CNS depression is seen when diazepam is combined with other CNS depressant drugs

ADVERSE REACTIONS
Central Nervous System:
Confusion, drowsiness, ataxia, depression, dysarthria, headache, hypoactivity, slurred speech, syncope, tremor, vertigo. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances and stimulation have been reported; should these occur, use of the drug

should be discontinued. Minor changes in EEG patterns, usually low-voltage fast activity, have been observed in patients during and after diazepam therapy and are of no known significance.

Gastrointestinal System:
Constipation, nausea, jaundice.
Genitourinary System:
Incontinence, urinary retention.
Cardiovascular System:
Bradycardia, cardiovascular collapse, hypotension
Skin:
Urticaria, skin rash.
Haematological System:
Neutropaenia

Diclofenac Sodium [1 tablet 15 cents, 1 suppository 25mg 18 cents]

ADMINISTRATION ROUTES:
PO, PR

ALTERNATIVE NAMES:
Cataflam, Flameril, Voltaren, Diclax, Voltfast

ICU INDICATIONS:
1. Analgesic

PRESENTATION AND ADMINISTRATION:
PO:
Tablets:
Cataflam 25mg (pale red), Voltaren Rapid 25mg (pale red)
Dispersible Tablets:
Voltaren D Dispersible 50mg for dispersal in water
Enteric Coated tablets:
Apo-Diclo EC tablets 25mg (yellow), Apo-Diclo EC tablets 50mg (light brown), Flameril 25mg tablets (yellow), Flameril 50mg tablets (light brown), Voltaren 50mg tablets (light brown)
Sustained release tablets:
Apo-Diclo SR tablets 75mg (pink), Apo-Diclo SR tablets 100mg (pink), Diclax SR tablets 75mg (pink), Diclax SR tablets 100mg (light red), Flameril Retard 75mg (pale pink), Flameril Retard 100mg (pink), Voltaren SR 75mg (pale pink)

PR:
Voltaren Suppositories 12.5mg and 25mg

DOSAGE:
PO or PR:
50mg 8 hourly or 75mg 12 hourly of sustained release

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	use only if on long-term dialysis; dose as in normal renal function
10-20	dose as in normal renal function but avoid if possible
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	dose as in normal renal function
HD	dose as in normal renal function
CVVHDF	use only if on long-term dialysis; dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO or PR:
1mg/kg 8-12 hourly

CLINICAL PHARMACOLOGY:
Diclofenac is a non steroidal anti-inflammatory drug that exhibits anti-inflammatory, analgesic, and antipyretic activities.

CONTRAINDICATIONS
1. Known hypersensitivity to Voltaren
2. Should not be given to patients who have experienced asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs.

WARNINGS
Use in ICU
Risks often outweigh benefits in ICU patients; careful consideration is required
GI bleeding
Serious gastrointestinal toxicity such as inflammation, bleeding, ulceration, and perforation of the stomach, small intestine or large intestine, can occur at any time, with or without warning symptoms, in patients treated with nonsteroidal anti-inflammatory drugs (NSAIDs). Minor upper gastrointestinal problems, such as dyspepsia, are common and may also occur at any time during NSAID therapy.
Anaphylactoid Reactions
As with other NSAIDs, anaphylactoid reactions may occur in patients without known prior exposure to diclofenac sodium. Diclofenac sodium should not be given to patients with the aspirin triad. This symptom complex typically occurs in asthmatic patients who experience rhinitis with or without nasal polyps, or who exhibit severe, potentially fatal bronchospasm after taking aspirin or other NSAIDs.
Advanced Renal Disease
In cases with advanced kidney disease, treatment with diclofenac sodium is not recommended unless the patient is already on dialysis.

PRECAUTIONS
General
Hepatic Effects
Borderline elevations of one or more liver tests may occur in up to 15% of patients taking NSAIDs including diclofenac sodium. These laboratory abnormalities may progress, may remain unchanged, or may be transient with continued therapy. In addition, rare cases of severe hepatic reactions, including jaundice and fatal fulminant hepatitis, liver necrosis and hepatic failure, some of them with fatal outcomes have been reported.
Haematological Effects
Anaemia is sometimes seen in patients receiving NSAIDs, including diclofenac sodium. This may be due to fluid retention, GI loss, or an incompletely described effect upon erythropoiesis.
Fluid Retention and Oedema
Fluid retention and oedema have been observed in some patients taking NSAIDs. Therefore, as with other NSAIDs, diclofenac sodium should be used with caution in patients with fluid retention, hypertension, or heart failure.

Laboratory Tests:
No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:
None known.

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Aspirin:

When diclofenac sodium is administered with aspirin, its protein binding is reduced. The clinical significance of this interaction is not known; however, as with other NSAIDs, concomitant administration of diclofenac and aspirin is not generally recommended because of the potential of increased adverse effects.

Methotrexate:

NSAIDs have been reported to competitively inhibit methotrexate accumulation in rabbit kidney slices. This may indicate that they could enhance the toxicity of methotrexate. Caution should be used when NSAIDs are administered concomitantly with methotrexate.

Cyclosporin:

Diclofenac sodium, like other NSAIDs, may affect renal prostaglandins and increase the toxicity of certain drugs. Therefore, concomitant therapy with diclofenac sodium may increase cyclosporin's nephrotoxicity. Caution should be used when diclofenac sodium is administered concomitantly with cyclosporin.

ACE-Inhibitors:

Reports suggest that NSAIDs may diminish the antihypertensive effect of ACE-inhibitors. This interaction should be given consideration in patients taking NSAIDs concomitantly with ACE-inhibitors.

Furosemide:

Clinical studies, as well as postmarketing observations, have shown that diclofenac sodium can reduce the natriuretic effect of furosemide and thiazides in some patients. This response has been attributed to inhibition of renal prostaglandin synthesis.

Lithium:

NSAIDs have produced an elevation of plasma lithium levels and a reduction in renal lithium clearance. The mean minimum lithium concentration increased 15% and the renal clearance was decreased by approximately 20%. These effects have been attributed to inhibition of renal prostaglandin synthesis by the NSAID. Thus, when NSAIDs and lithium are administered concurrently, subjects should be observed carefully for signs of lithium toxicity.

Warfarin:

The effects of warfarin and NSAIDs on GI bleeding are synergistic, such that users of both drugs together have a risk of serious GI bleeding higher than users of either drug alone.

ADVERSE REACTIONS

Body as a Whole:

Anaphylactic reactions

Cardiovascular System:

Congestive heart failure, hypertension, tachycardia, syncope.

Digestive System:

Abdominal pain, constipation, diarrhoea, dyspepsia, flatulence, gross bleeding/ perforation, heartburn, nausea, GI ulcers (gastric/duodenal), vomiting, dry mouth, oesophagitis, gastric/peptic ulcers, gastritis, gastrointestinal bleeding, glossitis, hematemesis, hepatitis, jaundice.

Haematological System:

Ecchymosis, eosinophilia, leukopaenia, melena, purpura, rectal bleeding, stomatitis, thrombocytopaenia.

Nervous System:
Anxiety, asthenia, confusion, depression, dream abnormalities, drowsiness, insomnia, malaise, nervousness, paraesthesia, somnolence, tremors, vertigo.
Respiratory System:
Asthma, dyspnea.
Skin and Appendages:
Alopecia, photosensitivity, sweating increased.
Urogenital System:
Cystitis, dysuria, haematuria, interstitial nephritis, oliguria/polyuria, proteinuria, renal failure.

Digoxin [1 vial $2.58, 1 tablet 250mcg 6 cents]

ADMINISTRATION ROUTES:
IV, PO

ALTERNATIVE NAMES:
Lanoxin

ICU INDICATIONS:
1. Atrial fibrillation
2. Cardiac failure

PRESENTATION AND ADMINISTRATION:
PO:
Lanoxin PG tablets 62.5mcg tablets (blue), Lanoxin 250mcg tablets (white), Lanoxin Paediatric Elixir 50mcg/ml.

IV:
Digoxin 500mcg/2ml
Solution may be injected slowly over at least 10-20 minutes. Alternatively, dilute required dose to four or more times its volume (eg 2ml with at least 8ml of diluent) with dextrose 5%, normal saline, glucose and sodium chloride or water for injection and administer slowly over at least 10-20 minutes.
The preferred method of administration is to add the required dose to 50-100ml of compatible IV fluid and to infuse over at least 10-20 minutes but preferably two or more hours.
Discard any solution not used within 24 hours of preparation.
Store at room temperature and protect from light.
Compatible with the following IV fluids:
Normal saline 5% Dextrose Glucose and sodium chloride
Hartmanns

DOSAGE:
Before administering a loading dose of digoxin, check that the patient has not received any digoxin during this hospital admission. If they have, you must check with the prescriber prior to administration.

IV:
Digitalising (loading) dose: 500mcg; followed by 250mcg 6 hours later and a further 250mcg 6 hours after that

IV/PO:
Oral loading:
750-1500mcg 1-2 doses 6 hours apart
Maintenance dose:
62.5mcg – 250mcg daily
Note: when converting from the oral to the IV formulation the dosage should be reduced by 33% to take account of the difference in bioavailability

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:

Dose in renal impairment [GFR (ml/min)]

<10	62.5mcg three times a week to 62.5mcg daily
10-20	usually 125mcg daily
>20-50	usually 125mcg daily

Dose in renal replacement therapy

CAPD	62.5mcg three times a week to 62.5mcg daily
HD	62.5mcg three times a week to 62.5mcg daily
CVVHDF	usually 125mcg daily

Note: for patients with renal impairment the interval between doses given during digitalisation should be lengthened to 8-10 hours.

DOSAGE IN PAEDIATRICS:

IV

Digitalising (loading) dose: 15mcg/kg stat and then 5mcg/kg after 6 hours

IV/PO

Maintenance dose:

3-5mcg/kg 12 hourly

Note: when converting from the oral to the IV formulation the dosage should be reduced by 33% to take account of the difference in bioavailability

CLINICAL PHARMACOLOGY:

Lanoxin (digoxin) is one of the cardiac (or digitalis) glycosides, a closely related group of drugs having in common specific effects on the myocardium. Digoxin inhibits sodium-potassium ATPase, an enzyme that regulates the quantity of sodium and potassium inside cells. Inhibition of the enzyme leads to an increase in the intracellular concentration of sodium and thus (by stimulation of sodium-calcium exchange) an increase in the intracellular concentration of calcium. The beneficial effects of digoxin result from direct actions on cardiac muscle, as well as indirect actions on the cardiovascular system mediated by effects on the autonomic nervous system.

CONTRAINDICATIONS

1. Hypersensitivity to digoxin

WARNINGS

Sinus Node Disease and AV Block

Because digoxin slows sinoatrial and AV conduction, the drug commonly prolongs the PR interval. The drug may cause severe sinus bradycardia or sinoatrial block in patients with pre-existing sinus node disease and may cause advanced or complete heart block in patients with pre-existing incomplete AV block. In such patients consideration should be given to the insertion of a pacemaker before treatment with digoxin.

Accessory AV Pathway (Wolff-Parkinson-White Syndrome)

After intravenous digoxin therapy, some patients with paroxysmal atrial fibrillation or flutter and a coexisting accessory AV pathway have developed increased antegrade conduction across the accessory pathway bypassing the AV node, leading to a very rapid ventricular response or ventricular fibrillation.

PRECAUTIONS

General

Use in Patients With Electrolyte Disorders

In patients with hypokalaemia or hypomagnesemia, toxicity may occur despite serum digoxin concentrations below 2.0 ng/ml, because potassium or magnesium depletion sensitizes the myocardium to digoxin. Therefore, it is desirable to maintain normal serum potassium and magnesium concentrations in patients being treated with digoxin.

Hypercalcaemia from any cause predisposes the patient to digitalis toxicity. Calcium, particularly when administered rapidly by the intravenous route, may produce serious arrhythmias in digitalized patients. On the other hand, hypocalcaemia can nullify the effects of digoxin in humans; thus, digoxin may be ineffective until serum calcium is restored to normal.

Use in Thyroid Disorders and Hypermetabolic States
Hypothyroidism may reduce the requirements for digoxin. Heart failure and/or atrial arrhythmias resulting from hypermetabolic or hyperdynamic states (e.g., hyperthyroidism, hypoxia, or arteriovenous shunt) are best treated by addressing the underlying condition. Atrial arrhythmias associated with hypermetabolic states are particularly resistant to digoxin treatment. Care must be taken to avoid toxicity if digoxin is used.

Laboratory Tests:
Digoxin toxicity may develop in the critically ill, particularly if the patient has renal impairment. Monitoring is not routinely required but should be considered.
Spec Collection: Plain (Red) or SST (Yellow); Paediatric and Neonatal only: 0.4 mL green microtainer.
Therapeutic Range 0.6-1.2 nmol/L. Recommended sampling: 8-24 hours post dose.
If a patient is commenced on digoxin in the ICU levels should not be measured until the drug has achieved steady state at 5-7 days.

Drug/Laboratory Test Interactions:
None if note

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Potassium-depleting diuretics are a major contributing factor to digitalis toxicity.
Calcium, particularly if administered rapidly by the intravenous route, may produce serious arrhythmias in digitalized patients.
Quinidine, verapamil, amiodarone, propafenone, indomethacin, itraconazole, alprazolam, and spironolactone raise the serum digoxin concentration due to a reduction in clearance and/or in volume of distribution of the drug, with the implication that digitalis intoxication may result. Erythromycin and clarithromycin (and possibly other macrolide antibiotics) and tetracycline may increase digoxin absorption in patients who inactivate digoxin by bacterial metabolism in the lower intestine, so that digitalis intoxication may result.
Rifampin may decrease serum digoxin concentration, especially in patients with renal dysfunction, by increasing the non-renal clearance of digoxin.

ADVERSE REACTIONS
Cardiovascular System:
Ventricular extrasystoles, tachycardia, bradycardias, heart block, cardiac arrest
Gastrointestinal System:
Anorexia, nausea, vomiting, diarrhoea, abdominal pain
CNS:
Headache, dizziness, mental disturbances, visual disturbances.

Infants and Children
The side effects of digoxin in infants and children differ from those seen in adults in several respects. Although digoxin may produce anorexia, nausea, vomiting, diarrhoea, and CNS disturbances in young patients, these are rarely the initial symptoms of overdosage. Rather, the earliest and most frequent manifestation of excessive dosing with digoxin in infants and children is the appearance of cardiac arrhythmias, including sinus bradycardia. In children, the use of digoxin may produce any arrhythmia. The most common are conduction disturbances or supraventricular tachyarrhythmias, such as atrial tachycardia (with or without block) and junctional (nodal) tachycardia.

Ventricular arrhythmias are less common. Sinus bradycardia may be a sign of impending digoxin intoxication, especially in infants, even in the absence of first-degree heart block. Any arrhythmia or alteration in cardiac conduction that develops in a child taking digoxin should be assumed to be caused by digoxin, until further evaluation proves otherwise.

Diltiazem [1 tablet 30mg 5 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Dilzem, Cardizem

ICU INDICATIONS:
1. Rate control in atrial fibrillation
2. Angina

PRESENTATION AND ADMINISTRATION:
PO:
Immediate Release Tablets:
Dilzem 30mg tablets (white), Dilzem 60mg tablets (white)
Twice Daily Sustained Release Capsules:
Dilzem SR 90mg capsules (green/white), Dilzem SR 120mg capsules (medium brown / light brown)
Once Daily Long Acting Tablets and Controlled Delivery Capsules:
Dilzem LA 180mg tablets (white), Dilzem LA 240mg tablets (white), Cardizem CD 120mg tablets (light turquoise / opaque), Cardizem CD 180mg tablets (light turquoise blue/ blue), Cardizem CD 240mg tablets (blue)

DOSAGE:
PO / NG:
In ICU it is usually appropriate to commence with 30mg 6-8 hourly and to increase as required to up to 360mg a day in divided doses. Immediate release tablets are the only formulation that can be administered via a nasogastric tube.
Note: dosage errors with diltiazem are common due to the variety of formulations that exist. Always make sure you are administering the correct formulation (see PRESENTATION AND ADMINISTRATION)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO
Use Immediate Release Only
1mg/kg 8 hourly; increase to maximum of 3mg/kg 8 hourly as required

CLINICAL PHARMACOLOGY:
Calcium channel blocker

CONTRAINDICATIONS
1. Sick sinus syndrome except in the presence of a functioning ventricular pacemaker
2. Patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker
3. Hypotension
4. Hypersensitivity to diltiazem

WARNINGS

Hypotension

Decreases in blood pressure associated with Diltiazem therapy may occasionally result in symptomatic hypotension.

Acute Hepatic Injury

Mild elevations of transaminases with and without concomitant elevation in alkaline phosphatase and bilirubin have been observed in clinical studies. Such elevations were usually transient and frequently resolved even with continued diltiazem treatment. In rare instances, significant elevations in enzymes such as alkaline phosphatase, LDH, ALT, AST, and other phenomena consistent with acute hepatic injury have been noted.

PRECAUTIONS

General:

See WARNINGS

Laboratory Tests:

No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:

None if note

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Due to the potential for additive effects, caution and careful titration are warranted in patients receiving diltiazem concomitantly with other agents known to affect cardiac contractility and/or conduction.

Concomitant administration of diltiazem with carbamazepine has been reported to result in elevated serum levels of carbamazepine (40-72% increase), resulting in toxicity in some cases.

A pharmacokinetic interaction between diltiazem and cyclosporin has been observed during studies involving renal and cardiac transplant patients. In renal and cardiac transplant recipients, a reduction of cyclosporin dose ranging from 15-48% was necessary to maintain cyclosporin trough concentrations similar to those seen prior to the addition of diltiazem. If these agents are to be administered concurrently, cyclosporin concentrations should be monitored, especially when diltiazem therapy is initiated, adjusted, or discontinued.

Coadministration of rifampin with diltiazem lowered the diltiazem plasma concentrations to undetectable levels. Coadministration of diltiazem with rifampin should be avoided when possible, and alternative therapy considered.

ADVERSE REACTIONS

Cardiovascular:

Oedema, angina, arrhythmia, AV block (second- or third-degree), bundle branch block, congestive heart failure, ECG abnormalities, hypotension, palpitations, syncope, tachycardia, ventricular extrasystoles.

Nervous System:

Headache, abnormal dreams, amnesia, depression, gait abnormality, hallucinations, insomnia, nervousness, paraesthesia, personality change, somnolence, tinnitus, tremor.

Gastrointestinal:
Nausea, anorexia, constipation, diarrhoea, dry mouth, dysgeusia, dyspepsia, mild elevations of SGOT, SGPT, LDH, and alkaline phosphatase, thirst, vomiting, weight increase.
Dermatologic:
Rash, petechiae, photosensitivity, pruritus, urticaria.

Dipyridamole [1 tablet 19 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Persantin, Pytazen

ICU INDICATIONS:
1. Adjunct to oral anticoagulants in circumstances where there is high risk of thrombosis

PRESENTATION AND ADMINISTRATION:
PO:
Immediate Release Tablets:
25mg tablets (orange)
Twice Daily Sustained Release Tablets and Modified Release Capsules:
Pytazen SR 150mg tablets (yellow), Persantin Perlongets 150mg Capsules (pink/white)

DOSAGE:
PO / NG:
Usual dosage 150mg of sustained release twice a day (or equivalent daily dose of immediate release tablets divided and administered 6 to 8 hourly). Use immediate release tablets if administering via NG tube.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO
1-2mg/kg 6-8 hourly oral
See PRECAUTIONS *Paediatric Use*

CLINICAL PHARMACOLOGY:
Platelet aggregation inhibitor

CONTRAINDICATIONS
1. Hypersensitivity to dipyridamole

WARNINGS
See PRECAUTIONS

PRECAUTIONS
General:
Coronary Artery Disease:
Dipyridamole has a vasodilatory effect and should be used with caution in patients with severe coronary artery disease (e.g., unstable angina or recently sustained myocardial infarction). Chest pain may be aggravated in patients with underlying coronary artery disease who are receiving dipyridamole.
Hepatic Insufficiency:
Elevations of hepatic enzymes and hepatic failure have been reported in association with dipyridamole administration.

Hypotension:
Dipyridamole should be used with caution in patients with hypotension since it can produce peripheral vasodilation.

Laboratory Tests:
No tests in addition to standard ICU tests are required

Drug/Laboratory Test Interactions:
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Adenosine:
Dipyridamole has been reported to increase the plasma levels and cardiovascular effects of adenosine. Adjustment of adenosine dosage may be necessary.
Cholinesterase Inhibitors:
Dipyridamole may counteract the anticholinesterase effect of cholinesterase inhibitors, thereby potentially aggravating myasthenia gravis.

ADVERSE REACTIONS
Body as a Whole:
Fatigue, malaise, myalgia
Neurological System:
Headache
Cardiovascular System:
Hypotension, palpitations, and tachycardia
Respiratory System:
severe bronchospasm, larynx oedema, angioedema
Gastrointestinal System:
Cholelithiasis, nausea, diarrhoea, vomiting, hepatitis.
Dermatological System:
Rash, urticaria
Haematological System:
Thrombocytopaenia

Dobutamine [1 vial $100.00]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Dobutamine

ICU INDICATIONS:
1. Inotrope

PRESENTATION AND ADMINISTRATION:
IV:
Each 20ml vial contains 250mg of dobutamine
Add 250mg of dobutamine (20ml) to 80ml of compatible IV fluid (i.e. 250mg in 100ml)
Compatible with the following IV fluids:

Normal saline	Glucose and sodium chloride	5% Dextrose
10% Dextrose	Hartmanns	

Store at room temperature
Protect from light

DOSAGE:
IV:
Administered by infusion at rates of 2.5-20 mcg/kg/min

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
15mg/kg in 50ml of 5% dextrose or normal saline at 2.5-20mcg/kg/min (0.5-4ml/hr)
1ml/hr equals 5mcg/kg/min

CLINICAL PHARMACOLOGY:
Dobutamine is a direct-acting inotropic agent whose primary activity results from stimulation of the beta²-receptors of the heart while producing comparatively mild chronotropic, hypertensive, arrhythmogenic, and vasodilative effects.

CONTRAINDICATIONS
1. Idiopathic hypertrophic subaortic stenosis
2. Hypersensitivity to dobutamine

WARNINGS
Increase in Heart Rate or Blood Pressure:
Dobutamine may cause a marked increase in heart rate or blood pressure, especially systolic pressure.
Ectopic Activity:
Dobutamine may precipitate or exacerbate ventricular ectopic activity, but only rarely causes ventricular tachycardia.

Hypersensitivity:
Reactions suggestive of hypersensitivity associated with administration of dobutamine in 5% dextrose injection, including skin rash, fever, eosinophilia, and bronchospasm, have been reported occasionally.

PRECAUTIONS
General:
Hypovolemia should be corrected with suitable volume expanders before treatment with dobutamine

Laboratory Tests:
No tests additional to routine ICU tests are indicated

Drug/Laboratory Test Interactions:
None known.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note

ADVERSE REACTIONS
Cardiovascular system:
Increased heart rate, hypotension, ventricular ectopy, atrial fibrillation, chest pain
Respiratory system:
Shortness of breath
Gastrointestinal system:
Nausea

Dopamine [1 vial $6.97]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Dopamine

ICU INDICATIONS:
1. Inotrope

PRESENTATION AND ADMINISTRATION:
IV:
Each 5ml vial contains 200mg of dopamine
Add 200mg of dopamine (5ml) to 95ml of compatible IV fluid (i.e. 200mg in 100ml)
Compatible with the following IV fluids:
Normal saline Glucose and sodium chloride 5% Dextrose
Hartmanns
Store at room temperature
Protect from light
Prepare solution immediately prior to use. Stable in compatible IV fluid for 24 hours at room temperature. Coloured solutions indicate decomposition of dopamine and should not be used

DOSAGE:
IV:
Administered by infusion at rates of 0-20 mcg/kg/min

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
15mg/kg in 50ml of 5% dextrose or normal saline at 0-20mcg/kg/min (0-4ml/hr)
1ml/hr equal 5mcg/kg/min

CLINICAL PHARMACOLOGY:
The predominant effects of dopamine are dose-related, although it should be noted that actual response of an individual patient will largely depend on the clinical status of the patient at the time the drug is administered.

At low rates of infusion (0.5 to 2 mcg/kg/min) dopamine causes vasodilation that is presumed to be due to a specific agonist action on dopamine receptors (distinct from alpha- and beta-adrenoceptors) in the renal, mesenteric, coronary and intracerebral vascular beds. At these dopamine receptors, haloperidol is an antagonist. The vasodilation in these vascular beds is accompanied by increased glomerular filtration rate, renal blood flow, sodium excretion and urine flow. Hypotension sometimes occurs. An increase in urinary output produced by dopamine is usually not associated with a decrease in osmolality of the urine.

At intermediate rates of infusion (2-10 mcg/kg/min), dopamine acts to stimulate the beta1-adrenoceptors, resulting in improved myocardial contractility, increased SA rate and enhanced impulse conduction in the heart. There is little, if any, stimulation of the beta2-adrenoceptors (peripheral vasodilation). Blood flow to the peripheral vascular beds may decrease while mesenteric flow increases due to increased cardiac output. Total peripheral resistance (alpha effects) at low and intermediate doses is usually unchanged.

At higher rates of infusion (10-20 mcg/kg/min), there is some effect on alpha-adrenoceptors, with consequent vasoconstrictor effects and a rise in blood pressure. The vasoconstrictor effects are first seen in the skeletal muscle vascular beds, but with increasing doses, they are also evident in the renal and mesenteric vessels.

At very high rates of infusion (above 20 mcg/kg/min), stimulation of alpha-adrenoceptors predominates and vasoconstriction may compromise the circulation of the limbs and override the dopaminergic effects of dopamine, reversing renal dilation and natriuresis.

CONTRAINDICATIONS

1. Idiopathic hypertrophic subaortic stenosis
2. Hypersensitivity to dopamine

WARNINGS

Dopamine contains sodium metabisulphite, a sulphite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulphite sensitivity in the general population is unknown and probably low. Sulphite sensitivity is seen more frequently in asthmatic than in non-asthmatic people.

PRECAUTIONS

General:

Hypovolemia should be corrected with suitable volume expanders before treatment with dopamine

If an increased number of ectopic beats are observed the dose should be reduced if possible.

At lower infusion rates, if hypotension occurs, the infusion rate should be rapidly increased until adequate blood pressure is obtained. If hypotension persists, dopamine should be discontinued and a more potent vasoconstrictor agent such as noradrenaline should be added.

Laboratory Tests:

No tests additional to routine ICU tests are indicated

Drug/Laboratory Test Interactions:

None known.

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Patients who have been receiving monoamine oxidase (MAO) inhibitors prior to the administration of dopamine should receive substantially reduced dosage of the latter.

Concurrent administration of low-dose dopamine and diuretic agents may produce an additive or potentiating effect on urine flow.

Administration of phenytoin to patients receiving dopamine has been reported to lead to hypotension and bradycardia. It is suggested that in patients receiving dopamine, alternatives to phenytoin should be considered if anticonvulsant therapy is needed.

ADVERSE REACTIONS
Cardiovascular System:
Ventricular arrhythmia (at very high doses), ectopic beats, tachycardia, anginal pain, palpitation, cardiac conduction abnormalities, widened QRS complex, bradycardia, hypotension, hypertension, vasoconstriction.
Respiratory System:
Dyspnea.
Gastrointestinal System:
Nausea, vomiting.
Central Nervous System:
Headache, anxiety.
Other:
Gangrene of the extremities has occurred when high doses were administered for prolonged periods or in patients with occlusive vascular disease receiving low doses of dopamine.

Doxazosin [1 tablet 2 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Dosan, Apo-Doxazosin

ICU INDICATIONS:
1. Hypertension refractory to other oral agents
2. Patients may also be taking this medication at the time of ICU admission for benign prostatic hypertrophy (it is usually appropriate to withhold doxazosin given for this indication)

PRESENTATION AND ADMINISTRATION:
PO:
Apo-Doxazosin 2mg (white), Apo-Doxazosin 4mg (white), Dosan 4mg (white)

DOSAGE:
PO / NG:
Commence with 1mg daily
Increase as required. Maximum 16mg daily

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO:
0.02-0.1mg/kg daily

CLINICAL PHARMACOLOGY:
Doxazosin mesylate is a selective inhibitor of the $alpha_1$-subtype of alpha adrenergic receptors.

CONTRAINDICATIONS
1. Known hypersensitivity to doxazosin

WARNINGS
First-Dose Effect
Doxazosin, like other alpha-adrenergic blocking agents, can cause marked hypotension, particularly with the first dose.
Priapism:
Doxazosin may cause priapism; if this occurs, urgent urological advice is required.

PRECAUTIONS
General:
Doxazosin should be administered with caution to patients with evidence of impaired hepatic function

Laboratory Tests:
No tests additional to routine ICU tests are required.

Drug/Laboratory Test Interactions:
None known.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Hypotension is more likely to occur when doxazosin is combined with other antihypertensives

ADVERSE REACTIONS
Body as a Whole:
Malaise
Cardiovascular System
Dizziness, hypotension
Skin & Appendages
Rash
Central & Peripheral Nervous System
Headache, paraesthesia, muscle cramps, somnolence
Gastrointestinal System
Nausea, diarrhoea, constipation
Respiratory System
Rhinitis

Enalapril [1 tablet 2 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Renitec

ICU INDICATIONS:
1. Hypertension
2. Congestive heart failure or left ventricular dysfunction after myocardial infarction
3. Diabetic nephropathy

PRESENTATION AND ADMINISTRATION:
PO:
M-enalapril 5mg (white), M-enalapril 10mg (light salmon), M-enalapril 20mg (light beige), Renitec 5mg (white), Renitec 10mg (rust-red), Renitec 20mg (peach)

DOSAGE:
PO / NG:
2.5mg daily; increased as required to 5-20mg 12 hourly.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment
start with 2.5mg and increase gradually

Dose in renal replacement therapy
CAPD start with 2.5mg and increase gradually
HD start with 2.5mg and increase gradually
CVVHDF start with 2.5mg and increase gradually
Note: Recent clinical observations have shown an association of hypersensitivity-like (anaphylactoid) reactions during haemodialysis with high-flux dialysis membranes (e.g., AN69) in patients receiving ACE inhibitors.

DOSAGE IN PAEDIATRICS:
PO:
0.1mg/kg daily oral, increased to max of 0.5mg/kg 12 hourly

CLINICAL PHARMACOLOGY:
Enalapril is an inhibitor of angiotensin I-converting enzyme (ACE), the enzyme responsible for the conversion of angiotensin I to angiotensin II.

CONTRAINDICATIONS
1. Hypersensitivity to enalapril or any other angiotensin-converting enzyme inhibitor (e.g. a patient who has experienced angioedema during therapy with any other ACE inhibitor).
2. Cardiogenic shock

WARNINGS

Anaphylactoid and Possibly Related Reactions

Enalapril can cause anaphylactoid reactions

Head and Neck Angioedema

Angioedema involving the extremities, face, lips, mucous membranes, tongue, glottis or larynx has been seen in patients treated with ACE inhibitors, including enalapril. If angioedema involves the tongue, glottis or larynx, airway obstruction may occur and be fatal. Swelling confined to the face, mucous membranes of the mouth, lips and extremities has usually resolved with discontinuation of enalapril; some cases required medical therapy.

Intestinal Angioedema

Intestinal angioedema has been reported in patients treated with ACE inhibitors. These patients presented with abdominal pain (with or without nausea or vomiting); in some cases there was no prior history of facial angioedema and C-1 esterase levels were normal.

Hypotension in Heart Failure Patients

Caution should be observed when initiating therapy in patients with heart failure. Patients with heart failure given enalapril commonly have some reduction in blood pressure. In patients with symptomatic hypotension this may require temporarily reducing the dose of enalapril, or diuretic, or both, and volume repletion

Hepatic Failure

Rarely, ACE inhibitors have been associated with a syndrome that starts with cholestatic jaundice and progresses to fulminant hepatic necrosis and (sometimes) death. The mechanism of this syndrome is not understood. Patients receiving ACE inhibitors who develop jaundice or marked elevations of hepatic enzymes should discontinue the ACE inhibitor.

Hyperkalaemia

Elevated serum potassium (greater than 5.7 mEq/L) was observed in approximately 1% of hypertensive patients in clinical trials. In most cases these were isolated values which resolved despite continued therapy. Hyperkalaemia was a cause of discontinuation of therapy in 0.28% of hypertensive patients. In clinical trials in heart failure, hyperkalaemia was observed in 3.8% of patients but was not a cause for discontinuation.

PRECAUTIONS

General:

Some patients with renal disease, particularly those with severe renal artery stenosis, have developed increases in serum creatinine after reduction of blood pressure with enalapril. Enalapril dosage reduction and/or discontinuation of diuretic may be required.

Elevations in serum potassium have been observed in some patients treated with ACE inhibitors, including enalapril.

Presumably due to the inhibition of the degradation of endogenous bradykinin, persistent nonproductive cough has been reported with all ACE inhibitors, always resolving after discontinuation of therapy. ACE inhibitor-induced cough should be considered in the differential diagnosis of cough.

Laboratory Tests:

No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions:

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Increased serum lithium levels and symptoms of lithium toxicity have been reported in patients receiving concomitant lithium and ACE inhibitor therapy.
The risk of hypotension increases if enalapril is coadministered with other antihypertensives

ADVERSE REACTIONS
Body as a Whole:
Gynaecomastia, anaphylactoid reactions, angioedema
Cardiovascular:
Cardiac arrest, cerebrovascular accident / insufficiency, rhythm disturbances, orthostatic hypotension, syncope
Dermatological:
Bullous pemphigus, erythema multiforme (Stevens Johnson syndrome), exfoliatice dermatitis
Gastrointestinal:
Pancreatitis, glossitis, dyspepsia, jaundice, hepatitis, rare causes of hepatic necrosis, cholestasis
Haematological:
Anaemia (including cases of haemolytic anaemia), thrombocytopaenia, neutropaenia
Metabolic:
Hyponatraemia
Musculoskeletal:
Myalgia, myasthenia
Nervous system:
Ataxia, confusion, depression, nervousness, somnolence
Respiratory system;
Bronchospasm, eosinophilic pneumonia, angioedema
Urogenital system;
Renal failure, proteinuria

Enoxaparin [1 pre-mixed syringe 40mg $4.96]

ADMINISTRATION ROUTES:
SC

ALTERNATIVE NAMES:
Clexane

ICU INDICATIONS:
1. Therapeutic anticoagulation
2. DVT prophylaxis

PRESENTATION AND ADMINISTRATION:
SC:
Pre-mixed syringes 20mg/0.2ml, 40mg/0.4ml, 100mg/ml
Do not remove air bubble from pre-mixed syringe prior to injection
Inject at 90 degrees to the skin on the lower abdomen. Alternate between the left and right anterolateral abdominal wall
Do not rub injection site after injection

DOSAGE:
SC:
DVT prophylaxis:
40mg sc daily (ALWAYS chart this at night. As most procedures happen during daylight hours, prescribing enoxaparin at night reduces the risk of procedural bleeding secondary to enoxaparin)

Therapeutic enoxaparin:
The standard treatment doses of enoxaparin (weight adjusted) are either 1mg/kg twice daily or 1.5mg/kg once daily
Enoxaparin dosing in extremes of bodyweight
The dose of enoxaparin does not need to be adjusted in the morbidly obese (BMI >35, or greater than 150kg), or those with a BMI <20 (underweight). These patients should be dosed on a mg/kg basis in the same way as patients of normal bodyweight, with adjustment for renal impairment if needed. There is evidence that twice daily dosing is safer for patients with BMI >35 or weight >150kg.
People at extremes of bodyweight (BMI <20 or >35) should have their Anti Xa level checked after 48 hours of dosing of enoxaparin, and the dose of enoxaparin adjusted as above.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<30	0.66mg/kg 12 hourly
30-59	0.8mg/kg 12 hourly

Note: the above doses are for therapeutic clexane; the recommended dose for DVT prophylaxis in patients with a GFR of <30 is 20mg daily
Dose in renal replacement therapy
Use systemic heparinisation in ICU in these patients

DOSAGE IN PAEDIATRICS:
Therapeutic Enoxaparin:
1mg/kg 12 hourly sc
Prophylactic Enoxaparin:
<2 months: 0.75mg/kg 12 hourly
2 months – 18 years: 0.5mg/kg 12 hourly

CLINICAL PHARMACOLOGY:
Low molecular weight heparin

CONTRAINDICATIONS
1. Hypersensitivity to enoxaparin
2. Active bleeding
3. Presence of an external ventricular drain

WARNINGS
Bleeding Risk:
Every patient being considered for enoxaparin therapy should be assessed for their risk of bleeding. This assessment should be documented in the patient's notes. There is an increased risk of any bleeding with enoxaparin use in patients who: are elderly (>65yo), have a BMI <20, have renal impairment, require a prolonged period of treatment, take concomitant clopidogrel (an 8-fold increased risk of major bleeding), aspirin or NSAID (3-4 fold increased risk), have had a previous upper GI bleed, have moderate hypertension (BP 140-180 systolic, 90-110 diastolic, even if on treatment), have multiple medical co-morbidities (especially diabetes, previous CVA or heart failure), have undiagnosed iron deficiency anaemia (in non-menstruating woman).

PRECAUTIONS
General
Many ICU procedures require reversal of anticoagulation. As enoxaparin is a not readily reversed, therapeutic systemic heparinisation may be a more appropriate choice in the many ICU patients

Laboratory Tests:
Routine Anti Xa monitoring is **not** recommended.
<u>Patients requiring Anti Xa monitoring</u>
Measuring peak Anti Xa activity is recommended for patients on therapeutic doses of clexane in the following situations:
- patients with moderate renal impairment (CrCl <60ml/min)
- patients who weigh <50kg
- patients who are morbidly obese (BMI >35)
- pregnant patients
- patients receiving treatment dose enoxaparin for longer than 14 days
- patients with changing renal function
- have increased risk of bleeding (see above)

<u>When to monitor Anti Xa</u>
- Peak Anti-Xa concentration yields the best correlation with clinical effect, and risk of bleeding.

- Anti Xa monitoring should only occur when enoxaparin is at steady state, which occurs after about 48 hours (5 half lives). It is not recommended that Xa levels are taken prior to this, as they are unable to be interpreted. Patients receiving enoxaparin for less than 48 hours do not need Anti Xa monitoring.
- Peak Anti Xa should be taken 4 hours after the dose of enoxaparin is given.

Trough measurements

- Measuring trough Anti Xa activity routinely is not recommended as the correlation between bleeding risk and trough Anti Xa has not been clearly established. Trough Anti Xa concentrations should however be monitored at the end of the dosing interval for patients with severe renal impairment (GFR <30ml/min) if the decision to use enoxaparin has been made. These patients should also have peak Anti-Xa levels taken. For twice daily dosing, the sample should be taken 12 hours after a dose, immediately preceding the next dose, and should be ≤ 0.5IU/ml. If the trough level is > 0.5 IU/ml, the patient should be changed to once daily dosing of enoxaparin, using the above nomogram. For once daily dosing, the sample should be taken 20 hours after a dose, and should be ≤ 0.4 IU/ml.

Therapeutic range

- The therapeutic peak Anti Xa range for treatment dose enoxaparin is 0.5–1.2 IU/ml for twice daily dosing, or 1–2 IU/ml for once daily dosing. The dose should be adjusted using the following nomogram:

Enoxaparin dose adjustment after Peak Anti Xa monitoring (TWICE daily dosing only)			
Anti Xa level	***Hold next dose***	***Dose change***	***Next Peak Anti Xa level (Always take level 4 hours after dose)***
<0.25	No	Increase by 50%	48 hours
0.25 - 0.49	No	Increase by 25%	48 hours
0.5 - 1.2	No	No	1 week
1.21 - 1.5	No	Decrease by 25%	48 hours
1.51 - 2	For 3 hours	Decrease by 30%	48 hours after next dose
>2	Until Anti Xa <0.5 IU/ml (check every 6 hours)	Decrease by 50%	48 hours after next dose Consider changing to UFH

Enoxaparin dose adjustment after Peak Anti Xa monitoring (ONCE daily dosing only)			
Anti Xa level	***Hold next dose***	***Dose change Peak***	***Next Peak Anti Xa level (Always take level 4 hours after dose)***
<0.5	No	Increase by 50%	48 hours
0.51 - 0.99	No	Increase by 25%	48 hours
1 - 2	No	No	1 week
2.1 - 3	No	Decrease by 30%	48 hours
>3	Until Anti Xa <0.5 IU/ml (check every 6 hours)	Decrease by 50%	48 hours after next dose Consider changing to UFH

NB: These nomograms are only valid if the patient is not bleeding and the renal function is stable.

Drug/Laboratory Test Interactions
None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Increased risk of bleeding when combined with other anti-platelet and anticoagulant agents

ADVERSE REACTIONS
Body as a Whole:
Bleeding, anaphylaxis, fever
Cardiovascular System:
Peripheral oedema,
Haematological System:
Anaemia, thrombocytopaenia, HITTS
Gastrointestinal System:
GI upset, elevated LFTs
Local:
haematoma (at injection site), skin necrosis

Ephedrine [1 vial $6.60]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Ephedrine

ICU INDICATIONS:
1. Drug-induced hypotension (particularly in association with bradycardia)

Note: used commonly in Anaesthesia but of limited utility in the ICU setting

PRESENTATION AND ADMINISTRATION:
IV:
Vial contains 30mg in 1ml
Dilute 30mg to a total of 10ml using normal saline (giving a concentration of 3mg/ml)
Store at room temperature
Protect from light
Compatible with the following IV fluids:

Normal saline	5% Dextrose	10% Dextrose	Glucose and sodium chloride
Hartmanns			

DOSAGE:
IV:
Administer by direct IV injection of 3-9mg (1-3ml) and repeat as required

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
0.25-1mg/kg (max 5mg/dose)

CLINICAL PHARMACOLOGY:
Ephedrine stimulates both alpha and beta receptors and its peripheral actions are due partly to norepinephrine release and partly to direct effect on receptors. Ephedrine may deplete norepinephrine stores in sympathetic nerve endings, so that tachyphylaxis to cardiac and pressor effects of the drug may develop.

CONTRAINDICATIONS
1. Hypersensitivity to ephedrine

WARNINGS
Ephedrine may cause hypertension resulting in intracranial haemorrhage. Ephedrine may induce anginal pain in patients with coronary insufficiency or ischaemic heart disease. The drug also may induce potentially fatal arrhythmias in patients with organic heart disease or who are receiving drugs that sensitise the myocardium

PRECAUTIONS

General:

Ephedrine should be used cautiously in patients with hyperthyroidism, hypertension, heart disease (including coronary insufficiency, angina pectoris and patients receiving digitalis), cardiac arrhythmias, diabetes or unstable vasomotor system.

Laboratory Tests:

No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions:

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Ephedrine should not be administered concomitantly with other sympathomimetic drugs because of possible additive effects and increased toxicity.

Alpha-adrenergic blocking agents may reduce the vasopressor response to ephedrine by causing vasodilation.

Beta-adrenergic blocking drugs may block the cardiac and bronchodilating effects of ephedrine.

Ephedrine also should be used cautiously with other drugs (e.g., digitalis glycosides) that sensitise the myocardium to the actions of sympathomimetic agents.

ADVERSE REACTIONS

Cardiovascular system:

Hypertension, tachyarrhythmias, palpitations

Neurological system:

headache, restlessness, anxiety, tension, tremor, weakness, dizziness, confusion, delirium hallucinations

Gastrointestinal system:

nausea or vomiting

Erythromycin

[1 vial $10.93, 1 tablet 400mg 17 cents, suspension 1mg 4 cents]

ADMINISTRATION ROUTES:
PO, NG, IV

ALTERNATIVE NAMES:
E-mycin

ICU INDICATIONS:
1. Empirical treatment of atypical pneumonia
2. Treatment of infections caused by other susceptible organisms
3. Gut prokinetic

PRESENTATION AND ADMINISTRATION:
PO:
E-Mycin 400mg tablets (pink)
E-Mycin 200 Suspension 200mg/5ml (pink)
E-Mycin 400 Suspension 400mg/5ml (pink)
ERA 250mg tablets (white)
ERA 500mg tablets (white)

IV:
1gm vial of powder
Add 20ml of water for injection ONLY to 1gm vial
Shake until all of the powder is dissolved (concentration = 50mg/ml). Expected time for dissolution is 4 minutes of shaking.
Add required dose to compatible IV fluid to give a concentration between 1mg/ml and 5mg/ml (when erythromycin being administered through a central line in ICU 5mg/ml is usually appropriate)

Final Volume	Amount of Erythromycin	Final Concentration
100ml	500mg	5mg/ml
250ml	500mg	2mg/ml
500ml	500mg	1mg/ml
200ml	1000mg	5mg/ml
250ml	1000mg	4mg/ml
500ml	1000mg	2mg/ml
1000ml	1000mg	1mg/ml

Administer over 60 minutes. For patients with high risk of cardiac arrhythmia infusion should be administered over 2 hours. Risk factors for cardiac arrhythmia due to erythromycin are as follows:
- history of cardiac disease,
- long QT syndrome,
- quinidine, procainamide or disopyramide
- impaired hepatic metabolism
- hypokalaemia or hypomagnesaemia

Compatible with the following IV fluids:
Normal saline Hartmanns
Reconstituted solution containing 50mg/ml is stable for 24 hours at room temperature. When further diluted with saline or Hartmanns, solutions should be used within 8 hours.

DOSAGE:
IV:
For infections requiring intensive care the usual dose is 1gm 6 hourly
For use as a prokinetic 125mg-250mg 6 hourly is usually appropriate

PO:
500mg 6 hourly.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	50% of normal dose
10-20	dose as in normal renal function
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	50% of normal dose
HD	50% of normal dose
CVVHDF	dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV/ PO:
For infections requiring intensive care 15-25mg/kg 6 hourly
For use as a prokinetic 2mg/kg 8 hourly

CLINICAL PHARMACOLOGY:
Erythromycin belongs to the macrolide group of antibiotics. Erythromycin acts by inhibition of protein synthesis in susceptible organisms by reversibly binding to 50 S ribosomal subunits, thereby inhibiting translocation of aminoacyl transfer-RNA and inhibiting polypeptide synthesis.

Erythromycin is usually active against the following organisms in vitro and in clinical infections:
Streptococcus pyogenes (group A Beta-haemolytic streptococci), Alpha-haemolytic streptococci (viridans group), Staphylococcus aureus (resistant organisms may emerge during treatment), Streptococcus pneumoniae, Mycoplasma pneumoniae, Treponema pallidum, Corynebacterium diphtheriae, Corynebacterium minutissimum, Entamoeba histolytica, Listeria monocytogenes, Neisseria gonorrhoeae, Bordetella pertussis, Legionella pneumophila (agent of Legionnaires' disease), Ureaplasma urealyticum, Chlamydia trachomatis.

CONTRAINDICATIONS:
1. Hypersensitivity to erythromycin

WARNINGS
Hepatic dysfunction:
There have been reports of hepatic dysfunction, including increased liver enzymes, and hepatocellular and/or cholestatic hepatitis, with or without jaundice, occurring in patients receiving oral erythromycin products.
Pseudomembranous colitis:
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including erythromycin, and may range in severity from mild to life threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents

PRECAUTIONS

General

There have been reports that erythromycin may aggravate the weakness of patients with myasthenia gravis.

Laboratory Tests:

No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:

Erythromycin interferes with the fluorometric determination of urinary catecholamines.

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Erythromycin use in patients who are receiving high doses of theophylline may be associated with an increase in serum theophylline levels and potential theophylline toxicity. In case of theophylline toxicity and/or elevated serum theophylline levels, the dose of theophylline should be reduced while the patient is receiving concomitant erythromycin therapy.

Concomitant administration of erythromycin and digoxin has been reported to result in elevated digoxin serum levels.

There have been reports of increased anticoagulant effects when erythromycin and oral anticoagulants were used concomitantly. Increased anticoagulation effects due to interactions of erythromycin with various oral anticoagulents may be more pronounced in the elderly.

Erythromycin has been reported to decrease the clearance of triazolam and midazolam and thus may increase the pharmacologic effect of these benzodiazepines.

The use of erythromycin in patients concurrently taking drugs metabolized by the cytochrome P450 system may be associated with elevations in serum levels of these other drugs. There have been reports of interactions of erythromycin with carbamazepine, cyclosporin, tacrolimus, hexobarbital, phenytoin, alfentanil, cisapride, disopyramide, lovastatin, bromocriptine, valproate, terfenadine, and astemizole. Serum concentrations of drugs metabolized by the cytochrome P450 system should be monitored closely in patients concurrently receiving erythromycin.

ADVERSE REACTIONS

Body as a Whole:

Anaphylaxis

Gastrointestinal System:

Nausea, vomiting, abdominal pain, diarrhoea and anorexia. Symptoms of hepatitis, hepatic dysfunction and/or abnormal liver function test results may occur.

Cardiovascular System:

Rarely, erythromycin has been associated with the production of ventricular arrhythmias, including ventricular tachycardia and torsades de pointes, in individuals with prolonged QT intervals.

Local:

thrombophlebitis

Esmolol [1 vial $39.20]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Breviblock

ICU INDICATIONS:
1. Hypertension
2. Tachydysrhythmia

Note: esmolol is primarily used where there is concern that beta blockade will not be well tolerated. If an adverse reaction occurs, esmolol has a very short action so the drug will wear off rapidly.

PRESENTATION AND ADMINISTRATION:
IV:
100mg in 10ml vial (10mg/ml)
Use 10mg/ml solution undiluted for loading dose and infusion
Store at room temperature.
Freezing does not adversely affect the product, but exposure to elevated temperatures should be avoided.
Protect from light
Esmolol loading dose should be administered by a doctor.
Note: Section 29 drug (requires specific notification to Director-General of Health)

DOSAGE:
IV:
Loading dose: 500mcg/kg over one minute (eg 70kg patient = 3.5ml of 10mg/ml)
Maintenance dose: 0-200mcg/kg/minute
Note: due to its high cost and the fact that cheaper alternatives exist, esmolol is rarely given by infusion

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
Loading dose: 500mcg/kg over one minute
Maintenance dose: 0-300mcg/kg/minute

CLINICAL PHARMACOLOGY:
Esmolol hydrochloride is a beta1-selective (cardioselective) adrenergic receptor blocking agent with a very short duration of action (elimination half-life is approximately 9 minutes).

CONTRAINDICATIONS
1. Sinus bradycardia,
2. Heart block greater than first degree,
3. Cardiogenic shock
4. Overt heart failure

WARNINGS

Risk of death in unstable patients
Despite the rapid onset and offset of esmolol effects, several cases of death have been reported in complex clinical states where esmolol was being used to control ventricular rate.
Bronchospastic Diseases
Because of its relative beta[1] selectivity and titratability, esmolol may be used with caution in patients with bronchospastic diseases. However, since beta[1] selectivity is not absolute, esmolol should be carefully titrated to obtain the lowest possible effective dose. In the event of bronchospasm, the infusion should be terminated immediately; a beta[2] stimulating agent may be administered if conditions warrant but should be used with particular caution as patients already have rapid ventricular rates.

PRECAUTIONS
General:
See WARNINGS

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions:
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Caution should be exercised when considering the use of esmolol and verapamil in patients with depressed myocardial function. Fatal cardiac arrests have occurred in patients receiving both drugs.
Esmolol should not be used to control supraventricular tachycardia in the presence of agents which are vasoconstrictive and inotropic such as dopamine, epinephrine, and norepinephrine because of the danger of blocking cardiac contractility when systemic vascular resistance is high.

ADVERSE REACTIONS
Cardiovascular System:
Symptomatic hypotension, pallor, flushing, bradycardia (heart rate less than 50 beats per minute), chest pain, syncope, pulmonary oedema and heart block.
Central Nervous System:
Dizziness, somnolence, confusion, headache, and agitation
Respiratory System:
Bronchospasm, wheezing, and dyspnoea.
Gastrointestinal System:
Nausea, vomiting, dyspepsia, constipation, dry mouth, and abdominal discomfort
Skin (infusion site):
Infusion site reactions including inflammation and induration

Etomidate [1 vial $4.95]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Etomidate

ICU INDICATIONS:
1. Induction of anaesthesia (particularly in the hypotensive patient)

PRESENTATION AND ADMINISTRATION:
IV:
20mg in 10ml vial
Inject undiluted by slow IV injection
Store at room temperature

DOSAGE:
IV:
0.3mg/kg slow IV

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
0.3mg/kg slow IV

CLINICAL PHARMACOLOGY:
Etomidate is a hypnotic drug without analgesic activity. Intravenous injection of etomidate produces hypnosis characterised by a rapid onset of action, usually within 1 minute. Duration of hypnosis is dose dependent but relatively brief, usually 3-5 minutes when an average dose of 0.3 mg/kg is employed. Reduced cortisol plasma levels have been reported with induction doses of 0.3 mg/kg etomidate. These persist for approximately 6-8 hours and appear to be unresponsive to ACTH

CONTRAINDICATIONS
1. Hypersensitivity to etomidate

WARNINGS
BECAUSE OF THE HAZARDS OF PROLONGED SUPPRESSION OF ENDOGENOUS CORTISOL AND ALDOSTERONE PRODUCTION, THIS FORMULATION SHOULD **NOT** BE ADMINISTERED BY PROLONGED INFUSION.

PRECAUTIONS
General:
See WARNINGS

Laboratory Tests:
No tests additional to routine ICU tests are required

Drug/Laboratory Test Interactions:
None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note

ADVERSE REACTIONS
Body as a Whole:
Anaphylaxis, adrenal suppression
Central Nervous System:
myoclonus
Cardiovascular System:
Hypertension, hypotension, tachycardia, bradycardia and other arrhythmias have occasionally been observed during induction and maintenance of anaesthesia
Respiratory System:
Hyperventilation, hypoventilation, apnea of short duration (5-90 seconds with spontaneous recovery), laryngospasm, hiccup and snoring suggestive of partial upper airway obstruction have been observed in some patients.
Gastrointestinal System:
Nausea and vomiting
Local:
Pain on injection

Felodipine [1 tablet 5mg 10 cents]

ADMINISTRATION ROUTES:
PO

ALTERNATIVE NAMES:
Felo ER, Plendil ER

ICU INDICATIONS:
1. Hypertension
2. Afterload reduction
3. Angina (can be used for treatment of angina but is rarely used for this indication in the ICU setting)

PRESENTATION AND ADMINISTRATION:
PO:
Felo ER 5mg (light pink) and Felo ER 10mg (reddish-brown)
Plendil ER 2.5mg (yellow), Plendil ER 5mg (pink), Plendil ER 10mg (red-brown)

DOSAGE:
Hypertension & afterload reduction:
Usual dosage 5mg daily; increasing to maximum 10mg daily
Note: tablets must not be crushed; use an alternative if NG administration is necessary

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
0.1-0.5mg/kg daily oral

CLINICAL PHARMACOLOGY:
Felodipine is a dihydropyridine calcium channel blocker. Felodipine is a peripheral arterial vasodilator that acts directly on vascular smooth muscle to cause a reduction in peripheral vascular resistance and reduction in blood pressure. It does not cause significant negative inotropy.

CONTRAINDICATIONS:
1. Known hypersensitivity to felodipine

WARNINGS
Increased Angina and/or Myocardial Infarction
Rarely, patients, particularly those with severe obstructive coronary artery disease, have developed documented increased frequency, duration and/or severity of angina or acute myocardial infarction on starting calcium channel blocker therapy or at the time of dosage increase. The mechanism of this effect has not been elucidated.

PRECAUTIONS

General

Caution should be exercised when administering felodipine as with any other peripheral vasodilator particularly in patients with severe aortic stenosis.

Patients with impaired liver function may have elevated plasma concentrations of felodipine and may respond to lower doses of felodipine; therefore, a starting dose of 2.5 mg once a day is recommended.

Laboratory Tests:

No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions:

None known.

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Felodipine is metabolized by CYP3A4. Coadministration of CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, erythromycin, grapefruit juice, cimetidine) with felodipine may lead to several-fold increases in the plasma levels of felodipine, either due to an increase in bioavailability or due to a decrease in metabolism.

ADVERSE REACTIONS

Cardiovascular System:

Hypotension, syncope, angina pectoris, arrhythmia, tachycardia, premature beats.

Digestive System:

Abdominal pain, diarrhoea, vomiting, dry mouth, flatulence, acid regurgitation, increased ALT.

Musculoskeletal System:

Arthralgia, back pain, leg pain, foot pain, muscle cramps, myalgia, arm pain, knee pain, hip pain.

Respiratory System:

Dyspnea, pharyngitis, bronchitis, influenza, sinusitis, epistaxis, respiratory infection.

Skin:

Angioedema, contusion, erythema, urticaria, leukocytoclastic vasculitis.

Fentanyl [1 vial 100mcg $1.22, 1 vial 500mcg $3.13, 1 patch 100mcg/hr $34.24, 1 premix 1000mcg in 100ml bag $23.17]

ADMINISTRATION ROUTES:
IV, transdermal

ALTERNATIVE NAMES:
Fentanyl, Durogesic, Sublimaze

ICU INDICATIONS:
1. Opioid analgesia
2. Induction of anaesthesia

PRESENTATION AND ADMINISTRATION:
IV:
100mcg in 2ml (50mcg/ml), 500mcg in 10ml (50mcg/ml)
500mcg in 50ml premixed syringes
Compatible with the following IV fluids:
Normal saline 5% glucose Glucose and Sodium Chloride
Store at room temperature
Use pre-mixed syringes for IV infusions; can be given either diluted or undiluted by IV push if required.

Transdermal:
12.5mcg/hour, 25mcg/hour, 50mcg/hour, 75mcg/hour, and 100mcg/hour patches
Apply to clean, dry, non hairy, non-irritated skin of the torso or upper arm.
Rotate application site.
Wear patch continuously for 72 hours.

DOSAGE:
IV:
Infusion doses are typically 0-100mcg/hr
Doses as part of induction of anaesthesia are typically 50-200mcg in ICU patients; much higher doses are occasionally required.

Transdermal:
Usually commence with 25mcg/hour or less in the opioid naïve.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	50% of normal dose
10-20	75% of normal dose
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	50% of normal dose
HD	50% of normal dose
CVVHDF	75% of normal dose

Note: although these dosages provided here are indicative, fentanyl is titrated to effect and the required dose to achieve the desired effect is the correct dose (irrespective of the renal function)

DOSAGE IN PAEDIATRICS:
IV:
1-10 mcg/kg; infusion 5-10 mcg/kg/hr
For infusion in paediatrics:
<10kg 100mcg/kg in 50ml 5% dextrose at 1-2ml/hr
>10kg 50mcg/ml at 0.04-0.08ml/kg/hr

CLINICAL PHARMACOLOGY:
Fentanyl citrate is a narcotic analgesic. A dose of 100 mcg is approximately equivalent in analgesic activity to 10 mg of morphine.

CONTRAINDICATIONS
1. Hypersensitivity to fentanyl

WARNINGS
May cause muscle rigidity, particularly involving the muscles of respiration, when given rapidly.

PRECAUTIONS
General:
Fentanyl may produce bradycardias

Laboratory Tests:
No tests additional to routine ICU tests are required

Drug/Laboratory Test Interactions:
None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Other CNS depressant drugs (e.g., barbiturates, tranquilizers, narcotics and general anaesthetics) will have additive or potentiating effects with fentanyl

ADVERSE REACTIONS
Body as a Whole:
Anaphylaxis, pruritus, urticaria
Cardiovascular System:
hypertension, hypotension, and bradycardia
Respiratory System:
Laryngospasm, respiratory depression, and apnea
Gastrointestinal System:
Nausea, emesis,
Neurological System:
Dizziness, blurred vision, extrapyramidal symptoms (dystonia, akathisia and oculogyric crisis)

Flucloxacillin [1 vial 1gm $1.09]

ADMINISTRATION ROUTES:
IV, IM, PO, NG

ALTERNATIVE NAMES:
Flucoxin, Staphlex, Flucloxacillin

ICU INDICATIONS:
1. Treatment of infections caused by susceptible organisms (particularly susceptible *Staph aureus*)

PRESENTATION AND ADMINISTRATION:
IV:
250mg, 500mg and 1gm
Add 5ml of Water for injection to 250mg, 500mg or 1gm vial. Shake gently until all the powder is dissolved. Withdraw contents and dilute contents with Water for Injection in the syringe to 10ml for the 250mg and 500mg vials or to 15-20ml for the 1gm vial.
Compatible with the following IV fluids:
Normal saline Dextran solutions 5% dextrose Hartmanns
Glucose and sodium chloride
Solutions prepared for direct IV injection should be prepared immediately before use.
Store at room temperature
Protect from light

IM:
Not generally administered by this route in ICU

PO / NG:
Flucloxacillin 500mg capsules (grey/caramel)
Staphlex 250mg and 500mg capsules (black/yellow)
Flucloxacillin oral suspension (white/pinkish)
Note: absorption of oral doses is significantly reduced by food so NG administration is impractical in patients being fed NG

DOSAGE:
IV:
1-2gm 6 hourly

PO:
500mg 6 hourly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	dose as in normal renal function up to a total daily dose of 4gm
10-20	dose as in normal renal function
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	dose as in normal renal function up to a total daily dose of 4gm
HD	dose as in normal renal function up to a total daily dose of 4gm
CVVHDF	dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
In the 1st week of life use 50mg/kg 12 hourly; in the 2nd to 4th weeks of life use 50mg/kg 8 hourly otherwise 25-50mcg/kg IV 6 hourly

PO:
12.5-25mg/kg 6 hourly

CLINICAL PHARMACOLOGY:
All penicillins inhibit the biosynthesis of the bacterial cell wall. Flucloxacillin is highly resistant to inactivation by staphylococcal penicillinase and is active against penicillinase-producing and non penicillinase-producing strains of Staphylococcus aureus.

CONTRAINDICATIONS:
1. A history of allergic reaction to any of the penicillins is a contraindication.

WARNINGS
Anaphylaxis
Penicillins are a common cause of anaphylactic reactions
Pseudomembranous colitis
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including flucloxacillin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents.

PRECAUTIONS
General
Prescribing Flucloxacillin in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug resistant bacteria.

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions
None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Tetracycline, a bacteriostatic antibiotic, may antagonise the bactericidal effect of penicillin and concurrent use of these drugs should be avoided.

ADVERSE REACTIONS
Body as a Whole:
Serum sickness like reactions, Anaphylaxis
Digestive System:
Nausea, vomiting, diarrhoea, and haemorrhagic/pseudomembranous colitis. Hepatic dysfunction including cholestatic jaundice, hepatic cholestasis and acute cytolytic hepatitis have been reported.

Nervous System:
Reversible hyperactivity, agitation, anxiety, insomnia, confusion, convulsions, behavioural changes, and/or dizziness have been reported rarely.
Skin:
Stevens-Johnson Syndrome, exfoliative dermatitis, toxic epidermal necrolysis, acute generalised exanthematous pustulosis, hypersensitivity vasculitis and urticaria have been reported
Haematological System:
Anaemia, including haemolytic anaemia, thrombocytopaenia, thrombocytopaenic purpura, eosinophilia, leukopaenia, and agranulocytosis have been reported during therapy with penicillins.

Fluconazole [1 vial 100mg 95 cents, 1 tablet 200mg 47 cents]

ADMINISTRATION ROUTES:
IV, PO

ALTERNATIVE NAMES:
Canesten Fluconazole, Diflucan, Flucazole

ICU INDICATIONS:
1. Candidiasis
2. Cryptococcal meningitis
3. Prophylaxis against Candida infections in patients after bone marrow transplantation

PRESENTATION AND ADMINISTRATION:
IV:
*100*mg in 50ml (formulated in normal saline)
Administer undiluted solution at a constant rate not exceeding 200mg/hr (eg one vial over 30 minutes or two vials over 60 minutes); dilution is not recommended.
Fluconazole may be administered through an existing line with the following IV fluids:

Hartmanns	Sodium bicarbonate	Sodium chloride
5% dextrose	20% dextrose	20mmol & 50mmol KCl in 5% dextrose

Discard any solution not used within 24 hours or opening
Do not use if solution is cloudy
Store at room temperature

PO:
Capsules:
Canesten Fluconazole 150mg capsules (white), Diflucan 50mg capsule (light turquoise / white), Diflucan 200mg capsules (purple / white), Diflucan One 150mg capsules (light turquoise blue), Flucazole 150mg capsules (white), Fluconazole (pacific) 50mg capsules (dark blue / white), Fluconazole (pacific) 150mg capsules (white), Fluconazole (pacific) 200mg capsules (blue / white)
Oral Suspension:
Diflucan suspension 50mg/5ml

DOSAGE:
PO & IV:
Severe infections: - 400mg stat then 200-400mg daily
Mild infections: - 200mg stat then 100-200mg daily
Prophylaxis – 200mg – 400mg daily (usually oral)
Note: the IV and oral dosages are the same; fluconazole is rapidly and nearly completely absorbed when administered orally (under normal circumstances)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	50% of normal dose
10-20	dose as in normal renal function
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	50% of normal dose
HD	50% of normal dose; give post dialysis
CVVHDF	dose as in normal renal function

DOSAGE IN PAEDIATRICS:

PO & IV:

Severe infections: - 12mg/kg stat (max 800mg), then 6-12mg/kg daily

Mild infections: - 6mg/kg stat, then 3mg/kg daily

Note: the IV and oral dosages are the same; fluconazole is rapidly and nearly completely absorbed when administered orally (under normal circumstances)

CLINICAL PHARMACOLOGY:

Fluconazole is a highly selective inhibitor of fungal cytochrome P-450 sterol C-14 alpha-demethylation. Mammalian cell demethylation is much less sensitive to fluconazole inhibition. The subsequent loss of normal sterols correlates with the accumulation of 14 alpha-methyl sterols in fungi and may be responsible for the fungistatic activity of fluconazole. The bioavailability of orally administered fluconazole is over 90% compared with intravenous administration.

CONTRAINDICATIONS:

1. Hypersensitivity to fluconazole

WARNINGS

Hepatic Injury:

Fluconazole has been associated with rare cases of serious hepatic toxicity, including fatalities primarily in patients with serious underlying medical conditions. In cases of fluconazole associated hepatotoxicity, no obvious relationship to total daily dose, duration of therapy, sex or age of the patient has been observed. Fluconazole hepatotoxicity has usually, but not always, been reversible on discontinuation of therapy. Patients who develop abnormal liver function tests during fluconazole therapy should be monitored for the development of more severe hepatic injury. Fluconazole should be discontinued if clinical signs and symptoms consistent with liver disease develop that may be attributable to fluconazole.

Anaphylaxis:

In rare cases, anaphylaxis has been reported.

PRECAUTIONS

General

Patients have rarely developed exfoliative skin disorders during treatment with fluconazole. Patients who develop rashes during treatment with fluconazole should be monitored closely and the drug discontinued if lesions progress.

Laboratory Tests:

No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions

None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Clinically or potentially significant drug interactions between fluconazole and the following agents/classes have been observed. These are described in greater detail below:

Oral Hypoglycaemics:

Clinically significant hypoglycaemia may be precipitated by the use of fluconazole with oral hypoglycaemic agents: 1 fatality has been reported from hypoglycaemia in association with combined fluconazole and glyburide use. Fluconazole reduces the metabolism of tolbutamide, glyburide, and glipizide and increases the plasma concentration of these agents. When fluconazole is used concomitantly with these or other sulfonylurea oral hypoglycaemic agents, blood glucose concentrations should be carefully monitored and the dose of the sulfonylurea should be adjusted as necessary.

Warfarin:

Prothrombin time may be increased in patients receiving concomitant fluconazole and coumarin-type anticoagulants. Careful monitoring of prothrombin time in patients receiving fluconazole and coumarin-type anticoagulants is recommended.

Phenytoin:

Fluconazole increases the plasma concentrations of phenytoin. Careful monitoring of phenytoin concentrations in patients receiving fluconazole and phenytoin is recommended.

Cyclosporin:

Fluconazole may significantly increase cyclosporin levels in renal transplant patients with or without renal impairment. Careful monitoring of cyclosporin concentrations and serum creatinine is recommended in patients receiving fluconazole and cyclosporin.

Rifampin:

Rifampin enhances the metabolism of concurrently administered fluconazole. Depending on clinical circumstances, consideration should be given to increasing the dose of fluconazole when it is administered with rifampin.

Theophylline:

Fluconazole increases the serum concentrations of theophylline. Careful monitoring of serum theophylline concentrations in patients receiving fluconazole and theophylline is recommended.

ADVERSE REACTIONS

Body as a whole:

anaphylaxis

Gastrointestinal:

Nausea, vomiting, dyspepsia, abdominal pain, diarrhoea, hepatitis, cholestasis, fulminant hepatic failure

Neurological:

Seizures, headache

Haematological:

Leukopaenia, thrombocytopaenia.

Dermatological:

Skin rash, exfoliative skin disorders including Stevens-Johnson Syndrome and toxic epidermal necrolysis

Flumazenil [1 vial $25.14]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Anexate

ICU INDICATIONS:
1. Reversal of the sedative effects of benzodiazepines

PRESENTATION AND ADMINISTRATION:
IV:
0.5mg/5ml of solution
Inject undiluted solution over 15 seconds preferably through a freely running IV infusion of compatible IV fluid and into a large vein.
For continuous infusion add 0.5mg to 50ml or 1mg to 100ml of compatible IV fluid (concentration 0.01mg/ml). Infuse at a rate of 0.1-0.4mg/hr (10-40ml/hr) and titrate to effect.
Compatible with the following IV fluids:
0.9% sodium chloride 5% glucose glucose and sodium chloride Hartmanns

DOSAGE:
IV:
Initially 0.2mg, followed by 0.1mg every 60 seconds as required to a maximum of 1mg
Note: in hepatic impairment initial dose remains the same but subsequent doses should be reduced in size or frequency

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
5mcg/kg every 60 seconds to a maximum total of 40mcg/kg then 2-10mcg/kg/hr

CLINICAL PHARMACOLOGY:
Flumazenil, an imidazobenzodiazepine derivative, antagonizes the actions of benzodiazepines on the central nervous system. Flumazenil competitively inhibits the activity at the benzodiazepine recognition site on the GABA/benzodiazepine receptor complex.

CONTRAINDICATIONS:
1. Hypersensitivity to flumazenil or benzodiazepines
2. Benzodiazepine dependence

WARNINGS
THE USE OF FLUMAZENIL HAS BEEN ASSOCIATED WITH THE OCCURRENCE OF SEIZURES. THESE ARE MOST FREQUENT IN PATIENTS WHO HAVE BEEN ON

BENZODIAZEPINES FOR LONG-TERM SEDATION OR IN OVERDOSE CASES WHERE PATIENTS ARE SHOWING SIGNS OF SERIOUS CYCLIC ANTIDEPRESSANT OVERDOSE. PRACTITIONERS SHOULD INDIVIDUALISE THE DOSAGE OF FLUMAZENIL AND BE PREPARED TO MANAGE SEIZURES.

Flumazenil should be used with caution in the ICU because of the increased risk of unrecognized benzodiazepine dependence in such settings. Flumazenil may produce convulsions in patients physically dependent on benzodiazepines.

PRECAUTIONS
General
Risk of Seizures
The reversal of benzodiazepine effects may be associated with the onset of seizures in certain high-risk populations. Possible risk factors for seizures include: concurrent major sedative-hypnotic drug withdrawal, recent therapy with repeated doses of parenteral benzodiazepines, myoclonic jerking or seizure activity prior to flumazenil administration in overdose cases, or concurrent cyclic anti-depressant poisoning.
Hypoventilation
Patients who have received flumazenil for the reversal of benzodiazepine effects (after conscious sedation or general anaesthesia) should be monitored for resedation, respiratory depression, or other residual benzodiazepine effects for an appropriate period (up to 120 minutes) based on the dose and duration of effect of the benzodiazepine employed.

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions
None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Particular caution is necessary when using flumazenil in cases of mixed drug overdosage since the toxic effects (such as convulsions and cardiac dysrhythmias) of other drugs taken in overdose (especially cyclic antidepressants) may emerge with the reversal of the benzodiazepine effect by flumazenil.

ADVERSE REACTIONS
Body as a Whole:
Fatigue (asthenia, malaise), Headache, Injection Site Pain, Injection Site Reaction (thrombophlebitis, skin abnormality, rash).
Cardiovascular System:
Cutaneous vasodilation (sweating, flushing, hot flushes).
Digestive System:
Nausea and Vomiting.
Nervous System:
Agitation (anxiety, nervousness, dry mouth, tremor, palpitations, insomnia, dyspnea, hyperventilation), dizziness (vertigo, ataxia), emotional lability (crying abnormal, depersonalisation, euphoria, increased tears, depression, dysphoria, paranoia).
Special Senses:
Abnormal Vision (visual field defect, diplopia), Paraesthesia (sensation abnormal, hypoaesthesia).

Fluoxetine [1 capsule 20mg 3 cents]

ADMINISTRATION ROUTES:
PO

ALTERNATIVE NAMES:
Fluox, Prozac

ICU INDICATIONS:
1. Depression

Note: it is rare for antidepressants to be commenced in patients in the ICU. Most ICU patients have 'situational depression' and the risks of medication often outweigh the benefits. (see WARNINGS)

PRESENTATION AND ADMINISTRATION:
PO:
Capsules:
Fluox 20mg capsules (purple / light green), Prozac 20mg capsules (green / cream)
Dispersible Tablets:
Fluox dispersible 20mg tablets (white)

DOSAGE:
PO:
20mg-60mg daily

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	dose as in normal renal function or on alternate days
10-20	dose as in normal renal function or on alternate days
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	dose as in normal renal function or on alternate days
HD	dose as in normal renal function or on alternate days
CVVHDF	dose as in normal renal function or on alternate days

DOSAGE IN PAEDIATRICS:
PO:
0.5mg/kg (max 20mg) daily, increase to maximum of 1mg/kg (max 40mg) 12 hourly

CLINICAL PHARMACOLOGY:
Fluoxetine is a serotonin specific reuptake inhibitor antidepressant

CONTRAINDICATIONS:
1. Hypersensitivity to fluoxetine or other SSRIs

WARNINGS
Use in Patients With Concomitant Illness
Clinical experience with Prozac in patients with concomitant systemic illness is limited. Caution is advisable in using Prozac in patients with diseases or conditions that could affect metabolism or haemodynamic responses.

Suicidality
Patients with major depressive disorder (MDD), both adult and paediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behaviour (suicidality) or unusual changes in behaviour, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs.
Hyponatraemia
Cases of hyponatraemia (some with serum sodium lower than 110 mmol/L) have been reported. The hyponatraemia appeared to be reversible when Prozac was discontinued. Although these cases were complex with varying possible aetiologies, some were possibly due to the syndrome of inappropriate antidiuretic hormone secretion (SIADH).

PRECAUTIONS
General
Anaphylactoid events, including bronchospasm, angioedema, laryngospasm, and urticaria alone and in combination, have been reported.
Pulmonary events, including inflammatory processes of varying histopathology and/or fibrosis, have been reported rarely. These events have occurred with dyspnea as the only preceding symptom.
Published case reports have documented the occurrence of bleeding episodes in patients treated with psychotropic drugs that interfere with serotonin reuptake. Subsequent epidemiological studies, both of the case-control and cohort design, have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions
None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
The combination of Tramadol and SSRIs should be used with caution due to the increased risk of serotonin syndrome with concomitant use.
Patients on stable doses of phenytoin and carbamazepine have developed elevated plasma anticonvulsant concentrations and clinical anticonvulsant toxicity following initiation of concomitant fluoxetine treatment.

ADVERSE REACTIONS
Body as a Whole
Flu syndrome
Cardiovascular System
Vasodilatation
Digestive System
Nausea, diarrhoea, anorexia, dry mouth, dyspepsia
Nervous System
Insomnia, anxiety, nervousness, somnolence, tremor
Respiratory System
Pharyngitis, sinusitis
Skin and Appendages
Sweating, rash

Frusemide [1 vial 250mg $9.62, 1 vial 20mg 59 cents, 1 tablet 40mg 1 cent]

ADMINISTRATION ROUTES:
PO, IV

ALTERNATIVE NAMES:
Diurin, Lasix, Frusemide

ICU INDICATIONS:
1. Fluid retention manifesting as pulmonary or peripheral oedema
2. Hyperkalaemia

PRESENTATION AND ADMINISTRATION:
PO:
Tablets:
Diurin 40mg tablets (off white), Diurin 500mg tablets (off white)
Oral Solution:
Lasix oral solution 10mg/ml

IV:
IV formulations available are:
1. Frusemide injection 20mg/2ml solution
2. Lasix high dose infusion 250mg in 25ml with 1000mg of mannitol as a stabilising agent

Administer doses of up to 80mg by slow IV injection over 2-5 minutes
For infusion doses of up to 5mg/hr use low dose infusion mixture of 40mg in 40ml of compatible IV fluid; for infusion doses of greater than 5mg/hr use high dose infusion mixture with undiluted Lasix high dose infusion (ie 250mg in 25ml or 500mg in 50ml)
Rate of infusion should not exceed 4mg/min
Compatible with the following IV fluids:
Normal saline Hartmanns
Note: glucose solutions are unsuitable
Store at room temperature; protect from light
Dilutions in compatible IV fluid are stable for 24 hours at room temperature – discard if not used within 24 hours. Do not use if solutions have a yellow colour or contain crystal deposits

DOSAGE:
PO:
Usual dosage from 10mg daily to 80mg three times a day

IV:
Dosage is highly individualised. 5mg may be sufficient to cause significant diuresis in the frusemide naïve patient. Doses of 100mg/hr by infusion may be required in those with significant renal impairment.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	dose as in normal renal function; increased doses may be required
10-20	dose as in normal renal function; increased doses may be required
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	not indicated
HD	not indicated
CVVHDF	rarely indicated; increased doses may be required

DOSAGE IN PAEDIATRICS:
IV/ PO:
Usually, 0.5-1mg/kg 6 hourly to four times a day.
IV infusion: 50mg/kg in 50ml of normal saline at 0.1-1 mg/kg/hr (i.e 0.1-1ml/hr)

CLINICAL PHARMACOLOGY:
Frusemide is a potent diuretic that inhibits the absorption of sodium and chloride in the proximal and distal tubules and the loop of Henle.

CONTRAINDICATIONS:
1. Known hypersensitivity to frusemide

WARNINGS
Allergy to Sulfur drugs
Patients allergic to sulfonamides may also be allergic to frusemide.
Ototoxicity
Cases of tinnitus and reversible or irreversible hearing impairment have been reported. Usually, reports indicate that frusemide ototoxicity is associated with rapid injection, severe renal impairment, doses exceeding several times the usual recommended dose, or concomitant therapy with aminoglycoside antibiotics or other ototoxic drugs.

PRECAUTIONS
General
Excessive diuresis may cause dehydration and blood volume reduction with circulatory collapse
As with any effective diuretic, electrolyte depletion may occur during frusemide therapy, especially in patients receiving higher doses and a restricted salt intake. Hypokalaemia may develop with frusemide, especially with brisk diuresis, inadequate oral electrolyte intake, when cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Digitalis therapy may exaggerate metabolic effects of hypokalaemia, especially myocardial effects.
Asymptomatic hyperuricaemia can occur and gout may rarely be precipitated.

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions
None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Frusemide may increase the ototoxic potential of aminoglycoside antibiotics, especially in the presence of impaired renal function. Except in life-threatening situations, avoid this combination.

Lithium generally should not be given with diuretics because they reduce lithium's renal clearance and add a high risk of lithium toxicity.

ADVERSE REACTIONS

Gastrointestinal System Reactions:

Pancreatitis, jaundice (intrahepatic cholestatic jaundice), anorexia, oral and gastric irritation, cramping, diarrhoea, constipation, nausea, and vomiting.

Systemic Hypersensitivity Reactions:

Systemic vasculitis, interstitial nephritis, and necrotising angiitis.

Central Nervous System Reactions:

Tinnitus and hearing loss, paraesthesias, vertigo, dizziness, headache, blurred vision, and xanthopsia.

Haematologic Reactions:

Aplastic anaemia (rare), thrombocytopaenia, agranulocytosis (rare), haemolytic anaemia, leukopaenia, and anaemia.

Dermatologic-Hypersensitivity Reactions:

Exfoliative dermatitis, erythema multiforme, purpura, photosensitivity, urticaria, rash, and pruritus.

Cardiovascular Reaction:

Orthostatic hypotension may occur and be aggravated by alcohol, barbiturates or narcotics.

Other Reactions:

Hyperglycaemia, glycosuria, hyperuricaemia, muscle spasm, weaknesses, restlessness, urinary bladder spasm, thrombophlebitis, and fever.

Gabapentin [1 tablet 100mg 13 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Neurontin, Nupentin

ICU INDICATIONS:
1. Treatment of pain (particularly neuropathic pain)

Note: Gabapentin is an anticonvulsant but is not generally used for this indication in ICU

PRESENTATION AND ADMINISTRATION:
PO:
Capsules:
Neurontin 100mg capsules (white), Neurontin 300mg capsules (yellow), Neurontin 400mg capsules (orange)
Nupentin 100mg capsules (white), Nupentin 300mg capsules (yellow), Nupentin 400mg capsules (orange)

Tablets:
Neurontin 600mg tablets (white)

DOSAGE:
PO / NG:
Commence with 100mg three times a day and increase as tolerated to a usual maximum of 1800mg per day (in divided doses); doses of up to 3600mg per day (in divided doses) have occasionally been used.
Note: Neurontin capsules can be opened and contents mixed with 10ml of water for administration via NG tube

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<15	usual dose 300mg on alternate days
15-30	usual dose 300mg once daily
>30-60	usual dose 300mg twice daily
60-90	usual dose 400mg three times daily

Dose in renal replacement therapy

CAPD	usual dose 300mg on alternate days
HD	200-300mg after each HD session
CVVHDF	rarely indicated; increased doses may be required

DOSAGE IN PAEDIATRICS:
PO:
2mg/kg three times daily; increase to 15mg/kg or higher if tolerated

CLINICAL PHARMACOLOGY:
Gabapentin is structurally related to the neurotransmitter GABA (gamma-aminobutyric acid). Its mechanism of action is unknown.

CONTRAINDICATIONS:

1. Hypersensitivity to gabapentin

WARNINGS

When gabapentin is used as an anticonvulsant, abrupt withdrawal may precipitate seizures

PRECAUTIONS

General

See WARNINGS

Laboratory Tests:

No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions

Because false positive readings were reported with the Ames N-Multistix SG dipstick test for urinary protein when gabapentin was added to other antiepileptic drugs, the more specific sulfosalicylic acid precipitation procedure is recommended to determine the presence of urine protein.

IMPORTANT DRUG INTERACTIONS FOR THE ICU

None of note

ADVERSE REACTIONS

Body as a Whole

Headache, abdominal pain

Digestive System

Diarrhoea, dry mouth, constipation, nausea, vomiting, flatulence

Metabolic and Nutritional Disorders

Weight gain, Hyperglycaemia

Nervous System

Dizziness, Somnolence, Ataxia, Abnormal gait, Incoordination, Amnesia, Hypesthesia

Skin and Appendages

Rash

Ganciclovir [1 vial 500mg $76]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Cymevene

ICU INDICATIONS:
1. Treatment of life threatening or sight threatening CMV infection

PRESENTATION AND ADMINISTRATION:
IV Use
Warning: Gancicolovir is a cytotoxic drug. Cytotoxic precautions apply.
Each vial contains 500mg of powder
Reconstitute each vial with 10ml of water for injection (giving a concentration of 50mg/ml). Shake well to dissolve powder. Add to 50-100ml of compatible IV fluid and administer over at least 1 hour.
Prepare immediately before use; reconstituted solution is stable at room temperature for 12 hours
Store at room temperature. Do not refrigerate.
Compatible with the following IV fluids:
Normal saline Hartmanns 5% glucose
Do not mix with other medications

DOSAGE:
5mg/kg every 12 hours for 14 to 21 days followed by 5mg/kg daily.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	1.25mg/kg 24 hourly
10-25	1.25mg/kg 24 hourly
25-50	2.5mg/kg 24 hourly
>50-69	2.5mg/kg 12 hourly

Dose in renal replacement therapy

CAPD	1.25mg/kg 24 hourly
HD	1.25mg/kg post dialysis
CVVHDF	2.5mg/kg 24 hourly

DOSAGE IN PAEDIATRICS:
5mg/kg every 12 hours for 14 to 21 days followed by 5mg/kg daily

CLINICAL PHARMACOLOGY:
Ganciclovir is a synthetic guanine derivative active against cytomegalovirus (CMV).

CONTRAINDICATIONS:
1. Hypersensitivity to ganciclovir, valganciclovir, acyclovir or valacyclovir

WARNINGS
Haematological
Ganciclovir should not be administered if the absolute neutrophil count is less than 500 or the platelet count is less than 25,000. Granulocytopaenia (neutropaenia), anaemia and thrombocytopaenia have been observed in patients treated with ganciclovir. The frequency and severity of these events vary widely in different patient populations.

PRECAUTIONS
General
See WARNINGS

Laboratory Tests
No tests are required in addition to routine ICU blood tests.

Drug/Laboratory Test Interactions
None reported

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Since both zidovudine and ganciclovir have the potential to cause neutropaenia and anaemia, some patients may not tolerate concomitant therapy with these drugs at full dosage.
Generalized seizures have been reported in patients who received ganciclovir and imipenem-cilastatin. These drugs should not be used concomitantly; use meropenem instead of imipenem in this situation.

ADVERSE REACTIONS
Body as a Whole
Fever, Infection, Chills, Sepsis
Digestive System
Diarrhoea, anorexia, vomiting
Haematological System:
Leukopaenia, anaemia, thrombocytopaenia
Nervous System
Neuropathy
Other
Sweating, Pruritus

Gentamicin [1 vial 65 cents]

ADMINISTRATION ROUTES:
IV, IM

ALTERNATIVE NAMES:
Gentamycin

ICU INDICATIONS:
1. Treatment of infections caused by susceptible organisms
2. Antibiotic synergism for infections caused by Pseudomonas, Acinetobacter and Enterobacteriaceae

PRESENTATION AND ADMINISTRATION:
IV:
80mg in 2ml solution
Add required dose to 100ml of compatible IV fluid and administer over 30 minutes
Dilutions in compatible IV fluid should be prepared immediately before use and any solution not used within 24 hours should be discarded
Store at room temperature

IM:
Not recommended by this route in ICU

DOSAGE:
7mg/kg once daily (round dose up to nearest 40mg)
Monitor levels & see below for repeat dosing

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	2 mg/kg 48 hourly and measure levels
10-20	3 mg/kg 48 hourly and measure levels
>20-30	4 mg/kg 48 hourly and measure levels
>30-40	2.5mg/kg 24 hourly and measure levels
>40-60	3.5mg/kg 24 hourly and measure levels
>60-80	4mg/kg 24 hourly and measure levels

Dose in renal replacement therapy

CAPD	2 mg/kg 48 hourly and measure levels
HD	2 mg/kg post dialysis and measure levels
CVVHDF	4 mg/kg 48 hourly and measure levels

DOSAGE IN PAEDIATRICS:
5-7mg/kg daily

CLINICAL PHARMACOLOGY:
In vitro tests have demonstrated that gentamicin is a bactericidal antibiotic which acts by inhibiting normal protein synthesis in susceptible microorganisms.

It is active against a wide variety of pathogenic bacteria including Escherichia coli, Proteus species (indole-positive and indole-negative), Pseudomonas aeruginosa, species of the Klebsiella-Enterobacter-Serratia group, Citrobacter species, and

Staphylococcus species (including penicillin- and methicillin-resistant strains). Gentamicin is also active in vitro against species of Salmonella and Shigella.

The following bacteria are usually resistant to aminoglycosides: Streptococcus pneumoniae, most species of streptococci, particularly group D and anaerobic organisms, such as Bacteroides species or Clostridium species.

CONTRAINDICATIONS:

1. Hypersensitivity to gentamicin or other aminoglycosides

WARNINGS

Nephrotoxicity

As with other aminoglycosides, gentamicin is potentially nephrotoxic. The risk of nephrotoxicity is greater in patients with impaired renal function and in those who receive high dosage or prolonged therapy.

Ototoxicity

Neurotoxicity manifested by ototoxicity, both vestibular and auditory, can occur in patients treated with gentamicin, primarily in those with pre-existing renal damage and in patients with normal renal function treated with higher doses and/or for longer periods than recommended; however, it may occur in the absence of these risk factors. Aminoglycoside-induced ototoxicity is usually irreversible.

PRECAUTIONS

General

Gentamicin sulphate contains sodium bisulphite, a sulphite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people.

Aminoglycosides should be used with caution in patients with neuromuscular disorders, such as myasthenia gravis, since these drugs may aggravate muscle weakness because of their potential curare-like effects on the neuromuscular junction.

Laboratory Tests

Monitor gentamicin levels:

Collect trough specimens in a SST (Yellow) or Plain (Red) Tube.

For Paediatric and Neonatal patients use a 0.4 mL green microtainer

Trough Level Interpretation:

- Take a trough level 2-4 hours before the second dose is due
- If the level is ≤ 0.3mg/L continue on the same dose every 24 hours
- If the level is >0.3mg/L withhold the next dose & repeat the level after 12 hours
- If the second level is ≤ 0.3mg/L continue on the same dose every 36 hours
- If the second level is >0.3mg/L contact the ID registrar or ICU SMO for advice

Drug/Laboratory Test Interactions

None reported

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Concurrent and/or sequential use of other potentially neurotoxic and/or nephrotoxic drugs, such as cisplatin, amikacin, neomycin, polymyxin B, colistin, and vancomycin, should be avoided.

The concurrent use of gentamicin with potent diuretics, such as frusemide, should be avoided, since certain diuretics by themselves may cause ototoxicity. In addition, when administered intravenously, diuretics may enhance aminoglycoside toxicity by altering the antibiotic concentration in serum and tissue.

ADVERSE REACTIONS

Body as a Whole:

lethargy, urticaria, generalised burning, anaphylactoid reactions

Nervous System:

Ototoxicity, headache, confusion, visual disturbances

Renal System:

Renal failure

Respiratory System:

Respiratory depression, laryngeal oedema

Cardiovascular System:

Hypotension and hypertension

Gastrointestinal System:

Decreased appetite, nausea, vomiting, increased salivation, hepatitis, cholestasis and stomatitis

Haematological System:

Anaemia, leukopaenia, granulocytopaenia, transient agranulocytosis, eosinophilia, increased and decreased reticulocyte counts, and thrombocytopaenia.

Glucagon [1 syringe 1mg $32.00]

ADMINISTRATION ROUTES:
IV, IM

ALTERNATIVE NAMES:
Glucagon Hypokit

ICU INDICATIONS:
1. Treatment of beta blocker or calcium channel blocker overdoses that are refractory to standard management with fluids, inotropes and calcium

Note: glucagon is not recommended as a 1st line treatment of hypoglycaemia in the ICU

PRESENTATION AND ADMINISTRATION:
IV Use
1mg vial + phenol containing solvent (prefilled syringe)
1 unit = 1 mg
FOR INFUSIONS, DO NOT USE SOLVENT THAT COMES WITH THE VIAL. Instead, reconstitute 25 vials of glucagon using water for injection, then dilute to a total of 25ml using 5% dextrose (i.e. 1mg/ml)
Compatible with the following IV fluids:
5% dextrose Water for injection
Store at room temperature
Note: glucagon administration can rapidly deplete the hospital glucagon supplies and alternative sources of glucagon should be sourced. Call the Pharmacist if commencing a glucagon infusion.

IM:
Dissolve 1mg vial in phenol containing solvent (prefilled syringe) and administer by IM injection

DOSAGE:
For treatment of beta blocker or calcium channel blocker overdoses:
1. Give an initial bolus of 5mg IV. If no response, repeat after 5 minutes.
2. If there is an adequate clinical response to the loading dose, commence an IV infusion of 2-5mg/hr

Note: if there is no clinical response to an initial loading dose of 10mg of glucagon, further administration of the drug is futile and use of glucagon should be abandoned.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
Beta blocker overdose: 0.1mg/kg IV stat followed by 0.3-2 mcg/kg/min

CLINICAL PHARMACOLOGY:
Glucagon for injection (rDNA origin) is a polypeptide hormone identical to human glucagon that increases blood glucose and relaxes smooth muscle of the gastrointestinal tract. Glucagon has positive inotropic and chronotropic effects similar to those of beta adrenergic agonists. These occur due to binding to specific intracellular glucagon receptors leading to activation of cardiac adenylate cyclise and increase cAMP concentrations

CONTRAINDICATIONS:
1. Hypersensitivity to glucagon

WARNINGS
Glucagon is not a first line therapy for beta blocker or calcium channel overdose. Its use is not supported by adequate clinical trials. Glucagon therapy should be used only for patients who are refractory to fluids and inotropes.

PRECAUTIONS
General
Generalised allergic reactions, including urticaria, respiratory distress, and hypotension, have been reported in patients who received glucagon by injection

Laboratory Tests
No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions
None reported

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note

ADVERSE REACTIONS
Body as a whole
Allergic reaction
Metabolic and endocrine
Hyperglycaemia, hypokalaemia
Gastrointestinal
Nausea, vomiting

Glyceryl Trinitrate

[1 vial 50mg in 50ml $8.66, 1 patch 5mg/24 hours 80 cents]

ADMINISTRATION ROUTES:
IV, Sublingual, Transdermal

ALTERNATIVE NAMES:
GTN, Nitronal, Lycinate, Glytrin, Nitrolingual, Minitran, Nitroderm

ICU INDICATIONS:
1. Afterload reduction / peripheral vasodilation
2. Treatment of hypertension
3. Treatment of angina

PRESENTATION AND ADMINISTRATION:
IV:
Nitronal 50ml contains 50mg of GTN in 50ml of 5% dextrose
Use undiluted
GTN is readily absorbed into many plastics. Original Perfusor PE tubing causes minimal absorption and is preferred. If other plastics are used, GTN may be absorbed by the tubing particular when running at low rates: IT SHOULD BE NOTED THAT WHEN THE APPROPRIATE INFUSION SETS ARE USED, THE CALCULATED DOSE WILL BE DELIVERED TO THE PATIENT BECAUSE THE LOSS OF NITROGLYCERIN DUE TO ABSORPTION IN STANDARD PVC TUBING WILL BE KEPT TO A MINIMUM. NOTE THAT THE DOSAGES COMMONLY USED IN PUBLISHED STUDIES UTILIZED GENERAL-USE PVC INFUSION SETS, AND RECOMMENDED DOSES BASED ON THIS EXPERIENCE ARE TOO HIGH IF THE LOW ABSORBING INFUSION SETS ARE USED.
Compatible with the following IV fluids:
5% dextrose Normal saline Glucose and sodium chloride
Do not mix with other medications
Store at room temperature and protect for light

Transdermal:
Apply once daily to chest or upper arm for 12-18 hours (brand dependent) followed by a 6-12 hour nitrate-free period (usually overnight)
Minitran 5mg/24 hours and 10mg/24 hours
Nitroderm TTS 5mg/24 hours (25mg) and 10mg/24 hours (50mg)
Sublingual tablets:
Lycinate 600mcg tablets
Sublingual spray:
Glytrin spray 400mcg/dose
Nitrolingual pump spray 400mcg/dose

DOSAGE:
IV infusion:
IV infusion dose range is 0-12ml/hr (equivalent to 0-200mcg/min). In ICU it is usually appropriate to commence the infusion at 5ml/hr and to titrate to effect.

Transdermal:
Usually commence with 5mg/24 hours patch; maximum two 10mg/24 hours patches

Sublingual tablets:
1 tablet under the tongue every 3-5 minutes as required

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV infusion:
<30kg 3mg/kg in 50ml 5% dextrose at 0.5-5ml/hr (0.5-5mcg/kg/min)
>30kg 3mg/kg in100ml 5% dextrose at 1-10ml/hr (0.5-5mcg/kg/min)

CLINICAL PHARMACOLOGY:
The principal pharmacologic action of nitroglycerin is relaxation of vascular smooth muscle, producing a vasodilator effect on both peripheral arteries and veins with more prominent effects on the latter. Dilation of the postcapillary vessels, including large veins, promotes peripheral pooling of blood and decreases venous return to the heart, thereby reducing left ventricular end-diastolic pressure (preload). Arteriolar relaxation reduces systemic vascular resistance and arterial pressure (afterload).

CONTRAINDICATIONS:
1. Known hypersensitivity to glyceryl trinitrate

WARNINGS
Occasionally, high dose GTN may lead to worsened oxygenation due to increased shunting

PRECAUTIONS
General
GTN may lead to severe hypotension in patients with haemodynamically significant aortic stenosis.
Laboratory Tests
No tests in addition to routine ICU tests are required
Drug/Laboratory Test Interactions
None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Amplification of the vasodilatory effects of nitroglycerin by sildenafil can result in severe hypotension.
Additive effects may be observed when GTN is combined with other antihypertensives

ADVERSE REACTIONS
Body as a Whole:
Allergic reactions
Cardiovascular System:
Tachycardia, hypotension, syncope, rebound hypertension, palpitations
Gastrointestinal System;
Nausea, vomiting, abdominal pain
Central Nervous System:
Headache
Haematological System:
Methaemoglobinaemia

Glycopyrrolate [1 vial $7.32]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Robinul

ICU INDICATIONS:
1. Protection against the peripheral muscarinic effects of cholinergics given to reverse neuromuscular blockade
2. To reduce secretions

PRESENTATION AND ADMINISTRATION:
IV:
Robinul contains 0.2mg of glycopyrrolate in a 1ml vial.
In order to minimize the appearance of cardiac side effects, glycopyrrolate and neostigmine may be administered simultaneously by IV injection and may be mixed in the same syringe when given for reversal of neuromuscular paralysis.
Compatible in the following IV fluids:
Dextrose 5% and 10% in water, or saline, dextrose 5% in sodium chloride 0.45%, and sodium chloride 0.9%
Store room temperature

DOSAGE:
IV:
To prevent bradycardia during reversal of neuromuscular blockade
The recommended dose of glycopyrrolate injection is 0.2 mg for each 1.0 mg of neostigmine.

To Reduce Secretions & Treating Bradycardia
0.2mg 6-8 hourly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Glycopyrrolate is renally excreted and its effect is significantly prolonged by renal impairment. However, dosage adjustment is generally not required.

DOSAGE IN PAEDIATRICS:
Reversal of Neuromuscular Blockade:
10mcg/kg of glycopyrrolate with 0.05mg/kg neostigmine

To Reduce Secretions or Treat Bradycardia:
5-10mcg/kg 6-8 hourly IV

CLINICAL PHARMACOLOGY:
Glycopyrrolate is a synthetic anticholinergic agent. Glycopyrrolate, like other anticholinergic (antimuscarinic) agents, inhibits the action of acetylcholine on structures innervated by postganglionic cholinergic nerves and on smooth muscles that respond to acetylcholine but lack cholinergic innervation.

CONTRAINDICATIONS:
1. Hypersensitivity to glycopyrrolate

WARNINGS
This drug should be used with great caution, if at all, in patients with glaucoma.
Exposure to excessive amounts of benzyl alcohol has been associated with toxicity (hypotension, metabolic acidosis), particularly in neonates.

PRECAUTIONS
General
Investigate any tachycardia before giving glycopyrrolate injection since an increase in the heart rate may occur.
Use with caution in patients with: coronary artery disease; congestive heart failure; cardiac arrhythmias; hypertension; hyperthyroidism.
Infants, patients with Down's syndrome, and paediatric patients with spastic paralysis or brain damage may experience an increased response to anticholinergics, thus increasing the potential for side effects.

Laboratory Tests
No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions
None noted

IMPORTANT DRUG INTERACTIONS FOR THE ICU
The concurrent use of glycopyrrolate injection with other anticholinergics or medications with anticholinergic activity, such as phenothiazines, antiparkinson drugs, or tricyclic antidepressants, may intensify the antimuscarinic effects and may result in an increase in anticholinergic side effects.

ADVERSE REACTIONS
Body as a Whole:
Anaphylactic/anaphylactoid reactions, malignant hyperthermia
Cardiovascular System:
Tachycardia, cardiac arrhythmias (including bradycardia, ventricular tachycardia, ventricular fibrillation)
Gastrointestinal System:
Nausea, vomiting, dry mouth, constipation
Renal System:
Urinary hesitancy and retention

Haloperidol [1 vial $1.87, 1 tablet 0.5mg 5 cents]

ADMINISTRATION ROUTES:
IV, IM, PO

ALTERNATIVE NAMES:
Serenace
Note: this monograph does **not** apply to Haldol (Haloperidol decanoate) which has an extended duration of action, is administered by IM depot injection and is not used in ICU

ICU INDICATIONS:
1. Delirium
2. Psychosis

PRESENTATION AND ADMINISTRATION:
IV:
Haloperidol 5mg in 1ml (solution)
Administer slowly over 1-2 minutes or as a bolus, undiluted or diluted in 5-10ml of normal saline.
May be diluted in compatible IV fluid and administered over 10-30 minutes
Undiluted solution may discolour if exposed to light. Discoloured solutions should not be used.
Compatible with the following IV fluid subject to concentration limits:

Normal saline	up to a concentration of 0.75mg/ml
5% dextrose	up to a concentration of 3mg/ml
Glucose and sodium chloride	up to a concentration of 1mg/ml
Hartmanns	up to a concentration of 1mg/ml

Store at room temperature and protect from light

PO:
Tablets:
Serenace 0.5mg tablets (green), Serenace 1.5mg (white), Serenace 5mg (red)
Liquid:
Serenace 2mg/ml (20 drops is equal to 1ml)

DOSAGE:
IV/IM:
ICU delirium and psychosis
0.5mg-10mg as required. Usual maximum daily dose is 100mg although much higher doses have been described.

PO:
0.5mg-20mg as required. Usual maximum daily dose is 100mg although much higher doses have been described.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	Start with lower doses. For single doses use 100% of normal dose. Avoid repeated dosage because of accumulation
10-20	Dose as in normal renal function
>20-50	Dose as in normal renal function

Dose in renal replacement therapy

CAPD	Start with lower doses. For single doses use 100% of normal dose. Avoid repeated dosage because of accumulation
HD	Start with lower doses. For single doses use 100% of normal dose. Avoid repeated dosage because of accumulation
CVVHDF	Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV, IM, PO:
0.01mg/kg daily; increased to 0.1mg/kg 12 hourly

CLINICAL PHARMACOLOGY:
Haloperidol is the first of the butyrophenone series of major tranquilisers. The precise mechanism of action has not been clearly established.

CONTRAINDICATIONS:
1. Hypersensitivity to haloperidol
2. Parkinson's disease

WARNINGS
Tardive Dyskinesia
A syndrome consisting of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. The syndrome usually develops with high doses given over a prolonged period; however, it can develop, although much less commonly, after relatively brief treatment periods at low doses.

Neuroleptic Malignant Syndrome (NMS)
A potentially fatal symptom complex referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with antipsychotic drugs.

PRECAUTIONS
General
Haloperidol may lower the seizure threshold
Severe neurotoxicity (rigidity, inability to walk or talk) may occur in patients with thyrotoxicosis who are also receiving antipsychotic medication, including haloperidol.

Laboratory Tests
No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions
None noted

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Combined Use of Haloperidol and Lithium

An encephalopathic syndrome (characterised by weakness, lethargy, fever, tremulousness and confusion, extrapyramidal symptoms, leukocytosis, elevated serum enzymes, BUN, and FBS) followed by irreversible brain damage has occurred in a few patients treated with lithium plus haloperidol. A causal relationship between these events and the concomitant administration of lithium and haloperidol has not been established; however, patients receiving such combined therapy should be monitored closely for early evidence of neurological toxicity and treatment discontinued promptly if such signs appear.

ADVERSE REACTIONS

Body as a Whole:

Neuroleptic malignant syndrome (NMS), hyperpyrexia and heat stroke have been reported with haloperidol.

Central Nervous System:

Extrapyramidal Symptoms (EPS), tardive dyskinesia, insomnia, restlessness, anxiety, euphoria, agitation, drowsiness, depression, lethargy, headache, confusion, vertigo, grand mal seizures, exacerbation of psychotic symptoms including hallucinations, and catatonic-like behavioural states

Cardiovascular:

Tachycardia, hypotension, hypertension and ECG changes including prolongation of the Q-T interval and torsades de pointes.

Haematological:

Mild and usually transient leukopaenia and leukocytosis, minimal decreases in red blood cell counts, anaemia, or a tendency toward lymphomonocytosis. Agranulocytosis has rarely been reported to have occurred with the use of haloperidol, and then only in association with other medication.

Endocrine Disorders:

Lactation, breast engorgement, mastalgia, menstrual irregularities, gynecomastia, impotence, increased libido, hyperglycaemia, hypoglycaemia and hyponatraemia.

Gastrointestinal Effects:

Anorexia, constipation, diarrhoea, hypersalivation, dyspepsia, jaundice, nausea and vomiting.

Autonomic Reactions:

Dry mouth, blurred vision, urinary retention, diaphoresis and priapism.

Respiratory Effects:

Laryngospasm, bronchospasm and increased depth of respiration.

Heparin [1 vial 25000 IU in 5ml $3.64]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Heparin, Multiparin

ICU INDICATIONS:
1. Anticoagulation

PRESENTATION AND ADMINISTRATION:
IV:
5000 units/ml in 5ml vials (25000 units); other formulations also available
For administration of heparin by infusion, prepare 25000 units of heparin in 50mls of compatible IV fluid
Administer via a dedicated central line or peripheral line.
Discard any solution not used within 24 hours or preparation
Compatible with the following IV fluids:
5% dextrose Normal saline Glucose and sodium chloride
Hartmanns
Store at room temperature

DOSAGE:
IV:
To reduce error, print an individualised 'Heparin Infusion Calculation' from the ICU database. Use this & the following protocol for heparin infusion **in ICU only**.
All doses are in units/kg and should be rounded to the nearest 100 units. APTT is measured 6 hourly for patients on a heparin infusion. (Note: 100 units equals 0.2ml when heparin is prepared according to the standard dilution above)

aPTT (sec)	Bolus Dose	Infusion Rate
Initial dose	**80 units/kg bolus**	**Begin infusion at 18 units/kg/hr**
aPTT <35 sec	80 units/kg bolus	Increase infusion rate by 4 units/kg/hr
aPTT 35-45 sec	40 units/kg bolus	Increase infusion rate by 2 units/kg/hr
aPTT >45-60	**No bolus**	Increase infusion rate by 2 units/kg/hr
aPTT >60-80	**No bolus**	**No change**
aPTT >80-90	**No bolus**	Decrease infusion rate by 2 units/kg/hr
aPTT >90	**No bolus**	Hold infusion for 1 hour then restart & decrease infusion rate by 3 units/kg/hr

(Adapted from Raschke RA, Reilly BM, Guidry JR, et al: The weight-based heparin dosing nomogram compared with a "standard care" nomogram. Ann Intern Med 1993;119:874.)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV
75-200 units/kg stat followed by infusion commencing at 15 units/kg/hr
Infusion made up as follows: 500 units / kg in 50ml at 0-2.5 ml/hr (0-25 units/kg/hr) adjusted according to APTT

CLINICAL PHARMACOLOGY:
Heparin inhibits reactions that lead to the clotting of blood and the formation of fibrin clots both in vitro and in vivo. Heparin acts at multiple sites in the normal coagulation system. Small amounts of heparin in combination with antithrombin III (heparin cofactor) can inhibit thrombosis by inactivating activated Factor X and inhibiting the conversion of prothrombin to thrombin.

CONTRAINDICATIONS:
1. Severe thrombocytopaenia
2. Heparin Induced Thromobsis-Thrombocytopaenia Syndrome (HITTS)

WARNINGS
Hypersensitivity
Patients with documented hypersensitivity to heparin should be given the drug only in clearly life-threatening situations.
Haemorrhage
Haemorrhage can occur at virtually any site in patients receiving heparin. An unexplained fall in hematocrit, fall in blood pressure, or any other unexplained symptom should lead to serious consideration of a haemorrhagic event.
Heparin sodium should be used with extreme caution in disease states in which there is increased danger of haemorrhage
Thrombocytopaenia
Thrombocytopaenia has been reported to occur in patients receiving heparin with a reported incidence of 0% to 30%. Mild thrombocytopaenia (count greater than 100,000/ mm^3) may remain stable or reverse even if heparin is continued. However, reduction in platelet count of any degree should be monitored closely. If the count falls below 100,000/mm^3 or if recurrent thrombosis develops, the heparin product should be discontinued.

PRECAUTIONS
General
Heparin Induced Thromobsis-Thrombocytopaenia Syndrome (HITTS):
It has been reported that patients on heparin may develop new thrombus formation in association with thrombocytopaenia resulting from irreversible aggregation of platelets induced by heparin, the so-called "white clot syndrome". The process may lead to severe thromboembolic complications like skin necrosis, gangrene of the extremities that may lead to amputation, myocardial infarction, pulmonary embolism, stroke, and possibly death. Therefore, heparin administration should be promptly discontinued if a patient develops new thrombosis in association with a reduction in platelet count.

Heparin Resistance:
Increased resistance to heparin is frequently encountered in fever, thrombosis, thrombophlebitis, infections with thrombosing tendencies, myocardial infarction, cancer, in postsurgical patients, and patients with antithrombin III deficiency.
Laboratory Tests
Patients in ICU on a heparin infusion should have their aPTT measured 6 hourly.

Drug/Laboratory Test Interactions
None noted

Pregnancy
Animal reproduction studies have not been conducted with heparin sodium. It is also not known whether heparin sodium can cause foetal harm when administered to a pregnant woman or can affect reproduction capacity. Heparin sodium should be given to a pregnant woman only if clearly needed.

Nursing Mothers
Heparin is not excreted in human milk.

Paediatric Use
See DOSAGE IN PAEDIATRICS

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Concomitant administration with warfarin, aspirin, activated protein C and enoxaparin increases the risk of bleeding.
Digitalis, tetracyclines, nicotine, or antihistamines may partially counteract the anticoagulant action of heparin sodium.

ADVERSE REACTIONS
Body as a Whole:
Haemorrhage, anaphylactic reactions
Gastrointestinal System:
Nausea, vomiting
Respiratory System:
Angioedema, asthma-like symptoms
Haematological System:
Thrombocytopaenia, HITTS (see PRECAUTIONS)

Hydralazine [1 vial $5.18, 1 tablet 25mg 54 cents]

ADMINISTRATION ROUTES:
IV, PO

ALTERNATIVE NAMES:
Apresoline

ICU INDICATIONS:
1. Afterload reduction / peripheral vasodilation

PRESENTATION AND ADMINISTRATION:
IV:
20mg vial of powder
Reconstitute with 1ml of water for injection
For direct injection, inject as either reconstituted solution or further dilute with a small volume of normal saline. Give over 1-2 minutes
For IV infusion reconstitute 100mg and add to 100ml of compatible IV fluid
Compatible with the following IV fluids:
Normal saline Hartmanns
Note 5% dextrose should not be used as glucose rapidly causes hydralazine to be broken down.
Prepare solutions immediately before use and discard after 24 hours. Hydralazine undergoes colour changes in most infusion fluids; however, these changes generally do not indicate loss of potency.
Store at room temperature.

PO:
Rarely indicated in ICU

DOSAGE:
IV:
5mg IV stat, then up to 20mg per hour by infusion.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Start with a small dose and adjust in accordance with response

DOSAGE IN PAEDIATRICS:
IV:
0.1-0.2mg/kg stat, then 4-6mcg/kg/min

CLINICAL PHARMACOLOGY:
Although the precise mechanism of action of hydralazine is not fully understood, the major effects are on the cardiovascular system. Hydralazine apparently lowers blood pressure by exerting a peripheral vasodilating effect through a direct relaxation of vascular smooth muscle

CONTRAINDICATIONS:
1. Hypersensitivity to hydralazine

WARNINGS

In a few patients hydralazine may produce a clinical picture simulating systemic lupus erythematosus including glomerulonephritis. In such patients hydralazine should be discontinued unless the benefit-to-risk determination requires continued antihypertensive therapy with this drug.

PRECAUTIONS

General

Myocardial stimulation produced by hydralazine can cause anginal attacks and ECG changes of myocardial ischaemia. The drug has been implicated in the production of myocardial infarction. It must, therefore, be used with caution in patients with suspected coronary artery disease

Peripheral neuritis, evidenced by paraesthesia, numbness, and tingling, has been observed.

Laboratory Tests

No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Concomitant administration with other antihypertensives increases the risk of hypotension

ADVERSE REACTIONS

Body as a Whole:

Rash, urticaria, pruritus, fever, chills

Cardiovascular System:

Hypotension, paradoxical pressor response, oedema, palpitations, tachycardia, angina pectoris

Respiratory System:

Dyspnea.

Gastrointestinal System:

Constipation, paralytic ileus, anorexia, vomiting, diarrhoea,

Haematological System:

Blood dyscrasias, consisting of reduction in haemoglobin and red cell count, leukopaenia, agranulocytosis, purpura; lymphadenopathy; splenomegaly.

Neurological System:

Headache, peripheral neuritis, evidenced by paraesthesia, numbness, and tingling; dizziness; tremors; muscle cramps; psychotic reactions characterised by depression, disorientation, or anxiety.

Hydrocortisone [1 vial 100mg $3.93, 1 tablet 20mg 20 cents]

ADMINISTRATION ROUTES:
IV, PO

ALTERNATIVE NAMES:
Solu-Cortef

ICU INDICATIONS:
1. Relative corticosteroid insufficiency in patients with severe septic shock
2. Adrenal insufficiency
3. Steroid responsive inflammatory conditions

PRESENTATION AND ADMINISTRATION:
IV:
100mg/2ml vial plus benzyl alcohol diluent
Reconstitute by pressing down on the plastic activator. This forces the diluent into the lower compartment. Gently agitate to dissolve powder. To withdraw solution, remove the plastic tab covering the stopper. Wipe the top of the stopper with an alcohol swab. Insert drawing up needle through the centre of the stopper until the tip is just visible. Invert vial and withdraw dose.
Reconstituted solutions and solutions with concentrations not exceeding 1mg/ml are stable for up to 24 hours.
Compatible with the following IV fluids:
Normal saline 5% Dextrose Glucose and sodium chloride
Hartmanns
Can be administered by infusion; however, preferred method in our ICU is administration by direct IV injection. Reconstituted solution is generally injection undiluted by slow IV injection.

PO:
Hydrocortisone 5mg and 20mg tablets (white)

DOSAGE:
IV:
Usual dose is 50mg 6 hourly for septic shock; however, many different dosage regimens exist for various indications (for most ICU indications 50mg 6 hourly is an appropriate dose)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV
0.5-4mg/kg 6 hourly

CLINICAL PHARMACOLOGY:
Hydrocortisone is a naturally occurring steroid hormone which has glucocorticoid and mineralocorticoid properties

CONTRAINDICATIONS:

1. The use of hydrocortisone sodium succinate sterile powder is contraindicated in premature infants because the 100, 250, 500and 1000 mg ACT-O-VIAL System contain benzyl alcohol. Benzyl alcohol has been reported to be associated with a fatal "Gasping Syndrome" in premature infants.

WARNINGS

Steroid induced myopathy:

An acute myopathy has been observed with the use of high doses of corticosteroids, most often occurring in patients with disorders of neuromuscular transmission (e.g., myasthenia gravis), or in patients receiving concomitant therapy with neuromuscular blocking drugs. This acute myopathy is generalized, may involve ocular and respiratory muscles, and may result in quadriparesis. Elevations of creatine kinase may occur. Clinical improvement or recovery after stopping corticosteroids may require weeks to years.

Adrenal-insufficiency due to steroids:

In patients on corticosteroid therapy subjected to unusual stress, increased dosage of rapidly acting corticosteroids before, during, and after the stressful situation is indicated.

Infections:

Corticosteroids may mask some signs of infection, and new infections may appear during their use.

Blood pressure:

Average and large doses of hydrocortisone can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. These effects are less likely to occur with the synthetic derivatives except when used in large doses.

PRECAUTIONS

General

There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis.

Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes, and severe depression to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Laboratory Tests

No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

The pharmacokinetic interactions listed below are potentially clinically important. Drugs that induce hepatic enzymes such as phenobarbital, phenytoin and rifampin may increase the clearance of corticosteroids and may require increases in corticosteroid dose to achieve the desired response.

ADVERSE REACTIONS

Fluid and Electrolyte Disturbances:

Sodium retention; fluid retention; congestive heart failure in susceptible patients; potassium loss; hypokalemic alkalosis; hypertension.

Musculoskeletal:
Muscle weakness; steroid myopathy, loss of muscle mass; osteoporosis; tendon rupture, particularly of the Achilles tendon; vertebral compression fractures; aseptic necrosis of femoral and humeral heads; pathologic fracture of long bones.

Gastrointestinal:
Peptic ulcer with possible perforation and haemorrhage; pancreatitis; abdominal distention; ulcerative oesophagitis; increases in alanine transaminase (ALT, SGPT), aspartate transaminase (AST, SGOT) and alkaline phosphatase have been observed following corticosteroid treatment.
Dermatologic:
Impaired wound healing; thin fragile skin; petechiae and ecchymoses; facial erythema; increased sweating; may suppress reactions to skin tests.
Neurological:
Convulsions; increased intracranial pressure with papilloedema (pseudotumour cerebri) usually after treatment; vertigo; headache.
Endocrine:
Menstrual irregularities; development of Cushingoid state; suppression of growth in children; secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery or illness; decreased carbohydrate tolerance; manifestations of latent diabetes mellitus; increased requirements for insulin or oral hypoglycaemic agents in diabetics.

Hyoscine Butylbromide [1 vial $1.91]

Note: this monograph does **not** apply to hyoscine hydrobromide (see next entry)

ADMINISTRATION ROUTES:
IV, PO, IM, SC

ALTERNATIVE NAMES:
Buscopan, Gastro-Soothe

ICU INDICATIONS:
1. Gastrointestinal tract spasm

PRESENTATION AND ADMINISTRATION:
IV:
20mg in 1ml (solution)
Room temperature. Protect from light.
Dilute required dose to 10ml with normal saline. Inject slowly over 3-5 minutes.
Compatible with the following IV fluids:
Normal saline 5% Glucose Glucose and sodium chloride
May be given into the side arm when the above IV fluids are being infused.

IM or SC:
Inject undiluted into a large muscle mass or subcutaneously

PO:
Buscopan 10mg (white)
Gastro-Soothe 10mg (white)

DOSAGE:
IV, IM, SC, PO:
20-40mg 6-8 hourly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV
0.5mg/kg 6-8 hourly IV

CLINICAL PHARMACOLOGY:
Buscopan exerts a spasmolytic action on the smooth muscle of the gastrointestinal, biliary and urinary tracts. As a quaternary ammonium derivative, hyoscine-N-butylbromide does not enter the central nervous system. Therefore, anticholinergic side effects at the central nervous system do not occur. Peripheral anticholinergic effects result from a ganglion-blocking action within the visceral wall as well as from anti-muscarinic activity.

CONTRAINDICATIONS:

1. Myasthenia gravis
2. Mechanical gastrointestinal tract obstruction

WARNINGS

Tachycardia:

Hyoscine butylbromide may cause marked tachycardia

Urinary retention:

Hyoscine butylbromide may precipitate urinary retention

PRECAUTIONS

General

Hyoscine butylbromide should not be given by intramuscular injection to patients being treated with anticoagulant drugs since intramuscular haematoma may occur. In these patients, the subcutaneous or intravenous routes may be used

Laboratory Tests

No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

The anticholinergic effect of drugs such as tricyclic antidepressants, antihistamines, quinidine, amantadine, disopyramide and other anticholinergics (e.g. tiotropium, ipratropium) may be intensified by Hyoscine-N-butylbromide.

Concomitant treatment with dopamine antagonists such as metoclopramide may result in diminution of the effects of both drugs on the gastrointestinal tract.

The tachycardic effects of beta-adrenergic agents may be enhanced by Hyoscine-N-butylbromide

ADVERSE REACTIONS

Body as a Whole

Anaphylactic shock, anaphylactoid reactions and other hypersensitivity, skin reactions

Cardiovascular

Tachycardia, hypotension, dizziness, flushing

Respiratory

Dyspnoea

Gastrointestinal

Dry mouth

Renal and urinary disorders

Urinary retention

Hyoscine Hydrobromide [1 vial $1.33]

Note: this monograph does **not** apply to hyoscine butylbromide (see previous entry)

ADMINISTRATION ROUTES:
IV, IM, SC

ALTERNATIVE NAMES:
Scopolamine hydrobromide

ICU INDICATIONS:
1. Reduction of respiratory tract and oral secretions (particularly in the palliative setting). Note, for this indication, hyoscine butylbromide is preferred by the palliative care team.

PRESENTATION AND ADMINISTRATION:
IV:
0.4mg in 1ml (solution)
Room temperature. Protect from light.
Dilute required dose to 10ml with normal saline. Inject slowly over 3-5 minutes.
Compatible with the following IV fluids:
Normal saline 5% Glucose Hartmanns

IM or SC:
Inject undiluted into a large muscle mass or subcutaneously

DOSAGE:
IV, IM, SC:
0.3-0.6 mg 6-8 hourly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV, IM, SC:
6-8mcg/kg 6-8 hourly

CLINICAL PHARMACOLOGY:
Hyoscine hydrobromide is one of the major antimuscarinic agents that inhibit the action of acetylcholine (ACh) on autonomic effectors innervated by postganglionic cholinergic nerves as well as on smooth muscles that lack cholinergic innervation. It exerts little effects on the actions of ACh at nicotinic receptor sites such as autonomic ganglia.

CONTRAINDICATIONS:
1. Hypersensitivity to hyoscine hydrobromide

WARNINGS
May cause significant sedation

PRECAUTIONS

General

Because of the tachycardic effects of the drugs, care must be exercised when tachycardia, other tachyarrhythmias, coronary heart disease, congestive heart disease or hyperthyroidism preexist.

Laboratory Tests

No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Other drugs, such as phenothiazines, tricyclic antidepressants, certain antihistamines, which have weak antimuscarinic activity, may considerably intensify the effects of antimuscarinic drugs.

ADVERSE REACTIONS

Body as a Whole:

Suppression of sweating causes reflexive flushing and heat intolerance

Nervous System:

Sedation, confusion, hallucinations

Cardiovascular

Hypotension, tachycardia

Gastrointestinal

Dry mouth

Urogenital:

Urinary Retention

Ibuprofen [1 tablet 1 cent]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Ibuprofen, Brufen, I-Profen, Nurofen, Panafen, ACT-3, Fenpaed

ICU INDICATIONS:
1. Analgesia

PRESENTATION AND ADMINISTRATION:
PO:
Tablets:
Apo-ibuprofen 200mg (yellow), Brufen 400mg (white), I-Profen 200mg, Ibuprofen 200mg (white), Nurofen 200mg (white), Panafen 200mg
Sustained Release Tablets:
Brufen Retard 800mg
Capsules:
ACT-3 200mg (green), Nurofen liquid capsules 200mg
Oral Suspension:
Fenpaed oral suspension 100mg/5ml, Nurofen for children 100mg/5ml

DOSAGE:
PO / NG:
400mg 6 hourly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	dose as in normal renal function, but avoid unless ESRF on dialysis
10-20	dose as in normal renal function, but avoid if possible
>20-50	dose as in normal renal function, but avoid if possible

Dose in renal replacement therapy

CAPD	dose as in normal renal function
HD	dose as in normal renal function
CVVHDF	dose as in normal renal function, but avoid unless ESRF on long-term dialysis

DOSAGE IN PAEDIATRICS:
PO:
5-10mg/kg 6 hourly

CLINICAL PHARMACOLOGY:
Ibuprofen is a non-steroidal anti-inflammatory drug

CONTRAINDICATIONS:
1. Hypersensitivity to ibuprofen
2. The syndrome of nasal polyps, angioedema, and bronchospastic reactivity to aspirin or other nonsteroidal anti-inflammatory agents.

WARNINGS

Risk of GI Ulceration, Bleeding and Perforation

Serious gastrointestinal toxicity such as bleeding, ulceration, and perforation, can occur at any time, with or without warning symptoms, in patients treated with nonsteroidal anti-inflammatory drugs.

Bleeding Risk:

Ibuprofen, like other nonsteroidal anti-inflammatory agents, can inhibit platelet aggregation but the effect is quantitatively less and of shorter duration than that seen with aspirin. Ibuprofen has been shown to prolong bleeding time (but within the normal range) in normal subjects. Because this prolonged bleeding effect may be exaggerated in patients with underlying haemostatic defects, ibuprofen should be used with caution in persons with intrinsic coagulation defects and those on anticoagulant therapy.

Renal Effects:

As with other nonsteroidal anti-inflammatory drugs, long-term administration of ibuprofen to animals has resulted in renal papillary necrosis and other abnormal renal pathology. In humans, there have been reports of acute interstitial nephritis with haematuria, proteinuria, and occasionally nephrotic syndrome.

A second form of renal toxicity has been seen in patients with prerenal conditions leading to a reduction in renal blood flow or blood volume, where the renal prostaglandins have a supportive role in the maintenance of renal perfusion. In these patients administration of a nonsteroidal anti-inflammatory drug may cause a dose dependent reduction in prostaglandin formation and may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, those taking diuretics and the elderly.

PRECAUTIONS

General

Liver effects

As with other nonsteroidal anti-inflammatory drugs, borderline elevations of one or more liver function tests may occur in up to 15% of patients. These abnormalities may progress, may remain essentially unchanged, or may be transient with continued therapy. Severe hepatic reactions, including jaundice and cases of fatal hepatitis, have been reported with ibuprofen as with other nonsteroidal anti-inflammatory drugs. Although such reactions are rare, if abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), ibuprofen should be discontinued.

Aseptic Meningitis

Aseptic meningitis with fever and coma has been observed on rare occasions in patients on ibuprofen therapy. Although it is probably more likely to occur in patients with systemic lupus erythematosus and related connective tissue diseases, it has been reported in patients who do not have an underlying chronic disease.

Laboratory Tests

No tests additional to routine ICU tests are indicated

Drug/Laboratory Test Interactions

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Diuretics:

Clinical studies have shown that ibuprofen can reduce the natriuretic effect of furosemide and thiazides in some patients. This response has been attributed to inhibition of renal prostaglandin synthesis. During concomitant therapy with ibuprofen, the patient should be observed closely for signs of renal failure, as well as to assure diuretic efficacy.

Lithium:

Ibuprofen produces an elevation of plasma lithium levels and a reduction in renal lithium clearance in patients on concomitant therapy.

Anticoagulants:

Risk of bleeding is additive with other anticoagulant drugs.

ADVERSE REACTIONS

Haematologic

Neutropaenia, agranulocytosis, aplastic anaemia, haemolytic anaemia (sometimes Coombs positive), thrombocytopaenia with or without purpura, eosinophilia,

Cardiovascular

Oedema, palpitations, rrhythmias (sinus tachycardia, sinus bradycardia)

Renal

Acute renal failure, decreased creatinine clearance, polyuria, azotaemia, cystitis, haematuria, renal papillary necrosis

Gastrointestinal

Nausea, epigastric pain , heartburn , diarrhoea, abdominal distress, nausea and vomiting, indigestion, constipation, abdominal cramps or pain, fullness of GI tract (bloating and flatulence) Gastric or duodenal ulcer with bleeding and/or perforation, gastritis, hepatitis, jaundice, abnormal liver function tests; pancreatitis

Central Nervous System

Dizziness, headache, nervousness, depression, insomnia, confusion, emotional lability, somnolence, aseptic meningitis with fever and coma, paraesthesias, hallucinations, dream abnormalities, pseudotumour cerebri

Dermatologic

Rash, (including maculopapular type), pruritus Vesiculobullous eruptions, urticaria, erythema multiform, Stevens-Johnson syndrome, allopecia Toxic epidermal necrolysis, photoallergic skin reactions

Special Senses

Tinnitus Hearing loss, amblyopia (blurred and/or diminished vision, scotomata and/or changes in colour vision) Conjunctivitis, diplopia, optic neuritis, cataracts

Iloprost [1 vial for nebulisation $39.50]

ADMINISTRATION ROUTES:
Nebulised

BRAND NAMES:
Ventavis

ICU INDICATIONS:
1. Right ventricular failure with pulmonary artery hypertension after separation from cardiopulmonary bypass and failure to improve with standard therapy.

Note: Administration in ICU is only possible after discussion with the Intensive Care Specialist.

PRESENTATION AND ADMINISTRATION:
Nebuliser:
20mcg in 2ml ampoule
Mix contents of ampoule with 3ml 0.9% saline & administer into ventilator tubing using an Aeroneb Pro X micropump nebuliser which will deliver the dose over 30 minutes.

The nebuliser is single patient but multiple use - **do not throw away**.
Do not mix with other inhaled or nebulised medications.
Information on how to set up the nebuliser is available on the ICU intranet & in policy TI ICU CD GEN-04.

DOSAGE:
Nebuliser:
20mcg nebulised up to a maximum of every 2 hours. At this frequency, the maximum duration of administration is 48 hours. Treatment may be continued on post-operative days 3 & 4 as 20mcg every 6 hours.
Initially reduce frequency of administration (rather than dose) to titrate to effect.
A response to iloprost is indicated by an increase in cardiac output or mixed venous oxygen saturation, often with reduction in central venous pressure. There may be minimal or no change in pulmonary artery pressure (even though pulmonary vascular resistance has fallen).

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose adjustment is not required for patients with creatinine clearance >30ml/min.
The effect of dialysis on iloprost is unknown.

DOSAGE IN PAEDIATRICS:
Iloprost should not be administered to children or adolescents under 18 years of age.

CLINICAL PHARMACOLOGY:
Iloprost is a synthetic prostacyclin analog. After inhalation, it causes direct vasodilatation of the pulmonary arterial bed with subsequent decrease in pulmonary vascular resistance & increase in cardiac output and mixed venous oxygen saturation. Effects on systemic vascular resistance & systemic arterial pressure are minor. The risk of rebound pulmonary artery hypertension seen with inhaled nitric oxide does not appear to be present with iloprost. Similarly, it does not cause hypotension & tends to improve oxygenation.

There may be an additional benefit to using iloprost with sildenafil as they have different pathways of action.

CONTRAINDICATIONS:
1. Known hypersensitivity to iloprost
2. Severe hepatic impairment (see WARNINGS below)
3. Severe asthma or COPD (relative contraindication - see WARNINGS below)
4. Pregnancy (iloprost should only be used in pregnancy if the potential benefits to the mother justify the risk to the fetus)

WARNINGS:
Use with caution in patients with mild to moderate hepatic dysfunction. The initial dosing frequency should be decreased with intervals of 3-4 hours between nebulisers. Thereafter the dosing interval may be shortened based on individual tolerability.

Bronchospasm of varying severity may be induced by iloprost. Patients with bronchial hyperreactivity are more susceptible. Use with caution in patients with severe asthma or chronic obstructive pulmonary disease.

PRECAUTIONS:
General
Iloprost should only be administered in the presence of a cardiac output monitor (such as a pulmonary artery catheter) so that its efficacy can be evaluated.

Laboratory Tests
No tests are required in addition to routine ICU blood tests

Drug/Laboratory Test Interactions
None known

Pregnancy
Relatively contraindicated. See CONTRAINDICATIONS above.

Nursing Mothers
Iloprost is excreted into maternal milk in animal studies. No human data is available.

Paediatric Use
Iloprost should not be administered to children or adolescents under 18 years of age.

IMPORTANT DRUG INTERACTIONS FOR THE ICU:
Iloprost may increase the antihypertensive effect of vasodilating and antihypertensive agents.

Iloprost inhibits platelet function so its use with anticoagulants (heparin, warfarin) or other inhibitors of platelet aggregation may increase the risk of bleeding. If bleeding occurs, iloprost administration should be stopped immediately.

ADVERSE REACTIONS:
General:
Bleeding events (epistaxis, haemoptysis, haematoma), thrombocytopaenia

Cardiovascular:
Vasodilation, hypotension, syncope
Respiratory:
Bronchospasm, chest pain, cough, dyspnoea, pharyngolaryngeal pain
Neurological:
Headache, dizziness
Gastrointestinal:
Nausea, diarrhoea, vomiting, mouth and tongue irritation
May increase liver enzymes
Skin:
Rash

Imipenem with Cilastatin [1 vial $3.67]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Primaxin

ICU INDICATIONS:
1. Treatment of infections caused by susceptible organisms
2. Broad spectrum cover of hospital-acquired infections (particularly in the setting of intra-abdominal sepsis)

PRESENTATION AND ADMINISTRATION:
IV:
Injection (vial) 500mg imipenem and 500mg cilastatin (powder)
Add 10ml of compatible IV fluid to the powder in each 500mg vial and shake to form a suspension (which must be further diluted before IV infusion). Transfer this suspension to IV fluid container. Each 500mg of dose should be diluted with 100ml of compatible IV fluid, whilst for a 1gm dose use a 250ml bag.
Agitate the contained until the solution is clear
Infuse doses of 500mg over 20 minutes. Infuse doses of 500mg to 1gm over 40 to 60 minutes.
If patient develops nausea during infusion, the rate of infusion may be slowed.
Compatible with the following IV fluids:

Normal saline	5% glucose and 0.15% KCL	5% or 10% glucose
5% and 10% Mannitol	Glucose and sodium chloride	

DOSAGE:
IV:
500mg - 1gm 6 hourly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<20	250mg (or 3.5mg/kg which ever is lower) every 12 hours
20-30	500mg-1gm every 12 hours
>30-70	500mg-1gm every 8 hours

Dose in renal replacement therapy

CAPD	500mg-1gm every 8 hours
HD	500mg-1gm every 12 hours
CVVHDF	500mg-1gm every 12 hours

DOSAGE IN PAEDIATRICS:
IV:
15-25mg/kg 6 hourly

CLINICAL PHARMACOLOGY:
Imipenem is a carbapenem antibiotic. The bactericidal activity of imipenem results from the inhibition of cell wall synthesis.
Imipenem has a high degree of stability in the presence of beta-lactamases, both

penicillinases and cephalosporinases produced by gram-negative and gram-positive bacteria. It is a potent inhibitor of betalactamases from certain gram-negative bacteria which are inherently resistant to most beta-lactam antibiotics, e.g., Pseudomonas aeruginosa, Serratia spp., and Enterobacter spp.

Imipenem has in vitro activity against a wide range of gram-positive and gram-negative organisms. In vitro tests show imipenem to act synergistically with aminoglycoside antibiotics against some isolates of Pseudomonas aeruginosa. Imipenem has been shown to be active against most strains of the following microorganisms, both in vitro and in clinical infections.

Gram-positive aerobes:
Enterococcus faecalis (NOTE: Imipenem is inactive in vitro against Enterococcus faecium)
Staphylococcus aureus including penicillinase-producing strains
Staphylococcus epidermidis including penicillinase-producing strains (NOTE: Methicillin-resistant staphylococci should be reported as resistant to imipenem.)
Streptococcus agalactiae (Group B streptococci)
Streptococcus pneumoniae
Streptococcus pyogenes
Gram-negative aerobes:
Acinetobacter spp.
Citrobacter spp.
Enterobacter spp.
Escherichia coli
Gardnerella vaginalis
Haemophilus influenzae
Haemophilus parainfluenzae
Klebsiella spp.
Morganella morganii
Proteus vulgaris
Providencia rettgeri
Pseudomonas aeruginosa (NOTE: Imipenem is inactive in vitro against Xanthomonas (Pseudomonas) maltophilia and some strains of P. cepacia.)
Serratia spp., including S. marcescens
Gram-positive anaerobes:
Bifidobacterium spp.
Clostridium spp.
Eubacterium spp.
Peptococcus spp.
Peptostreptococcus spp.
Propionibacterium spp.
Gram-negative anaerobes:
Bacteroides spp., including B. fragilis
Fusobacterium spp.

CONTRAINDICATIONS:

1. Hypersensitivity to carbapenems

WARNINGS

SERIOUS AND OCCASIONALLY FATAL HYPERSENSITIVITY (ANAPHYLACTIC) REACTIONS HAVE BEEN REPORTED IN PATIENTS RECEIVING THERAPY WITH BETA-LACTAMS. THESE REACTIONS ARE MORE APT TO OCCUR IN PERSONS WITH A HISTORY OF SENSITIVITY TO MULTIPLE ALLERGENS.

THERE HAVE BEEN REPORTS OF PATIENTS WITH A HISTORY OF PENICILLIN HYPERSENSITIVITY WHO HAVE EXPERIENCED SEVERE HYPERSENSITIVITY REACTIONS WHEN TREATED WITH ANOTHER BETA-LACTAM. BEFORE INITIATING THERAPY WITH IMIPENEM IV, CAREFUL INQUIRY SHOULD BE MADE CONCERNING PREVIOUS HYPERSENSITIVITY REACTIONS TO PENICILLINS, CEPHALOSPORINS, OTHER BETA-LACTAMS, AND OTHER ALLERGENS.

PRECAUTIONS

General

Seizures and other CNS adverse experiences, such as confusional states and myoclonic activity, have been reported during treatment with imipenem

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including imipenem-cilastatin sodium, and may range in severity from mild to life threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents.

Laboratory Tests:

No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions

None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU:

Generalised seizures have been reported in patients who received ganciclovir and imipenem. These drugs should not be used concomitantly unless the potential benefits outweigh the risks.

ADVERSE REACTIONS

Body as a whole:

Polyarthralgia, asthenia/weakness, drug fever.

Gastrointestinal:

Pseudomembranous colitis, diarrhoea, nausea, vomiting, haemorrhagic colitis, hepatitis (including fulminant hepatitis), jaundice, gastroenteritis, abdominal pain, glossitis, tongue papillar hypertrophy, staining of the teeth and/or tongue, heartburn, pharyngeal pain, increased salivation.

Haematologic:

Pancytopaenia, bone marrow depression, thrombocytopaenia, neutropaenia, leukopaenia, haemolytic anaemia.

CNS:

Seizures, encephalopathy, tremor, confusion, myoclonus, paraesthesia, vertigo, headache, psychic disturbances including hallucinations.

Respiratory:

Chest discomfort, dyspnea, hyperventilation, thoracic spine pain.

Cardiovascular:

Palpitations, tachycardia.

Skin:

Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme, angioneurotic edema, flushing, cyanosis, hyperhidrosis, skin texture changes, candidiasis, pruritus vulvae.

Renal:

Acute renal failure, oliguria/anuria, polyuria, urine discolouration.

Ipratropium Bromide [1 nebule 500mcg 20 cents]

ADMINISTRATION ROUTES:
Inhaled, Nebulised

ALTERNATIVE NAMES:
Atrovent, Combivent (ipratropium + salbutamol), Duolin (ipratropium + salbutamol)

ICU INDICATIONS:
1. Bronchospasm

PRESENTATION AND ADMINISTRATION:
Inh:
Atrovent inhaler 20mcg/dose
Combivent inhaler 20mcg atrovent per dose and 100mcg salbutamol per dose

Neb:
Ipratropium steri-neb 500mcg/2ml
Duolin 500mcg ipratropium and salbutamol 2.5mg per 2.5ml

DOSAGE:
Inh:
2 puffs 4 times per day or, if ventilated, 5 puffs via metered dose inhaler adaptor into ventilator circuit

Neb:
1 vial of Ipratropium or Duolin four times a day

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
Neb:
0.25-1ml of 250mcg/ml solution diluted to 4ml. In a severe attack administer every 20 minutes for 3 doses then administer 4 to 6 hourly after that.

CLINICAL PHARMACOLOGY:
Ipratropium bromide is an anticholinergic (parasympatholytic) agent. Anticholinergics prevent the increases in intracellular concentration of cyclic guanosine monophosphate (cyclic GMP) which are caused by interaction of acetylcholine with the muscarinic receptor on bronchial smooth muscle.

CONTRAINDICATIONS
1. Hypersensitivity to ipratropium bromide
2. Hypersensitivity to atropine or its derivatives.

WARNINGS
Immediate hypersensitivity reactions may occur after administration of ipratropium bromide, as demonstrated by rare cases of urticaria, angioedema, rash, bronchospasm, anaphylaxis and oropharyngeal edema.
Inhaled medicines, including ipratropium bromide, may cause paradoxical bronchospasm. If this occurs, treatment with ipratropium bromide aerosol should be stopped and other treatments

PRECAUTIONS
General
Ipratropium should be used with caution in patients with narrow-angle glaucoma, prostatic hypertrophy or bladder-neck obstruction.

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions
None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note.

ADVERSE REACTIONS
Body as a Whole
Back pain, headache
Central and Peripheral Nervous System
Dizziness
GI System
Dyspepsia, mouth dry, nausea
Respiratory System
Coughing, dyspnoea, rhinitis, sinusitis
Urinary System
Urinary tract infection

Isoprenaline Hydrochloride [1 vial $5.40]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Isuprel

ICU INDICATIONS:
1. Bradycardia

Note: current international guidelines do not recommend isoprenaline as the first line agent to treat any condition.

PRESENTATION AND ADMINISTRATION:
IV:
Isoprenaline 1mg in 5ml (1:5000) vials
For IV infusion, add 1mg to total volume of 50ml of compatible IV fluid and administer at 0-60ml/hr (0-20mcg/min)
Compatible with the following IV fluids:
Normal saline glucose and sodium chloride 5% glucose
Hartmanns
Does not require refrigeration. Do not freeze. Protect from light and air.
Discard any diluted fluid not used within 24 hours of preparation
Do not use solution if pinkish to brown in colour or contains precipitate

DOSAGE:
IV:
Usual dosage is 0.5mcg/min to 5mcg/min although doses of 20mcg/min or greater have been used. For bolus dosing, can dilute 200mcg in 20ml and administer 1ml bolus.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV infusion:
300mcg/kg in 50ml of compatible IV fluid. Commence infusion at 0.1mcg/kg/min (1ml/hr) and titrate to effect.

CLINICAL PHARMACOLOGY:
Isoproterenol hydrochloride is a synthetic sympathomimetic amine that is structurally related to epinephrine but acts almost exclusively on beta receptors.

CONTRAINDICATIONS
1. Heart block caused by digitalis intoxication
2. Known hypersensitivity to isoprenaline

WARNINGS
Potential for worsening of cardiac function
Isoprenaline, by increasing myocardial oxygen requirements while decreasing effective coronary perfusion, may have a deleterious effect on the injured or failing heart.

Worsening of heart block
In a few patients, presumably with organic disease of the AV node and its branches, isoprenaline has paradoxically been reported to worsen heart block or to precipitate Adams-Stokes attacks during normal sinus rhythm or transient heart block.
Contains sulfite
Contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people.

PRECAUTIONS
General
Isoprenaline should generally be started at the lowest recommended dose. This may be gradually increased if necessary while carefully monitoring the patient. Doses sufficient to increase the heart rate to more than 130 beats per minute may increase the likelihood of inducing ventricular arrhythmias. Such increases in heart rate will also tend to increase cardiac work and oxygen requirements which may adversely affect the failing heart or the heart with a significant degree of arteriosclerosis.
Particular caution is necessary in administering isoprenaline to patients with coronary artery disease, coronary insufficiency, diabetes, hyperthyroidism, and sensitivity to sympathomimetic amines.

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions
None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Isoprenaline and adrenalin should not be administered simultaneously because both drugs are direct cardiac stimulants and their combined effects may induce serious arrhythmias.
Beta receptor blocking agents and isoprenaline inhibit the effects of each other.

ADVERSE REACTIONS
CNS:
Nervousness, headache, dizziness.
Cardiovascular:
Tachycardia, palpitations, angina, Adams-Stokes attacks, pulmonary oedema, hypertension, hypotension, ventricular arrhythmias, tachyarrhythmias.
Other:
Flushing of the skin, sweating, mild tremors, weakness

Ketamine [1 vial $39.00]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Ketalar

ICU INDICATIONS:
1. Analgesia
2. Induction of anaesthesia

PRESENTATION AND ADMINISTRATION:
IV:
200mg/2ml vial
Compatible with the following IV fluids:
Normal saline 5% dextrose
Store at room temperature
For infusion dilute with compatible IV fluid to a dilution of 1mg/ml (e.g. 50mg in 50ml)

DOSAGE:
IV:
Induction of anaesthesia:
100-200mg IV
Analgesia:
Usual dilution 1mg/ml. Bolus doses of 1-2mg. Background infusion of 5mg/hr if required.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Specific guidelines for dosage adjustments in renal impairment are not available; it appears that no dosage adjustments are needed.

DOSAGE IN PAEDIATRICS:
Induction of anaesthesia:
1-2mg/kg IV
Analgesia
0-4mcg/kg/min

CLINICAL PHARMACOLOGY:
Ketamine is a rapid-acting general anaesthetic producing an anaesthetic state characterised by profound analgesia, normal pharyngeal-laryngeal reflexes, normal or slightly enhanced skeletal muscle tone, cardiovascular and respiratory stimulation, and occasionally a transient and minimal respiratory depression.

CONTRAINDICATIONS
1. Any condition where severe hypertension would constitute a serious hazard

WARNINGS
EMERGENCE REACTIONS HAVE OCCURRED IN APPROXIMATELY 12% OF PATIENTS. THE PSYCHOLOGICAL MANIFESTATIONS VARY IN SEVERITY BETWEEN PLEASANT DREAM-LIKE STATES, VIVID IMAGERY, HALLUCINATIONS, AND EMERGENCE DELIRIUM. IN SOME CASES THESE STATES HAVE BEEN ACCOMPANIED BY CONFUSION, EXCITEMENT, AND IRRATIONAL BEHAVIOUR WHICH A FEW PATIENTS RECALL AS AN UNPLEASANT EXPERIENCE. THE DURATION ORDINARILY IS NO MORE THAN A FEW HOURS; IN A FEW CASES, HOWEVER, RECURRENCES HAVE TAKEN PLACE UP TO 24 HOURS POSTOPERATIVELY. THE INCIDENCE OF THESE EMERGENCE PHENOMENA IS LEAST IN THE YOUNG (15 YEARS OF AGE OR LESS) AND ELDERLY (OVER 65 YEARS OF AGE) PATIENT.

PRECAUTIONS
General
An increase in intracranial pressure has been reported following administration of ketamine. Use with extreme caution in patients with raised intracranial pressure.

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions
None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note.

ADVERSE REACTIONS
General:
Anaphylaxis. Local pain and exanthema at the injection site have infrequently been reported. Transient erythema and/or morbilliform rash have also been reported.
Cardiovascular:
Blood pressure and pulse rate are frequently elevated following administration of ketamine. However, hypotension and bradycardia have been observed. Arrhythmia has also occurred.
Respiratory:
Although respiration is frequently stimulated, severe depression of respiration or apnea may occur following rapid intravenous administration of high doses of ketamine. Laryngospasms and other forms of airway obstruction have occurred during ketamine anaesthesia.
Neurological:
In some patients, enhanced skeletal muscle tone may be manifested by tonic and clonic movements sometimes resembling seizures
Gastrointestinal:
Anorexia, nausea and vomiting have been observed; however this is not usually severe

Labetalol [1 vial $17.72, 1 tablet 100mg 10 cents]

ADMINISTRATION ROUTES:
IV, PO

ALTERNATIVE NAMES:
Hybloc, Trandate

ICU INDICATIONS:
1. Hypertension

PRESENTATION AND ADMINISTRATION:
PO:
Hybloc 50mg, 100mg, 200mg, 400mg

IV:
100mg in 20ml (5 mg/ml). Administration undiluted is through central line only; peripheral administration requires dilution to 1 mg/ml
Bolus: 10-50 mg (2-10 mls over 2 mins), repeat every 5 mins to max total dose 200 mg
Infusion:
CVL only: 300 mg in 60 ml (undiluted = 5 mg/ml) at a rate of 0-30 ml/hr (0-150 mg/hr)
Peripheral line: add 200mg (2 ampoules) to 160 ml compatible fluid giving 200 mg in 200 ml = 1 mg/ml at a rate of 0-100 ml/hr (0-100 mg/hr)

Administering dilute labetalol via a peripheral line at high infusion rates may cause fluid overload and contribute to hypertension. Consider administration via central line, switch to oral/nasogastric route, or use of an alternative agent.

Compatible with the following IV fluids:
5% dextrose normal saline Hartmann's glucose & sodium chloride

DOSAGE:
PO:
50-100mg 12 hourly; may be increased to maximum of 600mg 6 hourly if required.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO:
1-2mg/kg 12 hourly; may increase to 10mg/kg 6 hourly

IV:
0.25-0.5mg/kg over 2 minutes repeated every 10 minutes if required
For infusion, 50mg/kg in 50ml of compatible IV fluid at 0-3ml/hr (0-3mg/kg/hr)

CLINICAL PHARMACOLOGY:
Labetalol hydrochloride is an adrenergic receptor blocking agent that has both selective alpha1-adrenergic and nonselective beta-adrenergic receptor blocking actions in a single substance. Labetalol is completely absorbed from the gastrointestinal tract with peak plasma levels occurring 1-2 hours after oral administration. The absolute bioavailability (fraction of drug reaching systemic circulation) of labetalol when

compared to an IV infusion is 25%; this is due to extensive "first-pass" metabolism. Despite "first-pass" metabolism there is a linear relationship between oral doses of 100-3000 mg and peak plasma levels. The absolute bioavailability of labetalol is increased when administered with food.

CONTRAINDICATIONS:

1. Sinus bradycardia,
2. Heart block greater than first degree,
3. Cardiogenic shock,
4. Overt cardiac failure
5. Asthma

WARNINGS

Hepatic Injury

Severe hepatocellular injury, confirmed by rechallenge in at least one case, occurs rarely with labetalol therapy. The hepatic injury is usually reversible, but hepatic necrosis and death have been reported.

Cardiac Failure

Sympathetic stimulation is necessary in supporting circulatory function in congestive heart failure, and beta blockade carries the potential hazard of further depressing myocardial contractility and precipitating more severe failure.

Discontinuation of therapy

Discontinuation of therapy in a patient with coronary artery disease may lead to rebound angina, arrhythmia or myocardial infarction.

Diabetes and Hypoglycaemia

Beta blockers may mask tachycardia occurring with hypoglycaemia.

Thyrotoxicosis

Beta-adrenergic blockade may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism. Abrupt withdrawal of beta blockade might precipitate a thyroid storm.

Rapid Decreases of Blood Pressure

Caution must be observed when reducing severely elevated blood pressure. A number of adverse reactions, including cerebral infarction, optic nerve infarction, angina, and ischemic changes in the electrocardiogram have been reported with other agents when severely elevated blood pressure was reduced over time courses of several hours to as long as 1 or 2 days. The desired blood pressure lowering should therefore be achieved over as long a period of time as is compatible with the patient's status.

Extravasation

Extravasation of undiluted labetalol (5 mg/ml) may cause ischaemia & necrosis due to the low pH of the solution. Only administer undiluted labetalol through a CVL.

PRECAUTIONS

General

Impaired Hepatic Function:

Labetalol should be used with caution in patients with impaired hepatic function since metabolism of the drug may be diminished.

Laboratory Tests:

No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions :
The presence of labetalol metabolites in the urine may result in falsely elevated levels of urinary catecholamines, metanephrine, normetanephrine, and vanillylmandelic acid when measured by fluorimetric or photometric methods. In screening patients suspected of having a pheochromocytoma and being treated with labetalol, a specific method, such as a high performance liquid chromatographic assay with solid phase extraction should be employed in determining levels of catecholamines. Labetalol has also been reported to produce a false-positive test for amphetamine when screening urine for the presence of drugs using the commercially available assay methods Toxi-Lab A (thin-layer chromatographic assay) and Emit-d.a.u. (radioenzymatic assay). When patients being treated with labetalol have a positive urine test for amphetamine using these techniques, confirmation should be made by using more specific methods, such as a gas chromatographic-mass spectrometer technique.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Beta blockers may exacerbate the rebound hypertension which can follow the withdrawal of clonidine. Drugs possessing beta-blocking properties can blunt the bronchodilator effect of beta-receptor agonist drugs in patients with bronchospasm; therefore, doses greater than the normal anti-asthmatic dose of beta-agonist bronchodilator drugs may be required.

ADVERSE REACTIONS
Body as a Whole:
Tiredness, Fatigue
Cardiovascular System:
Bradycardia, Cold extremities, Hypotension, Leg pain
Respiratory System:
Wheeziness, Dyspnoea
Digestive System:
Diarrhoea, Nausea, Hepatitis
Nervous System:
Dizziness, Vertigo, Light-headedness

Lactulose [syrup 10ml 7 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Duphalac

ICU INDICATIONS:
1. Constipation
2. Hepatic encephalopathy

PRESENTATION AND ADMINISTRATION:
PO:
Duphalac 10g/15ml
Store at room temperature

DOSAGE:
PO:
Constipation
10-20ml 12-24 hourly.
Hepatic Coma
Hourly doses of 30-45 ml of lactulose may be used to induce the rapid laxation in the initial phase of the therapy of portal-systemic encephalopathy. When the laxative effect has been achieved, the dose of lactulose may then be reduced to the recommended daily dose of 30-45ml 3-4 times daily. Continuous long-term therapy is indicated to lessen the severity and prevent the recurrence of portal-systemic encephalopathy. The dose for this purpose is the same as the recommended daily dose.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO:
Constipation
0.5mg/kg 12-24 hourly
Hepatic coma
1mg/kg hourly until bowel cleared then 1mg/kg 6-8 hourly

CLINICAL PHARMACOLOGY:
Lactulose is a synthetic disaccharide in solution form for oral administration. It is a colonic acidifier that promotes laxation. Lactulose causes a decrease in blood ammonia concentration and reduces the degree of portal systemic encephalopathy. These actions are considered to be results of the following: Bacterial degradation of lactulose in the colon acidifies the colonic contents. This acidification of colonic contents results in the retention of ammonia in the colon as the ammonium ion. Since the colonic contents are then more acid than the blood, ammonia can be expected to migrate from the blood into the colon to form the ammonium ion. The acid colonic contents convert NH3 to the ammonium ion (NH4)+, trapping it and preventing its absorption. The laxative action of the metabolites of lactulose then expels the trapped ammonium ion from the colon.

CONTRAINDICATIONS:

1. Mechanical bowel obstruction
2. Since lactulose contains galactose, it is contraindicated in patients who require a low galactose diet.

WARNINGS
Infants receiving lactulose may develop hyponatraemia and dehydration.

PRECAUTIONS
General
See WARNINGS and CONTRAINDICATIONS

Laboratory Tests:
No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions:
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Other laxatives should not be used, especially during the initial phase of therapy for portal-systemic encephalopathy, because the loose stools resulting from their use may falsely suggest that adequate Lactulose dosage has been achieved.

ADVERSE REACTIONS
Gastrointestinal:
Diarrhoea, nausea and vomiting, gaseous distention with flatulence or belching, abdominal discomfort
Metabolic:
Dehydration, hypokalaemia, hypernatraemia

Levetiracetam [1 vial $3.91, 1 tablet 250 mg 9 cents, 500 mg 15 cents]

ADMINISTRATION ROUTES:
IV, PO, NG

ALTERNATIVE NAMES:
Keppra, levetiracetam-AFT

ICU INDICATIONS:
1. Seizures and seizure prophylaxis

PRESENTATION AND ADMINISTRATION:
IV:
500mg in 5mL solution
Dilute dose in 100mL of compatible fluid and give over 15 minutes
Compatible with 0.9% normal saline, 5% dextrose, Hartmanns solution
Store at room temperature, discard if solution forms precipitates or becomes discoloured. Prepared infusions stable for 6 hours at room temperature
PO / NG:
Film coated tablets, tablets may be crushed and mixed with water for NG administration

DOSAGE:
No dose change is required for conversion between oral and IV doses

Status epilepticus: 60 mg/kg loading dose up to maximum of 4500 mg diluted in 100 mL of 0.9% normal saline or 5% dextrose and administered over 15 minutes
Maintenance dose of 500-1500 mg twice daily up to a maximum dose of 2000 mg twice daily if needed.

Seizure prophylaxis in traumatic brain injury, subarachnoid haemorrhage (usually short term): 20 mg/kg loading dose administered over 15 minutes
Maintenance dose: 1000 mg twice daily

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Loading dose not effected by renal impairment

Dose in renal impairment [GFR (mL/min)]

<15	250-500 mg once daily
15-30	250-500 mg twice daily
30-49	250-750 mg twice daily
50-79	500-1000 mg twice daily

Dose in renal replacement therapy

CAPD	250-500 mg once daily
HD	500-1000 mg once daily, give after dialysis
CVVHDF	750-1000 mg twice daily

No dose adjustment is required in patients with mild to moderate hepatic impairment

DOSAGE IN PAEDIATRICS:
Not recommended in infants and children under 4 years
IV:
Status epilepticus: loading dose 40-60 mg/kg dilute to a maximal concentration of 50 mg/mL in 0.9% normal saline or 5% dextrose and administered over 15mins
PO:
Age 4-16 and less than 50kg :initially 10mg/kg twice daily. May increase up to 30mg/kg twice daily
Over 50kg: dose as per adults

CLINICAL PHARMACOLOGY:
Exact mechanism of action is unknown. May modulate neurotransmission by binding to synaptic vesicle protein 2A

CONTRAINDICATIONS:
Hypersensitivity to levetiracetam

WARNINGS:
Use in pregnancy:
Levetiracetam should only be used during pregnancy if potential benefits justifies potential risk to fetus
Use in breastfeeding:
Levetiracetam is excreted in human breast milk. Decisions around discontinuation of drug should take into account importance of the drug to the mother

PRECAUTIONS:
General
Learning disability, history of psychiatric problems - increased risk of behavioural problems

Laboratory Test:
No specific tests are required

Drug/Laboratory Test Interactions:
None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU:
Methotrexate
Levetiracetam may increase methotrexate concentration when anti-neoplastic doses used. Monitor for toxicity and consider methotrexate concentration monitoring
Antidepressants
SSRIs & tricyclic antidepressants may decrease levetiracetam levels or effect

ADVERSE REACTIONS:
Body as a Whole:
Myalgia, malaise, rash
Digestive System:
Anorexia, nausea, vomiting, diarrhoea, pancreatitis
Nervous System:
Drowsiness, headache, behavioural effects, ataxia, aggression, depression, insomnia, irritability, psychosis, blurred vision, diplopia

Skin:
Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme, DRESS, alopecia
Haematological System:
*L*eucopenia, thrombocytopenia, pancytopenia

Levosimendan [1 vial $1400.00]

ADMINISTRATION ROUTES:
IV

BRAND NAMES:
Simdax

ICU INDICATIONS:
1. Patients undergoing cardiac surgery who have impaired systolic function & evidence of acute decompensated heart failure despite maximal medical therapy.

Note:Administration in ICU is only possible after discussion with the ICU Specialist.

PRESENTATION AND ADMINISTRATION:
IV
Levosimendan comes in a vial containing 12.5mg in 5ml (2.5mg/ml).
Refrigerate.
Compatible with the following IV fluids:
D5W
Levosimendan can be safely co-administered with frusemide (10mg/ml), digoxin (0.25mg/ml) or glyceryl trinitrate (0.1mg/ml)

Levosimendan is prepared by diluting **one 5ml** vial of 2.5mg/ml solution in **500ml of 5% dextrose** to make a **0.025mg/ml solution**. Administer by infusion only.
Do NOT administer a loading dose as this increases the risk of adverse events.
1. Begin the infusion at a rate of 0.05mcg/kg/min (see Dosage table below).
2. If this is tolerated for one hour, increase the infusion rate to 0.1mcg/kg/min.
3. If this is tolerated for the subsequent hour, increase the infusion rate to 0.2mcg/kg/min. This is the maximum dose.
4. Cease the levosimendan infusion after 24 hours.

The blood pressure should be checked both 15 minutes & 1 hour after either commencing the infusion or adjusting the infusion rate, if not already continuously monitored.

DOSAGE:
The following infusion rates apply only to the 0.025mg/ml preparation of Levosimendan prepared as directed above.

Patient's weight (kg)	Continuous infusion rate (mL/hr)		
	0.05mcg/kg/min	0.1mcg/kg/min	0.2mcg/kg/min
40	5	10	19
50	6	12	24
60	7	14	29
70	8	17	34
80	10	19	38
90	11	22	43
100	12	24	48
110	13	26	53

120	14	29	58

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
No dose adjustment is required for mild to moderate renal failure but the resultant increase in active metabolite concentration may cause a more pronounced and prolonged haemodynamic effect. Levosimendan is contraindicated in severe renal impairment (defined below). It is not removed by haemodialysis.

DOSAGE IN PAEDIATRICS:
Levosimendan should not be administered to children or adolescents under 18 years of age.

CLINICAL PHARMACOLOGY:
Levosimendan is a calcium sensitiser which increases cardiac contractility by enhancing the sensitivity of the heart to calcium. Haemodynamic effects persists for at least 24 hours and may be seen up to 9 days after discontinuation of a 24-hour infusion due to the presence of active metabolites that reach maximum plasma concentrations about 48 hours after the infusion has stopped.

CONTRAINDICATIONS:
1. Hypersensitivity to Levosimendan
2. Severe hepatic impairment
3. Severe renal impairment (creatinine clearance <30ml/min)
4. Severe hypovolaemia (this potentiates the hypotensive effects)

WARNINGS
Cardiovascular adverse effects
The most frequent adverse effects are hypotension, QT prolongation and arrhythmias (ectopy, atrial fibrillation and ventricular tachycardia). If hypotension or arrhythmias occur, the infusion should be stopped pending medical review after which the infusion may be restarted at a lower dose.
Patients receiving a Levosimendan infusion should undergo continuous ECG monitoring with blood pressure monitored as described in 'Administration' guidelines above.

Electrolytes
Levosimendan may cause a decrease in serum potassium concentration; hypokalaemia should be corrected prior to administration.

PRECAUTIONS
General
Co-administration with other drugs that prolong the QT interval should be undertaken with caution. Continuous ECG monitoring is required for these patients as well as for those already showing arrhythmias prior to Levosimendan administration.

Laboratory Tests
No tests are required in addition to routine ICU blood tests; vigilance for & correction of hypokalaemia is recommended.

Drug/Laboratory Test Interactions
None known

Pregnancy
Levosimendan has been given to only a limited number of pregnant women and women of childbearing age without an increase in the frequency of malformation on the human fetus having been observed. Animal studies have shown evidence of an increased occurrence of fetal damage of uncertain significance in humans.

Nursing Mothers
Levosimendan is excreted into maternal milk in animal studies. No human data is available.

Paediatric Use
Levosimendan should not be administered to children or adolescents under 18 years of age.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
See PRECAUTIONS

ADVERSE REACTIONS
Nervous system:
Headaches, dizziness, insomnia

Cardiovascular:
Arrhythmias (VT, AF, ventricular extrasystoles, tachycardia), hypotension

Digestive:
Diarrhoea, vomiting, constipation, nausea

Lithium [1 tablet 250mg 7 cents]

ADMINISTRATION ROUTES:
PO

ALTERNATIVE NAMES:
Lithicarb, lithium carbonate, priadel

ICU INDICATIONS:
1. Treatment of bipolar disorder

PRESENTATION AND ADMINISTRATION:
PO:
Tablets:
Lithicarb FC 250mg and 400mg tablets (white)
Capsules:
Lithium carbonate capsules 250mg (green / clear)
Controlled Release Tablets:
400mg tablets (white)

DOSAGE:
PO:
Bipolar disorder
Usual maintenance dosage 250mg – 1200mg daily in divided doses twice a day for tablets and capsules and daily for controlled release tablets (adjusted to levels)
Note: no information is available on NG administration; check with pharmacist if necessary

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Avoid is possible if GFR <50. If lithium must be used, reduce dosage and monitor plasma concentration carefully

DOSAGE IN PAEDIATRICS:
PO:
Bipolar disorder
5-20mg/kg 8-24 hourly; do not use controlled release tablets

CLINICAL PHARMACOLOGY:
Lithium is an element of the alkali-metal group. Preclinical studies have shown that lithium alters sodium transport in nerve and muscle cells and effects a shift toward intraneuronal metabolism of catecholamines, but the specific biochemical mechanism of lithium action in mania is unknown.

CONTRAINDICATIONS:
1. Significant renal or cardiovascular disease,
2. Severe dehydration,
3. Sodium depletion,
4. Patients receiving diuretics

WARNINGS

Lithium Toxicity

The likelihood of toxicity increases with increasing serum lithium levels. Serum lithium levels greater than 1.5 mEq/l carry a greater risk than lower levels. However, patients sensitive to lithium may exhibit toxic signs at serum levels below 1.5 mEq/l. Diarrhoea, vomiting, drowsiness, muscular weakness and lack of coordination may be early signs of lithium toxicity, and can occur at lithium levels below 2.0 mEq/l. At higher levels, giddiness, ataxia, blurred vision, tinnitus and a large output of dilute urine may be seen. Serum lithium levels above 3.0 mEq/l may produce a complex clinical picture involving multiple organs and organ systems. Serum lithium levels should not be permitted to exceed 2.0 mEq/l during the acute treatment phase.

Nephrogenic diabetes insipidus

Chronic lithium therapy may be associated with diminution of renal concentrating ability, occasionally presenting as nephrogenic diabetes insipidus, with polyuria and polydipsia. Such patients should be carefully managed to avoid dehydration with resulting lithium retention and toxicity. This condition is usually reversible when lithium is discontinued.

PRECAUTIONS

General

Lithium decreases sodium reabsorption by the renal tubules which could lead to sodium depletion. In addition to sweating and diarrhoea, concomitant infection with elevated temperatures may also necessitate a temporary reduction or cessation of medication.

Laboratory Tests:

Lithium levels should be checked in any patient on lithium admitted to the Intensive Care Unit. Samples should be collected in a yellow top tube (SST) and should be taken 12 hours post-dose. The therapeutic range is 0.6-1.2mmol/L

In the setting of acute overdose, peak levels of >5mmol/L 4-8 hours after ingestion are not unusual.

Drug/Laboratory Test Interactions:

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Combined use of Haloperidol and Lithium

An encephalopathic syndrome (characterised by weakness, lethargy, fever, tremulousness and confusion, extrapyramidal symptoms, leucocytosis, elevated serum enzymes, BUN and FBS) followed by irreversible brain damage has occurred in a few patients treated with lithium plus haloperidol. A causal relationship between these events and the concomitant administration of lithium and haloperidol has not been established; however, patients receiving such combined therapy should be monitored closely for early evidence of neurological toxicity and treatment discontinued promptly if such signs appear.

Lithium may prolong the effects of neuromuscular blocking agents. Therefore, neuromuscular blocking agents should be given with caution to patients receiving lithium.

Caution should be used when lithium and diuretics or angiotensin converting enzyme (ACE) inhibitors are used concomitantly because sodium loss may reduce the renal clearance of lithium and increase serum lithium levels with risk of lithium toxicity.

Lithium levels should be closely monitored when patients initiate or discontinue NSAID use. In some cases, lithium toxicity has resulted from interactions between an NSAID and lithium.

ADVERSE REACTIONS

Neuromuscular:

Tremor, muscle hyperirritability (fasciculations, twitching, clonic movements of whole limbs), ataxia, choreo-athetotic movements, hyperactive deep tendon reflexes.

Central Nervous System:

Blackout spells, epileptiform seizures, slurred speech, dizziness, vertigo, incontinence of urine or faeces, somnolence, psychomotor retardation, restlessness, confusion, stupor, coma, acute dystonia, downbeat nystagmus.

Cardiovascular:

Cardiac arrhythmia, hypotension, peripheral circulatory collapse, sinus node dysfunction with severe bradycardia (which may result in syncope).

Neurological:

Cases of pseudotumour cerebri (increased intracranial pressure and papilloedema) have been reported with lithium use.

Gastrointestinal:

Anorexia, nausea, vomiting, diarrhoea.

Genitourinary:

Albuminuria, oliguria, polyuria, glycosuria.

Dermatologic:

Drying and thinning of hair, anaesthesia of skin, chronic folliculitis, xerosis cutis, alopecia and exacerbation of psoriasis.

Loperamide [1 tablet 2 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Imodium, Nodia, Diamide

ICU INDICATIONS:
1. Diarrhoea

PRESENTATION AND ADMINISTRATION:
PO:
Tablets:
Imodium Caplets 2mg (light green)
Nodia 2mg tablets (green)
Capsules:
Diamide 2mg capsules (purple / dark green)
Imodium 2mg capsules (dark green / light grey)

DOSAGE:
PO:
Initially 4mg, then 2mg after each unformed stool. Maximum 16mg/day.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO:
0.05-0.1mg/kg 8-12 hourly; increase if required to 0.4mg/kg 8 hourly if required.

CLINICAL PHARMACOLOGY:
In vitro and animal studies show that loperamide acts by slowing intestinal motility and by affecting water and electrolyte movement through the bowel. Loperamide inhibits peristaltic activity by a direct effect on the circular and longitudinal muscles of the intestinal wall.

CONTRAINDICATIONS:
1. Pseudomembranous colitis or other infectious diarrhoea
2. Hypersensitivity to loperamide

WARNINGS
Loperamide therapy should be discontinued promptly if abdominal distention, constipation, or ileus occurs.

PRECAUTIONS

General

In acute diarrhoea, if clinical improvement is not observed in 48 hours, the administration of loperamide should be discontinued. Patients with hepatic dysfunction should be monitored closely for signs of CNS toxicity because of the apparent large first pass biotransformation. In patients with severe hepatic impairment, loperamide may cause CNS depression.

Laboratory Tests:

No tests are indicated in addition to routine ICU tests

Drug/Laboratory Test Interactions:

None known.

IMPORTANT DRUG INTERACTIONS FOR THE ICU

None of note

ADVERSE REACTIONS

Body as a Whole:

Hypersensitivity reactions (including skin rash), tiredness, drowsiness or dizziness.

Gastrointestinal:

Abdominal pain, distention, or discomfort, nausea and vomiting, constipation, dry mouth.

Losartan [1 tablet 78 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Cozaar, Hyzaar (contains losartan and hydrochlorothiazide)

ICU INDICATIONS:
1. Hypertension
2. Heart failure

PRESENTATION AND ADMINISTRATION:
PO / NG:
Tablets:
Hyzaar tablets – 50mg losartan, 12.5mg hydrochlorothiazide (yellow)
Cozaar 12.5mg tablets (blue), 25mg (white), 50mg (white), 100mg (white)
Note: tablets can be crushed for administration down NG tubes

DOSAGE:
PO:
Initially 12.5mg daily; increase to maximum of 100mg/day as required

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Start with small dose and adjust cautiously

DOSAGE IN PAEDIATRICS:
PO:
0.5-2mg/kg daily oral

CLINICAL PHARMACOLOGY:
Losartan potassium is an angiotensin II receptor (type AT1) antagonist.

CONTRAINDICATIONS:
1. Hypersensitivity to losartan

WARNINGS
Volume-Depleted Patients
In patients who are intravascularly volume-depleted (e.g., those treated with diuretics), symptomatic hypotension may occur after initiation of therapy with losartan.

PRECAUTIONS
General
Impaired Hepatic Function
Based on pharmacokinetic data which demonstrate significantly increased plasma concentrations of losartan in cirrhotic patients, a lower dose should be considered for patients with impaired liver function

Impaired Renal Function
In patients whose renal function may depend on the activity of the renin-angiotensin-aldosterone system (e.g., patients with severe congestive heart failure), treatment with angiotensin converting enzyme inhibitors has been associated with oliguria and/or progressive azotaemia and (rarely) with acute renal failure and/or death. Similar outcomes have been reported with losartan potassium. In studies of ACE inhibitors in patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or BUN have been reported. Similar effects have been reported with losartan potassium; in some patients, these effects were reversible upon discontinuation of therapy.
Electrolyte Imbalance
Electrolyte imbalances are common in patients with renal impairment, with or without diabetes, and should be addressed. In a clinical study conducted in Type 2 diabetic patients with proteinuria, the incidence of hyperkalaemia was higher in the group treated with losartan potassium as compared to the placebo group; however, few patients discontinued therapy due to hyperkalaemia.

Laboratory Tests:
No tests are indicated in addition to routine ICU tests

Drug/Laboratory Test Interactions:
None known.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
As with other drugs that block angiotensin II or its effects, concomitant use of potassium-sparing diuretics (e.g., spironolactone, triamterene, amiloride), potassium supplements, or salt substitutes containing potassium may lead to increases in serum potassium.

ADVERSE REACTIONS
Body as a whole:
Angiooedema, fatigue, anaphylaxis
Musculoskeletal
Cramp, back pain, rhabdomylosis
Cardiovascular:
Hypotension
Metabolic:
Hyperkalaemia, hyponatraemia
Gastrointestinal:
Hepatitis
Urogenital
Renal failure

Magnesium Sulphate [1 vial $1.84]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Magnesium Sulphate injection BP 49.3%

ICU INDICATIONS:
1. Hypomagnaesia
2. Atrial arrhythmias, torsades de pointes and ventricular ectopy
3. Eclampsia
4. Asthma

PRESENTATION AND ADMINISTRATION:
IV:
Injection 49.3% in 5ml solution contains 10mmol of magnesium sulphate
Store at room temperature
May be administered by direct IV injection provided that the concentration injected does not exceed 20% and the rate of infusion does not exceed 150mg/min (0.75ml/min of 20% solution). A 20% solution can achieved by diluting 5ml of 49.3% solution with at least 12.5ml of compatible IV fluid. In an emergency, to treat Torsade de pointes, 10mmol can be administered by direct IV injection over 1-2 minutes (preferably via a central line).
The usual means of administration in ICU is by intermittent infusion. When magnesium sulphate is administered by intermittent or continuous infusion, the required dose should be added to 50-500ml of compatible IV fluid and mixed thoroughly before being infused over 20-60 minutes at a rate no greater than 150mg/min.
Compatible with the following IV fluids:
Normal saline Glucose and sodium chloride 5% & 10% Dextrose
Hartmanns

DOSAGE:
IV:
Hypomagnesaemia, atrial arrhythmias and ventricular ectopy
10-20 mmol IV over 20-60 minutes

Eclampsia
Commence with a loading dose of 20mmol of Magnesium Sulphate in 100mls of normal saline administered over 20 minutes. For maintenance infusion add 40mmol to 500ml normal saline. Commence infusion at 50ml/hr (approximately 1gm/hr) if the patient weighes <55kg. Commence infusion at 75ml/hr (approximately 1.5gm/hr) if the mother weighs >55kg.
The target serum magnesium concentration in eclampsia is 2.0-3.0 mmol/L.

Torsades de pointes
10mmol over 1-2 minutes followed by 20mmol over 6 hours.

Severe asthma
Boluses of 5-10mmol can be given over 20 minutes or a continuous infusion can administered by diluting 100mmol in 100ml of compatible IV fluid and running at 5ml/hr (5mmol/hr)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Specific recommendations for dosage in renal failure are not available; however, patients with renal failure are at increased risk of magnesium toxicity (particularly when infusions are used) and dose reduction may be required.

DOSAGE IN PAEDIATRICS:
IV:
Hypomagnesaemia
0.2ml/kg

Asthma
IV magnesium sulphate bolus. Use magnesium sulphate 49.3% (493mg/ml). Give 0.1 ml/kg
(approx 50mg/kg) over 20 minutes (dilute to 20mls with normal saline and infuse via syringe
driver). Maximum dose 5 mls (2.5 g).

CLINICAL PHARMACOLOGY:
Magnesium is the second most plentiful cation of the intracellular fluids. It is essential for the activity of many enzyme systems and plays an important role with regard to neurochemical transmission and muscular excitability.

CONTRAINDICATIONS:
1. Heart block (unless pacing wires are present)

WARNINGS
Hypermagnesaemia
The principal hazard in parenteral magnesium therapy is the production of abnormally high levels of magnesium in the plasma. The most immediate danger to life is respiratory depression. Calcium chloride or calcium gluconate provide an effective antidote to life threatening hypermagnesaemia.
Toxicity in the newborn
When Magnesium Sulphate, is administered intravenously by a continuous infusion for longer than 24 hours before delivery, the possibility of the baby's showing signs of neuromuscular or respiratory depression of the newborn should be considered, since foetal toxicity can occur. A baby with hypermagnesemia my require resuscitation and assisted ventilation.

PRECAUTIONS
General
Since Magnesium is excreted almost entirely by the kidneys, it should be given very cautiously in the presence of serious impairment of renal function.

Laboratory Tests:
Patients with eclampsia treated with magnesium by infusion should have serum magnesium levels measured 6 hourly until stability is achieved. The target serum magnesium concentration in eclampsia is 2.0-3.0 mmol/L.

Drug/Laboratory Test Interactions:
None known.

IMPORTANT DRUG INTERACTIONS FOR THE ICU

When barbiturates, narcotics, hypnotics (or systemic anaesthetics), or other central nervous system depressants are to be given in conjunction with magnesium, their dosage should be adjusted with caution because of the additive central nervous system depressant effects of magnesium.

ADVERSE REACTIONS

Principal adverse reactions are related to the high plasma levels of magnesium and include flushing, sweating, hypotension, circulatory collapse, and cardiac and central nervous system depression. Respiratory depression is the most life-threatening effect.

Mannitol [1 bag $9.84]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Osmitrol

ICU INDICATIONS:
1. Cerebral oedema causing raised intracranial pressure
2. Raised intra-ocular pressure

Oral mannitol has also been used (together with activated charcoal) as an osmotic agent to increase intestinal removal of poisons

PRESENTATION AND ADMINISTRATION:
IV:

Solution	Volume of bag (mL)	Amount of mannitol in bag	Osmolality (mOsmol/kg)	pH
10%	1000	100g	550	5.5
20%	500	100g	1100	5.0

Mannitol may crystallise when exposed to low temperatures; this risk is increased with the 20% solution. The solution should be inspected prior to administration. If crystals are visible, they can be redissolved by warming whilst agitating. Check for crystals again on cooling prior to administration
Mannitol is incompatible with blood transfusions and some antibiotics (including cefepime, imipenem and cilastatin). Risk of precipitation if potassium or sodium chloride is added. Administer through in-line filter; do not use in-series connections.
Due to risk of thrombophlebitis, mannitol should be administered via a large peripheral or central vein where possible

DOSAGE:
0.5-1 g/kg by IV infusion of 10–20% solution over 15–30 min. Effects occur within 15-30 min and last 4-6 h

0.25–0.5 g/kg may follow 6-hourly for 24 h, unless diuresis has not occurred, cardiovascular instability ensues or plasma osmolality exceeds 315 mOsmol/kg

The table below shows the volume (in mL) of 20% mannitol to be administered for a dose of 0.5 g/kg (100 ml of 20% solution = 20 g):

Patient Weight (kg)	Volume of 20% mannitol at 0.5 g/kg (mL)
60	150
70	175
80	200
90	225
100	250
110	275
120	300

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Patients with pre-existing renal disease are at increased risk of renal failure. Mannitol is contraindicated in severe renal impairment. Will not induce diuresis in normally anuric patients. Reversible, acute renal failure has occurred in patients with previously normal renal function who receive large intravenous doses of mannitol

DOSAGE IN PAEDIATRICS:
For cerebral oedema or raised intra-ocular pressure:
IV infusion over 30-60 minutes
Neonates: 0.25-0.5 g/kg/dose
1 month - 12 years: 0.25 – 1.5 g/kg/dose. Repeat if necessary 1-2 times after 4-8 hours
12 - 18 years: 0.25-2g/kg/dose. Repeat if necessary 1-2 times after 4-8 hours

Peripheral oedema and ascites:
IV infusion over 2-6 hours
1 month-18 years: 1-2 g/kg

CLINICAL PHARMACOLOGY:
Plant-derived alcohol. Osmotic diuretic. Draws water from extracellular and intracellular spaces into vascular compartment. Relatively small amounts metabolised. Not reabsorbed once filtered in the kidneys, it continues to be osmotically active in the urine, causing diuresis. Efficacy in cerebral oedema depends on integrity of the blood–brain barrier that may be altered in neurological disease, although some benefit is derived from the systemic dehydration it produces. It may also act as a free radical scavenger

CONTRAINDICATIONS:
1. Hypersensitivity to mannitol
2. Severe heart failure
3. Severe pulmonary oedema
4. Anuric renal failure
5. Severe dehydration
6. Disturbance of the blood brain barrier
7. Shock
8. Hyperosmolarity

WARNINGS:
Extravasation causes inflammation and thrombophlebitis; bullous eruptions and compartment syndrome have also been described

PRECAUTIONS:
General
Renal impairment – use with caution in severe impairment
Laboratory Tests
Monitor fluid and electrolyte balance and serum osmolality and renal function. Maintain serum osmolality less than 315 mOsmol/kg

Drug/Laboratory Test Interactions
May cause false positive results in tests for blood ethylene glycol
Response to lithium and methotrexate may be impaired due to increased urinary excretion

Pregnancy
No safety data available - avoid unless essential

Nursing Mothers
Compatible with breast feeding

IMPORTANT DRUG INTERACTIONS FOR THE ICU:
Other diuretics potentiate the effects of mannitol. Dose adjustment may be required
Increased risk of nephrotoxicity with cyclosporin
Potentiation of ototoxic effects of aminoglycosides
Enhances effects of depolarising muscle relaxants
Decreased effect of oral anti-coagulants due to increased concentration of clotting factors secondary to dehydration
Increased risk of digoxin toxicity if resultant hypokalaemia is uncorrected

ADVERSE REACTIONS:
General:
Metabolic acidosis or alkalosis, fluid and electrolyte imbalances including hyper/hyponatraemia, hyper/hypokalaemia, dry mouth, thirst, chills, fever, urticaria
Cardiovascular System:
Increased vascular volume and CVP may cause cardiac failure, hypotension, hypertension, oedema, arrhythmia, chest pain, palpitations
Respiratory System:
Pulmonary oedema, rhinitis
Renal System:
Dehydration, focal osmotic nephrosis, acute renal failure, fluid and electrolyte imbalance, urinary retention
Neurological System:
Temporarily increases cerebral blood flow. ICP may rise slightly before falling, especially after rapid injection. Excessive brain shrinkage in the elderly may rupture subdural veins. A rebound increase in ICP may occur if treatment is prolonged due to eventual passage of mannitol into cerebral cells. This effect is more likely after repeated dosing. May also cause headache, convulsions, dizziness, blurred vision, confusion, lethargy
Gastro-intestinal System:
Nausea, vomiting, dry mouth, thirst

Meropenem [1 vial 1gm $21.00]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Merrem

ICU INDICATIONS:
1. Treatment of infections caused by susceptible organisms
2. Broad spectrum cover of hospital-acquired infections (particularly in the setting of intra-abdominal sepsis)

PRESENTATION AND ADMINISTRATION:
IV:
500mg and 1gm vials of white powder
Add 10ml of water for injection to 500mg vial or 20ml of water for injection to a 1gm vial. Shake vigorously until liquid is clear (approximately 3 minutes). The reconstituted solution has an approximate concentration of 50mg/ml. Inject required dose slowly over 5 minutes.
Initial reconstitution should be prepared as soon as practicable before use although solutions reconstituted with water for injection are stable for 8 hours at 25 degrees or 24 hours at 4 degrees.
Can be added to 50-200ml of compatible IV fluid for administration by infusion over 15-30 minutes.
Compatible with the following IV fluids:
Normal saline 5% or 10% glucose Glucose and sodium chloride
2.5% or 10% mannitol 5% glucose and 0.15% KCl
Store at room temperature

DOSAGE:
IV:
1gm 8 hourly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	250mg-1gm every 24 hours
10-20	250mg-1gm every 12 hours or 500mg every 8 hours
>20-50	500mg-1gm every 12 hours

Dose in renal replacement therapy

CAPD	250mg-1gm every 24 hours
HD	250mg-1gm every 24 hours
CVVHDF	250mg-1gm every 12 hours or 500mg every 8 hours

DOSAGE IN PAEDIATRICS:
IV:
20-40mg/kg 8 hourly

CLINICAL PHARMACOLOGY:
Meropenem is a carbapenem antibiotic. The bactericidal activity of meropenem results from the inhibition of cell wall synthesis.

Meropenem has been shown to be active against most isolates of the following microorganisms, both in vitro and in clinical infections
Aerobic and Facultative Gram-Positive Microorganisms:
Enterococcus faecalis (excluding vancomycin-resistant isolates).
Staphylococcus aureus (beta-lactamase and non-beta-lactamase producing, methicillin-susceptible isolates only).
Streptococcus agalactiae.
Streptococcus pneumoniae (penicillin-susceptible isolates only).
Streptococcus pyogenes.
Viridans group streptococci.

Aerobic and Facultative Gram-Negative Microorganisms:
Escherichia coli.
Haemophilus influenzae (beta-lactamase and non-beta-lactamase-producing).
Klebsiella pneumoniae.
Neisseria meningitidis.
Pseudomonas aeruginosa.
Proteus mirabilis.

Anaerobic Microorganisms:
Bacteroides fragilis.
Bacteroides thetaiotaomicron.
Peptostreptococcus species.

CONTRAINDICATIONS:
1. Hypersensitivity to carbapenems

WARNINGS
SERIOUS AND OCCASIONALLY FATAL HYPERSENSITIVITY (ANAPHYLACTIC) REACTIONS HAVE BEEN REPORTED IN PATIENTS RECEIVING THERAPY WITH BETA-LACTAMS. THESE REACTIONS ARE MORE APT TO OCCUR IN PERSONS WITH A HISTORY OF SENSITIVITY TO MULTIPLE ALLERGENS.
THERE HAVE BEEN REPORTS OF PATIENTS WITH A HISTORY OF PENICILLIN HYPERSENSITIVITY WHO HAVE EXPERIENCED SEVERE HYPERSENSITIVITY REACTIONS WHEN TREATED WITH ANOTHER BETA-LACTAM. BEFORE INITIATING THERAPY WITH MEROPENEM IV, CAREFUL INQUIRY SHOULD BE MADE CONCERNING PREVIOUS HYPERSENSITIVITY REACTIONS TO PENICILLINS, CEPHALOSPORINS, OTHER BETA-LACTAMS, AND OTHER ALLERGENS.

PRECAUTIONS
General
Seizures and other adverse CNS experiences have been reported during treatment with meropenem. These experiences have occurred most commonly in patients with CNS disorders (e.g., brain lesions or history of seizures) or with bacterial meningitis and/or compromised renal function (the risk of seizures is lower than the risk with imipenem).
In patients with renal dysfunction, thrombocytopaenia has been observed but no clinical bleeding reported.

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions
None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
There is evidence that meropenem may reduce serum levels of valproic acid to subtherapeutic

ADVERSE REACTIONS
Body as a Whole:
Pain, abdominal pain, chest pain, fever, back pain, abdominal enlargement, chills, pelvic pain.
Cardiovascular:
Heart failure, heart arrest, tachycardia, hypertension, myocardial infarction, pulmonary embolus, bradycardia, hypotension, syncope.
Digestive:
Oral moniliasis, anorexia, diarrhoea, nausea/vomiting, cholestatic jaundice/jaundice, flatulence, ileus, hepatic failure, dyspepsia, intestinal obstruction.
Haematological:
Anaemia, hypochromic anaemia, hypervolemia.
Metabolic/Nutritional:
Peripheral oedema, hypoxia.
Nervous system:
Insomnia, agitation/delirium, confusion, dizziness, seizure (see PRECAUTIONS), nervousness, paraesthesia, hallucinations, somnolence, anxiety, depression, asthenia.
Respiratory:
Respiratory disorder, dyspnea, pleural effusion, asthma, cough increased, lung edema.
Skin and appendages:
Urticaria, sweating, skin ulcer.
Urogenital system:
Dysuria, kidney failure, vaginal moniliasis, urinary incontinence.

Metaraminol [1 vial $6.01]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Aramine

ICU INDICATIONS:
1. Hypotension (particularly during induction of anaesthesia)

PRESENTATION AND ADMINISTRATION:
IV:
10mg in 1ml vial
Dilute 10mg in 20ml of compatible IV fluid (i.e. make up to a concentration of 0.5mg/ml)
Compatible with the following IV fluids:
Sodium Chloride 5% dextrose Hartmanns
Store at room temperature
Note: Section 29 drug (requires specific notification to Director-General of Health)

DOSAGE:
IV:
0.5-1mg PRN

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
0.01mg/kg PRN

CLINICAL PHARMACOLOGY:
Metaraminol is a potent sympathomimetic amine that increases both systolic and diastolic blood pressure.

CONTRAINDICATIONS:
1. hypersensitivity to metaraminol

WARNINGS
Metaraminol contains sodium bisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in non-asthmatic people.

PRECAUTIONS
General
Caution should be used to avoid excessive blood pressure response. Rapidly induced hypertensive responses have been reported to cause acute pulmonary oedema, arrhythmias, cerebral haemorrhage, or cardiac arrest.

Because of its vasoconstrictor effect metaraminol should be given with caution in heart or thyroid disease, hypertension, or diabetes.

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions
None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Metaraminol should be used with caution in digitalized patients, since the combination of digitalis and sympathomimetic amines may cause ectopic arrhythmias.
Monoamine oxidase inhibitors or tricyclic antidepressants may potentiate the action of sympathomimetic amines. Therefore, when initiating pressor therapy in patients receiving these drugs, the initial dose should be small and given with caution.

ADVERSE REACTIONS
Most adverse effects seen arise due to inadvertent excess dosing.
Cardiovascular:
Hypertension, tachycardia, bradycardia, pulmonary oedema, atrial or ventricular arrhythmia.
Central nervous system:
Cerebral haemorrhage, convulsions.

Metformin [1 tablet 500mg cents]

ADMINISTRATION ROUTES:
PO

ALTERNATIVE NAMES:
Arrow Metformin

ICU INDICATIONS:
1. Type 2 diabetes mellitus

PRESENTATION AND ADMINISTRATION:
PO:
Metformin 250mg, 500mg, 850mg and 1000mg tablets

DOSAGE:
PO:
Initially 500mg once to twice daily. Increasing to a maximum of 1000mg three times a day

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	avoid
10-40	avoid
>40-50	25-50% of dose

Dose in renal replacement therapy

CAPD	avoid
HD	avoid
CVVHDF	avoid

DOSAGE IN PAEDIATRICS:
PO:
Not applicable

CLINICAL PHARMACOLOGY:
Metformin is an antihyperglycaemic agent which improves glucose tolerance in patients with Type 2 diabetes, lowering both basal and postprandial plasma glucose. Its pharmacologic mechanisms of action are different from other classes of oral antihyperglycaemic agents. Metformin decreases hepatic glucose production, decreases intestinal absorption of glucose, and improves insulin sensitivity by increasing peripheral glucose uptake and utilization.

CONTRAINDICATIONS:
1. Renal dysfunction
2. Congestive heart failure requiring pharmacologic treatment.
3. Known hypersensitivity to metformin.
4. Acute or chronic metabolic acidosis including diabetic ketoacidosis
5. Use of intravenous contrast for angiography or CT within previous 72 hours

WARNINGS
Lactic Acidosis
Lactic acidosis is a rare, but serious, metabolic complication that can occur due to metformin accumulation; when it occurs, it is fatal in approximately 50% of cases.

PRECAUTIONS
General
Surgical Procedures
Metformin therapy should be temporarily suspended for any surgical procedure (except minor procedures not associated with restricted intake of food and fluids) and should not be restarted until the patient's oral intake has resumed and renal function has been evaluated as normal.
Hypoglycaemia
Hypoglycaemia does not occur in patients receiving metformin alone under usual circumstances of use, but could occur when caloric intake is deficient, when strenuous exercise is not compensated by caloric supplementation, or during concomitant use with other glucose-lowering agents (such as sulfonylureas and insulin)

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions
None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note

ADVERSE REACTIONS
Gastrointestinal:
Diarrhoea, nausea, vomiting, flatulence, abdominal discomfort
Metabolic and endocrine:
Lactic acidosis, hypoglycaemia

Methylene Blue [1 vial $7.06]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Methylene Blue

ICU INDICATIONS:
1. Methaemoglobinaemia
2. Vasoplegic shock (particularly after cardiopulmonary bypass)

PRESENTATION AND ADMINISTRATION:
IV:
1% Methylene Blue (10mg/1ml). 5 ml vials.
Inject Methylene Blue intravenously very slowly over a period of several minutes.
Store at room temperature

DOSAGE:
IV:
0.5-2mg/kg as a single dose; may give a subsequent dose if required.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
No data available

DOSAGE IN PAEDIATRICS:
IV:
0.5-2mg/kg as a single dose; may give a subsequent dose if required.

CLINICAL PHARMACOLOGY:
Methylene Blue is 3, 7-bis(Dimethylamino)-phenothiazin-5-ium chloride. It will produce two opposite actions on haemoglobin. Low concentrations will convert methaemoglobin to haemoglobin. High concentrations convert the ferrous iron of reduced haemoglobin to ferric iron which results in the formation of methaemoglobin. Methylene Blue is thought to reduce vasoplegia through actions involving nitric oxide.

CONTRAINDICATIONS:
1. Known hypersensitivity to methylene blue
2. Patients with Glucose-6-phosphate dehydrogenase deficiency
3. Severe renal impairment
4. Methaemoglobinaemia due to cyanide poisoning

WARNINGS
Administration of Methylene Blue leads to decreased oxygen saturation recorded by pulse oximetry or continuous mixed venous or central venous oxygen saturation monitoring.

PRECAUTIONS
General
Use of more than the recommended dose leads to methaemoglobinaemia. Do not exceed recommended dose.

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions
None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note

ADVERSE REACTIONS
Body as a Whole:
Dizziness, headache, confusion, methaemoglobinaemia
Gastrointestinal effects:
Abdominal pain

Methylprednisolone Sodium Succinate [1 vial 1gm $37.50]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Solu-Medrol

ICU INDICATIONS:
1. Steroid responsive lung diseases
2. ARDS
3. Stevens Johnson syndrome

PRESENTATION AND ADMINISTRATION:
IV
40mg/ml (Act-O-Vial), 125mg/2ml (Act-O-Vial), 500mg/4ml (Act-O-Vial), 1gm (+15.6ml solv)
Note: there is a depo product (Depo-Medrol); make sure you are using SOLU-Medrol for IV use

Directions for mixing Act-O-Vial:
Press down on plastic activator. This forces diluent into the lower compartment. Gently agitate to dissolve powder. To withdraw solution remove plastic tab covering the centre of stopper. Wipe top of stopper with alcohol swab. Insert needle squarely through centre of stopper until tip is just visible. Invert vial and withdraw dose.

Directions for mixing other vial preparations:
Add 1gm to 15.6ml of supplied diluent provided to make a final 62.5mg/ml.
Gently agitate to dissolve powder.

Doses of up to 250mg can be injected slowly by direct IV injection over at least 5 minutes
Doses of 125mg to 3gm may be diluted in 50ml of compatible IV fluid and administered over 30 minutes.

When reconstituted with water for injection use immediately and discard any unused solution. Small volume dilutions (50-100ml) are stable for 6 hours at room temperature. Large volume dilutions (250-1000ml) are stable for 24 hours at room temperature.

Compatible in the following IV fluids:
normal saline 5% dextrose glucose and sodium chloride

DOSAGE:
IV:
Doses vary widely depending in indication. Currently, the best available evidence for ARDs suggests dosages of 1-2mg/kg daily are the most appropriate. Doses of up to 30mg/kg have been used. For prophylaxis against laryngeal oedema in high risk patients, the recommended dose is 20mg 4 hourly for 4 doses beginning 12 hours prior to planned extubation.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
Doses vary widely depending in indication. Currently, the best available evidence for ARDs suggests dosages of 1-2mg/kg daily are the most appropriate. Doses of up to 30mg/kg have been used.

CLINICAL PHARMACOLOGY:
Methylprednisolone is a potent anti-inflammatory steroid synthesized in a laboratory. Methylprednisolone is a steroid. 1mg methylprednisolone equals 5mg hydrocortisone in glucocorticoid activity and 0.5mg in mineralocorticoid activity

CONTRAINDICATIONS:
1. The use of methylprednisolone sodium succinate sterile powder is contraindicated in premature infants because the 40, 125, 500, 1 g, and the accompanying diluent for the 500 mg and 2 g vials contain benzyl alcohol. Benzyl alcohol has been reported to be associated with a fatal "Gasping Syndrome" in premature infants.
2. Systemic fungal infections
3. Known hypersensitivity to the product and its constituents.

WARNINGS
In patients on corticosteroid therapy subjected to any unusual stress, increased dosage of rapidly acting corticosteroids before, during, and after the stressful situation is indicated.
Corticosteroids may mask some signs of infection, and new infections may appear during their use.

PRECAUTIONS
General
Drug-induced secondary adrenocortical insufficiency may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress o ccurring during that period, hormone therapy should be reinstituted. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.
There is an enhanced effect of corticosteroids on patients with hypothyroidism and in those with cirrhosis.
Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes, and severe depression, to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.
An acute myopathy has been observed with the use of high doses of corticosteroids, most often occurring in patients with disorders of neuromuscular transmission (e.g., myasthenia gravis), or in patients receiving concomitant therapy with neuromuscular blocking drugs (e.g., pancuronium). This acute myopathy is generalized, may involve ocular and respiratory muscles, and may result in quadriparesis. Elevations of creatine kinase may occur. Clinical improvement or recovery after stopping corticosteroids may require weeks to years.

Laboratory Tests:
No tests additional to usual ICU tests are required

Drug/Laboratory Test Interactions:
None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Convulsions have been reported with concurrent use of methylprednisolone and cyclosporin. Drugs that induce hepatic enzymes such as phenobarbital, phenytoin and rifampin may increase the clearance of methylprednisolone and may require increases in methylprednisolone dose to achieve the desired response.

ADVERSE REACTIONS
Fluid and Electrolyte Disturbances:
Sodium retention, potassium loss, fluid retention, hypokalemic alkalosis, congestive heart failure in susceptible patients, hypertension.
Musculoskeletal:
Muscle weakness, aseptic necrosis of femoral and humeral heads, steroid myopathy, loss of muscle mass, pathologic fracture of long bones, severe arthralgia, osteoporosis, vertebral compression fractures, tendon rupture (particularly of the Achilles tendon).
Gastrointestinal:
Peptic ulcer with possible perforation and haemorrhage, abdominal distention, ulcerative oesophagitis, pancreatitis. Increases in alanine transaminase (ALT, SGPT), aspartate transaminase (AST, SGOT), and alkaline phosphatase have been observed following corticosteroid treatment. These changes are usually small, not associated with any clinical syndrome and are reversible upon discontinuation.
Dermatologic:
Impaired wound healing, facial erythema, thin fragile skin, increased sweating, petechiae and ecchymoses, may suppress reactions to skin tests.
Neurological:
Increased intracranial pressure with papilloedema (pseudo-tumour cerebri) usually after treatment, convulsions, vertigo, headache.
Endocrine:
Development of Cushingoid state, menstrual irregularities, suppression of growth in children, decreased carbohydrate tolerance, secondary adrenocortical and pituitary unresponsiveness (particularly in times of stress, as in trauma, surgery or illness), manifestations of latent diabetes mellitus, increased requirements for insulin or oral hypoglycaemic agents in diabetics.

Metoclopramide [1 vial 45 cents, 1 tablet 6 cents]

ADMINISTRATION ROUTES:
PO, IV

ALTERNATIVE NAMES:
Maxolon, Metamide, Metoclopramide

ICU INDICATIONS:
1. Nausea
2. Gastroparesis

PRESENTATION AND ADMINISTRATION:
PO:
Maxalon 10mg tablets (white), Metamide 10mg tablets (white)

IV:
10mg/2ml vial
Inject undiluted over 1-2 minutes
Compatible with the following IV fluids:
Normal saline Glucose and sodium chloride 5%dextrose
Hartmanns
DO NOT USE if the solution is cloudy or precipitate is present
Store at room temperature. Protect from light

DOSAGE:
PO:
10mg 6-8 hourly

IV:
10-20mg 6-8 hourly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	50-100% of normal dose
10-20	75-100% of normal dose
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	50-100% of normal dose
HD	50-100% of normal dose
CVVHDF	75-100% of normal dose

DOSAGE IN PAEDIATRICS:
PO/IV:
0.15-0.30mg/kg 6-8 hourly

CLINICAL PHARMACOLOGY:
The antiemetic properties of metoclopramide appear to be a result of its antagonism of central and peripheral dopamine receptors. Dopamine produces nausea and vomiting by stimulation of the medullary chemoreceptor trigger zone (CTZ), and metoclopramide blocks stimulation of the CTZ by agents like l-dopa or apomorphine which are known to increase dopamine levels or to possess dopamine-like effects. Metoclopramide stimulates motility of the upper gastrointestinal tract without stimulating gastric, biliary, or pancreatic secretions. Its mode of action is unclear.

CONTRAINDICATIONS:
1. Parkinsons disease
2. Hypersensitivity to metoclopramide
3. Mechanical obstruction

WARNINGS
Acute dystonic reactions
Extrapyramidal symptoms, manifested primarily as acute dystonic reactions, occur in approximately 1 in 500 patients treated with the usual adult dosages of 30-40 mg/day of metoclopramide. These usually are seen during the first 24-48 hours of treatment with metoclopramide, occur more frequently in paediatric patients and adult patients less than 30 years of age and are even more frequent at the higher doses used in prophylaxis of vomiting due to cancer chemotherapy. These symptoms may include involuntary movements of limbs and facial grimacing, torticollis, oculogyric crisis, rhythmic protrusion of tongue, bulbar type of speech, trismus, or dystonic reactions resembling tetanus. Rarely, dystonic reactions may present as stridor and dyspnea, possibly due to laryngospasm. If these symptoms should occur, Benztropine, 1-2 mg intramuscularly, may be used to reverse these reactions.
Tardive Dyskinesia
Tardive dyskinesia, a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements, may develop in patients treated with metoclopramide.
Neuroleptic Malignant Syndrome (NMS)
There have been rare reports of an uncommon but potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) associated with metoclopramide.

PRECAUTIONS
General
See WARNINGS

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions
None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
The effects of metoclopramide on gastrointestinal motility are antagonized by anticholinergic drugs and narcotic analgesics. Additive sedative effects can occur when metoclopramide is given with alcohol, sedatives, hypnotics, narcotics, or tranquilizers.

ADVERSE REACTIONS

CNS Effects

Restlessness, drowsiness, fatigue, insomnia, headache, confusion, dizziness, depression, acute dystonic reactions, parkinsonian-like symptoms may include bradykinesia, tremor, cogwheel rigidity, mask-like facies, tardive dyskinesia, Neuroleptic Malignant Syndrome

Endocrine Disturbances

Galactorrhea, amenorrhea, gynaecomastia, fluid retention

Cardiovascular

Hypotension, hypertension, supraventricular tachycardia, bradycardia, fluid retention, acute congestive heart failure and possible AV block

Gastrointestinal

Nausea and bowel disturbances, primarily diarrhoea. hepatotoxicity,

Renal

Urinary frequency and incontinence.

Haematologic

neutropaenia, leukopaenia, or agranulocytosis, methaemoglobinaemia

Allergic Reactions

A few cases of rash, urticaria, or bronchospasm, especially in patients with a history of asthma. Rarely, angioneurotic edema, including glossal or laryngeal edema.

Metoprolol [1 vial $6.80, 1 tablet 50mg 16 cents, 1 tablet 47.5mg CR 25 cents]

ADMINISTRATION ROUTES:
PO, NG, IV

ALTERNATIVE NAMES:
Lopressor, Betaloc, Metoprolol CR

ICU INDICATIONS:
1. Hypertension
2. Acute myocardial infarction
3. Secondary prevention in patients with coronary artery disease
4. Angina
5. Rate control (including supraventricular & ventricular arrhythmias)

PRESENTATION AND ADMINISTRATION:
PO / NG:
Tablets:
Lopressor 50mg tablets (pink), Lopressor 100mg tablets (light blue)
Controlled Release tablets:
Betaloc CR 23.75mg, 47.5mg, 95mg and 190mg tablets (white to off white)
Oral Suspension:
Metoprolol Suspension 1mg/ml
Note: only **non** controlled release tablets should be crushed for NG administration.

IV:
Betaloc 5mg/5ml vial
Inject undiluted solution at a rate of 1-2mg/min; usual maximum dose 10mg
Compatible with the following IV fluids:
Normal saline 5% or 10% glucose Glucose and Sodium Chloride

DOSAGE:
PO:
25mg-100mg 8-12 hourly OR 23.75mg-190mg daily of controlled release tablets

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	start with small doses
10-20	start with small doses
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	start with small doses
HD	start with small doses
CVVHDF	start with small doses

DOSAGE IN PAEDIATRICS:
IV
0.1mg/kg over 5 minutes
PO
1-2mg/kg 6-12 hourly
CLINICAL PHARMACOLOGY:

Metoprolol is a beta-adrenergic receptor blocking agent. In vitro and in vivo animal studies have shown that it has a preferential effect on beta1 adrenoreceptors, chiefly located in cardiac muscle. This preferential effect is not absolute, however, and at higher doses, metoprolol also inhibits beta2 adrenoreceptors, chiefly located in the bronchial and vascular musculature.

CONTRAINDICATIONS:

1. Sinus bradycardia,
2. Heart block greater than first degree,
3. Cardiogenic shock,
4. Overt cardiac failure
5. Asthma

WARNINGS

Cardiac Failure

Sympathetic stimulation is necessary in supporting circulatory function in congestive heart failure, and beta blockade carries the potential hazard of further depressing myocardial contractility and precipitating more severe failure.

Discontinuation of therapy

Discontinuation of therapy in a patient with coronary artery disease may lead to rebound angina, arrhythmia or myocardial infarction.

Diabetes and Hypoglycaemia

Beta blockers may mask tachycardia occurring with hypoglycaemia.

Thyrotoxicosis

Beta-adrenergic blockade may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism. Abrupt withdrawal of beta blockade might precipitate a thyroid storm.

PRECAUTIONS

General

Metoprolol may aggravate peripheral arterial circulatory disorders.

Laboratory Tests:

No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions:

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Beta blockers may exacerbate the rebound hypertension which can follow the withdrawal of clonidine

ADVERSE REACTIONS

Body as a Whole:

Tiredness, Fatigue

Cardiovascular System:

Bradycardia, Cold extremities, Hypotension, Leg pain

Respiratory System:

Wheeziness, Dyspnoea

Digestive System:

Diarrhoea, Nausea

Nervous System:

Dizziness, Vertigo, Light-headedness

Metronidazole [1 vial $2.46, 1 tablet 400mg 18 cents]

ADMINISTRATION ROUTES:
IV, PO

ALTERNATIVE NAMES:
Flagyl, Metronidazole, Trichozole

ICU INDICATIONS:
1. Treatment of infections caused by susceptible organisms
2. Empirical cover where anaerobes are suspected to be causative

PRESENTATION AND ADMINISTRATION:
PO
Tablets:
Trichozole 200mg tablets (white), Trichozole 400mg tablets (yellow)
Suspension:
Flagyl-S oral suspension 200mg/5ml
Note: use suspension for NG administration

IV:
Infusion minibag 500mg in 100ml solution
Administer over 20-30 minutes
Dilution is not generally recommended. For patients maintained on IV fluids, metronidazole infusion may be diluted to 1 in 5 or greater with appropriate volumes of the following solutions:
Normal saline 5% glucose Glucose and sodium chloride
or the above with KCl 20-40mmol per 1000ml.
Protect from direct sunlight. Prolonged exposure to light will cause darkening or solution. Precipitation may occur if refrigerated. Do not use solution is it is cloudy, coloured or precipitate is visible.

DOSAGE:
IV:
500mg 8 hourly

PO:
400mg 8 hourly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<20	normal dose every 12 hours
21-30	dose as in normal renal function
>31-70	dose as in normal renal function

Dose in renal replacement therapy

CAPD	normal dose every 12 hours
HD	dose as in normal renal function
CVVHDF	dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
15mg/kg stat then 7.5mg/kg 8 hourly

CLINICAL PHARMACOLOGY:
Metronidazole is a synthetic antibacterial compound. Metronidazole is active in vitro against most obligate anaerobes, but does not appear to possess any clinically relevant activity against facultative anaerobes or obligate aerobes. Against susceptible organisms, metronidazole is generally bactericidal at concentrations equal to or slightly higher than the minimal inhibitory concentrations. Metronidazole has been shown to have in vitro and clinical activity against the following organisms:
Anaerobic Gram-Negative Bacilli, including:
Bacteroides species including the Bacteroides fragilis group (B. fragilis, B. distasonis, B. ovatus, B. thetaiotaomicron, B vulgatus) and Fusobacterium species.
Anaerobic Gram-Positive Bacilli, including:
Clostridium species and susceptible strains of Eubacterium.
Anaerobic Gram-Positive Cocci, including:
Peptococcus species and Peptostreptococcus species.

CONTRAINDICATIONS:
1. Hypersensitivity to metronidazole or other nitroimidazole derivatives

WARNINGS
Carcinogenicity
Metronidazole has been shown to be carcinogenic in mice and rats
Convulsive Seizures and Peripheral Neuropathy
Convulsive seizures and peripheral neuropathy, the latter characterised mainly by numbness or paraesthesia of an extremity, have been reported in patients treated with metronidazole.

PRECAUTIONS
General
Patients with severe hepatic disease metabolize metronidazole slowly, with resultant accumulation of metronidazole and its metabolites in the plasma. Accordingly, for such patients, doses below those usually recommended should be administered cautiously.

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions
Metronidazole may interfere with certain types of determinations of serum chemistry values, such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), triglycerides, and hexokinase glucose. Values of zero may be observed.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Metronidazole has been reported to potentiate the anticoagulant effect of warfarin, resulting in a prolongation of prothrombin time. This possible drug interaction should be considered when metronidazole is prescribed for patients on this type of anticoagulant therapy.

The simultaneous administration of drugs that induce microsomal liver enzymes, such as phenytoin or phenobarbital, may accelerate the elimination of metronidazole, resulting in reduced plasma levels; impaired clearance of phenytoin has also been reported.

Psychotic reactions have been reported in alcoholic patients who are using metronidazole and disulfiram concurrently. Metronidazole should not be given to patients who have taken disulfiram within the last 2 weeks.

ADVERSE REACTIONS
Gastrointestinal:
Nausea, vomiting, abdominal discomfort, diarrhoea, and an unpleasant metallic taste.
Hematopoietic:
Reversible neutropaenia (leukopaenia).
Dermatologic:
Erythematous rash and pruritus.
Central Nervous System:
Headache, dizziness, syncope, ataxia, and confusion.
Local Reactions:
Thrombophlebitis after IV infusion. This reaction can be minimized or avoided by avoiding prolonged use of indwelling IV catheters.
Other:
Fever. Instances of a darkened urine have also been reported, and this manifestation has been the subject of a special investigation. Although the pigment which is probably responsible for this phenomenon has not been positively identified, it is almost certainly a metabolite of metronidazole and seems to have no clinical significance.

Midazolam [1 vial 15mg/3ml $2.38, 1 vial 5mg/5ml $1.00]

ADMINISTRATION ROUTES:
IV, IM, PO

ALTERNATIVE NAMES:
Hypnovel

ICU INDICATIONS:
1. Sedation
2. Treatment of seizures

PRESENTATION AND ADMINISTRATION:
IV:
15mg/3ml vial and 5mg/5ml vial
For direct IV injection, usually diluted to a concentration of 1mg/ml using compatible IV fluid and injected slowly.
For continuous infusion dilute 60mg up to a total of 60ml with compatible IV fluid
Compatible with the following IV fluids:
Normal saline 5% dextrose 10% dextrose
Hartmanns
Any solutions not used within 24 hours should be discarded
Store at room temperature. Do not freeze.
IM:
Inject undiluted into a large muscle mass

DOSAGE:
IM:
Sedation: 1-5mg
IV:
Sedation: 1-10mg
Infusion: 0-20mg/hr
PO:
Premed: 7.5-15mg

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	50% of normal dose
10-20	dose as in normal renal function
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	50% of normal dose
HD	50% of normal dose
CVVHDF	dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IM:
Sedation: usually 0.1-0.5mg/kg.
IV:
Sedation: usually 0.1-0.5mg/kg.
Infusion (ventilated): Dilute 3mg/kg in 50ml 5% dextrose and run at 0-5ml/hr (0-5mcg/kg/min)
Intranasal:
Sedation: 0.2mg/kg nasal (repeated in 10 minutes if required)
PO:
Sedation: 0.5mg/kg (max 20mg)

CLINICAL PHARMACOLOGY:
Midazolam is a benzodiazepine. The precise mechanism by which midazolam exerts its antiseizure effect is unknown, although it is believed to be related to its ability to enhance the activity of gamma aminobutyric acid (GABA), the major inhibitory neurotransmitter in the central nervous system.

CONTRAINDICATIONS:
1. Hypersensitivity to benzodiazepines

WARNINGS
Withdrawal Symptoms
Withdrawal symptoms of the barbiturate type have occurred after the discontinuation of benzodiazepines including midazolam

PRECAUTIONS
General
Hypoventilation, airway obstruction, and apnoea can lead to hypoxia and/or cardiac arrest unless effective countermeasures are taken immediately.

Laboratory Tests:
No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:
None noted

IMPORTANT DRUG INTERACTIONS FOR THE ICU
The CNS-depressant action of the benzodiazepine class of drugs may be potentiated by alcohol, narcotics, barbiturates, nonbarbiturate hypnotics, antianxiety agents, the phenothiazines, thioxanthene and butyrophenone classes of antipsychotic agents, monoamine oxidase inhibitors and the tricyclic antidepressants, and by other anticonvulsant drugs.

ADVERSE REACTIONS
Neurologic:
Abnormal eye movements, aphonia, choreiform movements, coma, diplopia, dysarthria, dysdiadochokinesis, 'glassy-eyed' appearance, headache, hypotonia, nystagmus, respiratory depression, slurred speech, tremor, vertigo.

Psychiatric:
Confusion, depression, amnesia, hallucinations, hysteria, increased libido, insomnia, psychosis, suicidal attempt. The following paradoxical reactions have been observed: Excitability, irritability, aggressive behavior, agitation, nervousness, hostility, anxiety, sleep disturbances, nightmares and vivid dreams.
Respiratory:
Apnoea, hypoventilation
Cardiovascular:
Palpitations, hypotension.
Hematopoietic:
Anaemia, leukopaenia, thrombocytopaenia, eosinophilia.
Hepatic:
Hepatomegaly, transient elevations of serum transaminases and alkaline phosphatase.

Milrinone [1 vial $38.50]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Primacor

ICU INDICATIONS:
1. Low cardiac output states due to impaired myocardial contractility

PRESENTATION AND ADMINISTRATION:
Milrinone 1mg/ml (10ml vial)
Dilute 10mg up to 50ml using compatible IV fluid
Compatible in the following IV fluids:
0.45% saline 0.9% saline 5% dextrose
Store at room temperature
Preparations not used in 24 hours should be discarded

DOSAGE:
IV infusion:
0.375-0.75mcg/kg/min
Note: a loading dose of up to 50mcg/kg may be used but is not used in our ICU due to the risk of hypotension; patients may receive a loading dose in theatre prior to coming of bypass.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	usual dose 0.2mcg/kg/min
10-40	usual dose 0.3mcg/kg/min
>40-50	usual dose 0.4mcg/kg/min

Dose in renal replacement therapy

CAPD	usual dose 0.2mcg/kg/min
HD	usual dose 0.2mcg/kg/min
CVVHDF	dose as in normal renal function

Note: renal impairment significantly increases the terminal elimination half life of milrinone. Patients with renal impairment on milrinone infusions may develop progressive vasodilation leading to escalating noradrenaline requirements. If noradrenaline requirement is increasing consider whether it is appropriate to cease milrinone.

DOSAGE IN PAEDIATRICS:
IV infusion
<30kg: 1.5mg/kg in 50ml 5% dextrose at 0.5-1.5ml/hr (0.25-0.75mcg/kg/min)
>30kg: 1.5mg/kg in 100ml 5% dextrose a 1-3ml/hr (0.25-0.75mcg/kg/min)

CLINICAL PHARMACOLOGY:
Milrinone lactate is a positive inotrope and vasodilator, with little chronotropic activity different in structure and mode of action from either the digitalis glycosides or catecholamines.

Milrinone lactate, at relevant inotropic and vasorelaxant concentrations, is a selective inhibitor of peak III cAMP phosphodiesterase isozyme in cardiac and vascular muscle. This inhibitory action is consistent with cAMP mediated increases in intracellular ionized calcium and contractile force in cardiac muscle, as well as with cAMP dependent contractile protein phosphorylation and relaxation in vascular muscle.

CONTRAINDICATIONS:
1. Hypersensitivity to milrinone

WARNINGS
Milrinone is an inodilator. Significant hypotension due to peripheral vasodilation is common and is generally treated with noradrenaline.

PRECAUTIONS
General
The use of milrinone has been associated with increased frequency of ventricular and atrial arrhythmias.
Milrinone may aggravate outflow tract obstruction in hypertrophic subaortic stenosis.

Laboratory Tests:
No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:
None noted

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note.

ADVERSE REACTIONS
Cardiovascular:
SVT, VT, VF, hypotension
Respiratory:
bronchospasm
CNS:
Headaches, tremor.
Haematological:
Thrombocytopaenia
Metabolic:
Hypokalaemia

Morphine Sulphate and Morphine Tartrate

[1 vial 10mg in 10 ml $3.95,1 premixed bag 100mg in 100ml $18]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
RA morph (morphine hydrochloride), LA morph, m-Eslon, Sevredol

ICU INDICATIONS:
1. Analgesia
2. Sedation

PRESENTATION AND ADMINISTRATION:
IV
Morphine sulphate 10mg/1ml and 30mg/1ml vial; also, comes in 50mg in 50ml prefilled syringes. Also available, morphine tartrate 120mg in 1.5ml (used primary to make up morphine PCAs in double strength – i.e. 120mg in 60ml)
For direct injection, the usual method is to dilute 10mg into a total of 10ml of compatible IV fluid
For infusion, use prefilled syringes or dilute with compatible IV fluid to a dilution of 1mg/ml
Compatible in the following IV fluids:
Normal saline 5% dextrose Hartmanns Glucose and sodium chloride
Store at room temperature. Protect from light.
Store in controlled drug safe.

PO:
Tablets:
Sevredol 10mg tablets (blue), Sevredol 20mg tablets (pink)
Sustained Release Tablets:
LA Morph 10mg tablets (buff), LA Morph 30mg tablets (violet), LA Morph 60mg tablets (orange), LA Morph 100mg tablets (grey)
Sustained Release Capsules:
M-Eslon 10mg (yellow), M-Eslon 30mg (pink), M-Eslon 60mg (orange), M-Eslon 100mg (white)

DOSAGE:
PO:
Initially 5-20 mg every 4 hours of sevredol.
Sustained release formulations are administered 12 hourly

IV:
Analgesia: usually 1-5mg PRN
Infusion: 0-20mg/hr
PCA: usually 1mg with 5 minute lock-out and maximum of 12mg/hr

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:

Dose in renal impairment [GFR (ml/min)]

<10	use small doses (e.g. 1mg)
10-20	use small doses (e.g. 2mg)
>20-50	75% of normal

Dose in renal replacement therapy

CAPD	use small doses (e.g. 1mg)
HD	use small doses (e.g. 1mg)
CVVHDF	use small doses (e.g. 2mg)

Note: usually fentanyl is used in preference to morphine where there is significant renal impairment

DOSAGE IN PAEDIATRICS:

IM

0.1-0.2mg/kg

IV

0.05-0.1mg/kg by slow incremental injection over 5 to 15 minutes.
If ventilated, 0.1-0.2mg/kg/dose.

IV infusion

1mg/kg in 50ml 5% dextrose at 0-4ml/hr (0-80mcg/kg/hr)

PCA

PCA 20mcg/kg boluses (1ml of 1mg/kg in 50ml) with 5 minute lock-out time

CLINICAL PHARMACOLOGY:

Morphine, a pure opiate agonist

CONTRAINDICATIONS:

1. Hypersensitivity to morphine

WARNINGS

Impaired Respiration

Respiratory depression is the chief hazard of all morphine preparations. Respiratory depression occurs most frequently in the elderly and debilitated patients as well as in those suffering from conditions accompanied by hypoxia or hypercapnia when even moderate therapeutic doses may dangerously decrease pulmonary ventilation.
Morphine should be used with extreme caution in patients with chronic obstructive pulmonary disease or cor pulmonale, and in patients having a substantially decreased respiratory reserve, hypoxia, hypercapnia, or preexisting respiratory depression. In such patients, even usual therapeutic doses of morphine may decrease respiratory drive while simultaneously increasing airway resistance to the point of apnea.

Hypotensive Effect

Morphine sulphate controlled-release tablets, like all opioid analgesics, may cause severe hypotension in an individual whose ability to maintain his blood pressure has already been compromised by a depleted blood volume, or a concurrent administration of drugs that lower blood pressure.

Anaphylaxis

Although extremely rare, cases of anaphylaxis have been reported.

PRECAUTIONS

General

Morphine may aggravate pre-existing convulsions in patients with convulsive disorders.

Laboratory Tests:
No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:
None noted

IMPORTANT DRUG INTERACTIONS FOR THE ICU
The concomitant use of other central nervous system depressants including sedatives or hypnotics, general anaesthetics, phenothiazines, tranquilizers, and alcohol may produce additive depressant effects. Respiratory depression, hypotension, and profound sedation or coma may occur.

ADVERSE REACTIONS
Central Nervous System:
Weakness, headache, agitation, tremor, uncoordinated muscle movements, seizure, alterations of mood (nervousness, apprehension, depression, floating feelings), dreams, muscle rigidity, transient hallucinations and disorientation, visual disturbances, insomnia.
Respiratory:
Respiratory depression, apnoea, respiratory arrest,
Gastrointestinal:
Dry mouth, biliary tract spasm, laryngospasm, anorexia, diarrhoea, cramps, taste alteration, constipation, ileus, intestinal obstruction, increases in hepatic enzymes.
Cardiovascular:
Flushing of the face, chills, tachycardia, bradycardia, palpitation, faintness, syncope, hypotension, hypertension.
Genitourinary:
Urine retention or hesitance, reduced libido and/or potency.
Dermatologic:
Pruritus, urticaria, other skin rashes, oedema, diaphoresis.

Moxifloxacin [1 vial $70.00, 1 tablet 400mg $10.40]

ADMINISTRATION ROUTES:
IV, PO

ALTERNATIVE NAMES:
Avelox

ICU INDICATIONS:
1. Treatment of infections caused by susceptible organisms

PRESENTATION AND ADMINISTRATION:
IV
400mg in 250ml solution (pre-mixed bag)
Remove from aluminium overwrap bag immediately before use. If stored at cool temperatures precipitation may occur – this will redissolve at room temperature. Do not use solution unless it is clear and free of precipitate
Administer over not less than 60 minutes
Compatible with the following IV fluids:
Normal saline Hartmanns 5%, 10% & 40% dextrose
Glucose and sodium chloride
Store at room temperature
Do not store below 8°C

PO
Avelox 400mg tablets

DOSAGE:
IV:
400mg daily

PO:
400mg daily

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
10mg/kg daily
PO:
10mg/kg daily
Note: see WARNINGS

CLINICAL PHARMACOLOGY:
Moxifloxacin is a quinolone antibiotic. The bactericidal action of moxifloxacin results from inhibition of the topoisomerase II (DNA gyrase) and topoisomerase IV required for bacterial DNA replication, transcription, repair, and recombination. Moxifloxacin, given as an oral tablet, is well absorbed from the gastrointestinal tract. The absolute bioavailability of moxifloxacin is approximately 90%.

Moxifloxacin has been shown to be active against most strains of the following microorganisms, both in vitro and in clinical infections.
Aerobic Gram-Positive Microorganisms:
Staphylococcus aureus (methicillin-susceptible strains only), Streptococcus pneumoniae (including penicillin-resistant strains), Streptococcus pyogenes.
Aerobic Gram-Negative Microorganisms:
Haemophilus influenzae, Haemophilus parainfluenzae, Klebsiella pneumoniae, Moraxella catarrhalis.
Other Microorganisms:
Chlamydia pneumoniae, Mycoplasma pneumoniae.

CONTRAINDICATIONS:

1. Hypersensitivity to moxifloxacin or any member of the quinolone class of antimicrobials

WARNINGS
THE SAFETY AND EFFECTIVENESS OF MOXIFLOXACIN IN Paediatric PATIENTS, ADOLESCENTS (<18 YEARS OF AGE), PREGNANT WOMEN, AND LACTATING WOMEN HAVE NOT BEEN ESTABLISHED.
QTc prolongation
Moxifloxacin has been shown to prolong the QT interval of the electrocardiogram in some patients. The drug should be avoided in patients with known prolongation of the QT interval, patients with uncorrected hypokalaemia and patients receiving Class IA (e.g., quinidine, procainamide) or Class III (e.g., amiodarone, sotalol) antiarrhythmic agents, due to the lack of clinical experience with the drug in these patient populations.
Convulsions and neuropsychiatric complications
Convulsions have been reported in patients receiving quinolones. Quinolones may also cause central nervous system (CNS) events including: dizziness, confusion, tremors, hallucinations, depression, and, rarely, suicidal thoughts or acts. These reactions may occur following the first dose.
Hypersensitivity Reactions
Serious and occasionally fatal hypersensitivity (anaphylactic) reactions, some following the first dose, have been reported in patients receiving quinolone therapy.
Pseudomembranous Colitis
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including moxifloxacin, and may range in severity from mild to life-threatening.
Peripheral Neuropathy
Rare cases of sensory or sensorimotor axonal polyneuropathy affecting small and/or large axons resulting in paraesthesias, hypoesthesias, dysesthesias and weakness have been reported in patients receiving quinolones.
Tendon Effects
Ruptures of the shoulder, hand, achilles tendon or other tendons that required surgical repair or resulted in prolonged disability have been reported in patients receiving quinolones.

PRECAUTIONS
General
Prescribing moxifloxacin tablets and oral suspension in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Laboratory Tests:
No tests in addition to usual ICU tests are indicated

Drug/Laboratory Test Interactions:
None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Antacids, Sucralfate, Metal Cations, Multivitamins
Quinolones form chelates with alkaline earth and transition metal cations. Oral administration of quinolones with antacids containing aluminum or magnesium, with sucralfate, with metal cations such as iron, or with multivitamins containing iron or zinc, or with formulations containing divalent and trivalent cations such as (didanosine) chewable/buffered tablets or the paediatric powder for oral solution, may substantially interfere with the absorption of quinolones, resulting in systemic concentrations considerably lower than desired. Therefore, moxifloxacin should be taken at least 4 hours before or 8 hours after these agents

ADVERSE REACTIONS
Body as a Whole:
Headache, abdominal pain, injection site reaction, asthenia, moniliasis, pain, malaise, lab test abnormal (not specified), allergic reaction, leg pain, back pain, chest pain.
Cardiovascular:
Palpitation, tachycardia, hypertension, peripheral edema, QT interval prolonged.
Central Nervous System:
Insomnia, nervousness, anxiety, confusion, somnolence, tremor, vertigo, paraesthesia.
Digestive:
Vomiting, diarrhoea, abnormal liver function test, dyspepsia, dry mouth, constipation, oral moniliasis, anorexia, stomatitis, glossitis, flatulence, gastrointestinal disorder, GGTP increased.
Haematological:
Prothrombin decrease (prothrombin time prolonged/Internationl Normalized Ration (INR) increased), thrombocythemia, thrombocytopaenia, eosinophilia, leukopaenia.
Metabolic and Nutritional:
Amylase increased, lactic dehydrogenase increased.
Musculoskeletal:
Arthralgia, myalgia.
Respiratory:
Dyspnea.
Skin/Appendages:
Rash (maculopapular, purpuric, pustular), pruritus, sweating.

Naloxone [1 vial $6.60]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Narcan

ICU INDICATIONS:
1. Reversal of narcotic respiratory depression and coma

PRESENTATION AND ADMINISTRATION:
IV
0.4mg in 1ml vial
For bolus injection, usually dilute one vial in 10-20ml of compatible IV fluid
For continuous infusion, add 2mg to 500ml of compatible IV fluid to give a solution with a concentration of 4mcg/ml.
Discard any solution not used within 24 hours of preparation
Compatible with the following IV fluids:
Normal saline 5% dextrose Water for injection
Store at room temperature

DOSAGE:
IV:
For reversal of post-operative respiratory depression and coma: 20-40mcg IV PRN
For opioid overdose: 40-400mcg IV PRN
Infusion: If an infusion is required, commence the infusion with an hourly infusion rate calculated as 2/3rd of the total bolus dose given to achieve the desired opioid reversal effect

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
For post-operative respiratory depression or over-sedation, give 0.002mg/kg/dose (i.e. dilute 0.4mg to 20ml and then give 0.1ml/kg/dose). Repeat every 2 minutes x4 if required, then commence infusion by adding 0.3mg/kg to 30ml 5% dextrose and running at 0-1ml/hr (0.01mg/kg/hr).
For opiate overdose, give 0.01mg/kg (max 0.4mg) (i.e. dilute 0.4mg to 10ml and give 0.25ml/kg/dose). Repeat every 2 minutes x4 if required, then commence infusion by adding 0.3mg/kg to 30ml 5% dextrose and running at 0-1ml/hr (0.01mg/kg/hr).

CLINICAL PHARMACOLOGY:
Naloxone hydrochloride, is a narcotic antagonist. Naloxone prevents or reverses the effects of opioids including respiratory depression, sedation and hypotension.

CONTRAINDICATIONS:
1. Hypersensitivity to naloxone

WARNINGS

Naloxone injection should be administered cautiously to persons including newborns of mothers who are known or suspected to be physically dependent on opioids. In such cases, an abrupt and complete reversal of narcotic effects may precipitate an acute abstinence syndrome.
Naloxone is not effective against respiratory depression due to non-opioid drugs. Reversal of buprenorpinephrine-induced respiratory depression may be incomplete.

PRECAUTIONS
General
In addition to naloxone injection, other resuscitative measures, such as maintenance of a free airway, artificial ventilation, cardiac massage and vasopressor agents should be available and employed, when necessary, to counteract acute narcotic poisoning. Several instances of hypotension, hypertension, ventricular tachycardia and fibrillation, and pulmonary edema have been reported. These have occurred in postoperative patients most of whom had pre-existing cardiovascular disorders or received other drugs which may have similar adverse cardiovascular effects. Although a direct cause and effect relationship has not been established, naloxone injection should be used with caution in patients with pre-existing cardiac disease or patients who have received potentially cardiotoxic drugs.

Laboratory Tests:
No tests in addition to usual ICU tests are indicated

Drug/Laboratory Test Interactions:
None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Reverses opioid effects!

ADVERSE REACTIONS
Abrupt reversal of narcotic depression may result in nausea, vomiting, sweating, tachycardia, increased blood pressure and tremulousness. In post-operative patients, larger than necessary dosages of naloxone may result in significant reversal of analgesia.

Hypotension, hypertension, ventricular tachycardia and fibrillation, and pulmonary oedema have been associated with the use of naloxone postoperatively

Neostigmine [1 vial $2.80]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Neostigmine

ICU INDICATIONS:
1. Reversal of neuromuscular blockade
2. Ileus

PRESENTATION AND ADMINISTRATION:
IV
2.5mg in 1ml vial
For reversal of neuromuscular blockade administer with either atropine or glycopyrrolate
For ileus, add 2.5mg to 100ml of compatible IV fluid and administer over 1-5 hours (use the longer duration for younger patients or those at risk of bradycardia)
Compatible with the following IV fluids:
Normal saline 5% dextrose
Store at room temperature

DOSAGE:
IV:
For reversal of neuromuscular blockade, use 2.5mg of neostigmine with 0.6-1.2mg of atropine
For treatment of ileus give 2.5mg neostigmine over 1-5 hours by infusion (see PRESENTATION AND ADMINISTRATION above)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
For reversal of neuromuscular blockade, add 1.25mg (0.5ml) of neostigmine + 0.3mg (0.5ml) of atropine + 0.5ml of normal saline and then give 0.1ml/kg IV
Note: do not use as a treatment for ileus in children due to high risk of symptomatic bradycardia or asystole.

CLINICAL PHARMACOLOGY:
Neostigmine inhibits the hydrolysis of acetylcholine by competing with acetylcholine for attachment to acetylcholinesterase at sites of cholinergic transmission. It enhances cholinergic action by facilitating the transmission of impulses across neuromuscular junctions.

CONTRAINDICATIONS:
1. Hypersensitivity to neostigmine
2. Mechanical obstruction of the gastrointestinal tract

WARNINGS
Neostigmine can cause severe bradycardia and even asystole

PRECAUTIONS

General

Neostigmine methylsulfate should be used with caution in patients with epilepsy, bronchial asthma, bradycardia, recent coronary occlusion, vagotonia, hyperthyroidism, cardiac arrhythmias or peptic ulcer.

Laboratory Tests:

No tests in addition to usual ICU tests are indicated

Drug/Laboratory Test Interactions:

None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Neostigmine methylsulfate does not antagonize, and may in fact prolong, the Phase I block of depolarizing muscle relaxants such as succinylcholine.

ADVERSE REACTIONS

Body as a Whole

Anaphylaxis.

Neurologic:

Dizziness, convulsions, loss of consciousness, drowsiness, headache, dysarthria, miosis and visual changes.

Cardiovascular:

Cardiac arrhythmias (including bradycardia, tachycardia, A-V block and nodal rhythm), cardiac arrest, syncope and hypotension.

Respiratory:

Increased oral, pharyngeal and bronchial secretions, dyspnea, respiratory depression, respiratory arrest and bronchospasm.

Dermatologic:

Rash and urticaria.

Gastrointestinal:

Nausea, salivation, cramp, emesis, diarrhoea, flatulence and increased peristalsis.

Genitourinary:

Urinary frequency.

Musculoskeletal:

Muscle cramps and spasms, arthralgia.

Miscellaneous:

Diaphoresis, flushing and weakness.

Nicotine [1 patch $1.76]

ADMINISTRATION ROUTES:
TRANSDERMAL

ALTERNATIVE NAMES:
Habitrol, Nicorette, Nicotrol

ICU INDICATIONS:
1. Nicotine withdrawal

PRESENTATION AND ADMINISTRATION:
TD:
Habitrol 14mg/24 hours and 21mg/24 hours
Apply to clean, dry, non-hairy skin on hip, chest or upper arm
Store at room temperature

DOSAGE:
TD:
For patients who smoke less than 20 cigarettes per day use 14mg daily
For patients who smoke more than 20 cigarettes per day use 21mg daily

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
Not applicable

CLINICAL PHARMACOLOGY:
Nicotine replacement therapy

CONTRAINDICATIONS:
1. Active myocardial ischaemia
2. Subarachnoid haemorrhage
3. Recent cerebrovascular event
4. Generalised dermatological disorders such as psoriasis or chronic dermatitis

WARNINGS
Nicotine patches should be removed prior to undergoing an MRI
May cause arrhythmias

PRECAUTIONS
General
Nicotine patches should be used with caution in patients with:
• severe hypertension, stable angina pectoris, cerebrovascular disease, occlusive peripheral arterial disease, and heart failure.
• hyperthyroidism or pheochromocytoma.
• moderate to severe hepatic and/or severe renal impairment.

Laboratory Tests:

No tests in addition to usual ICU tests are indicated

Drug/Laboratory Test Interactions:
None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU
No clinically relevant interactions between NRT and other drugs have definitely been established.

ADVERSE REACTIONS
Body as a Whole:
Headache, sweating, pallor
Skin reactions:
Skin reactions consisted of erythema or pruritus at the patch site. Oedema, burning sensation, blisters, rash, or pinching at the application site were also noted.
Gastrointestinal reactions:
Nausea, vomiting, dyspepsia, abdominal pain, diarrhoea
Neurological System:
Abnormal dreams

Nimodipine [1 vial $67.50, 1 tablet $3.50]

ADMINISTRATION ROUTES:
PO, IV

ALTERNATIVE NAMES:
Nimotop

ICU INDICATIONS:
1. Prophylaxis and treatment of cerebral vasospasm after aneursymal subarachnoid haemorrhage

PRESENTATION AND ADMINISTRATION:
IV:
Nimotop infusion solution: 10mg nimodipine / 50ml
Use only infusion pumps with polyethylene (PE) infusion tubing, polypropylene (PP) syringes and polyethylene or polypropylene extensions, taps and connectors. Do not use polyvinylchloride (PVC) infusion tubing as nimodipine is absorbed by the tubing.
Administer nimodipine neat. Give via a three-way stopcock with a coinfusion of compatible IV fluid in a ratio of 1:4 (nimodipine: coinfusion). For example, an infusion running at 10ml/hr requires a co-infusion of 40ml/hr.
Compatible with the following IV fluids:

Normal saline	5% dextrose	Hartmanns
Mannitol 10%	5% albumin	

Store at room.
Protect from light. Infusion solution is light sensitive. Do not use in direct sunlight.
Note: administration of nimodipine via a central line is preferred as nimodipine causes thrombophlebitis when administered peripherally. If necessary, the peripheral route can be used (although administration via this route is not licensed)

PO:
Nimotop tablets 30mg (yellow)

DOSAGE:
IV:
Commence infusion at 1mg/hr (5ml/hr) for two hours and then increase to 2mg/hr (10ml/hr) if tolerated. For patients who are unable to tolerate infusion at 1mg/hr, commence infusion at 0.5mg/hr (2.5ml/hr)

Weaning from IV to oral therapy:
Commence regular oral therapy (see below). After the first dose of nimodipine is given, reduce infusion by 1 mL every hour for 5 hours, then cease infusion. If the patient becomes hypotensive after oral nimodipine is given, cease the infusion immediately.
Observe for neurological deterioration. If the patient does deteriorate neurologically, cease weaning off IV nimodipine and return to full IV therapy.

PO:
60mg 4 hourly for 21 days; if not tolerated due to hypotension, try a reduced dose of 30mg 4 hourly.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
10-15mcg/kg/hr IV for 2 hours then 10-45mcg/kg/hr

CLINICAL PHARMACOLOGY:
Nimodipine is a calcium channel blocker which has been shown to improve outcome after subarachnoid haemorrhage

CONTRAINDICATIONS:
1. Hypersensitivity to nimodipine

WARNINGS
Nimodipine can cause hypotension. If hypertensive therapy is being pursued or the patient develops significant hypotension during nimodipine treatment, the dose should be reduced or nimodipine should be withheld.

PRECAUTIONS
General
The metabolism of nimodipine is decreased in patients with impaired hepatic function. Such patients should have their blood pressure and pulse rate monitored closely and should be given a lower dose. (usually 50% of normal dose)

Laboratory Tests:
No tests in addition to usual ICU tests are indicated

Drug/Laboratory Test Interactions:
None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU
The risk of hypotension increases with concomitant administration of other antihypertensive drugs.

ADVERSE REACTIONS
Cardiovascular:
Hypotension, tachycardia, bradycardia
Respiratory:
Dyspnoea
Gastrointestinal:
Nausea, dyspepsia, deranged liver function tests, diarrhoea
Neurological:
Headache

Noradrenaline [1 bag $36.32]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Levophed

ICU INDICATIONS:
1. Septic shock
2. Other distributive shock

PRESENTATION AND ADMINISTRATION:
IV Use
Use 10mg in 100ml (0.1mg/ml) pre-mixed bags; 2mg in 2ml vials (1:1000) can be used to make up double strength noradrenaline if required by adding 20mg of noradrenaline to 100ml of compatible IV fluid.
Compatible with the following IV fluids:
5% dextrose dextrose with sodium chloride
Store at room temperature

DOSAGE:
IV:
0-20ml/hr (higher doses may occasionally be required)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
No dosage adjustment is required

DOSAGE IN PAEDIATRICS:
IV Infusion:
0.3mg/kg in 50ml D5W at 0.5-10ml/hr (equates to 0.05-1mcg/kg/min)

CLINICAL PHARMACOLOGY:
Norepinephrine bitartrate functions as a peripheral vasoconstrictor (alpha-adrenergic action) and as an inotropic stimulator of the heart and dilator of coronary arteries (beta-adrenergic action). The alpha action predominates.

CONTRAINDICATIONS:
Nil

WARNINGS
Norepinephrine injection contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people.

PRECAUTIONS
General
Norepinephrine should not be given to patients who are hypotensive from blood volume deficits except as an emergency measure to maintain coronary and cerebral artery perfusion until blood volume replacement therapy can be completed.

Laboratory Tests:
No tests additional to routine ICU tests are required.

Drug/Laboratory Test Interactions
None reported

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note

ADVERSE REACTIONS
Body as a Whole:
Ischemic injury due to potent vasoconstrictor action tissue hypoxia.
Cardiovascular System:
Bradycardia, probably as a reflex result of a rise in blood pressure, arrhythmias.
Nervous System:
Anxiety, transient headache.

Octreotide [1 vial 500mcg/ml $35.00]

ADMINISTRATION ROUTES:
SC, IV

ALTERNATIVE NAMES:
Sandostatin

ICU INDICATIONS:
1. variceal bleeding
2. chylothorax
3. carcinoid tumours, VIPomas and acromegally

PRESENTATION AND ADMINISTRATION:
SC:
Inject the required dose as undiluted solution by subcutaneous injection. Allow solution to come to room temperature to minimise pain at the injection site.

IV:
50mcg/ml, 100mcg/ml and 500mcg/ml vials
For continuous infusion dilute 500mcg vial in 50ml of normal saline
Dilutions stable for 24 hours at room temperature
Refrigerate vials for prolonged storage; may be stored at room temperature for up to two weeks. Protect from light.

DOSAGE:
SC:
Chylothorax: 100mcg 8 hourly

IV:
When commencing an octreotide infusion, start with 50mcg SC undiluted stat then run infusion at 25mcg/hr.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
No dosage adjustment is required

DOSAGE IN PAEDIATRICS:
Diarrhoea secondary to endocrine tumours:
1 mcg/kg stat then 1-5mcg/kg/kg IV

CLINICAL PHARMACOLOGY:
Octreotide exerts pharmacologic actions similar to the natural hormone somatostatin. It is an even more potent inhibitor of growth hormone, glucagon, and insulin than somatostatin. Like somatostatin, it also suppresses LH response to GnRH, decreases splanchnic blood flow, and inhibits release of serotonin, gastrin, vasoactive intestinal peptide, secretin, motilin, and pancreatic polypeptide.

CONTRAINDICATIONS:
1. sensitivity to octreotide

WARNINGS
Octreotide inhibits gallbladder contractility and may predispose to biliary tract disease such as cholecystitis and ascending cholangitis.

PRECAUTIONS
General
Nil

Laboratory Tests:
Baseline thyroid function tests should be performed for people who require chronic therapy (although such patients are extremely rare in ICU)

Drug/Laboratory Test Interactions
None reported

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Concomitant administration of Octreotide with cyclosporin may decrease blood levels of cyclosporin and result in transplant rejection.
Patients receiving insulin, oral hypoglycaemic agents, beta blockers, calcium channel blockers, or agents to control fluid and electrolyte balance, may require dose adjustments of these therapeutic agents.

ADVERSE REACTIONS
Gastrointestinal
Diarrhoea, vomiting, abdominal distention, constipation, biliary sludge, gallstones, nausea and abdominal discomfort
Cardiac
bradycardia
Metabolic and endocrine
Hypoglycaemia, hyperglycaemia, hypothyroidism
Neurological:
headache

Olanzapine [1 tablet 5mg $3.61, 1 wafer 5mg $3.65]

ADMINISTRATION ROUTES:
PO, IM, NG

ALTERNATIVE NAMES:
Zyprexa

ICU INDICATIONS:
1. Agitation and delirium
2. Psychosis

PRESENTATION AND ADMINISTRATION:
IM:
Zyprexa IM 10mg. Reconstitute with 2.1ml of sterile water for injection and administer by IM injection.

PO / NG:
Tablets:
Zyprexa 2.5mg tablets (white), Zyprexa 5mg tablets (white), Zyprexa 10mg tablets (white)
Wafers:
Zyprexa 5mg wafer (yellow), Zyprexa 10mg wafer (yellow)
Note: for NG administration, dissolve wafers and give via NG tube

DOSAGE:
IM:
Initially 5-10mg; may administer an additional dose of up to 10mg after 2 hours and a further dose of up to 10mg 4 hours after the second dose (max dose 30mg / 24 hours)

PO:
5-20mg daily (can be administered in divided doses)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	initial dose of 5mg and titrate as necessary
10-20	initial dose of 5mg and titrate as necessary
>20-50	initial dose of 5mg and titrate as necessary

Dose in renal replacement therapy

CAPD	initial dose of 5mg and titrate as necessary
HD	initial dose of 5mg and titrate as necessary
CVVHDF	initial dose of 5mg and titrate as necessary

DOSAGE IN PAEDIATRICS:
0.1-0.2mg/kg daily oral; increase to 0.4mg/kg daily oral if required

CLINICAL PHARMACOLOGY:
Olanzapine is a selective monoaminergic antagonist. The mechanism of action of olanzapine is unknown; however, it has been proposed that this drug's efficacy is mediated through a combination of dopamine and serotonin type 2 (5HT2) antagonism.
CONTRAINDICATIONS:
1. Sensitivity to olanzapine

WARNINGS
Increased risk of deaths in patients with dementia
Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo.
Hyperglycaemia and Diabetes Mellitus
Hyperglycaemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics including olanzapine.
Neuroleptic Malignant Syndrome (NMS)
A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with administration of antipsychotic drugs, including olanzapine.
Tardive Dyskinesia
A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs.

PRECAUTIONS
General
Olanzapine may induce hypotension. Olanzapine has not been evaluated or used to any appreciable extent in patients with a recent history of myocardial infarction or unstable heart disease. Patients with these diagnoses were excluded from premarketing clinical studies. Because of the risk of orthostatic hypotension with olanzapine, caution should be observed in cardiac patients
During premarketing testing, seizures occurred in 0.9%. Olanzapine should be used cautiously in patients with a history of seizures or with conditions that potentially lower the seizure threshold

Laboratory Tests:
No tests additional to routine ICU tests are indicated

Drug/Laboratory Test Interactions
None reported

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Because of its potential for inducing hypotension, olanzapine may enhance the effects of antihypertensive agents.

ADVERSE REACTIONS
Body as a Whole
Fever
Cardiovascular System
Hypotension, Tachycardia, Hypertension
Digestive System
Dry mouth, Constipation, Dyspepsia, Vomiting
Nervous System
Somnolence, Dizziness, Tremor, Hypertonia

Omeprazole [1 vial $5.73, 1 capsule 40mg 6 cents]

ADMINISTRATION ROUTES:
PO, IV

ALTERNATIVE NAMES:
Dr Reddy's Omeprazole, Losec, Omezol

ICU INDICATIONS:
1. Ulcer prophylaxis
2. Upper gastrointestinal bleeding

PRESENTATION AND ADMINISTRATION:
IV:
Omeprazole 40mg vial (powder) plus 10ml of specialised solvent
Use only solvent provided for reconstitution as follows:
1. Draw up 10ml of solvent from the vial
2. Slowly add approximately 5 ml of solvent to the vial
3. Withdraw as much air as possible from the vial to reduce positive pressure
4. Transfer the remaining solvent into the vial
5. Rotate and shake the vial to dissolve the powder

Inject solution over at least two and a half minutes at a rate not exceeding 4ml per minute
Note: the omeprazole formulation available in the ICU cannot be given by infusion (see DOSAGE for recommendations)
Store at room temperature
Protect from light
Prepare immediately before use. Reconstituted solution is stable at room temperature for four hours.

PO / NG:
Capsules:
Dr Reddys Omeprazole Capsules 10mg (purple / yellow), 20mg (purple / light grey), 40mg (yellow / purple)
Losec Capsules 10mg (pink), 20mg (pink / reddish-brown), 40mg (reddish-brown)
Omezol Capsules 10mg (pale pink / white), 20mg (pink / white), 40mg (pink / beige)
Suspension:
10mg/5ml
Note: Tablets can be dispersed in water and given via NG immediately following dispersion but only if NG tubes >8Fr. For NG tubes <8Fr, liquid should be used.

DOSAGE:
IV:
Ulcer Prophylaxis:
40mg daily (change to oral as soon as possible)
High dose (for upper GI bleed):
40mg 6-12 hourly

PO:
Ulcer Prophylaxis:
40mg daily

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
0.4-0.8mg/kg 12 to 24 hourly

CLINICAL PHARMACOLOGY:
Omeprazole is a specific inhibition of the H+/K+ ATPase enzyme system at the secretory surface of the gastric parietal cell. Because this enzyme system is regarded as the acid (proton) pump within the gastric mucosa, omeprazole has been characterised as a gastric acid-pump inhibitor, in that it blocks the final step of acid production.

CONTRAINDICATIONS:
1. Hypersensitivity to omeprazole

WARNINGS
Nil

PRECAUTIONS
General
Nil

Laboratory Tests:
No tests additional to routine ICU tests are indicated

Drug/Laboratory Test Interactions
None reported

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Omeprazole can prolong the elimination of diazepam, warfarin and phenytoin, drugs that are metabolized by oxidation in the liver. There have been reports of increased INR and prothrombin time in patients receiving proton pump inhibitors, including omeprazole, and warfarin concomitantly.

ADVERSE REACTIONS
Body as a Whole:
Allergic reactions
Gastrointestinal
Abdominal pain, constipation, diarrhoea, flatulence, nausea, vomiting, elevated LFTs
Renal
Interstitial nephritis
Nervous System
Headache, somnolence

Ondansetron [1 vial 4mg $4.93, 1 tablet 4mg $1.72]

ADMINISTRATION ROUTES:
PO, IV, IM

ALTERNATIVE NAMES:
Zofran

ICU INDICATIONS:
1. Nausea and vomiting

PRESENTATION AND ADMINISTRATION:
IV:
Ondansetron 4mg/2ml and 8mg/4ml
Doses of up to 8mg can be administered undiluted by slow IV injection over 2 to 5 minutes
Doses of 8mg to 32mg, which are rarely if every administered in ICU, should be diluted in 50-100ml of compatible IV fluid and infused over 15 minutes or more.
Compatible with the following IV fluids:

Normal saline	5% dextrose	Glucose and sodium chloride
Hartmanns	10% mannitol	

Store at room temperature. Protect from light

IM:
Inject undiluted into a large muscle (this route is not routinely used in ICU)

PO:
Tablets:
Zofran 4mg and 8 mg tablets (yellow)
Dispersible tablets:
Zofran zydis 4mg and 8mg tablets (white)

DOSAGE:
IV:
4-8mg 6 hourly

PO:
4-8mg 6 hourly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
0.2mg/kg 6-12 hourly

CLINICAL PHARMACOLOGY:
Ondansetron is a selective 5-HT_3 receptor antagonist. While ondansetron's mechanism of action has not been fully characterised, it is not a dopamine-receptor antagonist.

Serotonin receptors of the 5-HT_3 type are present both peripherally on vagal nerve terminals and centrally in the chemoreceptor trigger zone of the area postrema. It is not certain whether ondansetron's antiemetic action in chemotherapy-induced nausea and vomiting is mediated centrally, peripherally, or in both sites.

CONTRAINDICATIONS:

1. Hypersensitivity to ondansetron

WARNINGS
Nil

PRECAUTIONS
General
Nil

Laboratory Tests:
No tests additional to routine ICU tests are indicated

Drug/Laboratory Test Interactions
None reported

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note

ADVERSE REACTIONS
Body as a Whole:
Rash, anaphylaxis
Cardiovascular:
Hypotension, tachycardia, flushing
Gastrointestinal:
Constipation, elevated transaminases
Neurological:
Headache

Oxycodone [1 tablet 20mg 94 cents]

ADMINISTRATION ROUTES:
PO, IV

ALTERNATIVE NAMES:
Oxynorm, Oxycontin, Oxynorm oral solution

ICU INDICATIONS:
1. Opioid analgesia

PRESENTATION AND ADMINISTRATION:
IV:
Oxynorm injection 10mg/ml and 20mg/ml vials
Usually dilute to a concentration of 1mg/ml using compatible IV fluid and administer by direct IV injection
Compatible in the following IV fluids:
Normal saline 5% dextrose Water for injection
Store at room temperature

PO:
Capsules:
Oxynorm 5mg, 10mg and 20mg capsule
Modified release tablets:
Oxycontin 5mg (pale blue), Oxycontin 10mg (white), Oxycontin 20mg (pink), Oxycontin 40mg (yellow), Oxycontin 80mg (green)
Oral solution
Oxynorm oral solution 5mg/5ml

DOSAGE:
IV:
1-10mg IV 4hourly (higher doses may be required)

PO:
Oxynorm:
Initially 5-10mg 4-6 hourly
Oxycontin:
Dosage equivalent to oxynorm but sustained release (therefore administered only every 12 hours)
Transferring patients between oral and parenteral oxycodone:
The dose should be based on the following ratio: 2 mg of oral oxycodone is equivalent to 1 mg of parenteral oxycodone. It must be emphasised that this is a guide to the dose required. Inter-patient variability requires that each patient is carefully titrated to the appropriate dose.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	avoid
10-20	dose as in normal renal function
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	avoid
HD	avoid
CVVHDF	dose as in normal renal function

DOSAGE IN PAEDIATRICS:
Oxynorm:
0.1-0.2mg/kg 4-6 hourly
Oxycontin:
0.6-0.9mg/kg 12 hourly

CLINICAL PHARMACOLOGY:
Oxycodone is a pure agonist opioid whose principal therapeutic action is analgesia.

CONTRAINDICATIONS:
1. Hypersensitivity to oxycodone

WARNINGS
Oxycodone should be used with extreme caution in patients with significant chronic obstructive pulmonary disease or cor pulmonale, and in patients having a substantially decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression.
OxyContin may cause hypotension.
A study of OxyContin in patients with hepatic impairment indicates greater plasma concentrations than those with normal function. The initiation of therapy at 1/3 to 1/2 the usual doses and careful dose titration is warranted in such patients.

PRECAUTIONS
General
Opioid analgesics have a narrow therapeutic index in certain patient populations, especially when combined with CNS depressant drugs, and should be reserved for cases where the benefits of opioid analgesia outweigh the known risks of respiratory depression, altered mental state, and postural hypotension.
OxyContin and other morphine-like opioids have been shown to decrease bowel motility.

Laboratory Tests:
No tests indicated in addition to routine ICU tests

Drug/Laboratory Test Interactions
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
CNS depression is more marked when oxycodone is administered with other CNS depressants

ADVERSE REACTIONS
Body as a Whole:
Pruritus, sweating, anorexia

Cardiovascular
Postural hypotension
Gastrointestinal
Constipation, nausea, vomiting, ileus, dry mouth, abdominal pain, gastritis
Respiratory
Dyspnoea, hiccups, respiratory depression
Nervous system
Somnolence, headache, confusion, convulsions.
Renal:
Urinary retention

Paracetamol

[1 vial 1g $3.96, 1 tablet 17 cents, 1 suppository 500mg 39 cents]

ADMINISTRATION ROUTES:
PO, IV, PR

ALTERNATIVE NAMES:
Pamol, Panadol, Perfalgan

ICU INDICATIONS:
1. Analgesia
2. Antipyretic

PRESENTATION AND ADMINISTRATION:
IV:
Perfalgan 10mg/mL solution contains 1gm of paracetamol in 100ml
Administer by infusion over 15 minutes

Can also be diluted in compatible IV fluid. In this case, use the diluted solution within the hour following its preparation (infusion time included).
Compatible in the following IV fluids:
Normal saline 5% dextrose

As for all solution for infusion presented in glass vials, it should be remembered that close monitoring is needed notably at the end of the infusion, regardless of the administration route. This monitoring at the end of the perfusion applies particularly for central route infusion, in order to avoid air embolism.

It is recommended that for the administration of Perfalgan 10mg/mL solution for infusion a syringe or giving set with a diameter equal to or below 0.8mm should be used for solution sampling. In addition, it is recommended that the bung is pierced at the location specifically designed for needle introduction (where the thickness of the bung is the lowest). If these recommendations are not adhered to the likelihood of bung fragmentation or the bung being forced into the vial is increased.

Store at room temperature

PO:
Available in 500mg capsules, tablets, soluble tablets and suppositories

DOSAGE:
IV:
1gm 4 hourly (maximum 4gm/24 hours)

PO/PR:
1gm 4 hourly (maximum 4gm/24 hours)

Note: In patients with chronic or active hepatic disease, especially those with hepatocellular insufficiency, chronic alcoholism, chronic malnutrition (low reserves of hepatic glutathione), and dehydration the dose should not exceed 3g/day.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:

Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO / IV
20mg/kg stat, then 15mg/kg 4 hourly; usual daily maximum of 90mg/kg for 48 hours then 60mg/kg.

PR
40mg/kg stat then 30mg/kg 6 hourly (max 5gm/day)

CLINICAL PHARMACOLOGY:
Paracetamol is analgesic and antipyretic. The precise mechanism of the analgesic and antipyretic properties of paracetamol has yet to be established; it may involve central and peripheral actions.

CONTRAINDICATIONS:
1. Hypersensitivity to paracetamol
2. Fulminant hepatic failure

WARNINGS
Patients with hepatic insufficiency, chronic alcoholism, chronic malnutrition or dehydration may be at a higher risk of liver damage following administration of paracetamol

PRECAUTIONS
General
Paracetamol should be used with caution in the following settings:
Glucose 6 Phosphate Dehydrogenase (G6PD) deficiency (may lead to haemolytic anaemia), chronic alcoholism, excessive alcohol intake (3 or more alcoholic drinks every day), anorexia, bulimia or cachexia, chronic malnutrition (low reserves of hepatic glutathione)

Laboratory Tests:
No tests indicated in addition to routine ICU tests

Drug/Laboratory Test Interactions
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note

ADVERSE REACTIONS
Neurological
Dizziness, headache, dystonia
Gastrointestinal
Vomiting, dry mouth, diarrhoea, constipation, nausea, dyspepsia, enlarged abdomen, transaminitis
Haematological
Anaemia

Parecoxib [1 vial $15.00]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Dynastat

ICU INDICATIONS:
1. Analgesia

PRESENTATION AND ADMINISTRATION:
IV:
Parecoxib 40mg (powder) plus 2ml of 0.9% saline for reconstitution (can also be reconstituted with 5% dextrose)
Reconstitute then administer rapidly as a bolus.
Use as soon as practicable after reconstitution (may be stored at room temperature after reconstitution for up to 24 hours if required)

DOSAGE:
IV:
40mg stat then 40mg every 12 to 24 hours

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Contraindicated in renal failure. Do not use of CrCl is less than 50ml/min

DOSAGE IN PAEDIATRICS:
IV
There are insufficient data to support the use of parecoxib in the paediatric population

CLINICAL PHARMACOLOGY:
Parecoxib is COX-2 inhibitor non-steroidal anti-inflammatory drug

CONTRAINDICATIONS:
1. Ischaemic heart disease (including after coronary artery bypass graft surgery)
2. Renal impairment
3. Allergy to sulphur drugs

WARNINGS
Due to an increased risk of death associated with the use of COX-2 inhibitors in patients with coronary artery disease, it is prudent to avoid these drugs in patients who are at high risk of coronary artery disease due to the presence of cardiovascular risk factors.

PRECAUTIONS
General
May cause fluid retention

Laboratory Tests:
No tests indicated in addition to routine ICU tests

Drug/Laboratory Test Interactions
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Avoid concomitant use with other non-steroidal anti-inflammatory drugs (including aspirin)

ADVERSE REACTIONS
Body as a Whole:
Anaphylaxis
Neurological
Dizziness, aseptic meningitis
Gastrointestinal
GI upset, transaminitis
Haematological
Anaemia, thrombocytopaenia
Renal
Renal failure

Paroxetine [1 tablet 8 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Aropax, Loxamine

ICU INDICATIONS:
1. Antidepressant

Note: it is rare for antidepressants to be commenced in patients in the ICU. Most ICU patients have 'situational depression' and the risks of medication often outweigh the benefits. (see WARNINGS)

PRESENTATION AND ADMINISTRATION:
PO:
Tablets:
Aropax 20mg tablets (white), Loxamine 20mg tablets (white)
NG:
Tablets can be crushed for administration via NG tube

DOSAGE:
PO:
20mg-60mg daily

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	20mg daily
10-30	20mg daily
>30-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	20mg daily
HD	20mg daily
CVVHDF	20mg daily

DOSAGE IN PAEDIATRICS:
0.4mg/kg daily, increase to maximum of 1mg/kg daily

CLINICAL PHARMACOLOGY:
Paroxetine is a serotonin specific reuptake inhibitor antidepressant

CONTRAINDICATIONS:
1. Hypersensitivity to paroxetine or other SSRIs

WARNINGS
Use in Patients With Concomitant Illness
Clinical experience with SSRIs in patients with concomitant systemic illness is limited. Caution is advisable in using SSRIs in patients with diseases or conditions that could affect metabolism or haemodynamic responses.

Suicidality
Patients with major depressive disorder (MDD), both adult and paediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behaviour (suicidality) or unusual changes in behaviour, whether or not they are taking antidepressant medications, and this risk may persist until significant remission occurs.
Hyponatraemia
Cases of hyponatraemia (some with serum sodium lower than 110 mmol/L) have been reported. The hyponatraemia appeared to be reversible when SSRI was discontinued.

PRECAUTIONS
General
Anaphylactoid events, including bronchospasm, angioedema, laryngospasm, and urticaria alone and in combination, have been reported.
Pulmonary events, including inflammatory processes of varying histopathology and/or fibrosis, have been reported rarely. These events have occurred with dyspnea as the only preceding symptom.
Published case reports have documented the occurrence of bleeding episodes in patients treated with psychotropic drugs that interfere with serotonin reuptake. Subsequent epidemiological studies, both of the case-control and cohort design, have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding.

Laboratory Tests:
No tests in addition to routine ICU tests are required.
Drug/Laboratory Test Interactions
None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
The combination of Tramadol and SSRIs should be used with caution due to the increased risk of serotonin syndrome with concomitant use.
Patients on stable doses of phenytoin and carbamazepine have developed elevated plasma anticonvulsant concentrations and clinical anticonvulsant toxicity following initiation of concomitant fluoxetine treatment.
Serotonin release by platelets plays an important role in haemostasis. Epidemiological studies of the case-control and cohort design that have demonstrated an association between use of psychotropic drugs that interfere with serotonin reuptake and the occurrence of upper gastrointestinal bleeding have also shown that concurrent use of an NSAID or aspirin potentiated the risk of bleeding.
ADVERSE REACTIONS
Body as a Whole
Flu syndrome
Cardiovascular System
Vasodilatation
Digestive System
Nausea, diarrhoea, anorexia, dry mouth, dyspepsia
Nervous System
Insomnia, anxiety, nervousness, somnolence, tremor
Respiratory System
Pharyngitis, sinusitis
Skin and Appendages
Sweating, rash

Pethidine Hydrochloride [1 vial 100mg $1.16]

ADMINISTRATION ROUTES:
IV, IM, PO

ALTERNATIVE NAMES:
Meperidine

ICU INDICATIONS:
1. Analgesia
2. Shivering

PRESENTATION AND ADMINISTRATION:
IV:
Pethidine 100mg in 2ml 50mg in 1ml vial.
Dilute solution to 10mg/ml with Water for Injection. Inject slowly over 3-5 minutes (do not exceed 50mg per dose when administering via this route)
Compatible with the following IV fluids:
0.9% sodium chloride Hartmanns 5% or 10% dextros
Glucose and sodium chloride
Store at room temperature

IM:
Preferred route for repeated or large doses (as it is less irritating than IV)

PO:
Tablets:
Pethidine 50mg tablets (white), Pethidine 100mg tablets (white)

DOSAGE:
IV:
Usually 25-50mg IV 4 hourly (rare for more than a single dose to be used in the ICU setting)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	avoid
10-20	use small doses; increase dosing interval to 6 hours.
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	avoid
HD	avoid
CVVHDF	use small doses; increase dosing interval to 6 hours.

DOSAGE IN PAEDIATRICS:
IM
0.5-2mg/kg 4 hourly
IV
0.5-1mg/kg 4 hourly

CLINICAL PHARMACOLOGY:
Pethidine is a narcotic analgesic with multiple actions qualitatively similar to those of morphine; the most prominent of these involve the central nervous system and organs composed of smooth muscle. The principal actions of therapeutic value are analgesia and sedation.

CONTRAINDICATIONS:
1. Hypersensitivity to pethidine

WARNINGS
Impaired Respiration
Respiratory depression is the chief hazard of all opioids. Respiratory depression occurs most frequently in the elderly and debilitated patients as well as in those suffering from conditions accompanied by hypoxia or hypercapnia when even moderate therapeutic doses may dangerously decrease pulmonary ventilation.
Pethidine should be used with extreme caution in patients with chronic obstructive pulmonary disease or cor pulmonale, and in patients having a substantially decreased respiratory reserve, hypoxia, hypercapnia, or preexisting respiratory depression. In such patients, even usual therapeutic doses of morphine may decrease respiratory drive while simultaneously increasing airway resistance to the point of apnoea.
Hypotensive Effect
Morphine sulphate controlled-release tablets, like all opioid analgesics, may cause severe hypotension in an individual whose ability to maintain his blood pressure has already been compromised by a depleted blood volume, or a concurrent administration of drugs that lower blood pressure.
Anaphylaxis
Although extremely rare, cases of anaphylaxis have been reported.

PRECAUTIONS
General
Supraventricular Tachycardias
Pethidine should be used with caution in patients with atrial flutter and other supraventricular tachycardias because of a possible vagolytic action which may produce a significant increase in the ventricular response rate.
Convulsions
Pethidine may aggravate pre-existing convulsions in patients with convulsive disorders. If dosage is escalated substantially above recommended levels because of tolerance development, convulsions may occur in individuals without a history of convulsive disorders.

Laboratory Tests:
No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:
None noted

IMPORTANT DRUG INTERACTIONS FOR THE ICU
The concomitant use of other central nervous system depressants including sedatives or hypnotics, general anaesthetics, phenothiazines, tranquilizers, and alcohol may produce additive depressant effects. Respiratory depression, hypotension, and profound sedation or coma may occur.

ADVERSE REACTIONS

Central Nervous System:

Euphoria, sedation, dysphoria, weakness, headache, agitation, tremor, uncoordinated muscle movements, severe convulsions, transient hallucinations and disorientation, visual disturbances.

Respiratory:

Gastrointestinal:

Nausea and vomiting, dry mouth, biliary tract spasm, constipation, ileus, intestinal obstruction.

Cardiovascular:

Flushing of the face, chills, tachycardia, bradycardia, palpitation, faintness, syncope, hypotension, hypertension.

Genitourinary:

Urine retention or hesitance, reduced libido and/or potency.

Dermatologic:

Pruritus, urticaria, other skin rashes, oedema, diaphoresis.

Phenobarbitone [1 vial $9.48, 1 tablet 20 cents]

ADMINISTRATION ROUTES:
IV, PO

ALTERNATIVE NAMES:
Phenobarbitone

ICU INDICATIONS:
1. Treatment of status epilepticus in children (in accordance with the Starship protocol)

PRESENTATION AND ADMINISTRATION:
IV
200mg in 1ml of phenobarbitone
For direct IV injection, dilute dose to at least ten times its volume with water for injection. Inject slowly at a rate not exceeding 60mg/min.
Dilute immediately before use. Do not store diluted solution. Do not use any solution that contains a precipitate or is more than slightly discoloured.
May be given into side arm when any of the following fluids are being infused;
0.9% sodium chloride Hartmanns 5% and 10% dextrose
Glucose and sodium chloride
Store at room temperature
Protect from light
Controlled Drug – stored in ICU CD cupboard

IM
May be given IM – no more than 5ml of solution at any one site

PO:
Tablets:
Phenobarbitone 15mg and 30mg tablets (white)
Oral Liquid:
Phenobarbitone oral liquid 10mg/ml

DOSAGE:
IV:
Loading dose of 20mg/kg.
PO, IM, IV
Usual maintenance 300mg/day

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	reduce dose by 25-50%; avoid very large doses
10-20	dose as in normal renal function but avoid very large doses
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	reduce dose by 25-50%; avoid very large doses
HD	reduce dose by 25-50%; avoid very large doses
CVVHDF	dose as in normal renal function but avoid very large doses

DOSAGE IN PAEDIATRICS:
IV
20mg/kg over 20 minutes. If necessary may be given as IV push over 5-10 mins

CLINICAL PHARMACOLOGY:
The barbiturates are nonselective central nervous system (CNS) depressants which are primarily used as sedative hypnotics and are also anticonvulsants in subhypnotic doses.

CONTRAINDICATIONS:
1. Known barbiturate sensitivity
2. Porphyria
3. Marked impairment of liver function

WARNINGS
IV Administration
Rapid administration may cause respiratory depression, apnea, laryngospasm, or vasodilation with fall in blood pressure.

PRECAUTIONS
General
Parenteral solutions of barbiturates are highly alkaline. Therefore, extreme care should be taken to avoid perivascular extravasation or intra-arterial injection. Extravascular injection may cause local tissue damage with subsequent necrosis; consequences of intra-arterial injection may vary from transient pain to gangrene of the limb. Any complaint of pain in the limb warrants stopping the injection.

Laboratory Tests:
No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:
None noted

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Warfarin
Phenobarbital lowers the plasma levels of warfarin and causes a decrease in anticoagulant activity as measured by the prothrombin time.
Corticosteroids
Barbiturates appear to enhance the metabolism of exogenous corticosteroids, probably through the induction of hepatic microsomal enzymes. Patients stabilized on corticosteroid therapy may require dosage adjustments if barbiturates are added to or withdrawn from their dosage regimen.
Phenytoin, Sodium Valproate
The effect of barbiturates on the metabolism of phenytoin appears to be variable. Some investigators report an accelerating effect, while others report no effect. Because the effect of barbiturates on the metabolism of phenytoin is not predictable, phenytoin and barbiturate blood levels should be monitored more frequently if these drugs are given concurrently. Sodium valproate appear to decrease barbiturate metabolism; therefore, barbiturate blood levels should be monitored and appropriate dosage adjustments made as indicated.

Central Nervous System Depressants
The concomitant use of other central nervous system depressants, including other sedatives or hypnotics, antihistamines, tranquilizers, or alcohol, may produce additive depressant effects.

ADVERSE REACTIONS
Body as a Whole:
hypersensitivity reactions (angioedema, skin rashes, exfoliative dermatitis), fever
Nervous System:
Agitation, headache, confusion, hyperkinesia, ataxia, CNS depression, nightmares, nervousness, psychiatric disturbance, hallucinations, insomnia, anxiety, dizziness, thinking abnormality.
Respiratory System:
Hypoventilation, apnea.
Cardiovascular System:
Bradycardia, hypotension, syncope.
Digestive System:
Nausea, vomiting, constipation, liver damage.
Haematological System:
Megaloblastic anaemia following chronic phenobarbital use.

Phenylephrine [1 vial $4.62]

ADMINISTRATION ROUTES:
IV, PO

ALTERNATIVE NAMES:
Neo-Synephrine

ICU INDICATIONS:
1. Hypotension

PRESENTATION AND ADMINISTRATION:
IV
10mg in 1ml (10%) solution
Add 10mg to 100ml of compatible IV fluid and administered by infusion
Compatible with the following IV fluids:
Normal saline 5% glucose Glucose and sodium chloride
Hartmanns
Discard any solution not used within 24 hours of preparation
Store at room temperature.

DOSAGE:
IV:
For hypotension, 100-500mcg PRN
For infusion, administer by infusion at 0-60ml/hr (at higher doses, consider commencing noradrenaline)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV
2-10 mcg/kg stat (adult 500mcg), then 1-5mcg/kg/min

CLINICAL PHARMACOLOGY:
Phenylephrine hydrochloride is a powerful postsynaptic alpha-receptor stimulant with little effect on the beta-receptors of the heart. The predominant actions of phenylephrine hydrochloride are on the cardiovascular system.

CONTRAINDICATIONS:
1. Hypotension solely due to low cardiac output
2. Hypersensitivity to phenylephrine

WARNINGS
Contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in nonasthmatic people.

PRECAUTIONS

General

Phenylephrine hydrochloride should be employed only with extreme caution in elderly patients or in patients with hyperthyroidism, bradycardia, partial heart block, myocardial disease, or severe arteriosclerosis.

Laboratory Tests:

No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:

None noted

IMPORTANT DRUG INTERACTIONS FOR THE ICU

None of note

ADVERSE REACTIONS

Cardiovascular:

Arrhythmia (rare), decreased cardiac output, hypertension, pallor, precordial pain or discomfort, reflex bradycardia, severe peripheral and visceral vasoconstriction

Central nervous system:

Anxiety, dizziness, excitability, giddiness, headache, insomnia, nervousness, restlessness

Endocrine & metabolic:

Metabolic acidosis

Gastrointestinal:

Gastric irritation, nausea

Neuromuscular & skeletal:

Paraesthesia, pilomotor response, tremor, weakness

Renal:

Decreased renal perfusion, reduced urine output

Respiratory:

Respiratory distress

Miscellaneous:

Hypersensitivity reactions (including rash, urticaria, leukopaenia, agranulocytosis, thrombocytopaenia)

Phenytoin [1 vial 100mg $13.85, 1 tablet 100mg 9 cents]

ADMINISTRATION ROUTES:
IV, PO

ALTERNATIVE NAMES:
Dilantin, Phenytoin

ICU INDICATIONS:
1. Seizures and seizure prophylaxis

PRESENTATION AND ADMINISTRATION:
IV
100mg/2ml and 250mg/5ml
Direct IV injection:
Inject undiluted into a large vein at a rate not exceeding 50mg/min and for children and neonates not exceeding 3mg/kg/min. A slower rate of administration (e.g. not exceeding 25mg/min and if necessary as slow as 5-10mg/min) is recommended in patients with cardiovascular disease and the elderly in order to reduce cardiovascular side effects. Follow injection into a vein with 20ml of normal saline to reduce the irritation caused by the alkalinity of the solution (if administering via a peripheral vein)
Intermittent infusion:
Dilute phenytoin in 50-100ml of normal saline immediately before use (final concentration not to exceed 6.7mg/ml). Infuse within 1 hour. Infuse via an in-line filter (0.22-0.5 micron) at a rate not exceeding 50mg/min (children and neonates, give at a rate of 1-3mg/kg/min). Inspect closely for appearance of precipitate during infusion. Note that intermittent infusion, although widely used, is not recommended by the manufacturer due to the risk of precipitation.
Compatible with normal saline ONLY.

PO:
Dilantin infatabs 50mg tablets (yellow)
Dilantin 30mg capsules (white), 100mg capsules (white/orange)
Dilantin paediatric suspension 30mg/5ml

DOSAGE:
IV:
Loading dose in an emergency: 15-20mg/kg (max 1.5gm) IV over 1 hour. Maintenance, 100mg three times daily IV or PO. 300mg once daily can also be used for maintenance therapy.

PO / NG:
For NG use, stop feed for 2 hours before and 2 hours after administration of oral phenytoin dose. 300mg once daily can also be used for maintenance therapy.

Note: Oral Capsules, IV medication & liquid are NOT bioequivalent dose adjustment is needed

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
Loading dose in an emergency: 15-20mg/kg (max 1.5gm) IV over 1 hour. Initial maintenance, oral of IV: 2mg/kg 12 hourly (preterm); 3mg/kg 12 hourly (1st week of life), 8 hourly (2wk-4yr), 12 hourly (5-12 yr); 2mg/kg (usual max 100mg) 8 hourly (12 yrs)

CLINICAL PHARMACOLOGY:
Phenytoin sodium is an antiepileptic drug. Phenytoin sodium is related to the barbiturates in chemical structure.

CONTRAINDICATIONS:
1. Hypersensitivity to phenytoin

WARNINGS
Withdrawal
Abrupt withdrawal of phenytoin in epileptic patients may precipitate status epilepticus. When, in the judgment of the clinician, the need for dosage reduction, discontinuation, or substitution of alternative antiepileptic medication arises, this should be done gradually. However, in the event of an allergic or hypersensitivity reaction, rapid substitution of alternative therapy may be necessary.
Effect of alcohol
Acute alcoholic intake may increase phenytoin serum levels, while chronic alcohol use may decrease serum levels.
Use in pregnancy
A number of reports suggest an association between the use of antiepileptic drugs, including phenytoin, by women with epilepsy and a higher incidence of birth defects in children born to these women.

PRECAUTIONS
General
Phenytoin is NOT indicated for toxicological seizures or seizures due to hypoglycaemia.
Phenytoin should be discontinued if a skin rash appears. If the rash is exfoliative, purpuric, or bullous or if lupus erythematosus, Stevens-Johnson syndrome, or toxic epidermal necrolysis is suspected, use of this drug should not be resumed and alternative therapy should be considered.
The liver is the chief site of biotransformation of phenytoin; patients with impaired liver function, elderly patients, or those who are gravely ill may show early signs of toxicity.
A small percentage of individuals who have been treated with phenytoin have been shown to metabolize the drug slowly. Slow metabolism may be due to limited enzyme availability and lack of induction; it appears to be genetically determined.
Phenytoin is not effective for absence (petit mal) seizures. If tonic-clonic (grand mal) and absence (petit mal) seizures are present, combined drug therapy is needed.

Laboratory Tests:
Phenytoin levels should only be measured if there is a specific clinical indication (i.e. if there is concern about toxicity or ongoing seizures despite phenytoin administration) Specimens should be collected in SST (Yellow) or Plain (Red). Sampling time is not critical. Routine specimens are for total phenytoin. It is possible to measure free phenytoin (green tube); however, this is a send away test and is not routinely indicated.
For patients with low albumin total phenytoin levels will not represent active phenytoin levels in the blood.

Drug/Laboratory Test Interactions:
None known.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Drugs which may increase phenytoin serum levels include: acute alcohol intake, amiodarone, diazepam, warfarin, H2-antagonists, isoniazid, and ulfonamides.
Drugs which may decrease phenytoin levels include: carbamazepine, chronic alcohol abuse,
Drugs which may either increase or decrease phenytoin serum levels include: phenobarbital, sodium valproate, and valproic acid.
Although not a true drug interaction, tricyclic antidepressants may precipitate seizures in susceptible patients and phenytoin dosage may need to be adjusted.
Drugs whose efficacy is impaired by phenytoin include: corticosteroids, warfarin, frusemide, oral contraceptives, rifampin, and theophylline.

ADVERSE REACTIONS
Central Nervous System
Nystagmus, ataxia, slurred speech, decreased coordination and mental confusion.
Gastrointestinal System
Nausea, vomiting, constipation, toxic hepatitis and liver damage.
Skin
Dermatological manifestations sometimes accompanied by fever have included scarlatiniform or morbilliform rashes. A morbilliform rash (measles-like) is the most common; other types of dermatitis are seen more rarely. Other more serious forms which may be fatal have included bullous, exfoliative or purpuric dermatitis, lupus erythematosus, Stevens-Johnson syndrome, and toxic epidermal necrolysis.
Haemopoietic System
Thrombocytopaenia, leukopaenia, granulocytopaenia, agranulocytosis, and pancytopaenia with or without bone marrow suppression. While macrocytosis and megaloblastic anaemia have occurred, these conditions usually respond to folic acid therapy. Lymphadenopathy including benign lymph node hyperplasia, pseudolymphoma, lymphoma, and Hodgkin's disease have been reported.
Cardiovascular
Bradycardia, heart block, periarteritis nodosa.
Immunologic
Hypersensitivity syndrome (which may include, but is not limited to, symptoms such as arthralgias, eosinophilia, fever, liver dysfunction, lymphadenopathy or rash), systemic lupus erythematosus, and immunoglobulin abnormalities.

Potassium Chloride

[1 vial 10 mmol $1.10, 1 tablet 600 mg 4 cents]

ADMINISTRATION ROUTES:
IV, PO, NG

ALTERNATIVE NAMES:
Potassium Chloride, chlorvescent, slow K, span K

ICU INDICATIONS:
1. Hypokalaemia

PRESENTATION AND ADMINISTRATION:
IV:
750 mg/10 ml (1 mmol/ml) vial
Add 10-20 mmol KCl to 100 ml of compatible IV fluid and infuse over 1 hour via a central line. If fluid overload is a concern, the same amount could be concentrated into 50 ml for administration by a central line only. Rates of up to 40 mmol/hr have been used via central line for severe hypokalaemia (<2 mmol/L) when cardiac abnormalities were present
When infused via a peripheral vein, it is preferable to use a concentration of **not greater than 40 mmol/L**. Consider whether oral or NG replacement is possible.
When KCl has been added to IV fluids or when commercial preparations are opened, discard any solution not used within 24 hours. Do not use cloudy solutions.
Compatible with the following IV fluids:
0.9% sodium chloride Hartmanns 5%, 10% & 20% glucose
Glucose and sodium chloride
Store at room temperature

PO:
Chlorvescent Effervescent tablets (each contains 14mmol of potassium)
Span K sustained release tablets (each contains 8mmol of potassium)

DOSAGE:
IV:
For cardiac patients: <4 mmol give 20 mmol KCl; if <4.5 give 10 mmol KCl
For non cardiac patients usually <3.5 mmol give 20 mmol KCl; <4.0 mmol give 10 mmol KCl

PO:
Dose according to requirements and response.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	dose according to response
10-20	dose according to response
20-50	dose according to response

Dose in renal replacement therapy

CAPD	dose according to response
HD	dose according to response
CVVHDF	dose according to response

DOSAGE IN PAEDIATRICS:
IV:
Deficiency: usually 0.3 mmol/kg/hr (max 0.4 mmol/kg/hr) for 4-6 hours IV, then 4 mmol/kg/day Max oral dose 1 mmol/kg (<5years); 0.5 mmol/kg (>5years).
If given peripherally via IV route, max 0.05 mmol/ml

CLINICAL PHARMACOLOGY:
The potassium ion is the principal intracellular cation of most body tissues. Potassium ions participate in a number of essential physiological processes including the maintenance of intracellular tonicity, the transmission of nerve impulses, the contraction of cardiac, skeletal and smooth muscle and the maintenance of normal renal function.

CONTRAINDICATIONS:
1. Hyperkalaemia

WARNINGS
In patients with impaired mechanisms for excreting potassium, the administration of potassium salts can produce hyperkalaemia and cardiac arrest.

PRECAUTIONS
General
Solid oral dosage forms of potassium chloride can produce ulcerative and/or stenotic lesions of the gastrointestinal tract.

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Simultaneous administration of ACE inhibitors or potassium sparing diuretics (eg spironolactone) with KCl may lead to hyperkalaemia.

ADVERSE REACTIONS
Body as a Whole:
Hyperkalaemia
Gastrointestinal system (with oral preparations):
GI upset, ulcer, perforation, bleeding
Local:
Injection site pain

Phosphate [1 vial $5.20, 1 tablet 83 cents]

ADMINISTRATION ROUTES:
IV, PO

ALTERNATIVE NAMES:
Potassium dihydrogen phosphate, Phosphate Sandoz

ICU INDICATIONS:
1. Hypophosphataemia

PRESENTATION AND ADMINISTRATION:
IV:
10ml vial (1mmol/ml potassium, 1mmol/ml phosphate)
Add required dose to 100ml of compatible IV fluid. Administer at no greater than 20mmol per hour.
Use a central line if possible; if administration is necessary via a peripheral line it is preferable to add the required dose to 500ml or 1000ml
Discard any solution not used within 24 hours of preparation
Do not use solution that is cloudy or shows precipitate
Compatible with the following IV fluids:
0.9% sodium chloride 5% glucose Glucose and sodium chloride
Store at room temperature.

PO:
Phosphate Sandoz Effervescent tablets

DOSAGE:
IV:
Individualise dosage. Usually in ICU administer 1vial over 1 hour and repeat as required

PO:
Dose according to requirements and response. Note oral phosphate replacement is often not particularly effective in the ICU setting and is generally not indicated

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	dose according to response
10-20	dose according to response
20-50	dose according to response

Dose in renal replacement therapy

CAPD	dose according to response
HD	dose according to response
CVVHDF	dose according to response

Note: usually phosphate replacement is not appropriate in the setting of renal failure unless the patient is on renal replacement therapy

DOSAGE IN PAEDIATRICS:
IV:
0.15-0.33mmol/kg administered over 6 hours; may be repeated at 6 hour intervals until serum phosphate exceeds 0.6mmol/L. Dose should not exceed the maximum recommended adult dose. Rate of infusion should not exceed 0.2mmol/kg/hr.

CLINICAL PHARMACOLOGY:
Phosphorus in the form of organic and inorganic phosphate has a variety of important biochemical functions in the body and is involved in many significant metabolic and enzyme reactions in almost all organs and tissues. It exerts a modifying influence on the steady state of calcium levels, a buffering effect on acid-base equilibrium and a primary role in the renal excretion of hydrogen ion.

CONTRAINDICATIONS:
1. Hyperphosphataemia
2. Hyperkalaemia

WARNINGS
To avoid potassium or phosphorus intoxication, infuse solutions containing potassium phosphates slowly. In patients with severe renal or adrenal insufficiency, administration of potassium phosphates injection may cause potassium intoxication. Infusing high concentrations of phosphorus may cause hypocalcaemia, and calcium levels should be monitored.

PRECAUTIONS
General
Phosphorus replacement therapy with potassium phosphates should be guided primarily by the serum inorganic phosphorus levels and the limits imposed by the accompanying potassium (K^+) ion.

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note.

ADVERSE REACTIONS
Hyperphosphataemia
Hyperkalaemia
Hypomagnesaemia
Hypocalcaemia

Prednisone [1 tablet 5mg 3 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Apo-Prednisone

ICU INDICATIONS:
1. Relative corticosteroid insufficiency in patients with severe septic shock
2. Adrenal insufficiency
3. Steroid responsive inflammatory conditions

PRESENTATION AND ADMINISTRATION:
PO / NG:
Prednisone sodium phosphate liquid 5mg/ml
Apo-prednisone 20mg (pink), 20mg (white), 5mg, 1mg

DOSAGE:
PO:
Initially 10mg-100mg daily as a single morning dose or divided doses depending on indication.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function
DOSAGE IN PAEDIATRICS:
PO:
Asthma: 0.5-1mg/kg for 24 hours, then every 12 hours for two doses, then 1mg/kg daily.
Croup: 1mg/kg stat and in 12 hours; severe 4mg/kg then 1mg/kg 8 hourly
CLINICAL PHARMACOLOGY:
Prednisone is a steroid hormone which has glucocorticoid and mineralocorticoid properties. 1mg prednisone = hydrocortisone 4mg in glucocorticoid activity, 0.8mg in mineralocorticoid

CONTRAINDICATIONS:
1. Systemic fungal infections

WARNINGS
Steroid induced myopathy:
An acute myopathy has been observed with the use of high doses of corticosteroids, most often occurring in patients with disorders of neuromuscular transmission (e.g., myasthenia gravis), or in patients receiving concomitant therapy with neuromuscular blocking drugs. This acute myopathy is generalized, may involve ocular and respiratory muscles, and may result in quadriparesis. Elevations of creatine kinase may occur. Clinical improvement or recovery after stopping corticosteroids may require weeks to years.
Adrenal-insufficiency due to steroids:
In patients on corticosteroid therapy subjected to unusual stress, increased dosage of rapidly acting corticosteroids before, during, and after the stressful situation is indicated.
Infections:
Corticosteroids may mask some signs of infection, and new infections may appear during their use.

Blood pressure:
Average and large doses of hydrocortisone can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. These effects are less likely to occur with the synthetic derivatives except when used in large doses.

PRECAUTIONS
General
There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis.
Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes, and severe depression to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Laboratory Tests
No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
The pharmacokinetic interactions listed below are potentially clinically important. Drugs that induce hepatic enzymes such as phenobarbital, phenytoin and rifampin may increase the clearance of corticosteroids and may require increases in corticosteroid dose to achieve the desired response.

ADVERSE REACTIONS
Fluid and Electrolyte Disturbances:
Sodium retention; fluid retention; congestive heart failure in susceptible patients; potassium loss; hypokalemic alkalosis; hypertension.
Musculoskeletal:
Muscle weakness; steroid myopathy, loss of muscle mass; osteoporosis; tendon rupture, particularly of the Achilles tendon; vertebral compression fractures; aseptic necrosis of femoral and humeral heads; pathologic fracture of long bones.
Gastrointestinal:
Peptic ulcer with possible perforation and haemorrhage; pancreatitis; abdominal distention; ulcerative oesophagitis; increases in alanine transaminase (ALT, SGPT), aspartate transaminase (AST, SGOT) and alkaline phosphatase have been observed following corticosteroid treatment.
Dermatologic:
Impaired wound healing; thin fragile skin; petechiae and ecchymoses; facial erythema; increased sweating; may suppress reactions to skin tests.
Neurological:
Convulsions; increased intracranial pressure with papilloedema (pseudotumour cerebri) usually after treatment; vertigo; headache.
Endocrine:
Menstrual irregularities; development of Cushingoid state; suppression of growth in children; secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery or illness; decreased carbohydrate tolerance; manifestations of latent diabetes mellitus; increased requirements for insulin or oral hypoglycaemic agents in diabetics.

Propofol [1 vial 100ml $7.60]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Fresofol, Diprivan

ICU INDICATIONS:
1. Sedation
2. Induction of Anaesthesia

PRESENTATION AND ADMINISTRATION:
IV:
1% propofol (diprivan) 200mg in 20ml and 500mg in 50ml.
Administer undiluted by bolus or IV infusion
Compatibility of propofol injectable emulsion with the coadministration of blood/serum/plasma has not been established. When administered using a y-type infusion set, propofol injectable emulsion has been shown to be compatible with the following intravenous fluids:
5% Dextrose injection Hartmanns 5% Dextrose and 0.45% sodium chloride
Store at room temperature

DOSAGE:
IV:
Induction of anaesthesia: doses vary widely in the critically ill (typically 20mg to 200mg)
Sedation: usual doses of 0-20ml/hr; doses of >20ml/hr should not be used for greater than 24 hours due to the risk of propofol infusion syndrome (see WARNINGS)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
Sedation in ICU: 1-3mg/kg/hr (max 4mg/kg/hr) IV for no longer than 48 hours.
Short term anaesthesia: child 2.5-3.5mg/kg stat, then 7.5-15mg/kg/hr IV.

CLINICAL PHARMACOLOGY:
Propofol injectable emulsion is an intravenous sedative-hypnotic agent for use in the induction and maintenance of anaesthesia or sedation.

CONTRAINDICATIONS:
1. known hypersensitivity to propofol

WARNINGS
STRICT ASEPTIC TECHNIQUE MUST ALWAYS BE MAINTAINED DURING HANDLING. PROPOFOL INJECTABLE EMULSION IS A SINGLE-USE PARENTERAL PRODUCT WHICH CONTAINS 0.005% DISODIUM EDETATE TO RETARD THE RATE OF GROWTH OF MICROORGANISMS IN THE EVENT OF ACCIDENTAL

EXTRINSIC CONTAMINATION. HOWEVER, PROPOFOL INJECTABLE EMULSION CAN STILL SUPPORT THE GROWTH OF MICROORGANISMS AS IT IS NOT AN ANTIMICROBIALLY PRESERVED PRODUCT UNDER USP STANDARDS. ACCORDINGLY, STRICT ASEPTIC TECHNIQUE MUST STILL BE ADHERED TO. DO NOT USE IF CONTAMINATION IS SUSPECTED. DISCARD UNUSED PORTIONS AS DIRECTED WITHIN THE REQUIRED TIME LIMITS. THERE HAVE BEEN REPORTS IN WHICH FAILURE TO USE ASEPTIC TECHNIQUE WHEN HANDLING PROPOFOL INJECTABLE EMULSION WAS ASSOCIATED WITH MICROBIAL CONTAMINATION OF THE PRODUCT AND WITH FEVER, INFECTION/SEPSIS, OTHER LIFE-THREATENING ILLNESS, AND/OR DEATH.

Propofol infusion syndrome is a rare syndrome which can lead to cardiac failure, rhabdomyolysis, metabolic acidosis and renal failure and is often fatal. It usually effects patients undergoing long-term treatment with high doses of propofol.

PRECAUTIONS

General

A lower dose of propofol should be used in patients with haemodynamic instability at the time of induction; consider the use of an alternative agent

Clinical features of anaphylaxis, which may include angioedema, bronchospasm, erythema, and hypotension, may occur following propofol injectable emulsion administration

Reports of bradycardia, asystole, and rarely, cardiac arrest have been associated with propofol injectable emulsion.

Laboratory Tests

No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Propofol requirements are reduced by concomitant administration of opioids and/or benzodiazepines

ADVERSE REACTIONS

Body as a Whole:

Propofol infusion syndrome

Cardiovascular:

Bradycardia; arrhythmia; tachycardia; hypotension; decreased cardiac output

Central Nervous System:

Myoclonic jerking (NOT seizure activity)

Metabolic/Nutritional:

Hyperlipemia

Injection Site:

Burning/stinging or pain.

Respiratory:

Apnea

Skin and Appendages:

Rash, pruritus.

Propranolol [1 tablet 4 cents]

ADMINISTRATION ROUTES:
PO

ALTERNATIVE NAMES:
Cardinol

ICU INDICATIONS:
1. Thyrotoxic crisis
2. Use as a centrally acting beta blocker

PRESENTATION AND ADMINISTRATION:
PO
Tablets:
Cardinol 10mg tablets (red) and 40mg (red)
Long Acting Capsules:
Cardinol 160mg long acting capsules

DOSAGE:
PO:
Usual dosage for thyrotoxicosis, 10mg- 40mg 3-4 times a day; usual maximum dosage 320mg daily in divided doses

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	start with small doses
10-20	start with small doses
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	start with small doses
HD	start with small doses
CVVHDF	start with small doses

DOSAGE IN PAEDIATRICS:
PO
0.2-0.5mg/kg 6-12 hourly oral; slowly increase to 1.5mg/kg 6-12 hrly if required

CLINICAL PHARMACOLOGY:
Propranolol hydrochloride is a synthetic non-selective beta-adrenergic receptor blocking agent. It is the first line agent for thyrotoxicosis because it reduces peripheral conversion of T4 to T3.

CONTRAINDICATIONS:
1. sinus bradycardia,
2. heart block greater than first degree,
3. cardiogenic shock,
4. overt cardiac failure
5. asthma

WARNINGS
Cardiac Failure
Sympathetic stimulation is necessary in supporting circulatory function in congestive heart failure, and beta blockade carries the potential hazard of further depressing myocardial contractility and precipitating more severe failure.
Discontinuation of therapy
Discontinuation of therapy in a patient with coronary artery disease may lead to rebound angina, arrhythmia or myocardial infarction.
Diabetes and Hypoglycaemia
Beta blockers may mask tachycardia occurring with hypoglycaemia.
Thyrotoxicosis
Beta-adrenergic blockade may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism. Abrupt withdrawal of beta blockade might precipitate a thyroid storm.

PRECAUTIONS
General
Beta blockers may aggravate peripheral arterial circulatory disorders.

Laboratory Tests:
No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions:
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Beta blockers may exacerbate the rebound hypertension which can follow the withdrawal of clonidine

ADVERSE REACTIONS
Body as a Whole:
Tiredness, Fatigue
Cardiovascular System:
Bradycardia , Cold extremities, Hypotension, Leg pain
Respiratory System:
Wheeziness, Dyspnoea
Digestive System:
Diarrhoea, Nausea
Nervous System:
Dizziness, Vertigo, Light-headedness

Protamine Sulphate [1 vial $9.59]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Protamine

ICU INDICATIONS:
1. Reversal of heparin

PRESENTATION AND ADMINISTRATION:
IV
50mg in 5ml (solution).
Administer by slow IV injection over no greater than 1ml/minute (i.e. 50mg over 5 minutes). Watch the blood pressure trace closely during administration and slow rate of infusion if the blood pressure drops.
Administration by IV infusion is described but is not generally preferred. To administer by IV infusion, add to a suitable volume of compatible IV fluid and administer over required time period
Compatible with the following IV fluids:
0.9% Sodium chloride 5% Dextrose Glucose and sodium chloride
Store at room temperature. Protect from light.

DOSAGE:
IV:
For neutralisation of unfractionated heparin:
1mg of protamine sulphate will usually neutralise at least 100 international units of mucous heparin or 80 units of lung heparin. The dose of protamine sulphate should be reduced if more than 15 minutes have elapsed since intravenous injection.
For example, if 30-60 minutes have elapsed since heparin was injected intravenously, 0.5-0.75mg protamine sulphate per 100 units of mucous heparin is recommended. If two hours or more have elapsed, 0.25-0.375mg per 100 units of mucous heparin should be administered.
If the patient is receiving an intravenous infusion of heparin, the infusion should be stopped and 25-50mg of protamine sulphate given by slow intravenous injection.
In the reversal of UF heparin following cardiopulmonary bypass, either a standard dose of protamine may be given, as above, or the dose may be titrated according to the activated clotting time or TEG.
Neutralisation of low molecular weight (LMW) heparin:
A dose of 1mg per 100 units is usually recommended. The anti-Xa activity of LMW heparins may not be completely reversible with protamine sulphate and may persist for up to 24 hours after administration.
The longer half-life of LMW heparins (approximately twice that of UF heparin) should also be borne in mind when estimating the dose of protamine sulphate required in relation to the time which has elapsed since the last heparin dose.
Theoretically, the dose of protamine sulphate should be halved when one half-life has elapsed since the last LMW heparin dose. Intermittent injections or continuous infusion of protamine sulphate have been recommended for the neutralisation of LMW heparin following subcutaneous administration, as there may be continuing absorption from the subcutaneous depot.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV
1mg/100 IU of heparin (0.5mg/100 IU of heparin if > 1 hour since heparin dose); subsequent doses of protamine 1mg/kg (max 50mg)

CLINICAL PHARMACOLOGY:
Protamine is used to counteract the anticoagulant effect of heparin through the formation of heparin-protamine complexes. The onset of action of protamine occurs within five minutes following intravenous administration. The fate of the protamine-heparin complex is unknown, but it may be partially degraded, thus freeing heparin.

CONTRAINDICATIONS:
1. Hypersensitivity to protamine

WARNINGS
Hypotension
Rapid administration of protamine may lead to severe hypotension and anaphylactoid reactions

PRECAUTIONS
General
In patients who have had cardiac surgery with cardiopulmonary bypass, a rebound bleeding effect may occur hours post-operatively. This responds to further doses of protamine.

Laboratory Tests:
No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions:
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None known

ADVERSE REACTIONS
Body as a Whole:
Anaphylaxis, angioedema
Cardiovascular System:
Hypotension, flushing
Respiratory System:
Non cardiogenic pulmonary oedema
Digestive System:
Nausea, vomiting

Quinapril [1 tablet 5mg 5 cents]

ADMINISTRATION ROUTES:
PO

ALTERNATIVE NAMES:
Accupril, Accuretic (quinapril + hydrochlorthiazide)

ICU INDICATIONS:
1. Hypertension
2. Congestive heart failure or left ventricular dysfunction after myocardial infarction
3. Diabetic nephropathy

PRESENTATION AND ADMINISTRATION:
PO
Accupril tablets 5mg, 10mg & 20mg (reddish-brown)
Accuretic tablets 10mg quinapil & 12.5mg hydrochlorthiazide (pink)

DOSAGE:
PO:
5-10mg once daily; increasing to 20-40mg daily as required

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	50% of normal dose
10-20	75-100% of normal dose
>20-50	75-100% of normal dose

Dose in renal replacement therapy

CAPD	50% of normal dose
HD	75-100% of normal dose
CVVHDF	75-100% of normal dose

Note: Recent clinical observations have shown an association of hypersensitivity-like (anaphylactoid) reactions during haemodialysis with high-flux dialysis membranes (e.g., AN69) in patients receiving ACE inhibitors.

DOSAGE IN PAEDIATRICS:
PO:
0.2-0.8mg/kg daily

CLINICAL PHARMACOLOGY:
Quinapril is a specific competitive inhibitor of angiotensin I-converting enzyme (ACE), the enzyme responsible for the conversion of angiotensin I to angiotensin II.

CONTRAINDICATIONS:
1. Hypersensitivity to quinapril or any other angiotensin-converting enzyme inhibitor (e.g. a patient who has experienced angioedema during therapy with any other ACE inhibitor).
2. Cardiogenic shock

WARNINGS

Anaphylactoid and Possibly Related Reactions

Quinapril can cause anaphylactoid reactions

Head and Neck Angioedema

Angioedema involving the extremities, face, lips, mucous membranes, tongue, glottis or larynx has been seen in patients treated with ACE inhibitors, including captopril. If angioedema involves the tongue, glottis or larynx, airway obstruction may occur and be fatal. Swelling confined to the face, mucous membranes of the mouth, lips and extremities has usually resolved with discontinuation of quinapril; some cases required medical therapy.

Intestinal Angioedema

Intestinal angioedema has been reported in patients treated with ACE inhibitors. These patients presented with abdominal pain (with or without nausea or vomiting); in some cases there was no prior history of facial angioedema and C-1 esterase levels were normal.

Neutropaenia/Agranulocytosis

Neutropaenia (<1000/mm3) with myeloid hypoplasia has resulted from use of quinapril.

Hypotension in Heart Failure Patients

Caution should be observed when initiating therapy in patients with heart failure. Patients with heart failure given quinapril commonly have some reduction in blood pressure. In patients with symptomatic hypotension this may require temporarily reducing the dose of quinapril, or diuretic, or both, and volume repletion

Hepatic Failure

Rarely, ACE inhibitors have been associated with a syndrome that starts with cholestatic jaundice and progresses to fulminant hepatic necrosis and (sometimes) death. The mechanism of this syndrome is not understood. Patients receiving ACE inhibitors who develop jaundice or marked elevations of hepatic enzymes should discontinue the ACE inhibitor.

PRECAUTIONS

General

Some patients with renal disease, particularly those with severe renal artery stenosis, have developed increases in serum creatinine after reduction of blood pressure with quinapril. Quinapril dosage reduction and/or discontinuation of diuretic may be required.

Elevations in serum potassium have been observed in some patients treated with ACE inhibitors, including quinapril.

Presumably due to the inhibition of the degradation of endogenous bradykinin, persistent nonproductive cough has been reported with all ACE inhibitors, always resolving after discontinuation of therapy. ACE inhibitor-induced cough should be considered in the differential diagnosis of cough.

Laboratory Tests:

No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions :

None known.

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Increased serum lithium levels and symptoms of lithium toxicity have been reported in patients receiving concomitant lithium and ACE inhibitor therapy.

The risk of hypotension increases if quinapril is coadministered with other antihypertensives.

ADVERSE REACTIONS:
Body as a Whole:
Gynaecomastia, anaphylactoid reactions, angioedema
Cardiovascular:
Cardiac arrest, cerebrovascular accident / insufficiency, rhythm disturbances, orthostatic hypotension, syncope
Dermatological:
Bullous pemphigus, erythema multiforme (Stevens Johnson syndrome), exfoliatice dermatitis
Gastrointestinal:
Pancreatitis, glossitis, dyspepsia, jaundice, hepatitis, rare causes of hepatic necrosis, cholestasis
Haematological:
Anaemia (including cases of haemolytic anaemia), thrombocytopaenia, neutropaenia
Metabolic:
Hyponatraemia
Musculoskeletal:
Myalgia, myasthenia
Nervous system:
Ataxia, confusion, depression, nervousness, somnolence
Respiratory system:
Bronchospasm, eosinophilic pneumonia, angioedema
Urogenital system:
Renal failure, proteinuria

Ranitidine [1 vial $1.75, 1 tablet 150mg 3 cents]

ADMINISTRATION ROUTES:
PO, IV

ALTERNATIVE NAMES:
Apo-Ranitidine, Zantac, Peptisoothe

ICU INDICATIONS:
1. Ulcer prophylaxis

PRESENTATION AND ADMINISTRATION:
IV
Dilute 50mg dose to 20ml with compatible IV fluid and administer into side arm over at least 2 minutes.
Compatible with the following IV fluids:
0.9% sodium chloride 5% and 10% dextrose Glucose and Sodium Chloride Hartmann's
Store at room temperature

PO
Tablets
Apo-Ranitidine 150mg tablets (white), Arrow Ranitidine 150mg tablets (white), Zantac relief tablets (150mg)
Oral solution:
Peptisoothe 150mg/10ml
Zantac Syrup 150mg/10ml

DOSAGE:
PO:
150mg 8-12 hourly or 300mg at night
IV:
50mg 8 hourly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	50-100% of normal dose
10-20	dose as in normal renal function
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	50-100% of normal dose
HD	50-100% of normal dose
CVVHDF	dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
1mg/kg 8 hourly
PO:
2-4mg/kg 8-12 hourly

CLINICAL PHARMACOLOGY:
Ranitidine is a selective, competitive antagonist of histamine at H2-receptor sites

CONTRAINDICATIONS:
1. Hypersensitivity to ranitidine

WARNINGS
Nil

PRECAUTIONS
General
Nil

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions:
None known.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note

ADVERSE REACTIONS:
Body as a Whole:
Hypersensitivity reactions (e.g. fever, bronchospasm, anaphylactic shock, rash, eosinophilia)
Central nervous system.
Malaise, dizziness, somnolence, insomnia, vertigo, mental confusion, depression and hallucinations.
Cardiovascular system.
Tachycardia, bradycardia, premature ventricular beats, A-V block and asystole.
Gastrointestinal system:
Constipation, diarrhoea, nausea/ vomiting, abdominal discomfort/ pain, hepatitis, pancreatitis.
Musculoskeletal system:
Rare reports of arthralgias and myalgia.
Haematological system:
Agranulocytosis or pancytopaenia, sometimes with marrow hypoplasia or aplasia, have been reported.
Dermatological system:
Rash including rare cases of mild erythema multiforme. Rare cases of vasculitis have been reported.

Remifentanil [1 vial 2mg $20.30]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Ultiva

ICU INDICATIONS:
1. Opioid analgesia

PRESENTATION AND ADMINISTRATION:
IV
Administer by intravenous infusion. Dilute 2mg in 40ml of compatible IV fluid to make a concentration of 50mcg/ml
Compatible with the following IV fluids:
Water for Injection. 5% Dextrose 0.9% Sodium Chloride

DOSAGE:
IV:
Initially, 0.1-0.15mcg/kg/min; may titrate by 0.025mcg/kg/min at intervals of at least 5 minutes to desired level of analgesia or sedation; consider initiation of another sedative if desired level of sedation is not achieved with 0.2mcg/kg/min

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
0.05-0.2mcg/kg/min. Ventilated: usually 0.5-1mcg/kg/min; occasionally up to 8mcg/min

CLINICAL PHARMACOLOGY:
Remifentanil opioid agonist

CONTRAINDICATIONS:
1. Hypersensitivity to remifentanil

WARNINGS
Muscle Rigidity
At the doses recommended muscle rigidity may occur. As with other opioids, the incidence of muscle rigidity is related to the dose and rate of administration

PRECAUTIONS
General
As with all potent opioids, profound analgesia is accompanied by marked respiratory depression.
Due to the very rapid offset of action of remifentanil, no residual opioid activity will be present within 5-10 minutes after the discontinuation of remifentanil
Symptoms including tachycardia, hypertension and agitation have been reported upon abrupt cessation, particularly after prolonged administration of remifentanil.

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions :
None known.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
The concomitant administration with other cardiovascular depressant drugs leads to an increased risk of hypotension; concomitant administration with other CNS depressant drugs also increases the risk of CNS depression.

ADVERSE REACTIONS:
Body as a Whole:
Anaphylaxis
Central nervous system.
Skeletal muscle rigidity, Sedation.
Cardiovascular system.
Asystole, bradycardia, hypotension.
Gastrointestinal system:
Constipation, nausea/ vomiting.
Respiratory system:
Apnoea
Dermatological system:
Pruritis

Risperidone [1 tablet 1mg 28 cents]

ADMINISTRATION ROUTES:
PO, IM

ALTERNATIVE NAMES:
Ridal, Risperidal

ICU INDICATIONS:
1. Agitation and delirium
2. Psychosis

PRESENTATION AND ADMINISTRATION:
IM:
Long-acting Depot ONLY (not for use in ICU)

PO:
Tablets:
Ridal 0.5mg (red), 1mg (white), 2mg (orange), 3mg (yellow), 4mg (green); Risperidal 0.5mg (brownish / red), 1mg (white), 2mg (orange), 3mg (yellow), 4mg (green)
Oral Disintegrating Tablets:
Risperdal Quicklet 0.5mg (light coral), 1mg (light coral), 2mg (coral)
Oral Solution:
Risperdal Solution 1mg/ml

DOSAGE:
PO:
0.5-1mg 12 hourly; increase to a maximum of 8mg 12 hourly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	initial dose of 0.5mg BD; increase slowly to 1-2mg BD
10-20	initial dose of 0.5mg BD; increase slowly to 1-2mg BD
>20-50	initial dose of 0.5mg BD; increase slowly to 1-2mg BD

Dose in renal replacement therapy

CAPD	initial dose of 0.5mg BD; increase slowly to 1-2mg BD
HD	initial dose of 0.5mg BD; increase slowly to 1-2mg BD
CVVHDF	initial dose of 0.5mg BD; increase slowly to 1-2mg BD

DOSAGE IN PAEDIATRICS:
0.02mg/kg 12 hourly; increase to 0.15mg/kg 12 hourly

CLINICAL PHARMACOLOGY:
Risperidone is a compound which belongs to a new class of antipsychotic agents, the benzisoxazole derivatives. Risperidone is a selective monoaminergic antagonist having a high affinity for serotoninergic 5-HT2 and dopaminergic D2 receptors. Risperidone binds also to alpha1-adrenergic receptors and, with lower affinity, to H1-histamine and alpha2-adrenergic receptors.

CONTRAINDICATIONS:
1. Sensitivity to risperidone

WARNINGS

Increased risk of deaths in patients with dementia

Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo.

Hyperglycaemia and Diabetes Mellitus

Hyperglycaemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics including risperidone.

Neuroleptic Malignant Syndrome (NMS)

A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with administration of antipsychotic drugs, including risperidone.

Tardive Dyskinesia

A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs.

PRECAUTIONS

General

Risperidone may induce hypotension.

Classical neuroleptics are known to lower the seizure threshold. Caution is recommended when treating patients with epilepsy.

Laboratory Tests:

No tests additional to routine ICU tests are indicated

Drug/Laboratory Test Interactions

None reported

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Given the primary CNS effects of risperidone, it should be used with caution in combination with other centrally-acting medicines.

Carbamazepine has been shown to decrease the plasma levels of the active antipsychotic fraction of risperidone. On discontinuation of carbamazepine the dosage of risperidone should be re-evaluated and, if necessary, decreased.

ADVERSE REACTIONS

Cardiovascular System

Hypotension, Tachycardia, Hypertension

Digestive System

Dry mouth, Constipation, Dyspepsia, Vomiting

Nervous System

Somnolence, Dizziness, Tremor, Hypertonia

Haematological System:

Decreased neutrophil count, decreased platelet count

Rocuronium [1 vial $18.43]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Esmeron

ICU INDICATIONS:
1. Muscle relaxant

PRESENTATION AND ADMINISTRATION:
IV
50mg in 5ml solution
Supplied as a clear, aqueous solution for intravenous injection.
Administer neat for IV injection or infusion
Compatible with the following IV fluids:
5% dextrose normal saline Hartmanns glucose and sodium chloride
Store in the refrigerator at 2-8°C. The product can be stored outside the refrigerator at a temperature of up to 30°C for a maximum of 12 weeks. The product may not be placed back, once kept outside the refrigerator.

DOSAGE:
IV:
0.6-1.2mg/kg stat, then 0.1-0.2mg/kg boluses or 5-15mcg/kg/min

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function (duration of action may be prolonged)

DOSAGE IN PAEDIATRICS:
IV
0.6-1.2mg/kg stat, then 0.1-0.2mg/kg boluses or 5-15mcg/kg/min

CLINICAL PHARMACOLOGY:
Rocuronium is a fast onset, intermediate acting non-depolarizing neuromuscular blocking agent.

CONTRAINDICATIONS:
1. Hypersensitivity to rocuronium

WARNINGS
Anaphylactic reactions can occur following the administration of neuromuscular blocking agents including rocuronium.

PRECAUTIONS

General

In general, following long term use of neuromuscular blocking agents in the ICU, prolonged paralysis and/or skeletal muscle weakness has been noted. Myopathy after long term administration of other non-depolarizing neuromuscular blocking agents in the ICU in combination with corticosteroid therapy has been reported regularly. Therefore, for patients receiving both neuromuscular blocking agents and corticosteroids, the period of use of the neuromuscular blocking agent should be limited as much as possible.

Like other neuromuscular blocking agents, rocuronium should be used with extreme caution in patients with a neuromuscular disease

Laboratory Tests:

No tests additional to routine ICU tests are required

Drug/Laboratory Test Interactions

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Drugs which may enhance the neuromuscular blocking action of rocuronium include: certain antibiotics, especially the aminoglycosides and polymyxins; lithium; magnesium salts; procainamide; and quinidine.

The prior administration of succinylcholine does not enhance the duration, but quickens the onset and may increase the depth, of neuromuscular block induced by rocuronium

ADVERSE REACTIONS

General:

Allergic reactions (anaphylactic or anaphylactoid responses) which, in rare instances, were severe (e.g., cardiac arrest).

Musculoskeletal:

Inadequate block, prolonged block.

Cardiovascular:

Hypotension, vasodilatation (flushing), tachycardia, bradycardia.

Respiratory:

Dyspnea, bronchospasm, laryngospasm.

Integumentary:

Rash, urticaria, reaction at injection site.

Roxithromycin [1 tablet 300mg 28 cents]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Arrow Roxithromycin

ICU INDICATIONS:
1. Empirical treatment of atypical pneumonia
2. Treatment of infections caused by other susceptible organisms

PRESENTATION AND ADMINISTRATION:
PO / NG:
Arrow Roxithromycin 150mg tablets (white), 300mg tablets (white)
Note: tablets may be crushed and administered via NG tube.

DOSAGE:
PO / NG:
150mg twice daily OR 300mg once daily

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO:
2.5mg-4mg/kg 12 hourly

CLINICAL PHARMACOLOGY:
Roxithromycin is a semi-synthetic macrolide antibiotic. Roxithromycin is bacteriostatic at low concentrations and bactericidal at high concentrations. It binds to the 50S subunit of the 70S ribosome, thereby disrupting bacterial protein synthesis.
Roxithromycin is usually active against the following organisms in vitro and in clinical infections:
Streptococcus pyogenes (group A Beta-haemolytic streptococci), Alpha-haemolytic streptococci (viridans group), Staphylococcus aureus (resistant organisms may emerge during treatment), Streptococcus pneumoniae, Mycoplasma pneumoniae, Treponema pallidum, Corynebacterium diphtheriae, Corynebacterium minutissimum, Entamoeba histolytica, Listeria monocytogenes, Neisseria gonorrhoeae, Bordetella pertussis, Legionella pneumophila (agent of Legionnaires' disease), Ureaplasma urealyticum, Chlamydia trachomatis.

CONTRAINDICATIONS:
1. Hypersensitivity to roxithromycin or other macrolide antibiotics

WARNINGS
Hepatic dysfunction:
There have been reports of hepatic dysfunction, including increased liver enzymes, and hepatocellular and/or cholestatic hepatitis, with or without jaundice, occurring in patients receiving oral erythromycin products.

Pseudomembranous colitis:
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including roxithromycin, and may range in severity from mild to life threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents

PRECAUTIONS
General
Caution should be exercised if roxithromycin is administered to patients with impaired hepatic function, as its serum half life is increased in patients with hepatic failure. If administered to patients with severe hepatic insufficiency (e.g. hepatic cirrhosis with jaundice and/or ascites), the dose should be reduced by half to 150 mg once daily.

Laboratory Tests:
No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:
Erythromycin interferes with the fluorometric determination of urinary catecholamines.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Roxithromycin has a much lower affinity for cytochrome P450 than erythromycin, and consequently has fewer interactions. Interactions may be observed, however, with drugs that bind to alpha-1-acid glycoprotein, e.g. disopyramide.
Increases in prothrombin time (international normalised ratio (INR) have been reported in patients treated concomitantly with roxithromycin and warfarin
Roxithromycin may increase the absorption of digoxin leading to increased serum levels

ADVERSE REACTIONS
Body as a Whole:
Anaphylaxis, angioedema.
Gastrointestinal System:
Nausea, vomiting, epigastric pain, diarrhoea, hepatitis
Skin:
Urticaria, rash, pruritus

Salbutamol [1 vial 5mg $13.02, 1 nebule 5mg 25 cents]

ADMINISTRATION ROUTES:
IV, Nebulised, Inhaler

BRAND NAMES:
Ventolin, Combivent, Duolin, Albuterol, Respigen, Salamol.

ICU INDICATIONS:
1. Bronchospasm
2. Hyperkalaemia (pending definitive treatment)

PRESENTATION AND ADMINISTRATION:
IV:
5mg in 5ml solution.
For infusion add 5mg to 50ml or 10mg to 100ml of compatible IV fluid.
Note that Ventolin solution for IV infusion (5mg in 5ml) should not be injected undiluted.
If a bolus dose of salbutamol is required, dilute with Water for injection prior to administration. For example, add 0.5ml (500mcg) to 10ml to make a solution of 50mcg/ml and inject bolus doses of up to 5ml (repeat as required)
Compatible with the following IV fluids:
0.9% sodium chloride 5% glucose Glucose and sodium chloride
Store at room temperature.
Protect from light

Inhaler:
Respigen, Salamol & ventolin: 100mcg/dose
Combivent: salbutamol 100mcg/dose plus ipratropium 20mcg/dose

Nebuliser:
Ventolin 2.5mg/2.5ml nebules and 5mg/2.5ml nebules
Duolin 2.5mg salbutamol and 500mcg ipratropium / 2.5ml nebules

DOSAGE:
IV:
Usual bolus dose 250mcg
Usual infusion range 0-10ml/hr when made up in standard ICU infusion dilution

Inhaler:
For intubated patients, use metered dose inhalers in preference to nebulisers.
Administer 5-10 puffs into ventilator circuit using MDI adaptor.

Nebuliser:
2.5-5mg nebulisers as required (initially continuously if required)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV salbutamol bolus:
Give 10 micrograms/kg (single dose maximum 500 micrograms). Over 2 minutes. Give in a minimum volume of 5ml (can be diluted with 0.9% Saline). Repeat dose at 10 minutes if still not improving
IV salbutamol infusion:
Dose
5 -10 microgram/kg/min for 1 hour then reduce to 1 - 2 microgram/kg/min
If Patient Weight < 16kg
Add 3 mg/kg of IV salbutamol solution (1 mg/ml) to a 50 ml syringe and make up to 50 ml with 5% dextrose
Then 1 ml/hr = 1 microgram/kg/min
If Patient Weight > 16kg
Draw up neat IV salbutamol solution (1 mg/ml) into a 50ml syringe (i.e. not diluted)
Then rate (ml/hr) = 0.06 x weight (kg) x dose (microgram/kg/min)
For example if you have a 20 kg child and want to infuse salbutamol at 5 microgram/kg/min then set rate at 0.06 x 20 x 5 = 6 ml/hr

CLINICAL PHARMACOLOGY:
Salbutamol is a selective β_2 adrenoceptor agonist which acts on bronchial smooth muscle to relieve bronchospasm

CONTRAINDICATIONS
1. Hypersensitivity to salbutamol

WARNINGS
Hypokalaemia:
Potentially serious hypokaliemia may result from β2 agonist therapy mainly from parenteral and nebulised administration. Particular caution is advised in acute severe asthma as this effect may be potentiated by concomitant treatment with xanthine derivatives, steroids, diuretics and hypoxia. It is recommended the serum potassium levels are monitored in such situations.

PRECAUTIONS
General
Salbutamol should be administered cautiously to patients suffering from hyperthyroidism, cardiovascular disease and diabetes.

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions
None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Salbutamol will enhance the activity of other β2 sympathomimetics. β receptor blocking agents such as propranolol inhibit the activity of salbutamol. The effects of salbutamol may be enhanced by concomitant administration of aminophylline or other xanthines.

ADVERSE REACTIONS

Musculoskeletal system:

fine tremor of skeletal muscle (particularly of the hands), palpitations and muscle cramps.

Cardiovascular system:

Tachycardia, peripheral vasodilation with hypotension

Hypersensitivity reactions:

Angioedema, urticaria, bronchospasm, hypotension and collapse have been reported rarely.

Respiratory system:

Paradoxical bronchospasm may also occur requiring immediate discontinuation of therapy and institution of appropriate treatment.

Sildenafil [1 tablet 50mg $7.96]

ADMINISTRATION ROUTES:
PO, NG

ALTERNATIVE NAMES:
Viagra

ICU INDICATIONS:
1. Patients undergoing cardiac surgery who are at risk of, or who suffer from, peri-operative right ventricular (RV) failure due to raised pulmonary vascular resistance or exacerbation of pre-existing pulmonary hypertension

PRESENTATION AND ADMINISTRATION:
Tablets
Viagra 25mg (blue) and 50mg (blue)

DOSAGE:
PO:
The typical dose is 50mg 3-4 times daily. In small or very sick patients an initial dose of 25mg would be appropriate. For most patients a duration of 3-5 days only is appropriate.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	initially 25mg doses
10-30	initially 25mg doses
>30-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	initially 25mg doses
HD	initially 25mg doses
CVVHDF	initially 25mg doses

DOSAGE IN PAEDIATRICS:
PO
Not applicable

CLINICAL PHARMACOLOGY:
Sildenafil is a potent, selective inhibitor of cGMP-specific phosphodiesterase-5 (PDE-5). It has an established therapeutic role as a selective pulmonary vasodilator in patients with pulmonary hypertension in the non-operative setting. Recent limited data suggests it may have a similar role in the peri-operative setting in cardiothoracic surgical patients; however, evidence is very limited.

CONTRAINDICATIONS:
See WARNINGS

WARNINGS
Patients with increased susceptibility to vasodilators (e.g. severe aortic stenosis, left ventricular outflow tract obstructon, hypovolaemia) may be at increased risk of hypotension with sildenafil.
There are no reports in the literature of use in such patients.

PRECAUTIONS
General
May cause significant hypotension

Laboratory Tests:
No tests are indicated in addition to routine ICU

Drug/Laboratory Test Interactions
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Sildenafil potentiates the hypotensive effects of nitrates. The data sheet states that the combination of nitrates (nitric oxide donors including GTN, isosorbide salts, sodium nitroprusside; organic nitrates or organic nitrites) and sildenafil is contraindicated. However, in a recent double-blind placebo-controlled randomised trial of males with coronary artery disease the combination of sildenafil or placebo and iv GTN up to a dose of 80 mcg/min was tolerated without significant hypotension by 70% in the sildenafil group. In the peri-operative environment with intensive monitoring instituted it is appropriate to use nitrates if indicated. Nitric oxide co-administration is safe and potentiates the pulmonary vasodilator effects of sildenafil without any adverse effects. Sildenafil has been used to facilitate weaning of NO.
The combination of sildenafil with potent CYP3A4 inhibitors (e.g. ketoconazole, itraconazole, ritonavir) is contraindicated.

ADVERSE REACTIONS
Cardiovascular System:
flushing, hypotension
Nervous System:
headache, anterior ischemic optic neuropathy (causing sudden loss of vision)
Skin:
rash
Digestive System:
Diarrhoea, dyspepsia

Simvastatin [1 tablet 20mg 2 cents]

ADMINISTRATION ROUTES:
PO

ALTERNATIVE NAMES:
Arrow Simva, Lipex, Simvarex

ICU INDICATIONS:
1. Secondary prevention in patients with coronary artery disease
2. Treatment of hypercholesterolaemia

PRESENTATION AND ADMINISTRATION:
Tablets
Arrow Simva 10mg, 20mg, 40mg, 80mg
Lipex 10mg (peach), 20mg (tan), 40mg (red), 80mg (red)
Simvarex 10mg (light pink), 20mg (tan), 40mg and 80mg (pink)

DOSAGE:
PO:
Usually 40mg daily at night; slowly increase to a maximum of 80mg if required.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO
Not applicable

CLINICAL PHARMACOLOGY:
Simvastatin is a selective, competitive inhibitor of HMG-CoA reductase.

CONTRAINDICATIONS:
1. Active liver disease or unexplained persistent elevations of serum transaminases.
2. Hypersensitivity to any component of this medication.

WARNINGS
Liver Dysfunction
HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function.
Skeletal Muscle
Rare cases of rhabdomyolysis with acute renal failure secondary to myoglobinuria have been reported with Simvastatin and with other drugs in this class.

PRECAUTIONS
General
Patients should be advised to report promptly unexplained muscle pain, tenderness, or weakness, particularly if accompanied by malaise or fever.

Laboratory Tests:
CK should be measured if there is concern about development of myopathy due to statins.

Drug/Laboratory Test Interactions
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
The risk of myopathy during treatment with other drugs of this class is increased with concurrent administration of cyclosporin, fibric acid derivatives, niacin (nicotinic acid), erythromycin, and azole antifungals
When multiple doses of simvastatin and digoxin were coadministered, steady-state plasma digoxin concentrations increased by approximately 20%. Patients taking digoxin should be monitored appropriately.

ADVERSE REACTIONS
Body as a Whole:
Malaise
Digestive System:
Constipation, derangement of LFTs, flatulence, dyspepsia, and abdominal pain
Nervous System:
Insomnia, dizziness, paraesthesia, somnolence
Skin:
Pruritus
Musculoskeletal:
Myalgia, myopathy

Sodium Bicarbonate [1 vial10ml 8.4% $11.20]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Sodium Bicarbonate

ICU INDICATIONS:

1. Correction of normal anion gap acidosis
2. Correction of severe metabolic acidosis associated with myocardial dysfunction where acidosis may be contributory to myocardial dysfunction
3. Toxicological indications:

(i) cardiotoxicity secondary to fast sodium channel blockers
- tricyclics
- bupropion
- venlafaxine
- dextropropoxyphene
- propranolol
- type 1a and 1c antiarrhythmics (flecainide, quinidine and quinine)

(ii) prevention of restribution of drug to the CNS
- severe salicylate poisoning

(iii) immediate correction of profound life-threatening metabolic acidosis
- cyanide poisoning
- isoniazid poisoning
- toxic alcohol poisoning (ethylene glycol, methanol & other toxic alcohols)

(iv) enhanced urinary drug elimination
- salicylate intoxication (any symptomatic patient)
- phenobarbitone intoxication (any symptomatic patient)

(v) increased urinary solubility
- methotrexate toxicity
- drug induced rhabdomyolysis

PRESENTATION AND ADMINISTRATION:
IV:
8.4% (1mmol/ml) 10ml vial and 8.4% 50 & 100ml glass bottles
Store at room temperature
Compatible with the following IV fluids:
0.9% sodium chloride 5% glucose Glucose and sodium chloride
Do not use solutions which are cloudy or have visible precipitate
Administer via a central line if possible (i.e. if a central line is present this is the preferred route)
In ICU, it is usual to administer sodium bicarbonate undiluted over an hour; in an emergency situation it can be administered undiluted by direct IV injection.

DOSAGE:
IV:
Usual dose 1mmol/kg IV (repeated as required)
Alternative method to calculate dose is: Dose (mmol) = Base Excess x Weight/10 (these doses correct half the base deficit)
In severe cardiotoxicity due to fast sodium channel blockade in drug overdose give 2mmol/kg IV and repeat until cardiovascular stability is achieved

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	use with caution
10-20	dose as in normal renal function
>20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	use with caution
HD	use with caution
CVVHDF	dose as in normal renal function

DOSAGE IN PAEDIATRICS:
If Patient Weight < 5kg
Dose (mmol) = Base Excess x Weight/4
If Patient Weight > 5kg
Dose (mmol) = Base Excess x Weight/6

CLINICAL PHARMACOLOGY:
Sodium bicarbonate

CONTRAINDICATIONS
1. Severe hypernatraemia
2. Alkalosis
3. Hypokalaemia

WARNINGS
Fluid overload:
Sodium bicarbonate constitutes a significant sodium load and may precipitate fluid overload. Patients with poorly controlled congestive cardiac failure, renal failure and acute pulmonary oedema are at particular risk.

PRECAUTIONS
General
Alkalosis may precipitate hypokalaemia
Laboratory Tests:
No tests in addition to routine ICU tests are required.
Drug/Laboratory Test Interactions
None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None

ADVERSE REACTIONS

Cardiovascular System:

Fluid overload, Acute pulmonary oedema

Respiratory System:

Respiratory depression, hypoxia (secondary to compensatory respiratory acidosis)

Gastrointestinal System:

Metabolic System:

Alkalosis, hypernatraemia, hypokalaemia, hypocalcaemia, hyperosmolarity

Local:

Local tissue inflammation secondary to extravasation

Sodium Nitroprusside [1 vial $11.00]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Nipride, nitropress

ICU INDICATIONS:
1. Afterload reduction / peripheral vasodilation
2. Treatment of hypertension

PRESENTATION AND ADMINISTRATION:
IV:
50mg of powder in a vial.
Add 2-3ml of 5% glucose to dissolve the powder
Dilute reconstituted solution of 50mg up to a total of 50ml using 5% dextrose.
Sodium nitroprusside is compatible with 5% dextrose ONLY. No other drug may be administered via the side arm or added to the infusion while sodium nitroprusside is being infused.
Freshly prepared solution has a very faint brownish tinge
Prepare all solutions immediately before use.
In aqueous solution, sodium nitroprusside is photosensitive and must be protected from light. Immediately after dilution the solution should be wrapped in aluminium foil to protect it from light. Use yellow tubing. (it is not necessary to cover the tubing or the drip chamber with foil)
Any solution not used within 24 hours or preparation should be discarded. Any solution that is high coloured should be discarded.
Store at room temperature
Protect from light and heat.

DOSAGE:
IV infusion:
IV infusion dose range is 0-20ml/hr (usually used in the lower end of the dose range).

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function; avoid prolonged use.

DOSAGE IN PAEDIATRICS:
IV infusion:
<30kg 3mg/kg in 50ml 5% dextrose at 0.5-4ml/hr (0.5-4mcg/kg/min)
>30kg 3mg/kg in100ml 5% dextrose at 1-8ml/hr (0.5-4mcg/kg/min)

CLINICAL PHARMACOLOGY:
The principal pharmacological action of sodium nitroprusside is relaxation of vascular smooth muscle and consequent dilation of peripheral arteries and veins.

CONTRAINDICATIONS:
1. Known hypersensitivity to sodium nitroprusside

WARNINGS

Methaemoglobinaemia

Rare patients receiving more than 10mg/kg of sodium nitroprusside will develop methaemoglobinaemia

Cyanide Poisoning

Except when used briefly or at low (less than 2micrograms/kg/min) infusion rates, sodium nitroprusside can give rise to important quantities of cyanide ion, which can reach toxic, potentially lethal levels especially those with impaired renal function after prolonged, rapid infusions.

Excessive Hypotension

Sodium Nitroprusside can cause precipitous decreases in blood pressure. Because sodium nitroprusside's hypotensive effect is very rapid in onset and in dissipation, small variations in infusion rate can lead to wide, undesirable variations in blood pressure.

PRECAUTIONS

General

Sodium nitroprusside may lead to severe hypotension in patients with haemodynamically significant aortic stenosis.

Laboratory Tests

No tests in addition to routine ICU tests are required

Drug/Laboratory Test Interactions

None of note

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Amplification of the vasodilatory effects of sodium nitroprusside by sildenafil can result in severe hypotension.

Additive effects may be observed when sodium nitroprusside is combined with other antihypertensives

ADVERSE REACTIONS

Body as a Whole:

Allergic reactions

Cardiovascular System:

Tachycardia, hypotension, syncope, rebound hypertension, palpitations

Gastrointestinal System;

Nausea, vomiting, abdominal pain

Central Nervous System:

Headache

Haematological System:

Methaemoglobinaemia, thiocyanate toxicity

Sodium Valproate [1 vial $41.51, 1 tablet 14 cents]

ADMINISTRATION ROUTES:
IV, PO, NG

ALTERNATIVE NAMES:
Epilim

ICU INDICATIONS:
1. Seizures and seizure prophylaxis

PRESENTATION AND ADMINISTRATION:
IV
Injection (vial) 400mg (powder) plus diluent (4ml for Injection). Store at room temperature.
Prepare solutions immediately before use; reconstituted solution and solution prepared for infusion may be refrigerated for use within 24 hours
For direct IV injection, add diluent (4ml) to vial. Shake gently to dissolve powder. Concentration of reconstituted solution is 95mg/ml. Give required dose over 3 to 5 minutes.
For intermittent infusion, prepare as for direct IV injection then add required dose to 500ml of compatible IV fluid and infuse over a convenient period. Compatible with the following IV fluids:
0.9% normal saline 5% glucose Glucose and Sodium Chloride

PO / NG:
Crushable tablets:
Epilim crushable 100mg tablets (white)
Enteric coated tablets:
Epilim EC 200mg tablets (lilac)
Liquids:
Epilim sugar free liquid (200mg/5ml); Epilim 200mg/5ml syrup
Note: for NG administration, use liquid.

DOSAGE:
IV:
If previous oral dose satisfactory, continue at the same dose using intermittent infusion. For commencement of therapy use 400-800mg (up to 10mg/kg) followed by a continuous or repeated infusion dose of up to a maximum of 2500mg/day.

PO:
Administered in 2 divided doses. Initial dose 600mg/day. Increase by 200mg/day at 3 day intervals until control achieved. Usual dose range 1000-2000mg/day. Maximum dose 2500mg/day

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO, IV:
5mg/kg 8-12 hourly oral; increase to a maximum of 20mg/kg 8-12 hourly

CLINICAL PHARMACOLOGY:
Sodium valproate is an anticonvulsant. The mechanisms by which valproate exerts its therapeutic effects have not been established. It has been suggested that its activity in epilepsy is related to increased brain concentrations of gamma-aminobutyric acid (GABA).

CONTRAINDICATIONS:
1. Hypersensitivity to sodium valproate
2. Hepatic disease or dysfunction
3. Urea cycle disorders

WARNINGS
Hepatotoxicity
Hepatic failure resulting in fatalities has occurred in patients receiving valproic acid. Experience has indicated that children under the age of 2 years are at a considerably increased risk of developing fatal hepatotoxicity and this medication should only be used in this group with consideration of this risk.
Pancreatitis
Cases of life-threatening pancreatitis have been reported in both children and adults receiving valproate. If pancreatitis is diagnosed, valproate should ordinarily be discontinued.
Urea Cycle Disorders (UCD)
Valproate sodium is contraindicated in patients with known urea cycle disorders.
Post-Traumatic Seizures
There is some evidence that valproate increases the risk of death compared to phenytoin when used for seizure prophylaxis after head injury. It should not be used for this indication.
Use in pregnancy
Sodium valproate is teratogenic

PRECAUTIONS
General
Sodium Valproate is NOT indicated for toxicological seizures or seizures due to hypoglycaemia.
Sodium Valproate may cause thrombocytopaenia.

Laboratory Tests:
The relationship between plasma concentration and clinical response is not well documented. Some patients are well controlled with serum levels outside the therapeutic range. Serum levels should only be measured if there is a specific clinical indication.
Spec Collection: SST (Yellow) or Plain (Red)
Therapeutic Range: 300-600 umol/L (trough)
Clinical value: Used primarily to detect non-compliance or suspected toxicity
General Notes: Peak: 1-4 hr post dose. Steady State: 2-3 days. Half life: 7-9 hr. Recommended sampling: Pre-dose (trough) Toxic: >800 umol/L

Drug/Laboratory Test Interactions:
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Reduce serum levels of valproate are seen when valproate is coadministered with carbapenems or rifampicin. The concomitant use of valproic acid and clonazepam may induce absence status in patients with a history of absence type seizures. The dose of lamotrigine should be reduced when coadministered with valproate. Serious skin reactions (such as Stevens-Johnson Syndrome and toxic epidermal necrolysis) have been reported with concomitant lamotrigine and valproate administration. In patients with epilepsy, there have been reports of breakthrough seizures occurring with the combination of valproate and phenytoin. The dosage of phenytoin should be adjusted as required by the clinical situation. In an *in vitro* study, valproate increased the unbound fraction of warfarin by up to 32.6%. The therapeutic relevance of this is unknown; however, coagulation tests should be monitored if valproate therapy is instituted in patients taking anticoagulants. Other clinically significant drug interactions are possible.

ADVERSE REACTIONS

Body as a Whole

Chest Pain, Headache, Injection Site Inflammation & Pain

Cardiovascular System

Vasodilation, hypotension

Digestive System

Abdominal Pain, Diarrhoea, Nausea, Vomiting

Nervous System

Dizziness, Euphoria, Hyperaesthesia, Nervousness, Paraesthesia, Somnolence, Tremor.

Respiratory System

Pharyngitis

Sotalol [1 vial $13.08, 1 tablet 80mg 5 cents]

ADMINISTRATION ROUTES:
PO, IV

ALTERNATIVE NAMES:
Sotalol, Sotacor

ICU INDICATIONS:
1. Acute treatment and prevention of supraventricular tachycardia

PRESENTATION AND ADMINISTRATION:
IV:
Injection vial (40mg/4ml solution)
Add required dose to an appropriate volume of compatible IV fluid to prepare a solution with a concentration of 0.1-2mg/ml (see examples in table below). Infuse over 10 minutes.

Volume of Sotalol Injection	Diluent Volume	Total Volume	Sotalol Concentration
4ml	16ml	20ml	2mg/ml
4ml	36ml	40ml	1mg/ml
4ml	46ml	50ml	0.8mg/ml
4ml	96ml	100ml	0.4mg/ml
8ml	32ml	40ml	2mg/ml
8ml	72ml	80ml	1mg/ml

Compatible with the following IV fluids:
0.9% sodium chloride 5% glucose
Store at room temperature; if storage is necessary after dilution, refrigerate for no more than 24 hours.

PO:
Tablets:
Sotalol 80mg tablets (white), Sotalol 160mg (white)

DOSAGE:
IV:
Individualise dose. 0.5 to 1.5mg/kg (20 – 120mg). Repeat 6 hourly if necessary. Usual maximum daily dose 320mg.

PO:
Initially 80mg twice daily; may increase gradually to 240-320mg/day

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]
<10 Avoid or use with caution
10-20 25% of normal dose
>20-50 50% of normal dose
Dose in renal replacement therapy
CAPD Avoid
HD Avoid

CVVHDF 25% of normal dose
DOSAGE IN PAEDIATRICS:
IV:
0.5 - 2mg/kg over 10 minutes 6 hourly

PO:
1-4mg/kg 8 -12 hourly

CLINICAL PHARMACOLOGY:
Sotalol hydrochloride is an antiarrhythmic drug with Class II (beta-adrenoreceptor blocking) and Class III (cardiac action potential duration prolongation) properties.

CONTRAINDICATIONS:
1. Sinus bradycardia,
2. Heart block greater than first degree,
3. Cardiogenic shock,
4. Overt cardiac failure
5. Asthma

WARNINGS
Proarrhythmia
Like other antiarrhythmic agents, sotalol can provoke new or worsened ventricular arrhythmias in some patients, including sustained ventricular tachycardia or ventricular fibrillation, with potentially fatal consequences
General
Cardiac Failure
Sympathetic stimulation is necessary in supporting circulatory function in congestive heart failure, and beta blockade carries the potential hazard of further depressing myocardial contractility and precipitating more severe failure.
Discontinuation of therapy
Discontinuation of therapy in a patient with coronary artery disease may lead to rebound angina, arrhythmia or myocardial infarction.
Diabetes and Hypoglycaemia
Beta blockers may mask tachycardia occurring with hypoglycaemia.
Thyrotoxicosis
Beta-adrenergic blockade may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism. Abrupt withdrawal of beta blockade might precipitate a thyroid storm.

PRECAUTIONS
Sotalol may aggravate peripheral circulatory disorders

Laboratory Tests:
No tests are required in addition to routine ICU tests

Drug/Laboratory Test Interactions:
The presence of sotalol in the urine may result in falsely elevated levels of urinary metanephrine when measured by fluorimetric or photometric methods.

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Class Ia antiarrhythmic drugs, such as disopyramide, quinidine and procainamide and other Class III drugs (e.g., amiodarone) are not recommended as concomitant therapy with Sotalol, because of their potential to prolong refractoriness leading to ventricular arrhythmia. Additive Class II effects would also be anticipated with the use of other beta-blocking agents concomitantly with Sotalol.

Sotalol should be administered with caution in conjunction with calcium blocking drugs because of possible additive effects on atrioventricular conduction or ventricular function. Additionally, concomitant use of these drugs may have additive effects on blood pressure, possibly leading to hypotension

Beta blockers may exacerbate the rebound hypertension which can follow the withdrawal of clonidine

ADVERSE REACTIONS

Body as a Whole:

Tiredness, Fatigue

Cardiovascular System:

Bradycardia, Ventricular tachycardia, Cold extremities, Hypotension, Leg pain

Respiratory System:

Wheeziness, Dyspnoea

Digestive System:

Diarrhoea, Nausea

Nervous System:

Dizziness, Vertigo, Light-headedness

Spironolactone [1 tablet 25mg 5 cents]

ADMINISTRATION ROUTES:
PO

ALTERNATIVE NAMES:
Spirotone, spironolactone

ICU INDICATIONS:
1. heart failure
2. essential hypertension
3. fluid overload

PRESENTATION AND ADMINISTRATION:
PO:
Tablets:
Spirotone 25mg and 100mg tablets (pale orange)
Oral Liquid:
Spironolactone oral liquid 5mg/ml
Note: crush tablets for NG administration.

DOSAGE:
PO:
Initially 25-100mg/day in single or divided doses; increase to maximum of 200mg/day as required.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	Avoid
10-30	Avoid
>30-50	25mg per day

Dose in renal replacement therapy

CAPD	Avoid
HD	Avoid
CVVHDF	Avoid

DOSAGE IN PAEDIATRICS:
PO (NOT/kg):
1-10kg: 6.25mg 12 hourly
11-20kg: 12.5mg 12 hourly
21-40kg: 25mg 12 hourly
>40kg: 25mg 8 hourly

CLINICAL PHARMACOLOGY:
Spironolactone is a potassium sparing diuretic.

CONTRAINDICATIONS:
1. Hyperkalaemia
2. Renal failure

WARNINGS
Hyperkalaemia
Excessive potassium intake may cause hyperkalaemia in patients receiving spironolactone

PRECAUTIONS
General
See WARNINGS

Laboratory Tests:
No tests are required in addition to routine ICU tests; close monitoring of potassium and renal function are important

Drug/Laboratory Test Interactions:
Several reports of possible interference with digoxin radioimmunoassays by spironolactone, or its metabolites, have appeared in the literature. Neither the extent nor the potential clinical significance of its interference (which may be assay-specific) has been fully established.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
ACE Inhibitors:
Concomitant administration of ACE inhibitors with potassium-sparing diuretics has been associated with severe hyperkalaemia.
Skeletal Muscle Relaxants, Nondepolarizing:
Possible increased responsiveness to the muscle relaxant may result.
Lithium:
Lithium generally should not be given with diuretics. Diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity.
Nonsteroidal Anti-inflammatory Drugs (NSAIDs):
In some patients, the administration of an NSAID can reduce the diuretic, natriuretic, and antihypertensive effect of loop, potassium-sparing and thiazide diuretics. Combination of NSAIDs, has been associated with severe hyperkalaemia.
Digoxin:
Spironolactone has been shown to increase the half-life of digoxin. This may result in increased serum digoxin levels and subsequent digitalis toxicity.

ADVERSE REACTIONS
Digestive:
Gastric bleeding, ulceration, gastritis, diarrhoea and cramping, nausea, vomiting.
Endocrine:
Gynecomastia, irregular menses or amenorrhea, postmenopausal bleeding.
Haematologic:
Agranulocytosis.
Hypersensitivity:
Fever, urticaria, maculopapular or erythematous cutaneous eruptions, anaphylactic reactions, vasculitis.
Nervous System/Psychiatric:
Mental confusion, ataxia, headache, drowsiness, lethargy.
Liver/Biliary:
A very few cases of mixed cholestatic/hepatocellular toxicity, with 1 reported fatality, have been reported with spironolactone administration.

Suxamethonium [1 vial $2.60]

ADMINISTRATION ROUTES:
IV, IM

ALTERNATIVE NAMES:
Succinyl Choline

ICU INDICATIONS:
1. Muscle Relaxant (for rapid sequence induction)

PRESENTATION AND ADMINISTRATION:
IV
Suxamethonium 100mg/2ml
Administer neat
Refrigerate - stable at room temperature for 14 days.

DOSAGE:
IV:
1mg/kg

IM:
3mg/kg
(this is **not** the preferred administration route in ICU and should be used in an emergency only when intravenous/intraosseous access cannot be established)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function; avoid if there is hyperkalaemia

DOSAGE IN PAEDIATRICS:
IV
Neonate: 3mg/kg
Child: 2mg/kg
Note: in children, there is a risk of bradycardia and asystole particularly if there is hypoxia. Suxamethonium should be given with atropine.

CLINICAL PHARMACOLOGY:
Suxamethonium is a depolarizing skeletal muscle relaxant.

CONTRAINDICATIONS:
1. Muscular dystrophy or other skeletal myopathies (including critical illness myopathy)
2. Personal or family history of malignant hyperthermia
3. Hypersensitivity to suxamethonium
4. Acute phase of injury following major burns, extensive denervation of skeletal muscle, or upper motor neuron injury [The risk of hyperkalaemia in these patients increases over time and usually peaks at 7-10 days after the injury. The risk is dependent on the extent and location of the injury. The precise time of onset and the duration of the risk period are not known.]

WARNINGS

Cardiac arrest in children

There have been rare reports of acute rhabdomyolysis with hyperkalaemia followed by ventricular dysrhythmias, cardiac arrest and death after the administration of suxamethonium to apparently healthy children who were subsequently found to have undiagnosed skeletal muscle myopathy, most frequently Duchenne's muscular dystrophy. Therefore, when a healthy appearing infant or child develops cardiac arrest soon after administration of suxamethonium not felt to be due to inadequate ventilation, oxygenation or anaesthetic overdose, immediate treatment for hyperkalaemia should be instituted.

Electrolyte disturbances & digoxin toxicity

Suxamethonium should be administered with GREAT CAUTION to patients suffering from electrolyte abnormalities and those who may have massive digitalis toxicity, because in these circumstances suxamethonium may induce serious cardiac arrhythmias or cardiac arrest due to hyperkalaemia.

Malignant Hyperthermia

Suxamethonium administration has been associated with acute onset of malignant hyperthermia, a potentially fatal hypermetabolic state of skeletal muscle.

PRECAUTIONS

General

Suxamethonium may cause raised intraocular pressure & raised intracranial pressure

Laboratory Tests:

No tests additional to routine ICU tests are required

Drug/Laboratory Test Interactions

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Drugs which may enhance the neuromuscular blocking action of suxamethonium include: gentamicin, lithium carbonate, magnesium salt and metoclopramide. The neuromuscular blocking effect of suxamethonium may be enhanced by drugs that reduce plasma cholinesterase activity (e.g., chronically administered oral contraceptives, glucocorticoids, or certain monoamine oxidase inhibitors).

ADVERSE REACTIONS

General:

Allergic reactions (anaphylactic or anaphylactoid responses), malignant hyperthermia

Musculoskeletal:

Inadequate block, prolonged block.

Cardiovascular:

Hypotension, hypertension, vasodilatation (flushing), tachycardia, bradycardia.

Respiratory:

Respiratory arrest, dyspnoea, bronchospasm, laryngospasm.

Renal system:

Rhabdomyolysis with possible myoglobinuric acute renal failure

Tazocin (Piperacillin & Tazobactam) [1 vial $12.00]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Tazocin

ICU INDICATIONS:
1. Treatment of infections caused by susceptible organisms
2. Broad spectrum cover of hospital-acquired infections

PRESENTATION AND ADMINISTRATION:
IV:
4.5gm vial of powder (4gm piperacillin and 500mg tazobactam)
Reconstitute with at least 20ml of Water for Injection, normal saline, 5% glucose or glucose and sodium chloride and administer via slow IV injection over 3-5 minutes.
Alternatively, further dilute to desired volume (e.g. 100ml) with compatible fluid and infuse over 20 to 30 minutes.
Prepare immediately before use. Dilutions should be used immediately.
Store at room temperature
Compatible with the following IV fluids:
Normal saline 5% glucose Glucose and Sodium Chloride

DOSAGE:
IV:
4.5gm 8 hourly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	4.5gm every 12 hours
10-20	4.5gm every 12 hours
20-50	dose as in normal renal function

Dose in renal replacement therapy

CAPD	4.5gm every 12 hours
HD	4.5gm every 12 hours
CVVHDF	4.5gm every 12 hours

DOSAGE IN PAEDIATRICS:
IV:
50-75mg/kg 6-8 hourly

CLINICAL PHARMACOLOGY:

Piperacillin/tazobactam has been shown to be active against most strains of the following microorganisms both *in vitro* and in clinical infections.

Aerobic and facultative gram-positive microorganisms:

Staphylococcus aureus (excluding methicillin and oxacillin-resistant isolates)

Aerobic and facultative gram-negative microorganisms:

Acinetobacter baumanii

Escherichia coli

Haemophilus influenzae (excluding beta-lactamase negative, ampicillin-resistant isolates)

Klebsiella pneumoniae

Pseudomonas aeruginosa (given in combination with an aminoglycoside to which the isolate is susceptible)

Gram-negative anaerobes:

Bacteroides fragilis group *(B. fragilis, B. ovatus, B. thetaiotaomicron,* and *B. vulgatus)*

The following *in vitro* data are available **but their clinical significance is unknown.** At least 90% of the following microorganisms exhibit an *in vitro* minimum inhibitory concentration (MIC) less than or equal to the susceptible breakpoint for piperacillin/tazobactam. However, the safety and effectiveness of piperacillin/tazobactam in treating clinical infections due to these bacteria have not been established in adequate and well-controlled clinical trials.

Aerobic and facultative gram-positive microorganisms:

Enterococcus faecalis (ampicillin or penicillin-susceptible isolates only)

Staphylococcus epidermidis (excluding methicillin and oxacillin resistant isolates)

*Streptococcus agalactiae**

*Streptococcus pneumoniae** (penicillin-susceptible isolates only)

*Streptococcus pyogenes**

Viridans group streptococci*

Aerobic and facultative Gram-negative microorganisms:

Citrobacter koseri

Moraxella catarrhalis

Morganella morganii

Neisseria gonorrhoeae

Proteus mirabilis

Proteus vulgaris

Serratia marcescens

Providencia stuartii

Providencia rettgeri

Salmonella enterica

Gram-positive anaerobes:

Clostridium perfringens

Gram-negative anaerobes:

Bacteroides distasonis

Prevotella melaninogenica

CONTRAINDICATIONS:

1. Hypersensitivity to piperacillin / tazobactam

WARNINGS
SERIOUS AND OCCASIONALLY FATAL HYPERSENSITIVITY (ANAPHYLACTIC) REACTIONS HAVE BEEN REPORTED IN PATIENTS RECEIVING THERAPY WITH BETA-LACTAMS. THESE REACTIONS ARE MORE LIKELY TO OCCUR IN PERSONS WITH A HISTORY OF SENSITIVITY TO MULTIPLE ALLERGENS.
THERE HAVE BEEN REPORTS OF PATIENTS WITH A HISTORY OF PENICILLIN HYPERSENSITIVITY WHO HAVE EXPERIENCED SEVERE HYPERSENSITIVITY REACTIONS WHEN TREATED WITH ANOTHER BETA-LACTAM. BEFORE INITIATING THERAPY WITH TAZOCIN IV. CAREFUL INQUIRY SHOULD BE MADE CONCERNING PREVIOUS HYPERSENSITIVITY REACTIONS TO PENICILLINS, CEPHALOSPORINS, OTHER BETA-LACTAMS, AND OTHER ALLERGENS.

PRECAUTIONS
General:
Bleeding manifestations have occurred in some patients receiving beta-lactam antibiotics, including piperacillin. These reactions have sometimes been associated with abnormalities of coagulation tests such as clotting time, platelet aggregation and prothrombin time, and are more likely to occur in patients with renal failure.
As with other penicillins, patients may experience neuromuscular excitability or convulsions if higher than recommended doses are given intravenously (particularly in the presence of renal failure).
Tazocin contains a total of 2.79mEq (64mg) of sodium per gram of piperacillin in the combination product. This should be considered when treating patients requiring restricted salt intake and in any patients with unexplained hypernatraemia.

Laboratory Tests:
No tests in addition to routine ICU tests are required.

Drug/Laboratory Test Interactions:
None noted.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note.

ADVERSE REACTIONS
Body as a whole:
Fever, agitation, pain
Gastrointestinal:
Diarrhoea, nausea, vomiting, dyspepsia, constipation, stool changes, abdominal pain
CNS:
Insomnia, headache, anxiety, dizziness
Respiratory:
Rhinitis, dyspnoea
Cardiovascular:
Hypertension, chest pain, oedema

Terlipressin [1 vial $90.00]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Glypressin

ICU INDICATIONS:
1. Acute variceal bleeding

PRESENTATION AND ADMINISTRATION:
IV:
Glypressin lyophilized powder is provided in a 6ml glass vial with a rubber stopper and green/silver coloured snap cap. Each vial of powder contains 1mg terlipressin acetate. The diluent is provided in a 5ml glass vial. Substance and diluent are provided together. Mix solvent with powder for injection via the rubber stopper in the vial. The clear reconstituted solution must be injected intravenously immediately after reconstitution.
Store at room temperature

DOSAGE:
IV:
Terlipressin is administered as an IV bolus every 6 hours. For acute variceal bleeding, the dose is 2mg 6 hourly for the first 24 hours, reducing to 1mg 6 hourly for the second 24 hours if bleeding has stabilised. If bleeding has ceased after 48 hours then Terlipressin can be stopped.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
No data available

DOSAGE IN PAEDIATRICS:
Not applicable

CLINICAL PHARMACOLOGY:
Terlipressin is a synthetic vasopressin analogue with relative specificity for the splanchnic circulation where it causes vasoconstriction. This reduces blood flow through these vessels with a reduction in portal pressure.

CONTRAINDICATIONS:
1. Hypersensitivity to terlipressin
2. Pregnancy

WARNINGS
Low cardiac output
Due is its profound vasoconstrictor effects, terlipressin may lead to reduced cardiac output secondary to increased afterload particularly in the setting of underlying reduced left ventricular function

PRECAUTIONS
General:
See WARNINGS

Laboratory Tests:
No tests additional to routine ICU tests are required

Drug/Laboratory Test Interactions:
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Concomitant treatment with medicinal products with a known bradycardic effect may lower the heart rate and cardiac output.

ADVERSE REACTIONS
Neurological:
Headache

Cardiovascular:
Bradycardia, atrial fibrillation, ventricular extrasystoles, tachycardia, chest pain, myocardial infarction, fluid overload with pulmonary oedema, torsade de pointes, left ventricular failure, peripheral vasoconstriction, peripheral ischaemia, hypertension, intestinal ischaemia, peripheral cyanosis

Respiratory:
Respiratory distress, respiratory failure

Gastrointestinal:
Abdominal pain, nausea, vomiting, diarrhoea

Metabolic and Endocrine:
Hyponatraemia

Thiamine [1 vial $30.48, 1 tablet 6 cents]

ADMINISTRATION ROUTES:
IV, IM, PO

ALTERNATIVE NAMES:
Apo thiamine, Vitamin B1

ICU INDICATIONS:
1. Treatment / prophylaxis of vitamin B1 deficiency

PRESENTATION AND ADMINISTRATION:
IV/IM:
100mg in 1ml solution
For IM administration, solution may be injected undiluted into a large muscle mass
For IV injection, administer by direct IV slow injection over 10 minutes into a vein or the side arm of a running infusion. Can be diluted in compatible IV fluid if required.
Compatible with the following IV fluids:
5% dextrose 0.9% sodium chloride
Store at room temperature
Protect from light
Note: Section 29 drug when administered IV (requires specific notification to Director-General of Health as unapproved route of administration)

PO:
Tablets:
Apo-thiamine 50mg tablets (white)

DOSAGE:
PO:
Usually given in doses of 50mg for treatment of thiamine deficiency; usual daily requirement is only 0.8-1.5mg/day

IV:
For treatment of deficiency in ICU, give 100mg IV once daily.
For Wernicke's encephalopathy give 200mg IV 8 hourly for 3 days then 100mg IV or oral once daily

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
1-2mg/kg *IV*, *IM* or *PO* daily

CLINICAL PHARMACOLOGY:
Vitamin B1

CONTRAINDICATIONS:
1. Hypersensitivity to thiamine preparations

WARNINGS
Administration of Glucose:
In patients with potential thiamine deficiency, thiamine should be administered prior to glucose even in the presence of hypoglycaemia. Thiamine is a necessary cofactor for glucose metabolism. Administration of IV glucose alone has caused permanent brain stem damage when administered to thiamine deficient patients (e.g alcoholics)

Sensitivity reactions and intravenous use:
Serious sensitivity reactions can occur. Deaths have resulted from intravenous use (use IV route with caution)

PRECAUTIONS
General:
See WARNINGS

Laboratory Tests:
No tests additional to routine ICU tests are required

Drug/Laboratory Test Interactions:
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note

ADVERSE REACTIONS
General:
An occasional individual may develop a sensitivity or intolerance to thiamine, especially after repeated intravenous administration. Some tenderness and induration may follow intramuscular use.
Skin:
Pruritis, urticaria,
Cardiovascular:
Pulmonary oedema
Respiratory:
Angioneurotic oedema,
Gastrointestinal:
Nausea, haemorrhage into the gastrointestinal tract.

Tobramycin [1 vial 80mg $5.86]

ADMINISTRATION ROUTES:
IV, IM

ALTERNATIVE NAMES:
DBL Tobramycin, Nebcin, Tobra-day

ICU INDICATIONS:
1. Treatment of infections caused by susceptible organisms
2. Pseudomonas and other gram negative infections (e.g. Burkholderia cepacia complex) susceptible to tobramycin, especially in patients with cystic fibrosis

PRESENTATION AND ADMINISTRATION:
IV:
80mg in 2ml solution
Add required dose to 100ml compatible IV fluid and administer over 30 minutes.
Store at room temperature and protect from light
Compatible with the following IV fluids:
Normal saline 5% dextrose

IM:
Not recommended by this route in ICU

DOSAGE:
10 mg/kg once daily dosing
Monitor levels & see below for repeat dosing

(For obese patients, calculate dose based on Ideal Body Weight plus 0.4 of the difference between actual and ideal body weight;consult ICU pharmacist)

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<30	2mg/kg 12 hourly and measure levels ensuring trough <1mg/L
30-60	Increase dose interval to 36 hours and measure levels

Dose in renal replacement therapy

CAPD	2mg/kg 48 hourly and measure levels
HD	2mg/kg post dialysis and measure levels
CVVHDF	2mg/kg 48 hourly and measure levels OR consider alternative antibiotics (Tobramycin is removed by dialysis

DOSAGE IN PAEDIATRICS:
10mg/kg once daily dosing
(reduce dose to 5mg/kg in first week of life)

CLINICAL PHARMACOLOGY:
Tobramycin is a bactericidal aminoglycoside antibiotic with concentration dependent bacterial killing & good post antibiotic effect. Its antibacterial action is by various mechanisms including inhibition of protein synthesis by binding to 30S and 50S ribosomal sub-units. It is usually active against a variety of bacteria including *Pseudomonas aeruginosa, Proteus sp* (including *Proteus mirabilis, morganii, rettgeri* and *vulgaris*), *Escheria coli, Klebseilla-Enterobacter-Serratia* group, *Citrobacter* sp,

Providencia sp, *Staphylococci* (including *Staphylococci aureus* - coagulase-positive & coagulase-negative). Aminoglycosides have a low order of activity against most gram-positive organisms including *Streptococcus pyogenes, pneumoniae* & *enterococci*.

CONTRAINDICATIONS:
1. Hypersensitivity to or previous toxic effects from tobramycin or other aminoglycoside antibiotics

WARNINGS:
Nephrotoxicity & ototoxicity
As with other aminoglycosides, tobramycin is nephro & ototoxic which is more likely with prolonged peak levels >12mg/L or trough levels >2mg/L. Concurrent use of other nephrotoxic agents should be avoided. Ototoxicity may manifest with both auditory and vestibular effects. The auditory changes are irreversible, usually bilateral and may be partial or total. Patients with pre-existing renal impairment are at higher risk, as are those exposed to higher doses or longer duration of tobramycin therapy.

PRECAUTIONS
General
Tobramycin sulphate contains sodium bisulphite, a sulphite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people.
Aminoglycosides should be used with caution in patients with neuromuscular disorders, such as myasthenia gravis, since these drugs may aggravate muscle weakness because of their potential curare-like effects on the neuromuscular junction. They may also be absorbed in significant quantities from body surfaces after local irrigation or application.

Laboratory Tests
Monitor tobramycin levels:
Collect specimens in a SST (yellow) or Plain (red) tube for peak level (within 30 minutes of finishing infusion) & trough level (taken within 1 hour before giving next dose)

Level interpretation:
- Aim for peak level of 20 - 30mg/L
- Increase next dose if peak too low, initially to 12.5mg/kg, then to maximum of 15mg/kg
- Do not give next dose if peak level >50mg/L
- Ensure that trough level is <1mg/L

Drug/Laboratory Test Interactions
None reported.

Pregnancy
Avoid due to placental transfer causing toxicity. Total irreversible bilateral congenital deafness has been described in children whose mothers received aminoglycosides during pregnancy.

Nursing Mothers
Likely to be safe though may alter neonatal gut flora.

Paediatric Use
Safe to use.

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Concurrent and/or sequential use of other potentially neurotoxic and/or nephrotoxic drugs, such as cisplatin, amikacin, neomycin, polymyxin B, colistin, and vancomycin, should be avoided. There is increased risk of nephrotoxicity when co-administered with cyclosporin or tacrolimus.

The concurrent use of tobramycin with potent diuretics, such as frusemide, should be avoided, since certain diuretics by themselves may cause ototoxicity. In addition, when administered intravenously, diuretics may enhance aminoglycoside toxicity by altering the antibiotic concentration in serum and tissue.

When used with muscle relaxants (non-depolarising agents and suxamethonium), there is an enhanced relaxant effect. Tobramycin will also cause antagonism of neostigmine and pyridostigmine effects.

ADVERSE REACTIONS

Nervous System:

Headache, lethargy, confusion, disorientation, convulsions, dizziness, hearing loss

Renal System:

Nephrotoxicity, which occurs in 2-10% of patients. Predisposing factors include advanced age, pre-existing renal impairment, dehydration and concomitant use of other potentially nephrotoxic medication

Respiratory System:

Risk of bronchospasm with **nebulised** therapy.

Cardiovascular System:

None known

Gastrointestinal System:

Nausea & vomiting, diarrhoea, may alter liver function tests

Skin

Rash, dermatitis, itching, urticaria

Haematological System:

Anaemia, granulocytopaenia, thrombocytopenia

Tranexamic Acid [1 vial $12.47]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Cyklokapron

ICU INDICATIONS:
1. Bleeding post cardiac surgery or other bleeding due to fibrinolysis
2. Major trauma with significant bleeding risk

PRESENTATION AND ADMINISTRATION:
IV:
500mg in 5ml (solution)
Preferred method of administration is via direct IV injection at a rate of 1ml (100mg) per minute
Can be administered by intermittent infusion by adding dose to a suitable volume of compatible IV fluid and infusing at a rate of 100mg/min
Compatible with the following IV fluids:
Normal saline, 5% dextrose
Store at room temperature.
Use dilutions in IV fluid within 24 hours of preparation

DOSAGE:
IV:
10-25 mg/kg 8 hourly
For major trauma: 1 gm over 10 mins then 1 gm over 8 hrs by infusion

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	5mg/kg 24 hourly
10-20	10mg/kg 24 hourly
>20-50	10mg/kg 12 hourly

Dose in renal replacement therapy

CAPD	5mg/kg 24 hourly
HD	5mg/kg 24 hourly
CVVHDF	10mg/kg 24 hourly

DOSAGE IN PAEDIATRICS:
IV:
10-20 mg/kg 8 hourly

CLINICAL PHARMACOLOGY:
Tranexamic acid is an antifibrinolytic.

CONTRAINDICATIONS:
1. Previous DVT or PE
2. Hypersensitivity to tranexamic acid

WARNINGS
Procoagulant effects
Tranexamic acid may cause thrombotic complications; it should be used with caution in patients at risk of such complications.

PRECAUTIONS
General:
See WARNINGS

Laboratory Tests:
No tests additional to routine ICU tests are required

Drug/Laboratory Test Interactions:
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
None of note.

ADVERSE REACTIONS
Body as a Whole:
Allergic reactions, thrombotic events
Cardiovascular:
Hypotension (particularly with rapid injection)
Gastrointestinal:
Nausea, vomiting, diarrhoea
Nervous System:
Impaired colour vision and other visual disturbances

Tramadol

[1 vial 100mg $1.41, 1 capsule 50mg 5 cents,1 tablet 50mg SR 12 cents]

ADMINISTRATION ROUTES:
IV, PO, IM, NG

ALTERNATIVE NAMES:
Tramal, Tramadol

ICU INDICATIONS:
1. Analgesia

PRESENTATION AND ADMINISTRATION:
IV / IM:
100mg in 2ml (solution)
For IM injection, inject undiluted into large muscle
For IV administration, dilute in compatible IV fluid and administer by IV injection over 2-3 minutes. Alternatively, dilute with a suitable volume of compatible IV fluid and administer over a convenient time period.
Compatible with the following IV fluids:

0.9% normal saline	5% dextrose	Glucose and Sodium Chloride
Hartmanns	8.4% sodium bicarbonate	

Dilutions in compatible IV fluids are stable for 24 hours at room temperature
Any solution not used within 24 hours of preparation should be discarded
Store at room temperature

PO:
Capsules:
Tramadol 50mg capsules (green / yellow)
Tramal 50mg capsules (green / pale yellow)
Tramedo 50mg capsules (orange / white)
Sustained Release capsules:
Tramal SR 50mg, 100mg and 200mg SR capsules
Oral Drops:
Tramal oral drops 100mg/ml

DOSAGE:
IV / PO/ NG:
50-100mg 4-6 hourly

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose in renal impairment [GFR (ml/min)]

<10	50mg every 12 hours
10-20	50-100mg every 12 hours
>20-50	Dose as in normal renal function

Dose in renal replacement therapy

CAPD	50mg every 12 hours
HD	50mg every 12 hours
CVVHDF	50-100mg every 12 hours

DOSAGE IN PAEDIATRICS:
IV:
2-3mg/kg stat, then 1-2mg/kg 4-6 hourly

CLINICAL PHARMACOLOGY:
Tramadol is a centrally acting synthetic analgesic compound. Although its mode of action is not completely understood, at least two complementary mechanisms appear applicable: binding of parent and M1 metabolite to opioid receptors and weak inhibition of reuptake of norepinephrine and serotonin.

CONTRAINDICATIONS:
1. Hypersensitivity to tramadol

WARNINGS
Seizure Risk
Seizures have been reported in patients receiving tramadol within the recommended dosage range. The risk of convulsions may be increased in patients with epilepsy, those with a history of seizures, or in patients with a recognized risk for seizure (such as head trauma, metabolic disorders, alcohol and drug withdrawal, CNS infections).
Anaphylactoid Reactions
Serious and rarely fatal anaphylactoid reactions have been reported in patients receiving therapy with tramadol.

PRECAUTIONS
General
Administer tramadol cautiously in patients at risk for respiratory depression.
In cirrhotic patients, dosing reduction is recommended. Reduce dose and / or increase dosing interval

Laboratory Tests:
No tests additional to routine ICU tests are required

Drug/Laboratory Test Interactions
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Concomitant use of tramadol increases the seizure risk in patients taking selective serotonin reuptake inhibitors and tricyclic antidepressants. Synergistic with other CNS depressant drugs. Post-marketing surveillance has revealed rare reports of digoxin toxicity and alteration of warfarin effect, including elevation of prothrombin times.

ADVERSE REACTIONS
Body as a Whole:
Itch
Cardiovascular:
Hypotension, Tachycardia
Gastrointestinal:
Nausea, vomiting, diarrhoea, constipation, dry mouth
Nervous System:
Anxiety, confusion, coordination disturbance, euphoria, headache, seizures

Thyroxine [1 tablet 100mcg 7 cents]

ADMINISTRATION ROUTES:
PO

ALTERNATIVE NAMES:
Eltroxin, Levothyroxine (Goldshield), Synthyroid

ICU INDICATIONS:
1. Treatment of hypothyroidism

PRESENTATION AND ADMINISTRATION:
PO:
Eltroxin 50mcg and 100mcg tablets (white to off white)
Levothyroxine (Goldshield) 50mcg and 100mcg tablets (white)
Synthyroid 50mcg tablets (white) and 100mcg tablets (yellow)

DOSAGE:
PO:
Thyroid hormone replacement
Usual dosage range 50-200mcg daily

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
PO:
Thyroid hormone replacement
Usual dose range is 100mcg/m^2 rounded to the nearest quarter tablet daily (see PRECAUTIONS *Paediatric Use*)

CLINICAL PHARMACOLOGY:
Thyroxine is a thyroid hormone.

CONTRAINDICATIONS:
1. Uncorrected adrenal insufficiency

WARNINGS
Patients with underlying cardiovascular disease:
Exercise caution when administering levothyroxine to patients with cardiovascular disorders and to the elderly in whom there is an increased risk of occult cardiac disease. In these patients, levothyroxine therapy should be initiated at lower doses than those recommended in younger individuals or in patients without cardiac disease.

PRECAUTIONS
General
Levothyroxine has a narrow therapeutic index. Regardless of the indication for use, careful dosage titration is necessary to avoid the consequences of over- or under-treatment.
Laboratory Tests:
It is reasonable to check thyroid hormone levels in patients on thyroxine when they are

admitted to the intensive care unit; however, interpretation of thyroid hormone levels in the setting of critical illness can be difficult

Drug/Laboratory Test Interactions :

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Many drugs affect thyroid hormone pharmacokinetics and metabolism (e.g., absorption, synthesis, secretion, catabolism, protein binding, and target tissue response) and may alter the therapeutic response. In addition, thyroid hormones and thyroid status have varied effects on the pharmacokinetics and actions of other drugs.

Drugs That Alter Thyroid Hormone Secretion

Drugs that may decrease thyroid hormone secretion, which may result in hypothyroidism:

Aminoglutethimide, amiodarone, iodide (including iodine-containing radiographic contrast agents), lithium, methimazole, propylthiouracil (PTU), sulfonamides, tolbutamide:

Long-term lithium therapy can result in goiter in up to 50% of patients, and either subclinical or overt hypothyroidism, each in up to 20% of patients. Oral cholecystographic agents and amiodarone are slowly excreted, producing more prolonged hypothyroidism than parenterally administered iodinated contrast agents. Long-term aminoglutethimide therapy may minimally decrease T4 and T3 levels and increase TSH, although all values remain within normal limits in most patients.

Drugs that may increase thyroid hormone secretion, which may result in hyperthyroidism:

Amiodarone, iodide (including iodine-containing radiographic contrast agents):

Iodide and drugs that contain pharmacologic amounts of iodide may cause hyperthyroidism in euthyroid patients with Grave's disease previously treated with antithyroid drugs or in euthyroid patients with thyroid autonomy (e.g., multinodular goiter or hyperfunctioning thyroid adenoma). Hyperthyroidism may develop over several weeks and may persist for several months after therapy discontinuation. Amiodarone may induce hyperthyroidism by causing thyroiditis.

Drugs that may decrease T4 absorption, which may result in hypothyroidism:

Antacids (aluminum and magnesium); hydroxides (simethicone); bile acid sequestrants (cholestyramine, colestipol); calcium carbonate; cation exchange resins (kayexalate); ferrous sulfate; sucralfate:

Concurrent use may reduce the efficacy of levothyroxine by binding and delaying or preventing absorption, potentially resulting in hypothyroidism. Calcium carbonate may form an insoluble chelate with levothyroxine, and ferrous sulfate likely forms a ferric-thyroxine complex. Administer levothyroxine at least 4 hours apart from these agents.

Drugs that may increase serum TBG concentration:

Clofibrate, estrogen-containing oral contraceptives, estrogens (oral), heroin/methadone, 5-fluorouracil, mitotane, tamoxifen.

Drugs that may decrease serum TBG concentration:

Androgens/anabolic steroids, asparaginase, glucocorticoids, slow-release nicotinic acid.

Drugs that may cause protein-binding site displacement:
Frusemide (>80 mg IV); heparin; hydantoins; non-steroidal anti-inflammatory drugs (fenamates, phenylbutazone); salicylates (>2 g/day):
Administration of these agents with levothyroxine results in an initial transient increase in FT4. Continued administration results in a decrease in serum T4 and normal FT4 and TSH concentrations and, therefore, patients are clinically euthyroid. Salicylates inhibit binding of T4 and T3 to TBG and transthyretin. An initial increase in serum FT4 is followed by return of FT4 to normal levels with sustained therapeutic serum salicylate concentrations, although total-T4 levels may decrease by as much as 30%.

Drugs That May Alter T4 and T3 Metabolism
Drugs that may increase hepatic metabolism, which may result in hypothyroidism:
Carbamazepine, hydantoins, phenobarbital, rifampin:
Stimulation of hepatic microsomal drug-metabolizing enzyme activity may cause increased hepatic degradation of levothyroxine, resulting in increased levothyroxine requirements. Phenytoin and carbamazepine reduce serum protein binding of levothyroxine, and total- and free-T4 may be reduced by 20-40%, but most patients have normal serum TSH levels and are clinically euthyroid.

Drugs That May Decrease T4 5 alpha-Deiodinase Activity
Amiodarone; beta-adrenergic antagonists
Administration of these enzyme inhibitors decreases the peripheral conversion of T4 to T3, leading to decreased T3 levels. However, serum T4 levels are usually normal but may occasionally be slightly increased. In patients treated with large doses of propranolol (>160 mg/day), T3 and T4 levels change slightly, TSH levels remain normal, and patients are clinically euthyroid. It should be noted that actions of particular beta-adrenergic antagonists may be impaired when the hypothyroid patient is converted to the euthyroid state. Short-term administration of large doses of glucocorticoids may decrease serum T3 concentrations by 30% with minimal change in serum T4 levels. However, long-term glucocorticoid therapy may result in slightly decreased T3 and T4 levels due to decreased TBG production (see above).

Miscellaneous
Anticoagulants coumarin derivatives, indandione derivatives:
Thyroid hormones appear to increase the catabolism of vitamin K-dependent clotting factors, thereby increasing the anticoagulant activity of oral anticoagulants. Concomitant use of these agents impairs the compensatory increases in clotting factor synthesis. Prothrombin time should be carefully monitored in patients taking levothyroxine and oral anticoagulants and the dose of anticoagulant therapy adjusted accordingly.

Antidepressants tricyclics
Concurrent use of tri/tetracyclic antidepressants and levothyroxine may increase the therapeutic and toxic effects of both drugs, possibly due to increased receptor sensitivity to catecholamines. Toxic effects may include increased risk of cardiac arrhythmias and CNS stimulation; onset of action of tricyclics may be accelerated. Administration of sertraline in patients stabilized on levothyroxine may result in increased levothyroxine requirements.
Antidiabetic agents: biguanides, meglitinides, sulfonylureas, thiazolidediones, insulin:
Addition of levothyroxine to antidiabetic or insulin therapy may result in increased antidiabetic agent or insulin requirements. Careful monitoring of diabetic control is recommended, especially when thyroid therapy is started, changed, or discontinued.
Cardiac glycosides:

Serum digitalis glycoside levels may be reduced in hyperthyroidism or when the hypothyroid patient is converted to the euthyroid state. Therapeutic effect of digitalis glycosides may be reduced.

Ketamine:

Concurrent use may produce marked hypertension and tachycardia; cautious administration to patients receiving thyroid hormone therapy is recommended.

Methylxanthine bronchodilators

Decreased theophylline clearance may occur in hypothyroid patients; clearance returns to normal when the euthyroid state is achieved.

Radiographic agents:

Thyroid hormones may reduce the uptake of 123I, 131I, and 99mTc.

Sympathomimetics:

Concurrent use may increase the effects of sympathomimetics or thyroid hormone. Thyroid hormones may increase the risk of coronary insufficiency when sympathomimetic agents are administered to patients with coronary artery disease.

ADVERSE REACTIONS

Adverse reactions associated with levothyroxine therapy are primarily those of hyperthyroidism due to therapeutic overdosage.

General:

Fatigue, increased appetite, weight loss, heat intolerance, fever, excessive sweating.

Central Nervous System:

Headache, hyperactivity, nervousness, anxiety, irritability, emotional lability, insomnia.

Musculoskeletal:

Tremors, muscle weakness.

Cardiovascular:

Palpitations, tachycardia, arrhythmias, increased pulse and blood pressure, heart failure, angina, myocardial infarction, cardiac arrest.

Respiratory:

Dyspnea.

Gastrointestinal:

Diarrhoea, vomiting, abdominal cramps and elevations in liver function tests.

Dermatologic:

Hair loss, flushing.

Endocrine:

Decreased bone mineral density.

Reproductive:

Menstrual irregularities, impaired fertility.

Thiopentone [1 vial $12.55]

ADMINISTRATION ROUTES:
IV, IM, PO

ALTERNATIVE NAMES:
Thiopentone

ICU INDICATIONS:
1. Induction of anaesthesia
2. Treatment of status epilepticus refractory to other measures (rarely used for this indication)
3. Treatment of intracranial hypertension (rarely used for this indication in our ICU)

PRESENTATION AND ADMINISTRATION:
IV
500mg vials for reconstitution
Reconstitute with Water for Injection
For IV injection dilute 500mg to a total of 20ml using Water for Injection (makes a solution with a concentration of 25mg/ml)
Store at room temperature
Note: Section 29 drug when administered IV (requires specific notification to Director-General of Health as unapproved route of administration)

DOSAGE:
IV:
2-5mg/kg slowly stat. In unstable patients (i.e. most ICU patients) administer 75mg at a time then assess effect on blood pressure and conscious state before administering more.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
2-5mg/kg slowly stat

CLINICAL PHARMACOLOGY:
Thiopental is an ultrashort-acting depressant of the central nervous system which induces hypnosis and anaesthesia, but not analgesia. It produces hypnosis within 30-40 seconds of intravenous injection. Repeated intravenous doses lead to prolonged anaesthesia because fatty tissues act as a reservoir; they accumulate thiopental in concentrations 6-12 times greater than the plasma concentration, and then release the drug slowly to cause prolonged anaesthesia.

CONTRAINDICATIONS:
1. Hypersensitivity to thiopentone
2. Acute intermittent porphyria

WARNINGS
Hypotension:
Administer with caution in haemodynamically unstable patients

PRECAUTIONS
General
Use with care in patients with reduced left ventricular function

Laboratory Tests:
No tests additional to routine ICU tests are required

Drug/Laboratory Test Interactions
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Thiopentone has a synergistic action with other CNS depressant drugs.

ADVERSE REACTIONS
Body as a Whole:
Anaphylactic and anaphylactoid reactions
Cardiovascular:
Hypotension, myocardial depression, arrhythmias
Respiratory:
Respiratory depression, coughing, bronchospasm and laryngospasm
Skin:
Urticaria.

Vancomycin [1 vial 500 mg $3.58]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Vancomycin

ICU INDICATIONS:
1. Infections due to susceptible organisms.

PRESENTATION AND ADMINISTRATION
IV:
500mg vial powder.

Preparation requires a two-step dilution.
Step One: reconstitute each 500 mg vial of vancomycin with 10ml of Water for Injection (making a 50 mg/ml solution)
Step Two: further dilution depends on whether administering loading dose or maintenance infusion. See below for both.

Administration: LOADING DOSE
Add the solution prepared in step one above (reconstituted vancomycin solution containing 50 mg/mL) to an infusion bag of either 0.9% sodium chloride or 5% dextrose. The volume of the bag depends on the dose to be administered.

For doses of ***up to* 2500mg** add to 250 mL of 5% dextrose to give through a central venous line (CVL) or peripherally inserted central catheter (PICC). If giving through a peripheral cannula, add to 500 mL of 5% dextrose.

For doses ***over* 2500mg** add to 500mL of 5% dextrose to give through a CVL or PICC. If giving through a peripheral cannula, add to 1000 mL of 5% dextrose.

The maximum infusion rate for the loading dose is 500 mg/hr
Rapid infusion must be avoided due to the risk of red man syndrome.

Administration: MAINTENANCE INFUSION
Can be administered by a continuous (preferred) or intermittent infusion.

<u>Continuous infusion:</u>
For administration **via CVL or PICC only**, add the solution prepared in step 1 to a 250 ml bag of either 5% dextrose (preferred) or 0.9% sodium chloride.

For administration **via peripheral cannula only**, add the solution prepared in step 1 to a 500 ml bag of either 5% dextrose (preferred) or 0.9% sodium chloride.

For microbiological safety reasons, each infusion bag should be prepared just prior to administration and used within 24 hours

<u>Intermittent Infusion</u>
Add the solution prepared in step 1 to a suitably sized bag of either 5% dextrose (preferred) or 0.9% sodium chloride depending on intended route of administration:

For administration via **CVL or PICC**, the maximum concentration is 10 mg/mL
For administration via **peripheral cannula**, the maximum concentration is 4 mg/mL (i.e. 1000 mg in 250 mL)

The maximum infusion rate for the maintenance dose is 500 mg/hr
Rapid infusion must be avoided due to the risk of red man syndrome.

DOSAGE
Dosage is divided into calculation of the loading dose & the maintenance infusion dose

Dosage 1: LOADING DOSE
Prescribed on the ONCE ONLY section of the drug chart.

Vancomycin requires a ONE TIME ONLY loading dose of 25–30 mg/kg, to reach adequate serum concentration to effectively treat infection. This loading dose is calculated on the patient's **ACTUAL** body weight and **does NOT depend on their renal function**.

Table 1: Vancomycin loading dose guide

VANCOMYCIN LOADING DOSE (once only)		INFUSION TIME
Actual Body Weight (kg)	**Dose (mg)**	
50-64 kg	1500 mg	3 hours
65-79 kg	2000 mg	4 hours
80-99 kg	2500 mg	5 hours
100-120 kg	3000 mg	6 hours
Over 120 kg	25 mg per kg (round up to nearest 250 mg) **Maximum 4000 mg**	500 mg per hour

Dosage 2: MAINTENANCE CONTINUOUS INFUSION DOSE
Prescribed on the REGULAR section of the drug chart.
The prescription MUST include the infusion **concentration** and **infusion rate**

Most patients in ICU will need to receive a continuous intravenous infusion **starting immediately after the loading dose** to maintain adequate serum levels. This dose is calculated based on the patient's renal function using the estimated glomerular filtration rate (eGFR) reported on laboratory biochemistry results. The eGFR is **NOT** the same as serum creatinine. Do **NOT** use serum creatinine in this calculation. Liaise with ICU pharmacist or medical staff if unsure.

Table 2: Vancomycin infusion rate for giving through CVL or PICC

eGFR	24 Hour Dose	Add 24 Hour Dose to a 250ml bag
Over 90	3000 mg	Run maintenance infusion at **12 ml/hour** for all patients.
75-90	2500 mg	
60-74	2000 mg	
45-59	1500 mg	
30-44	1000 mg	
Under 30, or on intermittent haemodialysis	See CCDHB renal guidance	
Continuous renal replacement therapy	Give loading dose as in Table 1 Commence infusion of 1000 mg/24 hours as above Measure vancomycin level **daily** and adjust as per Table 4	

Table 3: Vancomycin infusion rate for giving through peripheral cannula

eGFR	24 Hour Dose	Add 24 Hour Dose to a 500ml bag
Over 90	3000 mg	Run maintenance infusion at **23 ml/hour** for all patients.
75-90	2500 mg	
60-74	2000 mg	
45-59	1500 mg	
30-44	1000 mg	
Under 30, or on intermittent haemodialysis	See CCDHB renal guidance	
Continuous renal replacement therapy	Give loading dose as in Table 1 Commence infusion of 1000 mg/24 hours as above Measure vancomycin level **daily** and adjust as per Table 4	

Dosage 3: THERAPEUTIC DRUG MONITORING & DOSAGE ADJUSTMENTS

The target therapeutic serum vancomycin level is 18-25mg/L.

Vancomycin levels must be measured daily in routine morning bloods, beginning the day after starting the infusion. The infusion should continue at the current rate until the laboratory has reported the serum level. Once the level is known, use table 4 below to adjust the rate or dose accordingly.

Table 4. Dosage adjustment based on measured vancomycin serum level

Vancomycin serum level	Suggested dosage change
<18mg/L	Increase the 24 hour dose to the next level **up** in Table 2 or 3*
18 – 25mg/L	NO CHANGE
25.1-30 mg/L	Decrease the 24 hour dose to next level **down** in Table 2 or 3 **
>30mg/L	**Stop the infusion**. **Re-check level every 6 hours**. Restart infusion once level within target range at lower rate **

*If patient is on 3000 mg of vancomycin in 24 hours, liaise with Medical Staff for advice.

**If patient is on 1000 mg of vancomycin in 24 hours then stop the infusion. Re-check level every 24 hours until the level is <20mg/L and switch to intermittent dosing or consider an alternative antibiotic, if appropriate.

Dosage 4: CONVERSION TO WARD THERAPY

The use of continuous infusion dosing is restricted to ICU. As such patients will need to be converted to intermittent dosing for discharge to the ward (unless Infectious Diseases team request continued treatment by infusion). This conversion is described in table 5 below.

The first dose should be given immediately after stopping the continuous infusion. A serum vancomycin level must be checked after administration of the **second** intermittent dose. Note the conversion from continuous infusion to intermittent dosing requires roughly a 25% dose increase.

Table 5. Conversion to ward dosing

ICU 24 Hour Dose from Table 2 or 3	Dose conversion for ward
1000 mg	750 mg every 12 hours
1500 mg	1000 mg every 12 hours
2000 mg	1250 mg every 12 hours
2500 mg	1000 mg every 8 hours
3000 mg	1250 mg every 8 hours

CLINICAL PHARMACOLOGY:
Glycopeptide antibiotic. Vancomycin is active against most strains of the following microorganisms, both in vitro and in clinical infections:
Aerobic Gram-Positive Microorganisms including:
Staphylococci, including Staphylococcus aureus and Staphylococcus epidermidis (including MRSA).
Enterococci, viridans group Streptococci (e.g. Streptococcus bovis), & diphtheroids

CONTRAINDICATIONS:
1. Hypersensitivity to vancomycin

WARNINGS:

DO NOT GIVE BY BOLUS
Rapid bolus administration (e.g., over several minutes) may be associated with massive histamine release resulting in hypotension, shock, and, cardiac arrest.

Ototoxicity
Ototoxicity may occur in patients receiving vancomycin. It may be transient or permanent. It has been reported mostly in patients who have been given excessive doses, who have an underlying hearing loss, or who are receiving concomitant therapy with another ototoxic agent, such as an aminoglycoside.

Pseudomembranous colitis
Pseudomembranous colitis has been reported with nearly all antibacterial agents, including vancomycin, and may range in severity from mild to life-threatening. Therefore, it is important to consider this diagnosis inpatients who present with diarrhoea subsequent to the administration of antibacterial agents.

PRECAUTIONS
General
In order to minimise the risk of nephrotoxicity, renal function should be monitored, especially when treating patients with underlying renal dysfunction or patients receiving therapy with nephrotoxic drugs.
Reversible neutropaenia has been reported in patients receiving vancomycin
Flushing of the upper body may occur with IV infusion ‘red man syndrome’. This reaction is extremely rare when vancomycin is given over an appropriate time interval. (see PRESENTATION AND ADMINISTRATION)

Laboratory Tests:
See in DOSAGE Section 3: THERAPEUTIC DRUG MONITORING
Blood Sample Collection ideally in SST (Yellow) tube, alternatively in Plain (Red), Heparin (Green) or EDTA (Mauve)

Paediatric and Neonatal only: 0.2 mL serum in 0.4 mL Plain (Red) or EDTA (Mauve) Microtainer®.

Drug/Laboratory Test Interactions
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Administration with other nephrotoxic drugs greatly increases the risk of renal toxicity.

ADVERSE REACTIONS
Body as a Whole:
Anaphylaxis, drug fever, chills
Cardiovascular:
Hypotension (particularly with rapid injection)
Gastrointestinal:
Nausea, pseudomembranous colitis
Skin:
Toxic epidermal necrolysis, rashes (including exfoliative dermatitis),
Renal:
Rarely, nephrotoxicity
Haematological:
Neutropaenia, eosinophilia, thrombocytopaenia
Otological:
Hearing loss, vertigo

Vasopressin/Argipressin [1 vial $76.14]

ADMINISTRATION ROUTES:
IV

ALTERNATIVE NAMES:
Pitressin

ICU INDICATIONS:
1. Refractory septic shock
2. Severe post cardiopulmonary bypass vasoplegia

PRESENTATION AND ADMINISTRATION:
IV:
20 units in 1ml glass vials
Administer by IV infusion. Make 20 units of vasopressin up to a total of 20ml of compatible IV fluid.
Compatible with the following IV fluids:
5% dextrose normal saline
Administer via a central line.
Store at room temperature
Note: Section 29 drug (requires specific notification to Director-General of Health)

DOSAGE:
IV:
0-2 units/hr

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
IV:
Vasopressin has been shown to increase the risk of death in children with septic shock; it should not be used except on the advice of a Paediatric Intensivist (i.e. Starship Consultant)

CLINICAL PHARMACOLOGY:
Vasopressin is a potent vasopressor which is an analogue of the posterior pituitary hormone ADH. Vasopressin binds to different receptors than the catecholamine pressors. Vasoconstrictor effects are through the V_1 vascular receptors

CONTRAINDICATIONS:
1. hypersensitivity to vasopressin

WARNINGS
See PRECAUTIONS

PRECAUTIONS
General
Vasopressin is a potent vasoconstrictor. Due to its effect on afterload, vasopressin may increase myocardial oxygen demand and lead to myocardial ischaemia.

Laboratory Tests:
No tests are required in addition to routine ICU tests.

Drug/Laboratory Test Interactions
None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Vasopressin acts via different receptors than other vasoconstrictor agents; it may lead to significant reductions in noradrenaline requirements.

ADVERSE REACTIONS
Cardiovascular:
Arrhythmias including asystole, hypertension, reduced cardiac output, chest pain, MI, venous thrombosis
Central nervous system:
Pounding in head, fever, vertigo.
Dermatologic:
Ischemic skin lesions, circumoral pallor, urticaria
Gastrointestinal:
Abdominal cramps, flatulence, mesenteric ischemia, nausea, vomiting
Genitourinary:
Uterine contraction
Neuromuscular & skeletal:
Tremor
Respiratory:
Bronchial constriction
Metabolic:
Hyponatraemia & water retention

Vitamin K [1 vial $10.84]

ADMINISTRATION ROUTES:
IV, PO

ALTERNATIVE NAMES:
Phytomenadione, Konakion

ICU INDICATIONS:
1. Correction of elevated INR due to administration of warfarin or liver impairment

PRESENTATION AND ADMINISTRATION:
IV
2mg in 0.2ml vials and 10mg in 1ml vials
Usually administered in ICU by direct IV injection. Administer undiluted by very slow IV push over at least 30 seconds either direct or, where appropriate, into lower section of infusion set of a continuous infusion of normal saline or 5% glucose.
Compatible when injected into the tubing of a continuous infusion of:
Normal saline 5% glucose
Store at room temperature.

PO:
Konakion 10mg tablets (white to yellowish)

DOSAGE:
IV/ PO:
0.5-10mg; repeated as necessary (avoid large doses if anticoagulation is to be continued). SEE APPENDIX 2 - WARFARIN REVERSAL GUIDELINES.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function

DOSAGE IN PAEDIATRICS:
For warfarin reversal: 0.1mg/kg (max 5mg) IV or oral

CLINICAL PHARMACOLOGY:
Vitamin K is an essential cofactor for a microsomal enzyme that catalyzes the post-translational carboxylation of multiple, specific, peptide-bound glutamic acid residues in inactive hepatic precursors of factors II, VII, IX, and X. The resulting gamma-carboxyglutamic acid residues convert the precursors into active coagulation factors that are subsequently secreted by liver cells into the blood.

CONTRAINDICATIONS:
1. Hypersensitivity to the drug

WARNINGS
An immediate coagulant effect should not be expected after administration of vitamin K. Whole blood or component therapy is necessary if the patient is bleeding.
Repeated large doses of vitamin K are not warranted in liver disease if the response to initial use of the vitamin is unsatisfactory. Failure to respond to vitamin K may indicate that the condition being treated is inherently unresponsive to vitamin K.

PRECAUTIONS
General
Allergic reactions can occur with IV administration

Laboratory Tests:
No tests in addition to routine ICU tests are indicated

Drug/Laboratory Test Interactions:
No tests additional to routine ICU tests are required.

IMPORTANT DRUG INTERACTIONS FOR THE ICU
Temporary resistance to prothrombin-depressing anticoagulants may result, especially when larger doses of vitamin K are used. If relatively large doses have been employed, it may be necessary when reinstituting anticoagulant therapy to use somewhat larger doses of the prothrombin-depressing anticoagulant, or to use one which acts on a different principle, such as heparin.

ADVERSE REACTIONS
Body as a Whole:
Transient "flushing sensations" and "peculiar" sensations of taste have been observed, as well as rare instances of dizziness, rapid and weak pulse, profuse sweating, brief hypotension. The possibility of allergic sensitivity, including an anaphylactoid reaction, should be kept in mind.
Respiratory System:
Dyspnoea.
Local:
Pain, swelling, and tenderness at the injection site may occur.

Verapamil [1 vial $1.51, 1 tablet 10 cents]

ADMINISTRATION ROUTES:
PO, IV

BRAND NAMES:
Isoptin, Isoptin SR, Verpamil SR

ICU INDICATIONS:
1. Tachycardias including paroxysmal SVT, AF with rapid ventricular response (excluding WPW syndrome), atrial flutter with rapid ventricular response, extrasystoles
2. Hypertension
3. Acute coronary insufficiency

PRESENTATION AND ADMINISTRATION:
Oral:
Isoptin 40mg (white), 80mg (white)
Isoptin SR 240mg (light green)
Verpamil SR 120mg (white biconvex), 240mg (light green biconvex)

IV:
Isoptin 5mg in 2ml solution

DOSAGE:
Oral:
Administer in 2-3 divided doses.
Hypertension: 240-480mg/day, 160mg maximum single dose
Angina: 360-480mg/day

IV:
Injection: 5mg undiluted solution slowly over 2 minutes (longer in elderly) with continuous ECG & blood pressure monitoring
Can repeat if necessary after 5-10 minutes

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
No dose adjustment is required

DOSAGE IN PAEDIATRICS:
Oral 1-3mg/kg 8-12 hourly

CLINICAL PHARMACOLOGY:
Verapamil is a calcium ion influx inhibitor. It decreases the influx of ionic calcium across the cell membrane of arterial smooth muscle as well as conductile & contractile myocardial cells. It dilates the main coronary arteries & inhibits coronary artery spasm. It also reduces afterload so reducing myocardial energy consumption. By decreasing calcium influx through the slow channels of the AV node, the effective refractory period is increased so AV conduction is slowed in a rate-related manner. It has no effect on the normal atrial action potential or intraventricular conduction time.

CONTRAINDICATIONS:

1. Severe LV dysfunction
2. Hypotension (systolic <90mmHg) or cardiogenic shock
3. Sick sinus syndrome (except in patients with a functioning external ventricular pacemaker)
4. Second- or third-degree AV block (except in patients with a functioning external ventricular pacemaker)
5. Atrial flutter or atrial fibrillation and an accessory bypass tract (Wolff-Parkinson-White, Lown-Ganong-Levine syndromes)
6. Known hypersensitivity to verapamil

WARNINGS:

The negatively inotropic effects of verapamil are mostly compensated for by its afterload reduction without a net impairment of LV performance. It should be used in caution with patients with severe LV dysfunction (LVEF<30%), moderate to severe symptoms of cardiac failure, and in any patients with dysfunction also receiving beta-blockers.
Very rapid ventricular responses or VF have been described in patients with coexisting accessory AV pathways that may not become apparent until the administration of verapamil. First-degree AV block with transient bradycardia may be seen, sometimes accompanied by nodal escape rhythms. PR-interval prolongation corresponds with verapamil plasma concentrations. Serious adverse effects (including death) have been recorded in a series of patients with hypertrophic cardiomyopathy receiving verapamil. Elevation of liver enzymes have been reported.

PRECAUTIONS

General

Severe liver dysfunction prolongs elimination half-life; 30% of the dose should be administered to these patients. Verapamil decreases neuromuscular transmission in Duchenne's muscular dystrophy.

Laboratory Tests

No tests are required in addition to routine ICU blood tests

Drug/Laboratory Test Interactions

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Alcohol: may increase blood alcohol concentrations & prolong its effects
Beta-blockers: may result in additive negative effects on hear rate, AV conduction & cardiac contractility.
Digoxin: chronic verapamil usage can increase serum digoxin levels by 50-75% during first week of therapy. Effects exaggerated in hepatic cirrhosis.
Disopyramide: should not be given within 48 hours before or 24 hours after verapamil
Lithium: increased sensitivity to the effects of lithium (neurotoxicity) reported
Carbamazepine: levels may be increased by verapamil
Rifampicin: markedly reduces oral verapamil bioavailability
Cyclosporin: levels may be increased by verapamil
Theophylline: levels may be increased by verapamil
Neuromuscular blocking agents: verapamil may prolong the duration of action

ADVERSE REACTIONS
Nervous system:
CVA, confusion, insomnia, parasthesiae
Cardiovascular:
Angina, AV dissociation
Digestive:
Diarrhoea, dry mouth, gingival hyperplasia
Skin:
Rash, hair loss, Stevens-Johnson syndrome, erythema multiforme
Urogenital:
Gynaecomastia, impotence

Warfarin Sodium [1 tablet 3mg 8 cents]

ADMINISTRATION ROUTES:
PO, NG

BRAND NAMES:
Coumadin, Marevan

ICU INDICATIONS:
1. Anticoagulation for prophylaxis and/or treatment of venous thrombosis, pulmonary embolism, thromboembolism associated with atrial fibrillation or prosthetic valve insertion.

PRESENTATION AND ADMINISTRATION:
PO:
Coumadin 1mg (beige), 2mg (lavender) and 5mg (green) tablets
Marevan 1mg (brown), 3mg (blue) and 5mg (pink) tablets

DOSAGE:
The dosage is individualised according to the patient's sensitivity to the drug as indicated by their INR. Most patients are satisfactorily maintained with a dose of 2 to 10mg daily.
Several studies have shown that a loading regimen of 5mg/5mg/5mg produces a therapeutic INR by day 4 to 5 as rapidly as higher dosed regimens but with a reduced risk of bleeding complications. In patients after cardiac surgery, a loading regimen of 2.5mg for the first 2 days with the third dose adjusted only if the INR was <1.5 or >3.0 has been shown to reduce excessive anticoagulation; this is the recommended dosing schedule in these patients

Recommended INR ranges:

DVT andPE	2.0-3.0
Atrial fibrillation	2.0-3.0
Bioprosthetic heart valves	2.0-3.0
Mechanical heart valves	2.5-3.5

An INR greater than 4.0 appears to provide no additional therapeutic benefit in most patients & is associated with a higher risk of bleeding.
Duration of therapy is individualised and in general should be continued until the danger of thrombosis & embolism has passed.

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
Dose as in normal renal function. Active metabolites may accumulate in renal failure.
Not dialysed.

DOSAGE IN PAEDIATRICS:

Day 1	0.2mg/kg single dose
Day 2	0.2mg/kg single dose providing INR<1.3
Day 3 & onwards	0.05-0.2mg/kg single dose titrated to INR

CLINICAL PHARMACOLOGY:
Warfarin sodium acts by inhibiting the synthesis of vitamin K dependent clotting factors which include Factors II, VII, IX and X, and the anticoagulant proteins C and S.

Therapeutic warfarin doses decrease the total amount of the active form of each vitamin K dependent factor made by the liver by approximately 30-50%. An anticoagulant effect generally occurs within 24 hours after drug administration, however peak anticoagulant effect may be delayed by 72-96 hours. The duration of action of a single dose of warfarin is 2-5 days.
Warfarin may potentiate a more hypercoagulable state in the first 24-48 hours due to the more rapid depletion of the anticoagulant proteins C & S when compared to the clotting factors with longer half-lives. As such, any concomitant anticoagulant therapy such as Heparin or Enoxaparin should be continued until the desired therapeutic INR is reached. This initial pro-coagulant effect is increased with the use of higher loading doses.
Warfarin may increase the APTT test even in the absence of heparin. Heparin therapy may also affect the INR.

Anticoagulants have no direct effect on established thrombus but prevent further extension of the formed clot.

CONTRAINDICATIONS:
Any condition in which the hazard of haemorrhage is greater than the potential clinical benefits of anticoagulation, such as:

1. Pregnancy, threatened abortion, eclampsia and pre-eclampsia
2. Haemorrhagic tendencies or blood dyscrasias
3. Sever to moderate hepatic or renal insufficiency
4. Recent or contemplated surgery of the CNS, eye or traumatic surgery resulting in large open surfaces
5. Bleeding tendencies associated with active ulceration or overt bleeding of gastrointestinal/genitourinary or respiratory tracts, cerebrovascular haemorrhage, cerebral aneurysms, dissecting aorta, pericarditis and pericardial effusions, bacterial endocarditis
6. Inadequate laboratory facilities
7. Unsupervised senility, alcoholism, psychosis or lack of patient co-operation
8. Spinal puncture
9. Malignant hypertension
10. Known or suspected deficiency in protein C
11. Known hypersensitivity to warfarin

WARNINGS:
Risk of haemorrhage in any tissue or organ related to level of intensity & duration of anticoagulant therapy. Necrosis & gangrene of skin and other tissues is seen less frequently (<0.1%) and usually appears within a few days of the start of therapy.
Therapy in each patient is highly individualised and regular INR monitoring is required due to the narrow therapeutic index of warfarin which may be easily affected by other drugs and dietary vitamin K.

PRECAUTIONS
General
Patients of 60 years or older appear to exhibit a greater than expected INR response to the anticoagulant effects of warfarin for reasons unknown.
An increased INR response may also be seen with cancer, congestive heart failure,

hyperthermia, hyperthyroidism and in patients with a poor nutritional state.
A decreased INR response may be seen with oedema, hyperlipidaemia and hypothyroidism

Laboratory Tests
Therapeutic effect is monitored by regular measurement of the INR

Drug/Laboratory Test Interactions
None

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Drugs that may cause an **increased** INR include:
Alcohol, allopurinol, amiodarone, aspirin, azithromycin, cephazolin, ceftriaxone, chloramphenicol, chloral hydrate, ciprofloxacin, clarithromycin, diclofenac, doxycycline, erythromycin, fluconazole, fluoxetine, glucagon, heparin, ibuprofen, indomethacin, influenza flu vaccine, itraconazole, ketorolac, methyldopa, metronidazole, naproxen, neomycin, omeprazole, paracetamol, paroxetine, penicillin G (intravenous), phenytoin, prednisone, propranolol, quinine, ranitidine, simvastatin, tamoxifen, tetracycline, thyroid drugs, tramadol, valproate

Drugs that may cause a **decreased** INR include:
Alcohol, atorvastatin, azathioprine, carbamazepine, chloral hydrate, clozapine, cortisone, haloperidol, phenobarbitone, prednisone, rifampicin, spironolactone, sucralfate, vitamin C (high dose), vitamin K

ADVERSE REACTIONS
Nervous system:
Headache, dizziness.
Haemorrhagic complications may present as headache, paralysis, paraesthesia or altered consciousness & need to be excluded.
Cardiovascular:
None described
Digestive:
Nausea, vomiting, diarrhoea, flatulence, bloating
Skin:
Necrosis, bullous eruptions, urticaria, pruritus, alopecia

Zopiclone [1 tablet 10 cents]

ADMINISTRATION ROUTES:
PO, NG

BRAND NAMES:
Imovane, Zimovane, Apo-Zopiclone

ICU INDICATIONS:
1. Insomnia

PRESENTATION AND ADMINISTRATION:
PO / NG:
Zopiclone 7.5mg tablet

DOSAGE:
3.75-7.5mg nocte

DOSAGE IN RENAL FAILURE AND RENAL REPLACEMENT THERAPY:
No dose adjustment is required

DOSAGE IN PAEDIATRICS:
0.1-0.4mg/kg nocte

CLINICAL PHARMACOLOGY:
Zopiclone is a short-acting hypnotic with a pharmacological profile similar to that of the benzodiazepenes. It has hypnotic, sedative, anxiolytic, anti-convulsant & muscle-relaxant properties. It has negligible residual effects the following morning without rebound insomnia on cessation of treatment. It is rapidly & well absorbed after oral administration with an elimination half-life of 5 hours, prolonged to 7 hours in the elderly. It is not removed effectively by haemodialysis due to a large volume of distribution.

CONTRAINDICATIONS:
1. Hypersensitivity to Zopiclone
2. Myasthenia gravis
3. Severe sleep apnoea syndrome
4. Severe hepatic insufficiency
5. Respiratory failure

WARNINGS
Risk of dependence if treatment duration is longer than 4 weeks; this is increased in patients with a history of drug abuse, alcoholism or personality disorders.

Risk of rebound & withdrawal after abrupt discontinuation after prolonged treatment. Gradual dose decrement is recommended, especially so in patients with a history of seizures

Anterograde amnesia may occur especially in the elderly or with disruption of sleep. This effect is dose-related. The risk of confusion is also higher in the elderly & in patients with cerebral impairment.

PRECAUTIONS

General

Additive effect with concomitant use of other central depressant drugs.

Laboratory Tests

No tests are required in addition to routine ICU blood tests

Drug/Laboratory Test Interactions

None known

IMPORTANT DRUG INTERACTIONS FOR THE ICU

Activity may be enhanced when co-administered with drugs that inhibit hepatic enzymes (particularly cytochrome P450) such as cimetidine or erythromycin.

ADVERSE REACTIONS

Nervous system:

Drowsiness, un-co-ordination, headaches, fatigue

Cardiovascular:

Arrhythmias (especially in elderly patients)

Digestive:

Dry mouth, heartburn, constipation, diarrhoea, nausea, vomiting

Skin:

Urticaria, tingling

APPENDICES

APPENDIX 1

Administration of medicines via enteral feeding tubes – Quick tips

Janice Young, ICU Pharmacist , August 2010

- Narrow tubes and long tubes are more likely to become blocked.
- In general for tubes <8Fr diameter, check with your clinical pharmacist before administering dose
- The correct formulation and effective flushing is required to prevent blockage.
- **Do not** administer medicines via tubes being used for aspiration or those on free drainage
- For jejunally placed tubes, some medicines may have decreased absorption due to pH if administered via a jejunal tube. Discuss with your clinical pharmacist
- Consider withholding non-essential treatment if enteral tube administration is necessary
- **Do not** crush long acting/slow or controlled release tablets
- **Do not** crush enteric coated tablets
- Preferentially use liquid formulations where available
- If in doubt, check with your clinical pharmacist before administering medicines via enteral feeding tubes
- There may be differences in enteral tube administration between brands available. If in doubt check with your clinical pharmacist

Reference:

- *RPS Publishing Royal Pharmaceutical Society of Great Britain. London UK. White R, Badnam V (authors). Handbook of Drug Administration via Enteral Feeding Tubes. 2007 edition.*

APPENDIX 2

WARFARIN REVERSAL CONSENSUS GUIDELINES

Based on The Australasian Society of Thrombosis & Haemostasis recommendations for Australia & New Zealand (MJA 2004; 181(9):492-497)

Guidelines for the management of an elevated INR in adult patients with or without bleeding

Clinical setting		Therapy					
INR	Bleeding	Warfarin	Vitamin K	Prothrombinex	FFP	Measure INR	Comments
> therapeutic range but < 5	None	Reduce or omit next dose	-	-	-	-	Resume warfarin at reduced dose when INR approaches therapeutic range If INR < 10% above therapeutic, dose reduction may not be necessary
5-9*	None	Cease	-	-	-	Within 24 hrs	Resume warfarin at reduced dose when INR approaches therapeutic range
	None (high risk)^	Cease	1-2mg (po) or 0.5-1mg (iv)	-		Within 24 hrs	Resume warfarin at reduced dose when INR approaches therapeutic range
> 9	None (low risk)	Cease	2.5-5mg (po) or 1mg (iv)	-	-	In 6-12 hrs	Resume warfarin at reduced dose when INR < 5
	None (high risk)^	Cease	1mg (iv)	Consider 25-50 IU/kg	Consider 150-300 ml	In 6-12 hrs	Resume warfarin at reduced dose when INR < 5
Clinically significant bleeding where warfarin is a contributing factor		Cease	5-10mg (iv)	25-50 IU/kg	150-300 ml	Assess patient continuously until INR < 5 & bleeding stops If FFP is unavailable, give vitamin K (5-10mg iv) & Prothrombinex (25-50 IU/kg) If Prothrombinex is unavailable, give vitamin K (5-10mg iv) & FFP (10-15 ml/kg)	

* Bleeding risk increases exponentially from INR 5 to 9; INR ≥ 6 should be monitored closely
^ High bleeding risk factors include active gastrointestinal disorders, concomitant anti-platelet therapy, major surgical procedure within preceding 2 weeks, thrombocytopenia

In severe bleeding, prothrombinex is preferable to FFP as it is usually more immediately available.

SEEK EXPERT HAEMATOLOGY ADVICE IF UNSURE

Managing oral anticoagulation during invasive procedures according to risk of thromboembolism

Thromboembolism risk	Therapeutic procedures before and after surgery					
	4-5 days before	2-3 days before	Night/day before	Day of surgery	After surgery	72 hours + after
Low	Withhold warfarin	-	If INR > 2, 1-5 mg vitamin K (iv)	If INR ≤ 1.5 proceed If INR > 1.5 defer If surgery is urgent, Prothrombinex (25-50 IU/kg) + 150-300 ml FFP or FFP alone	Start warfarin on same day at previous maintenance dose Employ thromboprophylaxis as per usual practice	-
High	Withhold warfarin	Start treatment dose unfractionated heparin (iv) or low molecular weight heparin (LMWH)* (subcut)	If using LMWH, last dose (max dose of enoxaparin 1mg/kg) at least 24 hours before surgery	If using unfractionated heparin, discontinue 4-6 hours before surgery	Recommence warfarin ASAP Start heparin or LMWH 12-24 hours post-operatively If using LMWH, give thromboprophylactic dose If using unfractionated heparin, aim to prolong APTT 1.5x	Fully anticoagulate patient with warfarin if no evidence of bleeding Cease heparin or LMWH 48 hours after target INR is reached

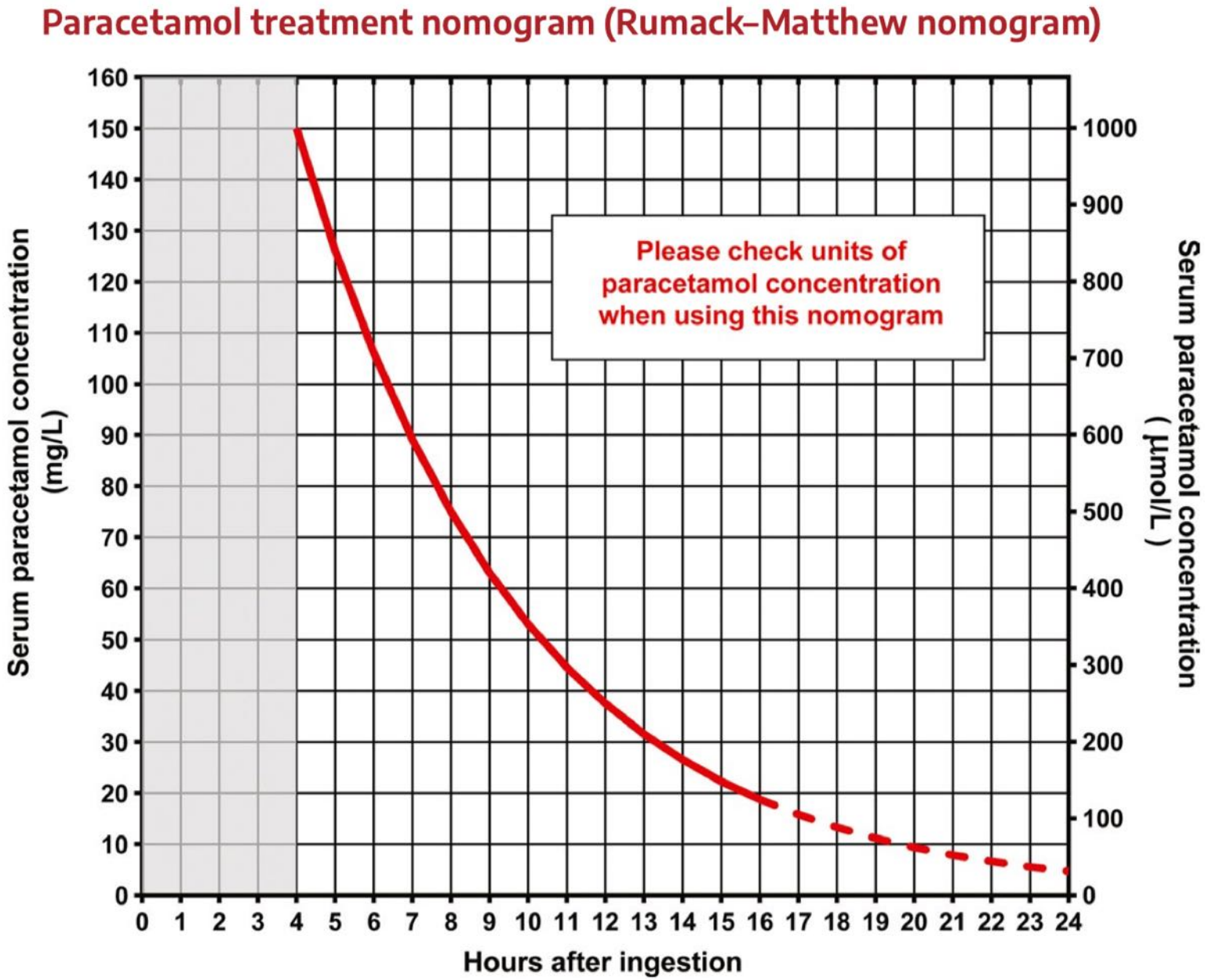
* Exercise caution in patients with impaired renal function (creatinine clearance rate < 30 ml/hour). LMWH can accumulate & contribute to bleeding.

NOTE: Patients with prosthetic valves & those who have had an acute thrombosis within the preceding three months should receive bridging anticoagulation peri- and post-operatively.

SEEK EXPERT HAEMATOLOGY ADVICE IF UNSURE

APPENDIX 3

PARACETAMOL POISONING NOMOGRAM - from Chiew et al. *Updated guidelines for the management of paracetamol poisoning in Australia and New Zealand.* ***MJA 212 (4) 2 March 2020***



ONLY FOR USE IN INGESTION OF IMMEDIATE RELEASE PARACETAMOL

APPENDIX 4
Therapeutic Drug Level Monitoring

General Principles

- Only clinically relevant tests should be performed; **do not** perform tests that cannot be interpreted or do not assist patient management. Random levels that do not conform to the timings indicated below are not clinically useful.
- 'Peak' levels refer to the highest blood concentration of a drug after administration
- 'Trough' levels refer to the lowest blood concentration of a drug after administration
- 'Steady-state' refers to the situation reached when the intake of a drug equals that of its removal from the body
- Blood samples should be collected only after the drug concentration has reached steady-state i**.e. at least 4 half-lives at a constant dosing regimen.** Levels close to steady state may be reached earlier if a loading dose has been administered. Drugs with long half-lives may be monitored before steady-state has been achieved to ensure patients with impaired metabolism or renal excretion are not at risk of developing toxicity at the initial dosage regimen
- Drug concentrations may be requested for any of the following reasons:
    - Suspected toxicity
    - Lack of response
    - To assess patient compliance
    - To assess therapy following a change in dosage regimen
    - A change in clinical state of the patient
    - Potential drug interaction due to a change in other medications
    - Where manifestations of toxicity and disease are similar
- To interpret a result, the details of the dosage regime (dose and duration) must be known
- For patients suspected of symptoms of drug toxicity, the best time to take the blood specimen is when the symptoms are occurring
- If there is a question as to whether an adequate dose of the drug is being achieved, it is usually best to obtain trough levels (rather than peak) as these are less influenced by absorption and distribution problems. However, for some drugs where toxicity is a concern (such as gentamicin), peak levels may be requested
- A range of drug concentrations is usually targeted rather than a specific value as the effect of a drug at a known concentration may vary greatly between individuals
- Trough levels are usually obtained at the end of the dosage interval i.e. immediately before the next dose is due to be given
- Peak levels are usually obtained:
    - 30 minutes after an intravenous dose (if given by infusion, 30 minutes after the infusion has been stopped); aminoglycoside antibiotics (gentamicin, tobramycin) given by bolus should have their levels checked 30 minutes post dose to avoid the distribution phase
    - one hour after an intramuscular dose
    - one to two hours after oral dosing
    - slow release drugs may not produce peak levels for several hours after ingestion

Drug	Timing of blood sample	Vacutainer tube	Therapeutic Range
Carbamazepine	Sample immediately before next dose (trough)	**Red or Yellow**	16-50 micmol/L
Clozapine	Sample immediately before next dose (trough) or at anytime if toxicity suspected	**Red**	Trough 1000 nmol/L; Toxicity >2000 nmol/L
Cyclosporin	Sample immediately before next dose *(C0)* or exactly 2 hours post dose *(C2)*	**Purple**	**See drug monograph for interpretation**
Digoxin	Sample 8-24 hours post dose	**Red or Yellow**	0.6-2.0 nmol/L
Gentamicin	Sample trough level 2-4 hours before next dose is due	**Yellow or Red (Green for paeds)**	**See drug monograph for interpretation**
Lithium	Sample 12 hours post dose	**Yellow**	0.6-1.2 mmol/L
Phenobarbitone	Sample immediately before next dose (trough)	**Yellow, Red or Green**	65-130 micmol/L
Phenytoin	Sample at least 12 hours post dose (trough)	**Yellow**	Trough 40-80 micmol/L
Theophylline	For i/v infusion, sample at any time	**Yellow, Red or Green**	55-110 micmol/L
Tobramycin	- Trough: immediately before next dose - Peak: 30 mins post dose	**Red or Yellow**	Trough <1mg/L Peak 20-30mg/L
Vancomycin	- Sample daily in routine morning bloods, beginning **day after** starting infusion	**Red, Yellow or Purple**	18-25mg/L **See drug monograph**

All table data taken from the CCDHB Laboratory Test Database (January 2013)

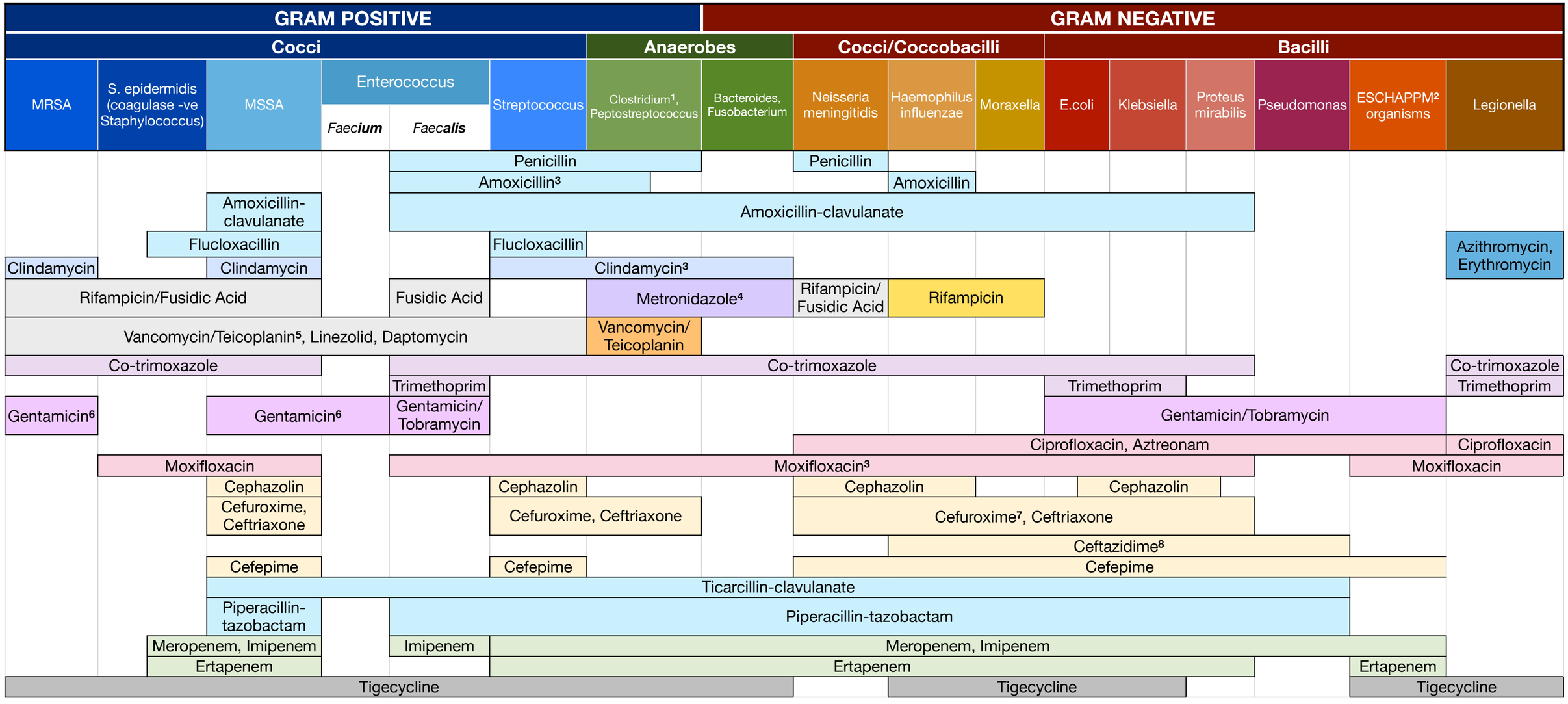
For Paracetamol toxicity see ***APPENDIX 3***

References

1. Gross AS. Best practice in therapeutic drug monitoring. Br J Clin Pharmacol 1998;46(2):95–9
2. Birkett DJ. Therapeutic drug monitoring. Austr Prescr 1997;20:9-11
3. Kang JS, Lee MH. Overview of therapeutic drug monitoring. Korean J Intern Med 2009;24(1):1–10

APPENDIX 5

Antibiotic Sensitivity Overview



For simplicity, atypical organisms are not included above. Partial columns indicate incomplete coverage. ESBL-producing organisms are not susceptible to most antibiotics containing a beta-lactam ring; carbapenems are the usual agent of choice.

1: *C. difficile* should only be treated with metronidazole or vancomycin. **2:** ESCHAPPM are β-lactamase producing organisms. These are *Enterobacter, Serratia, Citrobacter freundii*, *Hafnia*, *Acinetobacter/Aeromonas*, *Proteus* (**not** *mirabilis*), *Providencia & Morganella morganii*.

3: Not effective against *Clostridium.* **4:** Metronidazole is not effective against *Peptostreptococcus*, **5**: Teicoplanin is not effective against *Enterococcus faecium*, **6:** Gentamicin is not appropriate mono therapy for *Staphylococcus aureus* & should only be used in conjunction with a β-lactam.

7: Due to increasing MIC, Cefuxorime is not recommended therapy for *Moraxella.* **8**: Although it has other actions, Ceftazidime should only be used for *Pseudomonas*.

ANTIBIOTIC CLASS KEY

PENICILLINS	LINCOSAMIDE	MACROLIDES	NITROIMIDAZOLE	RIFAMYCIN	GLYCOPEPTIDES
SULFONAMIDES	AMINOGLYCOSIDES	FLUOROQUINOLONES	CEPHALOSPORINS	CARBAPENEMS	GLYCYLCYCLINE

*This chart is intended as a guide, pending specific identification & sensitivities - **it does not replace expert ID advice. Local antibiotic sensitivities & preferences will vary.**

APPENDIX 6
Opioid Dose Equivalence

Opioid	IV (mg)	Oral (mg)
Morphine	2	
Sevredol		15-30
Codeine Phosphate		120
Methadone	2	7.5-15
Oxycodone	2	5-10
Fentanyl	20 **mcg**	
Pethidine	20	

Fentanyl patch:
(use with caution in opioid naive patients; takes 8-12 hours for effect with residual effect for 14-24 hours after patch removed)

25mcg patch equivalent to:
- Morphine 50mg po over 24 hour period
- Morphine 16mg i/v over 24 hour period

50mcg patch equivalent to:
- Morphine 100mg po over 24 hour period
- Morphine 32mg i/v over 24 hour period

Morphine/Methadone conversion ratios:
The ratio changes as the morphine dose increases
Calculate equianalgesic dose then reduce by 25-50%

Ratio of **24-hour oral morphine: oral methadone**
For <90 mg of morphine = **4:1**
For 91-300 mg of morphine = **8:1**
For 301-600 mg of morphine = **12:1**

Oral methadone:IV/IM methadone = 2:1
Seek expert Pain Team or Palliative Care advice if unsure or complex patient

Ref: CCDHB Pain Management guidelines by Dr.Paul Glover, Dept. Anaesthesia 2009

APPENDIX 7

Intravenous vs Enteral Medication Costs

(All prices in NZ$ & are correct as of January 2015)

Medication	Intravenous Preparation		Tablets or Capsule/ Liquid		Note for NG Administration
	Strength	Cost	Strength	Cost	
Acetazolamide	500mg	$111	250mg	$0.17	Crush tablet
Ciprofloxacin	400mg	$8.20	500mg	$0.07/$6.50	Crush tablets (liquid sticks to tube)
Clindamycin	600mg	$10	600mg	$1.52	Open capsule
Co-trimoxazole	480mg	$23.50	480mg	$0.04	Use liquid
Fluconazole	100mg	$5	200mg	$0.35/$4	Open capsule
Levetiracetam	500mg	$48	500mg	$0.48	Crush tablet
Moxifloxacin	400mg	$70	400mg	$10	Crush tablet
Rifampicin	600mg	$128	600mg	$3	Use liquid

When prescribing, please consider enteral administration of these medications first unless it is contraindicated or absorption is thought unlikely. Although individual cost benefits may seem small, when considered for multiple doses for prolonged ICU stays across the whole unit, such savings may be significant for equivalent medical benefit. Please consult the unit pharmacist or ICU specialist if you are unsure.

APPENDIX 8
Intravenous To Enteral Antibiotic Conversion

Before converting from intravenous to oral antibiotics, the following **SWITCH** criteria should be met:

Suitable oral alternative available
When patient afebrile > 24 hours
Infectious condition suitable for oral treatment*
Tolerating oral/nasogastric food or fluid
Clinical & lab trend towards improvement**
Haematology/Oncology patients excluded

Benefits to SWITCH include decreased risk of infection from intravenous lines, decreased risk of thrombophlebitis, decreased patient discomfort, savings in nursing time and costs.
Please consult the unit pharmacist or ICU specialist if you are unsure before SWITCHing.

Intravenous Antibiotic	Oral Option	Oral Bioavailability
Amoxicillin	Amoxicillin 500 mg - 1 g TDS	72-93%
Amoxicillin clavulanate	Amoxicillin clavulanate 625 mg TDS	72-93%
Benzylpenicillin	Amoxicillin 500 mg - 1 g TDS	
Cefuroxime	Usually amoxicillin clavulanate 625 mg TDS	
Cephazolin	Cephalexin 1 g TDS	90%
Clindamycin	Clindamycin 450 mg - 600 mg TDS - QDS	90%
Erythromycin	Erythromycin 400 mg QDS	
Fluconazole	Same as intravenous dose	90%
Flucloxacillin	Flucloxacillin 1 g TDS	
Metronidazole	Metronidazole 400 mg BD (400 mg TDS for *C.difficile*)	80%

*Infections that are **unsuitable** for SWITCH include bone/joint/CNS infection, bacterial endocarditis, cystic fibrosis/bronchiectasis, undrained abscesses, infected prosthesis, *Staphylococcus aureus* bacteraemia

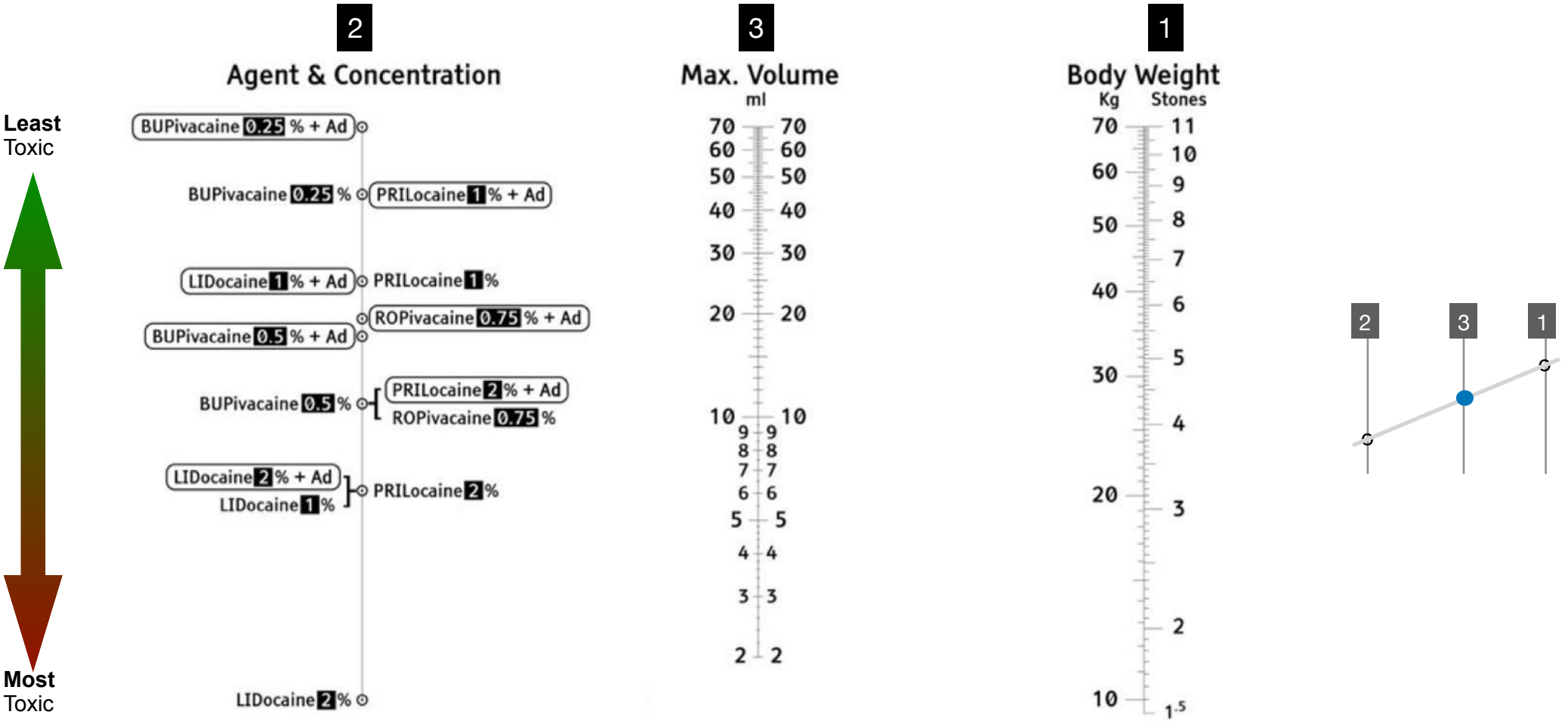
**WBC 4 - 11 or improving, vital signs normal or normalising

APPENDIX 9

Local Anaesthetic Safety Calculations*

(maximum safe amount administered within an 8 HOUR period)

(from Williams DJ, Walker JD. A nomogram for calculating maximum dose of local anaesthetic. Anaesthesia 2014)



HOW TO USE THIS NOMOGRAM: Take a ruler or straight edge. Place one end on scale **1** on the relevant value for the patient's body weight. Place the other end on line **2** crossing the preferred local anaesthetic agent & concentration. The maximum volume in millilitres that can be safely administered is shown where the straight line crosses the middle scale (marked **3**). For patients > 70 Kg, use 70 Kg; for obese patients, use ideal body weight. If body weight or maximum volume values fall between scale graduations, use next LOWEST values on each scale. **This nomogram is a guide and does not replace calculations for maximum dose toxicity**. See table on following page for guidance with this calculation.

***Ropivacaine 0.2% is the preferred agent in Wellington for local anaesthetic wound catheters. See next page for specific dosing guidelines.**

ROPIVACAINE 0.2% DOSING: This is the preferred local anaesthetic agent for administration through wound catheters (usually rectus sheath catheters) in Wellington Regional Hospital. **Ropivacaine 0.2% contains 2 mg /ml**. The **maximum safe dose in 24 hours is 8 mg / kg** (consider reduction in elderly patients). Follow steps 1-4 below to prescribe ropivacaine safely:

1. Calculate the **24 hour maximum safe volume** based on the patient's weight using the table:
2. Divide this volume by **4** to give the volume to be administered **every 6 hours**
3. Divide this volume by the **number of wound catheters** to give the **volume per catheter** every 6 hours
4. Prescribe '**Ropivacaine 0.2% q6 hrly via wound caths**' with the volume calculated in step 3

PATIENT WEIGHT (Kg):	40-49	50-59	60-69	70-79	80-89	90-99
Max volume 0.2% ropivacaine (ml per 24 hrs)	160-180	200-220	240-260	280-300	320-340	360-380

SAFELY DOSING OTHER LOCAL ANAESTHETIC AGENTS: Use the table below to calculate the maximum safe dose for other local anaesthetic agents in both plain preparation and preparations with adrenaline added. This is the maximum safe dose that can be administered **every 8 hours (TDS)**. **The maximum stated dose assumes normal plasma protein binding, normal hepatic & renal function, and no interactions with other co-administered drugs.** If variants in these factors are known or suspected then the administered dose should be reduced accordingly. Dose reduction should also be considered in elderly patients.

DRUG	Maximum 8 HOURLY DOSE (mg/kg)	
	PLAIN	WITH ADRENALINE
LIDocaine	3	7
BUPivacaine	2	2.5
PRILocaine	6	9
ROPivacaine	3	4

See Appendix 10 for assistance in calculating drug concentrations from solutions expressed in percentages.

APPENDIX 10
Drug Calculations

CALCULATING DOSES FROM PERCENTAGE SOLUTIONS:
The underlying principle of all drug dilutions is that a **100% solution** is **1 g** of drug in **1 ml** of volume (a '1 in 1' solution).
This solution has **100 g** of drug in **100 mls** of solution.
Therefore a **1% solution** of any drug = **1:100** solution = **1 g** in **100 ml** = **10 g** in **1 litre** = **10 mg** in **1 ml** = **10,000 mcg** in **1 ml**

Subsequent dilutions can be derived as shown in the table below (each row contains the same amount of drug):

Equivalent Drug Dilutions Expressed As:				
RATIO	**PERCENTAGE SOLUTION**	**GRAM PER 100 ml**	**MILLIGRAM PER MILLILITRE**	**MICROGRAMS PER MILLILITRE**
	%	**g / 100ml**	**mg / ml**	**mcg / ml** or **µg / ml**
1:100	1	1	10	10,000
1:200	0.5	0.5	5	5,000
1:1000	0.1	0.1	1	1000
1:10,000	0.01	0.01	0.1	100
1:100,000	0.001	0.001	0.01	10
1:200,000	0.0005	0.0005	0.005	5

EXAMPLES OF COMMON ICU DRUGS:
- 0.5% bupivacaine contains 5 mg in 1 ml (100 mg in a 20 ml vial)
- 0.2% ropivacaine contains 2 mg in 1 ml (40 mg in a 20 ml vial, 400 mg in a 200 ml bag)
- 2% lignocaine contains 20 mg in 1 ml (100 mg in a 5 ml vial)
- '1 in 1000' adrenaline contains 1 mg in 1 ml or 1000 mcg in 1 ml
- 10% calcium chloride contains 1 g in 10 ml; this is 6.8 mmol of calcium & 13.6 mmol of chloride
- 49.3% magnesium sulfate contains 493 mg in 1 ml; a single 5 ml vial therefore contains 2.465 g
- 8.4% sodium bicarbonate contains 84 mg in 1 ml; this is 23 mg (1 mmol or 1 mEq) of sodium & 61 mg (1 mmol or 1 mEq) of bicarbonate

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