Joint Formulary
North Sefton & West Lancashire
Area Medicines Management Committee

Southport & Ormskirk Hospital  NHS
NHS Trust

NHS
Sefton

NHS
Central Lancashire
# Contents

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Introduction</td>
<td>1</td>
</tr>
<tr>
<td>Chapter 1 Gastro-intestinal system</td>
<td>6</td>
</tr>
<tr>
<td>Chapter 2 Cardio-vascular system</td>
<td>22</td>
</tr>
<tr>
<td>Chapter 3 Respiratory system</td>
<td>42</td>
</tr>
<tr>
<td>Chapter 4 Central nervous system</td>
<td>54</td>
</tr>
<tr>
<td>Chapter 5 Infections</td>
<td>80</td>
</tr>
<tr>
<td>Chapter 6 Endocrine system</td>
<td>81</td>
</tr>
<tr>
<td>Chapter 7 Obstetrics, gynaecology &amp; Urinary tract disorders</td>
<td>97</td>
</tr>
<tr>
<td>Chapter 8 Malignant disease &amp; immunosuppression</td>
<td>112</td>
</tr>
<tr>
<td>Chapter 9 Nutrition &amp; blood</td>
<td>122</td>
</tr>
<tr>
<td>Chapter 10 Musculoskeletal &amp; joint diseases</td>
<td>131</td>
</tr>
<tr>
<td>Chapter 11 Eye</td>
<td>137</td>
</tr>
<tr>
<td>Chapter 12 Ear, nose &amp; oropharynx</td>
<td>149</td>
</tr>
<tr>
<td>Chapter 13 Skin</td>
<td>153</td>
</tr>
<tr>
<td>Chapter 14 Immunological products &amp; vaccines</td>
<td>170</td>
</tr>
<tr>
<td>Chapter 15 Anaesthesia</td>
<td>171</td>
</tr>
</tbody>
</table>
INTRODUCTION
The aim of this Formulary is to promote safe, effective, and economic prescribing in both primary and secondary care. The medicines included provide appropriate treatment for the vast majority of patients. All drugs listed have been approved for uses and are routinely stocked by all pharmacies.

The Joint Formulary provides all prescribers with guidance on first choice drugs. In turn, this will achieve two objectives. Firstly as a selective list this will lead to greater familiarity with a limited range of medicines and thus help to reduce prescribing errors. Secondly, with agreement across the interface between primary and secondary care, the Formulary will promote a seamless approach to prescribing which will benefit all patients who require medicines.
Development
Consultation on which medicines to include has been extensive and consideration given to current prescribing patterns and relative costs. Evidence of clinical effectiveness, safety, cost effectiveness and patient acceptability has been taken into account when making recommendations.
Final choices of medicines have been approved by the Formulary steering group and endorsed by the Area Medicines Management Committee (AMMC).

Content
As well as being a selective list of medicines, the Formulary also contains prescribing notes that highlight key messages about the medicines/conditions being treated. The first and second choice medicines are indicated in each section and prescribing notes follow. In some cases comments on other drugs are also included when they have a therapeutic use in particular circumstances. The drugs are listed in therapeutic categories following the well-known and recognised BNF classification system. Within some sections there are coloured boxes that contain specialist medicines for use within secondary care only.
The Formulary is not designed to replace the BNF and all prescribers should continue to refer to the current edition of the BNF for further information on doses, side effects, interactions and for more comprehensive information on a wider range of medicines.
Non Formulary medicines

The Formulary is not designed to contain all medicines that will be required by all patients. It is estimated that the drugs in the Formulary will be sufficient to meet the needs of the vast majority of patients. However it is recognised that there will always be some patients for whom a more extensive and complex drug treatment can be justified.

Non Formulary medicines are both appropriate and justifiable when there are contraindications to Formulary drugs or when patients require further medication in addition to Formulary choices. There must be clear communication between primary and secondary care as to the reasons why this is necessary. It is not considered appropriate to prescribe non-Formulary drugs in the place of recommended choices without explanation.

The Hospital Pharmacy departments only keep in stock medicines that are on the Formulary. If a patient is admitted on a non-formulary medicine, the procedure below should be followed:

- Use the patient’s own supply of medicines (after inspection by doctor, trained pharmacy staff or nurse).
- Arrange with the Pharmacy for a small quantity to be purchased on an individual patient basis.
- Change to a formulary product if not detrimental to patient care eg- antacid, haemorrhoid preparation etc.
Procedure for introducing new medicines to the Joint Formulary

All new medicines requests will be considered on a health-economy basis by the Area Medicines Management Committee. The process for submitting requests is as follows. This process CANNOT be deviated from.

- The hospital pharmacy is notified by a Consultant/GP that they require a new product to be added, or that an additional formulation of a current medicine is required.
- The Hospital Formulary Pharmacist sends the requestor a New Product Request form, to be completed and returned. This form requires information on the definite advantages of the product against existing agents, together with an estimate of the likely usage.
- The request will be considered at the next meeting of the AMMC. The requestor will be invited to attend the meeting to support the request and supply any additional information.
- A decision will be made by the AMMC to support or reject the introduction of the new product, together with any relevant remarks about whether the use is restricted to the Hospital Trust or if it will be available across Primary Care also. If a medicine is rejected, the committee will consider appeals against its decisions.
- Within the hospital, the Stores and Procurements staff of the Pharmacy will then be authorised to order the new product.
- Requests for medicines for use within the Hospital Trust will only be accepted from Consultants.
- If it is deemed necessary to procure a new product as an emergency treatment for an individual patient within the hospital trust, a verbal request from the Consultant to the deputy Chairman of the AMMC (Chairman of the DTC) for executive authorisation can be made. In such a case, the minimum quantity to treat that patient would be made available in the Pharmacy. Subsequent patients would not be supplied unless a formal request form had been submitted.

The Committee will audit all requests for new products and prescribers may be asked to report back to the Committee on their experiences of using a new product.

Nomenclature

The recommended international Non-proprietary Name (rINN) is used throughout the Formulary in line with the EU and UK legislation. Generic names are used for most medicines throughout the Formulary to ensure that when a generic product is available, it is prescribed and the cost benefit of this approach is obtained. On the few occasions where a particular brand is required, this is stated. In addition, occasionally for convenience, where approved names are not in general use for some products, the proprietary name has also been given in brackets after the approved name.
Unlicensed use of medicines
Where an unlicensed medicine is recommended, this is indicated in the Formulary. This may be a licensed medicine being used for an unlicensed indication or at a dose outside the current license, or it may be a medicinal product which does not currently have a product license e.g. a “Special”. In these cases, the medicine involved has been considered to be the most appropriate treatment and has been recognised as such by an appropriate peer group. The responsibility for prescribing, as for any medicine, lies with the doctor who signs the prescription. If any doctor is unsure about taking on the prescribing responsibility of any medicine contained in the Formulary, he/she should seek more information before proceeding.

Implementation
All Trusts within the health economy support the Joint Formulary. In addition, it is agreed that implementation will be co-ordinated by the individual medicines management committees. The Formulary steering group will review sections as and when is necessary and at least annually. Additions and future changes will be sent to all recipients.

Useful contact details

**Hospital pharmacy department**
Southport 01704 704162; Ormskirk 01695 656422

**Julie Kenyon/Kay Walsh - Interface Pharmacists**
01704 704164

**Kath Phillips - Hospital Formulary Pharmacist**
01704 705157

**Sefton PCT Medicines Management**
0151 478 1272

**Central Lancashire PCT Medicines Management**
01772 678068
Chapter 1 - Drugs acting on the Gastro-Intestinal System

1.1.1 Antacids

**First choice:** Magnesium trisilicate mixture (6mmol Na+ per 10ml)
**Low sodium alternative:** Maalox® suspension (<1mmol Na+ per 10ml)

1.1.2 Compound alginates

**First choice:** Peptac® suspension (6.2mmol Na+ per 10ml)
**Lower sodium alternative:** Gastrocote® tablets (1mmol Na+ per tab)
**Paediatric alternative:** Gaviscon® Infant Sachets

**Additional Prescribing Advice**
- Liquid preparations are most effective.
- Magnesium salts can cause diarrhoea
- Aluminium salts can cause constipation
- Peptac® is more expensive and should be reserved for reflux oesophagitis. It should not be used in situations where plain antacids would suffice
1.2 Antispasmodics and Mobility stimulants

a) Antispasmodics

First choice: Mebeverine tablets

Additional Prescribing Advice

- Pain relief is best achieved by other means e.g. diet, fluids, exercise, bulking agents etc. Antispasmodics should not be used as initial agents and should not be given on a continuous basis.
- Does not cause antimuscarinic side effects like other agents that can be a particular problem in the elderly.

b) Mobility stimulants

First choice: Metoclopramide

Second choice: Domperidone

Additional Prescribing Advice

- Domperidone does not cross the blood brain barrier and is less likely to cause dystonic reactions than metoclopramide. It should be used for the young and elderly; treatment should not exceed 12 weeks.
1.3 Ulcer Healing Drugs

NICE guidance on Dyspepsia (August 2004) recommends:

- Self-treatment with antacid and / or alginate therapy taken as required may be appropriate for immediate symptom relief. This might be either prescribed or purchased over-the-counter.
- If the symptoms persistently affect patient’s quality of life, additional therapy is appropriate.
- Patients should be reviewed regularly and encouraged to try stepping down or stopping treatment.

Uninvestigated dyspepsia

Initial therapeutic strategies are:
- Test & treat for H. pylori or
- Empirical treatment with a Proton Pump Inhibitor (PPI).

A 2 week washout period following PPI use is necessary before testing for H. pylori with a breath test.

Gastro-oesophageal reflux disease (GORD)

Full dose PPI for 4 - 8 weeks

Recurrent symptoms after initial treatment - Use PPI at lowest dose possible to control symptoms, with limited number of repeat prescriptions.

Peptic ulcer disease (PUD)

Eradication therapy for H. pylori positive patients with PUD.

Proven NSAID-associated PUD

Stop NSAID if possible & prescribe full dose PPI or H2RA for 8 weeks. H. Pylori eradication subsequently if H. pylori positive.
If NSAID cannot be stopped, use low dose PPI as prophylaxis.
Non-ulcer dyspepsia
Eradicate H. Pylori if present.
Symptomatic management, with periodic monitoring.

PPI therapy is indicated
- As a treatment course for:
  - Gastric ulcer - 4 - 8 week course
  - Duodenal ulcer - 4 week course
  - Oesophagitis - 8 week course
  - Endoscopy-negative GORD where 8 week H2 receptor antagonist failed - 4 - 8 week course
  - Part of H.pylori eradication regime (please refer to current BNF for recommended regimes)
- As long term maintenance therapy for:
  - Severe oesophagitis or complicated by stricture or Barretts oesophagus - full dose PPI
  - Prophylaxis for bleeding ulcers in patients who are elderly/frail and would not tolerate further bleeding.

On presentation with dyspepsia, the ALARM symptoms should be first considered and patients referred for urgent gastroscopy if symptoms are present:
- Anaemia
- Loss of Weight
- Anorexia
- Recurrent problems
- Melaena
- Swallowing problems
1.3.1 - H2 Receptor Antagonist

**First choice:** Ranitidine

**Additional Prescribing Advice**
- H2 - Receptor antagonists have not been shown to be beneficial in haematemesis and malaena but prophylactic use reduces the frequency of bleeding.
- Intravenous H2 - receptor antagonists should only be used in patients unable to take oral medication. Most patients with an acute upper GI bleed can be managed on an oral agent.

1.3.2 - Not recommended

1.3.3 - Chelates and complexes

**First choice:** Sucralfate (Consultant initiated only)

**Additional Prescribing Advice**
- Sucralfate may be useful for resistant ulcers or for prophylaxis of stress ulceration.

1.3.4 - Not recommended
1.3.5 - Proton Pump Inhibitors

Lansoprazole Capsules
Omeprazole Capsules

Additional Prescribing Advice

- Omeprazole should be used for patients with severe or complicated oesophagitis who require high dose (40mg) therapy - or those patients still symptomatic after standard treatment with Lansoprazole.
- The possibility of gastric carcinoma should be excluded, since acid suppression may mask the symptoms.
- In most patients with GORD, a step down approach is encouraged starting with optimum doses and then adjusting to maintain symptomatic control using the lowest dose of the most cost-effective agent (antacid, H2 - antagonist, PPI). An on-demand regimen is acceptable if adequate symptom control is achieved.
- PPIs and antibiotics must be stopped two weeks before H.pylori breath test or endoscopy.
- If NSAID induced bleed or ulcer occurs, stop NSAID and prescribe a PPI.
- Esomeprazole may be used in patients with no response or who have relapsed with high dose lansoprazole or omeprazole.

1.3.6 - Not recommended

Additional medicines for Hospital use only

Pantoprazole inj - strictly in accordance with hospital guidelines
- Most patients with an acute upper GI bleed can be managed on an oral agent.
1.4.1 Not recommended

1.4.2 Anti-motility drugs

First choice: Loperamide
Second choice: Codeine Phosphate

Additional Prescribing Advice

• First-line treatment for acute diarrhoea is rehydration therapy (see section 9.2.1)
• Codeine phosphate has problems with dependency, narrow dose range and a worse side effect profile than loperamide - short courses only.
• Spurious (overflow) diarrhoea is common in the elderly and anti-diarrhoeals should only be prescribed when constipation has been excluded by rectal examination.
• Antidiarrhoeal drugs should not be given in acute inflammatory bowel disease or pseudomembranous colitis, megacolon, nor in acute infective diarrhoea with bloody stools.
• Cholestyramine should only be used for post cholecystectomy diarrhoea (see section 1.9.2).
1.5 Inflammatory Bowel Disease

First choice: Mesalazine (see notes below)
   - Prednisolone
   - Hydrocortisone foam enema

Second choice: Sulfasalazine
   - Budesonide MR caps

Additional Prescribing Advice
- Specialist advice should be sought if diagnosis is unclear.
- Local therapies using retention enemas will resolve symptoms in most patients who have bloody diarrhoea from ulcerative proctitis, without side effects. Some systemic absorption of steroid occurs from steroid foam enemas; prolonged uses may lead to adrenal suppression and steroid side effects. Patients should be issued with a steroid card.
- Different formulations of mesalazine have different release characteristics and should not be regarded as interchangeable; the proprietary name should be specified.

Additional Medicines for Hospital Use Only
- Azathioprine tablets - consultant advice only. Until shared-care protocols are in place, prescribing should be maintained within secondary care.
- Infliximab
1.6 Laxatives

Treatment of Constipation in Adults

Consider cause:
- Drugs
- Low Fibre intake
- Inadequate fluid intake
- Lack of exercise/immobility
- Disease
- Pregnancy

Chronic constipation - emphasis on patient education
1. Increase dietary fibre intake
2. Add bulk forming agent
3. Add faecal softener
4. Add stimulant laxative
5. Movicol® (specialist advice only)
6. REVIEW

Acute constipation without impaction
1. Establish cause
2. Stimulant laxative
3. Maintenance therapy

Acute constipation with impaction
1. Establish cause
2. Rectal administration of stimulant laxative
3. If still constipated, change to: Phosphate ± arachis oil enema
4. Movicol®
5. If still constipated, seek specialist advice

Drug induced constipation (e.g. - tricyclics, opioid analgesics, aluminium containing antacids, iron salts, antimuscarinics)
1. Avoid/change causative agent if possible
2. Combination of stimulant/osmotic laxative
3. Maintain on this combination whilst still taking causative agent
1.6.1 Bulk-forming agents

First choice: Ispaghula husk

1.6.2 Stimulant laxatives

First choice: Senna tablets

Second choice: Bisacodyl supp/Glycerol suppositories

Palliative care only: Co-danthramer/co-danthrusate (second-line)

1.6.3 Faecal softeners

First choice: Docusate sodium (acts as both softener and stimulant)

Second choice: Arachis oil enema

1.6.4 Osmotic laxatives

First choice: Magnesium Hydroxide (not in renal impairment)

Second choice: Phosphate enema/Movicol® sachets

Hepatic encephalopathy and renal impairment only: Lactulose
1.6.5 Bowel cleansing solutions

**First choice:** Picolax®

**Additional Prescribing Advice**
- All laxatives are contra-indicated in intestinal obstruction
- Bulk forming agents should be used with care in the elderly and patients with dysphagia, adhesions and stenosis.
- As a general rule, due to the amount of fluid required, bulk forming laxatives and Movicol® should not be used in Palliative care.
- Stimulants become less effective with long term use.
Drug Treatment of Constipation in Children

GENERAL PRINCIPLES

- Attention to diet & fluid intake may avoid the need for drugs.
- Whatever drug regime is employed diet & fluids are still the most important factor in determining long term outcome.
- The general approach to drug treatment is:
  Step 1: Soften retained faeces with softener
  Step 2: Add in stimulant to evacuate softened faeces
  Step 3: Maintain bowel habit with a combination of softener & stimulant
- Wherever possible, a licensed medicine should be prescribed. However the informed use of unlicensed medicines or of licensed medicines for unlicensed applications is necessary in paediatric practice.
- The approach should always be flexible to suit the individual child/family and these guidelines are not rigid.
- Laxatives generally have a low incidence of side effects and with careful supervision doses can be increased above those given in the BNF.
- There is no convincing evidence of laxative dependence or diminution of effect with continuing use.
- Various laxatives in multiple combinations may be used - there is little evidence based data to support any one laxative combination over the others.
- Support & frequent and prolonged follow up is essential in the treatment of constipation in childhood & it is important that the family realises that long term drug treatment is very often needed.
- 25% patients off laxatives within 6m of starting Rx
- 50% patients off laxatives within 1yr of starting Rx
- 75% patients off laxatives within 2yr of starting Rx
1.6.2 Stimulant laxatives

First choice: Senna

Second choice: Sodium picosulfate elixir

1.6.3 Faecal softeners

First choice: Lactulose

Second choice: Docusate sodium

1.6.4 Osmotic laxatives

First choice: Movicol® / Movicol-Half®

1.6.5 Bowel Cleansing solutions

First choice: Picolax®

Additional Prescribing Advice
- Lactulose takes 48hrs for full effect. Teeth should be brushed afterwards.
- Docusate taste may be off-putting
- Senna may cause gripes.
- Sodium picosulfate may be added to senna at weekends if required or used as an alternative.
- Picolax® sachets it may be advisable to use for intractable constipation or as a weekly laxative booster at weekends (Fri/Sat night). A second dose may be given if no stool is produced after 6 hrs. It may be advisable to use in hospital initially.
- Movicol® can be used as single daily doses regularly in severe chronic constipation. It may also be used as an alternative to enema/manual removal for faecal impaction. It may need to be administered in hospital or at home under nursing supervision.
- Please refer to full guidelines for further information.
1.7.1 Soothing haemorrhoidal preparations

**First choice:** Anusol®

1.7.2 Compound haemorrhoidal preparations with corticosteroids

**First choice:** Scheriproct or Hydrocortisone 1% cream

**Additional Prescribing Advice**
- Scheriproct® is suitable for occasional short-term use after exclusion of infection.

1.7.4 Anal fissures

**First choice:** Glyceryl trinitrate (Rectogesic®)

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**Additional Medicines for Hospital use only**

Lidocaine ointment

1.7.3 Oily Phenol Injection
1.8. Stoma Care

Before discharge from hospital, patients should be fully conversant with the management of their stoma. The patient will be provided with sufficient supplies to last until their prescription can be dispensed.

Clinical Nurse Specialists - Stoma Care
Poulton Road Clinic - Samantha Miller 01704 383206
Ormskirk DGH - Freda Rattigan 01695 577111 bleep 140

Prescribing for Stoma patients

Use caution when prescribing for stoma patients, especially with enteric-coated and slow-release preparations, laxatives, antidiarrhoeals, antibiotics, antacids, diuretics, digoxin, analgesics, iron preparations and oral contraceptives.

Available Appliances

With the abundance of stoma appliances now available on prescription it is the Stoma Specialist Nurse who uses her skill to select and advise the client on the most suitable appliance for their needs.

Additional Prescribing Advice

- Lactulose is occasionally prescribed for colostomy patients if they suffer from constipation initially. Long term use is not recommended.
- Loperamide and codeine phosphate are commonly used for loose stools.
1.9. Drugs affecting intestinal secretions

1.9.1 Drugs affecting biliary composition and flow

First choice: Ursodeoxycholic acid

1.9.2 Bile acid sequestrants

First choice: Cholestyramine

1.9.3 See section 2.11

1.9.4 Pancreatin

First choice: Creon®
            Pancrex V®

Additional Prescribing Advice

- Higher strength preparations are available but carry a CSM warning following reports of fibrotic strictures of the large bowel in children aged 2 - 13 years.
Chapter 2

2.1 – Positive Inotropes

2.1.1 Cardiac glycosides

First Choice: Digoxin

Additional Prescribing Advice:

- Digoxin is indicated for rate control in atrial fibrillation and symptomatic heart failure; it has no role in the prophylaxis of paroxysmal atrial fibrillation.

- For rapid rate control in atrial fibrillation, a loading dose of digoxin may be given intravenously or orally.

- Regular measurements of plasma digoxin concentrations are not usually required except to confirm toxic or sub-therapeutic levels, or to check compliance.

- Digoxin should be used with particular caution in the elderly and patients with renal impairment.

- Hypokalaemia predisposes to digoxin toxicity.

- Digoxin levels may be increased by drugs such as amiodarone, quinidine, quinine, hydroxychloroquine, verapamil and diltiazem.

- Older patients - loading and maintenance doses of digoxin should be adjusted according to renal function: age, sex and weight need to be considered. A lower maintenance dose is usually adequate in older patients.

- Dose adjustments may be required when changing from IV to oral.

- See Acute Trust guidelines for digoxin administration

2.1.2 Phosphodiesterase inhibitors

Not recommended.
2.2 Diuretics

2.2.1 Thiazides & related diuretics

**First Choice:** Bendroflumethiazide (bendrofluazide)

**Additional Prescribing Advice:**

- Bendroflumethiazide 2.5mg daily is the drug of choice for mild-moderate hypertension. Doses greater than 2.5mg are no more effective due to “dose ceiling” effect.
- Allow 4 weeks for maximal antihypertensive effect of bendroflumethiazide.
- Bendroflumethiazide may be prescribed with furosemide (frusemide) for severe heart failure under hospital supervision; this must be carefully monitored.
- Hypokalaemia and hyponatraemia are common in older people.

2.2.2 Loop diuretics

**First Choice:** Furosemide (frusemide)
**Second choice:** Bumetanide

**Additional Prescribing Advice:**

- Furosemide produces a dose-dependent diuresis within 1 hour if given orally or 30 minutes if given intravenously; duration of action, 6 hours.
- Furosemide 500mg tablets are scored and can be halved. Only for severe oliguria with consultant/nephrology advice.
- Loop diuretics are not recommended for hypertension except in presence of heart failure.

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**Medication for use by hospital only**

Metolozone - for severe resistant oedema only.
Daily monitoring of U&E’s essential.
2.2.3 Potassium-sparing diuretics and aldosterone antagonists

First Choice: Spironolactone or Amiloride

Additional Prescribing Advice:

- Amiloride and spironolactone are weak diuretics with potassium-sparing properties, given with other diuretics if hypokalaemia is a problem; may take 2-3 days for full effect.

- Spironolactone is an aldosterone antagonist used for oedema in hepatic cirrhosis or heart failure, and primary hyperaldosteronism (Note: Dose 100mg-200mg compared with heart failure dose as below)

- Spironolactone 25 - 50mg daily has been shown to reduce mortality in patients with severe heart failure receiving standard therapy including ACE inhibitors; renal function and electrolytes should be monitored.

- Care in patients already on ACE inhibitors as severe hyperkalaemia may occur. Use with caution in renal impairment.

- Eplerenone is licensed post MI in patients with evidence of heart failure.

2.2.4 Potassium-sparing diuretics with other diuretics

First Choice: Co-amilofruse 5/40 (only if compliance with furosemide/amiloride a problem)

Additional Prescribing Advice:

- Combination products containing a diuretic plus potassium do not contain sufficient potassium to correct hypokalaemia and are not recommended.

- Fixed combinations of diuretics should only be considered if compliance is a problem.

- Older Patients - All diuretics have the propensity to cause postural hypotension and thus collapse and falls in older patients.

- Monitor potassium
2.3 Drugs for arrhythmias

Initiation on specialist advice only

Prevention of Supraventricular Arrhythmias (oral)
First Choice: Sotalol or Flecainide
Second choice: Amiodarone

Wolff-Parkinson-White (pre-excitation) Syndrome
First Choice: Flecainide
Second choice: Sotalol or Amiodarone

Drugs used in bradyarrhythmias (acute)
(consider need for pacing)
First Choice: Atropine IV injection

Additional Prescribing Advice:

- Amiodarone may cause corneal microdeposits, thyroid dysfunction, pneumonitis, peripheral neuropathy and hepatotoxicity. Liver-function and thyroid-function tests should be performed before treatment, and 6 monthly thereafter; chest X-ray should be done before treatment.

- Patients receiving amiodarone should avoid exposure of the skin to direct sunlight or sun lamps; a sunscreening product providing SPF 25 should be applied if amiodarone is prescribed (see section 13.8.1).

- Flecainide should not be used in patients with co-existing heart failure/history of myocardial infarction.

- Amiodarone interacts with many drugs. There is a potential for drug interactions to occur for several months after treatment with it has been stopped, due to its very long half life.

- Sotalol may cause atypical VT (torsades de pointes); it should be given with extreme caution with drugs known to prolong the QT interval e.g. erythromycin, chloroquine, haloperidol, lithium, tricyclic antidepressants, chlorpromazine. It should not be used for angina, hypertension, thyrotoxicosis or secondary prevention after myocardial infarction. Sotalol should be avoided in patients on diuretics or with hypokalaemia (see CSM warning).

Medication for use by hospital only
Adenosine i/v - for terminating paroxysmal supraventricular tachycardia.
2.4 Beta-adrenoceptor blocking drugs

Angina/hypertension
First Choice: Atenolol
Second choice: Metoprolol

Heart failure
First Choice: Bisoprolol (Cardicor® is the only brand licensed for heart failure)
Second choice: Carvedilol

Additional Prescribing Advice:

- Atenolol is first choice beta-blocker except for stable chronic heart failure.

- Bisoprolol is first choice beta-blocker for stable, chronic heart failure initiated under specialist supervision. Carvedilol is second-line for patients intolerant of bisoprolol in heart failure.

- Beta-blockers may cause bronchospasm; avoid in patients suffering asthma/COPD.

- Sotalol is only used as an anti-arrhythmic; see section 2.3.

- Propranolol is indicated for treatment of migraine, anxiety, thyrotoxicosis and essential tremor.

- See Acute Trust guidelines for use of beta blockers in heart failure.
2.5 Drugs affecting the renin-angiotensin system & some other antihypertensive drugs

2.5.4 Alpha-adrenoceptor blocking drugs

**First Choice:** doxazosin

**Additional Prescribing Advice:**

- Doxazosin is a third-line agent in the treatment of hypertension. It should be used with caution in patients with heart failure or impaired left ventricular function.

- Doxazosin may cause postural hypotension and first dose hypotension. Treatment should be initiated at the lowest dose possible.

- Doxazosin may be prescribed with other antihypertensive drugs, particularly beta-blockers, in the treatment of hypertension. It may be especially useful in patients with prostatism.

2.5.5 Drugs affecting the renin-angiotensin system

2.5.5.1 Angiotensin-converting enzyme inhibitors

Perindopril or Ramipril

**Additional Prescribing Advice:**

- ACE inhibitors are useful alternatives for hypertension when thiazides are contra-indicated, not tolerated or fail to control blood pressure.

- For heart failure the dose of the ACE inhibitor should be titrated to a ‘target’ dose (or to the maximum tolerated dose if lower). See BNF.

- ACE inhibitors should be considered first-line antihypertensives in diabetics. In those who are intolerant of ACE inhibitors, an angiotensin-II receptor antagonist may be considered as an alternative (see section 2.5.5.2).

- Urea and electrolytes should be checked within 1 week of commencing therapy.

- See Acute Trust Guidelines for use of ACEI in CHF.

- Use of ACE inhibitor with thiazide diuretic after stroke has been shown to reduce recurrence and mortality independent of blood pressure lowering effect (PROGRESS study & see SIGN guidelines and RCP Stroke Guidelines).

2.5.5.2 Angiotensin-II receptor antagonists

**First choice:** Candesartan  
**Second choice:** Irbesartan

**Additional Prescribing Advice**

- Angiotensin-II receptor antagonists should be reserved for patients who develop a persistent cough with ACE inhibitors.
2.6 Nitrates, calcium-channel blockers and potassium-channel activators

2.6.1 Nitrates

First Choice: Glyceryl trinitrate or Isosorbide mononitrate

Additional Prescribing Advice:

- To reduce the risk of nitrate tolerance, isosorbide mononitrate should be given twice daily 6-8 hours apart.
- Long-acting and transdermal nitrate preparations are significantly more expensive than standard formulations. A cost-effective branded long-acting preparation should be prescribed only for patients who have a problem with compliance.
- Isosorbide dinitrate intravenous injection may be given when sublingual or buccal is ineffective in patients with chest pain due to myocardial infarction or severe ischaemia, and in treatment of acute left ventricular failure.

Medications for hospital use only
IV isosorbide dinitrate
2.6.2 Calcium-channel blockers

**Hypertension**
Amlodipine or Nifedipine LA

**Angina**
(a) patients not receiving beta-blocker
Diltiazem
(b) patients receiving beta-blocker
Amlodipine

**Supraventricular arrhythmias**
Verapamil (although other classes should be used in preference)

**Additional Prescribing Advice:**

- Amlodipine has been widely prescribed but is more expensive.
- Nifedipine LA is first choice calcium-channel blocker for hypertension. The brand of different calcium-channel blockers should be specified since different formulations may have different clinical effects.
- Sudden withdrawal of calcium-channel blockers may exacerbate angina; withdraw gradually if ischaemic pain occurs or worsens after starting treatment.
- Short-acting formulations of nifedipine capsules have been associated with large variations in blood pressure and reflex tachycardia; they are no longer recommended for angina or hypertension.
- Diltiazem is first choice calcium-channel blocker for angina if a beta-blocker cannot be used; it is also given for hypertension. It has less negative inotropic effects than verapamil and significant myocardial depression is rare. Use caution if given with beta-blockers due to risk of bradycardia. The most cost-effective brand should be prescribed.
- Verapamil is used for angina, hypertension and arrhythmia; it reduces cardiac output, slows the heart rate and may affect atrioventricular conduction. It may produce heart failure, exacerbate conduction disorders, and high doses may cause hypotension. **It should not be used with beta-blockers.**
2.6.3 Potassium-channel activators

Nicorandil

Additional Prescribing Advice:
• Potassium-channel activators are used when other anti-anginal drugs are insufficient; they have similar efficacy to other anti-anginal drugs in controlling symptoms.

2.6.4 Peripheral and cerebral vasodilators

Cilostazol (initiation by consultant in vascular surgery only)

Additional Prescribing Advice:
• Patients suffering intermittent claudication should be advised to exercise and stop smoking. First-line management of Raynaud's phenomenon includes avoiding exposure to cold and stopping smoking.
• Peripheral vasodilators are of limited value
2.7 Sympathomimetics (For Hospital Use Only)

2.7.1 Inotropic sympathomimetics
First Choice: Dobutamine

2.7.2 Vasoconstrictor sympathomimetics
First Choice: Noradrenaline acid tartrate (norepinephrine bitartrate)

2.7.3 Cardiopulmonary resuscitation sympathomimetics
First Choice: Adrenaline (epinephrine)

Additional Prescribing Advice:
- Inotropic and vasoconstrictor sympathomimetics should preferably be used only in the intensive care setting with invasive haemodynamic monitoring.
- See Acute Trust guidelines for use of dobutamine
2.8 Anticoagulants

2.8.1 Parenteral anticoagulants

Prophylaxis of DVT
First choice: Enoxaparin

Non-ST elevation Acute Coronary Syndrome (NSTEMI)
First choice: Enoxaparin

Treatment of DVT and PE
First choice: Enoxaparin

Additional Prescribing Advice:

- Treatment for DVT & PE with standard heparin/enoxaparin is continued for at least 5 days and until INR is in range for two consecutive readings.

- Heparin is monitored using activated partial thromboplastin time (APTT) to give a patient/control ratio of 1.5-2.5.

- Low molecular weight heparin does not require APTT monitoring; if necessary, anti-factor Xa can be monitored.

- Heparins may induce two types of thrombocytopenia: the first, usually develops within 1-4 days of initiation, is acute, usually mild, and may resolve spontaneously. The second type has an immunological basis and is more serious: it usually occurs after 6-10 days, or more quickly in previously exposed patients, and is often associated with serious thromboembolic complications or bleeding. Serial platelet counts should be measured if heparin is given for longer than 5 days (or sooner if previously exposed), and heparin stopped if thrombocytopenia develops or a 50% reduction in platelet count is seen.

- Protamine sulphate reverses the effects of standard heparin, but only partially reverses the effects of low molecular weight heparins.
2.8.2 Oral anticoagulants

First choice: Warfarin

Additional Prescribing Advice:

- The warfarin dose is adjusted according to the international normalised ratio (INR). The target INR should be clearly identified at initiation of therapy, and measured daily initially, then every 3 days (depending on response) then up to every 12 weeks.

- Indication and duration of treatment and target INR should be clearly recorded at initiation of treatment; the patient-held anticoagulant treatment booklet should be used. See BNF for details.

- The plasma half-life of warfarin is 35 hours; a steady anticoagulant effect is achieved after about one week. If immediate anticoagulation is required, heparin must be given concomitantly.

- There are many clinically important interactions with warfarin; clinicians are strongly advised to consult BNF before prescribing. In addition, many alternative and herbal remedies interact with warfarin and should be discussed with patients.

- Vitamin K (phytomenadione) can be given to reverse the effects of warfarin but takes 6-12 hours to become effective. Immediate reversal of the anticoagulant effect of warfarin may be achieved with fresh frozen plasma or prothrombin complex concentrate; see BNF for details. Specialist haematological advice should be sought.

- Older Patients - Warfarin should be used with caution in patients with confusion or a tendency to fall.

- Lower doses may be required for elderly patients, those with cardiac failure, and those with hepatic and/or renal failure.
2.9 Antiplatelet drugs

Secondary prevention of cerebrovascular disease or myocardial infarction

**First Choice:** Aspirin  
**Second Choice:** Dipyridamole MR (see prescribing notes below)

After an episode of unstable angina or non-ST elevation MI

**First Choice:** Aspirin + clopidogrel (for 12 months)

**Additional Prescribing Advice:**

- The e/c formulation of aspirin 75mg is not recommended.

- The combination of MR dipyridamole and low dose aspirin is recommended for people who have had an ischaemic stroke or a TIA for a period of 2 years from the most recent event. Thereafter, (or if MR dipyridamole not tolerated), preventative therapy should revert to long term low dose aspirin.

- Dipyridamole MR or low dose aspirin may be used with warfarin for prophylaxis of thromboembolism due to prosthetic heart valves.

- After STEMI, aspirin and clopidogrel may be used for up to 4 weeks only, before reverting to aspirin alone. Must be initiated in secondary care and whole 4 week course must be supplied.

- Clopidogrel does **not** represent an alternative to aspirin in patients with a past history of stomach problems (see guidelines)

- See Southport and Ormskirk NHS Trust - Guidelines for clopidogrel prescribing.
2.10 Fibrinolytic drugs

**First Choice:** Tenecteplase

**Additional Prescribing Advice:**

- Thrombolysis is effective if given as soon as possible after acute myocardial infarction; urgent transfer to hospital is essential.

- Tenecteplase has the advantage of availability as a single, weight adjusted, intravenous bolus injection. It can also be used in patients who have previously received streptokinase, suffered a recent streptococcal infection or developed a hypersensitivity reaction to streptokinase.

- If severe bleeding occurs, the fibrinolytic should be discontinued; coagulation factors and/or tranexamic acid may be required

- See MI pathway for contra-indications

2.11 Antifibrinolytic drugs and haemostatics

**First Choice:** Tranexamic acid (for menorrhagia)

**Additional Prescribing Advice**

- The manufacturer recommends regular eye examinations and liver function tests when tranexamic acid is used long-term for hereditary angioneurotic oedema; however, the BNF states that the need for regular eye examinations during long-term treatment is based on unsatisfactory evidence.

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**Medications for Hospital use only**
Drotrecogin alfa - see Acute Trust Guidelines and prescribing checklist
2.12 Lipid-regulating drugs

Statins
First choice: Simvastatin 40mg

Fibrates
First choice: Bezafibrate MR

Additional Prescribing Advice

- NICE guidance (May 2008) recommends Simvastatin 40mg for primary prevention for adults with a greater than 20% 10 year risk of developing CVD. A target is not recommended & repeat lipid measurement is not necessary.
- NICE guidance (May 2008) recommends Simvastatin 40mg for secondary prevention in all patients with CVD. For patients not reaching target on Simvastatin 40mg, consider increasing to Simvastatin 80mg.
- Fibrates have been less well tested in clinical trials. They are mainly of benefit in those with mixed hyperlipidaemia and low HDL cholesterol.
- Ezetimibe may be considered as an option in line with NICE guidance (TA132).
- If statin therapy is added to anticoagulant therapy or a drug/dose change made, an anticoagulant appointment should be made within 7 days - irrespective of which statin involved.
- For patients unable to tolerate Simvastatin, Pravastatin 40mg may be tried.
- For patients with ACS, Simvastatin 80mg should be used as per NICE guidance.
Southport & Ormskirk NHS Trust

Guidelines for Clopidogrel Prescribing
All patients with a history of cardiovascular disease, including previous MI, angina, stroke or TIA, should be treated with aspirin 75mg daily unless contraindicated.

**As an alternative to aspirin**

Clopidogrel 75mg daily should be used as an alternative to aspirin only where
- There is a documented allergy (hypersensitivity) to aspirin
- The patient is truly intolerant of aspirin because of previous GI bleed, active or recent peptic ulcer.
- A patient suffers a CVA despite aspirin therapy. (Please refer to stroke guidelines)

Clopidogrel does not represent an alternative to aspirin in patients with quiescent, old or operated peptic ulcer, mild dyspepsia, hiatus hernia or vague indigestion. Genuine intolerance to aspirin is defined as proven hypersensitivity to aspirin containing medicines or history of severe dyspepsia induced by low-dose aspirin. The best course of action for patients with severe dyspepsia induced by low dose aspirin is uncertain. In the first instance omeprazole could be added in. If this does not work, then Clopidogrel can be tried. **All anti-platelets should be avoided in patients with active bleeding.**

**Non-ST elevation Acute Coronary Syndromes**

After an episode of unstable angina or non-ST elevation MI, aspirin and clopidogrel 75mg can be used together in high risk patients scoring >3 on risk stratification (see Cheshire and Mersey guidelines for the management of patients with non-ST segment elevation acute coronary syndrome (NSTEMI) — see overleaf). When appropriately indicated as above, clopidogrel should be given as an initial 300mg oral dose followed by 75mg daily.

Clopidogrel should be continued in the absence of side effects for a maximum of 12 months at which point it should be stopped and aspirin alone continued, as there is no current evidence of benefit from longer-term prescription. If a cardiologist considers the patient should continue clopidogrel treatment beyond 12 months, he/she should inform the GP in writing and specify the period recommended.
ST elevation Myocardial Infarction

Clopidogrel is licensed, in combination with aspirin, in patients who are having a confirmed ST elevation MI and who are to be medically treated, with or without thrombolytic therapy. However, it is currently not hospital policy to routinely initiate clopidogrel in patients having an acute STEMI. Discuss use with individual patient’s consultant before prescribing.

PCI

Clopidogrel in combination with aspirin will normally be initiated in secondary care for patients undergoing PCI. (Unlicensed indication) This should continue in the absence of adverse effects for a maximum of 12 months at which point it should be stopped by the GP and aspirin alone continued. If a cardiologist considers the patient should continue clopidogrel treatment beyond 12 months, he/she should inform the GP in writing and specify the period recommended.

CABG

The consensus among surgeons regarding post-CABG patients is that they will normally initiate clopidogrel and aspirin in combination to continue for 6 weeks to 12 months. The surgeon should inform the GP in writing of the specific period recommended for clopidogrel treatment. Patients awaiting CABG should stop taking clopidogrel a minimum of 7 days before surgery. A cardiac surgeon may give specific advice to a patient to cease clopidogrel earlier.

Atrial Fibrillation

There is currently no evidence for using clopidogrel to prevent stroke in AF and clopidogrel is unlicensed for this indication. Refer to guidelines.

For specialist indications only, prescribing may be outside the guideline. For example

Clopidogrel can be used as an alternative to aspirin for Myeloproliferative disorders including Essential Thrombocythaemia and Polycythaemia. This is an unlicensed indication, and must be prescribed by a Consultant haematologist only.
SOUTHPORT AND ORMSKIRK NHS TRUST
GUIDELINES FOR THE USE OF BETA-BLOCKERS IN HEART FAILURE

Specialist supervision is required for initiation of B-Blocker therapy

Which patients are suitable?
- Clinically stable patients with all grades of heart failure who are already treated with diuretics and ACE inhibitors and/or Digoxin.
- Consultants and GPs can refer these patients to heart failure team for initiation of beta-blockers.

What is stable heart failure?
- No acute failure for past 6 weeks.
- No changes in HF therapy in past 2 weeks.
- On optimal dose of ACEi.
- Systolic blood pressure > 100mmHg.

SPECIALIST SUPERVISION IS REQUIRED FOR INITIATION OF B-BLOCKER THERAPY

Check for Contraindications
- Asthma, COPD, 2nd or 3rd degree heart block.
- Bradycardia (< 50bpm).
- Sick sinus syndrome.
- Metabolic Acidosis.
- Phaeochromocytoma.
- Liver dysfunction.
- Raynauds Syndrome.
Seek senior medical advice.

SUITABLE FOR TREATMENT INITIATION STEP 1
- Assess for oedema/breathlessness to identify change in condition.
- Check baseline U+Es. If Creatinine > 200umol/L or Urea > 20mmol/L, refer to doctor.
- Check ECG for heart block or bradycardia (< 50bpm).
- Start with low dose.
  - 1st choice agent - Bisoprolol 1.25mg od.
  - 2nd choice agent - Carvedilol 3.125mg bd.
- If systolic BP < 100 mmHg and/or heart rate < 60bpm monitor for 2-3 hours after initiation.
- Check U+Es 3-6monthly for stable patients or as required.
- Explain expected benefits to patient and advise patient of possible side effects and that symptoms may worsen initially. Advise daily weighing.
- Give patient an information leaflet with contact number for advice, and follow up appointment.
- Inform GP by letter.

STEP 2: DOSE TITRATION
- Prior to dose increase monitor blood pressure, heart rate, heart failure symptom control and renal function.
- Check U+Es 1-2 weeks after each dose increase.
- See below for titration schedules.
- Arrange follow up appointment.
- Inform GP by letter.

DOSE TITRATION FOR BETA-BLOCKERS IN HEART FAILURE

<table>
<thead>
<tr>
<th>Bisoprolol (1st choice)</th>
<th>Carvedilol</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.25mg daily for 1 week</td>
<td>3.125mg twice daily for 2 weeks</td>
</tr>
<tr>
<td>2.5mg daily for 1 week</td>
<td>6.25mg twice daily for 2 weeks</td>
</tr>
<tr>
<td>3.75mg daily for 1 week</td>
<td>12.5mg twice daily for 2 weeks</td>
</tr>
<tr>
<td>5mg daily for 4 weeks</td>
<td>25mg twice daily for 2 weeks (or continuous if &lt; 85kg)</td>
</tr>
<tr>
<td>7.5mg daily for 4 weeks</td>
<td>If &gt; 85kg 50mg twice daily thereafter</td>
</tr>
<tr>
<td>10mg daily thereafter</td>
<td></td>
</tr>
</tbody>
</table>

Bisoprolol is licensed for class III-IV heart failure (moderate to severe).
Carvedilol is licensed for class II-III heart failure (mild to moderate).

IF ADVERSE EFFECTS
- Symptomatic hypotension - review other anti-hypertensives (including dose and time of administration of ACEi). If no signs of congestion consider reducing diuretic dose. May need to withhold beta-blocker or leave on lower dose.
- Asymptomatic hypotension does not usually require alteration in therapy.
- If Heart rate < 50 bpm stop beta-blocker or leave on lower dose. Arrange ECG. Review other drugs which may slow the heart e.g. amiodarone, calcium channel blockers.
- If fluid retention occurs (weight increase of more than 1kg or increased symptoms) may require a temporary increase in diuretic therapy.
- If marked fatigue halve dose of beta-blocker.
- If symptoms persist or worsen despite increase in diuretics then a reduction in dose or temporary omission of beta-blocker therapy may be required.

Beta-blockers should not be stopped suddenly unless absolutely necessary (there is a risk of "rebound increase in myocardial ischaemia/infarction and arrhythmias). In severe hypotension, acute pulmonary oedema, cardiogenic shock, symptomatic bradycardia or AV block, beta-blockers can be stopped immediately.
Southport and Ormskirk NHS Trust
Guidelines for Use of ACE Inhibitors (ACEi)/Angiotensin II Antagonists (AIIA) in Heart Failure

Confirmed left ventricular systolic dysfunction

Contra-indications
- Known ACEi/AIIA allergy
- Bilateral renal artery stenosis
- Moderate to severe or Severe aortic stenosis
- Pregnancy
- Hyperkalaemia

Seek senior medical advice

Suitable for ACE inhibitor initiation
Step 1
- Stop potassium supplements/potassium sparing diuretics because of risk of hyperkalaemia with possible exemption of spironolactone.
- Where possible, stop NSAIDs because of risk of renal dysfunction.
- Consider temporarily stopping all diuretics for 24-48 hours before test dose.
- Omit nitrates on the day of the test dose
- Warn patient about possible symptomatic hypotension (i.e. dizziness, lightheadedness)
- Start with low dose ACE inhibitor/AIIA (see below)
- Frail elderly: consider observing for 2 hours for signs of hypotension
- If tolerated, uptitrate to target dose (see below)

IF ADVERSE EFFECTS
- Deterioration in renal function: creatinine increase >50%, or 200umol/L - stop and seek specialist advice. Consider dehydration as the cause. Stop other nephrotoxic drugs e.g. NSAIDs
- Symptomatic hypotension: systolic BP<100mmHg: Review other anti-hypertensives and/or reduce dose of ACEi/AIIA.
- Intolerable cough: consider angiotension II receptor antagonist, e.g. candesartan, if there are no CI. Initiation as per ACEinhibitor
- Allergy/Angioedema or C/I to ACEi/AIIA: Consider hydralazine and nitrate, seek specialist advice.
- K+>5.9mmol/L - check that potassium supplements/sparing diuretics have been discontinued and for evidence of renal dysfunction
- If K+ > 6.0mmol/L or creatinine ↑ >100% or > 350umol/L, STOP ACEi/AIIA and seek advice

Seek senior Medical advice before starting ACEi/AIIA
- Creatinine >200 micromol/L
- Urea >12mmol/L
- Sodium < 130mmol/L
- Systolic BP <100mmHg
- Diuretic dose > furosemide 80mg od or bumetanide 2mg od
- Frail elderly
- Unilateral renal artery stenosis

Suitable for ACE inhibitor initiation

Step 2: REVIEW AFTER ONE WEEK
- Check urea, creatinine, electrolytes
- Check for adverse effects e.g. symptomatic hypotension (systolic BP<100mmHg), renal dysfunction (creatinine increase >50%), hyperkalaemia (K+>5.9mmol/L), intolerable cough, loss of taste, rashes, abdominal pain, headache, weakness.

Step 3: REVIEW AFTER ONE MONTH
- Titrate to target dose. Inform GP by letter
- Check urea, creatinine, electrolytes and for adverse effects as above.

Step 4: Repeat urea, creatinine, electrolytes and BP
- If the patient becomes unwell
- If there is a dose change
- Every 3-6 months in every case

Target Doses for ACE inhibitors/Angiotensin II Antagonists in Heart Failure

<table>
<thead>
<tr>
<th>Drug</th>
<th>Starting Dose</th>
<th>Titration Steps</th>
<th>Heart Failure Target Dose</th>
<th>Licensed Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perindopril</td>
<td>2mg od</td>
<td>2</td>
<td>4mg-8mg per day</td>
<td>Heart failure, hypertension</td>
</tr>
<tr>
<td>Ramipril</td>
<td>1.25mg od</td>
<td>4</td>
<td>10mg per day (single or divided dose)</td>
<td>Heart failure, hypertension, post MI, reduction of risk of cardiovascular events in patients over 55 with C/V disease or in patients with diabetes and risk factors for C/V disease</td>
</tr>
<tr>
<td>Candesartan</td>
<td>4mg</td>
<td>3</td>
<td>32mg</td>
<td>Heart failure, hypertension</td>
</tr>
</tbody>
</table>

Third Edition. Original Adapted from University Hospital Aintree
by Laura Gibson/Nicky Hennessy, Cardiology Pharmacist, and Barbara Flowers, Heart Failure Nurse.
Approved by Dr Pulya, Consultant Cardiologist
General notes

- Prescribers should refer to the ‘British Guideline on the Management of Asthma’ produced by the British Thoracic Society (BTS) and SIGN (see www.sign.ac.uk). For chronic obstructive pulmonary disease (COPD) refer to: BTS guidelines for COPD and use of nebulisers (www.brit-thoracic.org.uk); Global Initiative for Chronic Obstructive Lung Disease (www.goldcopd.com); NICE Clinical Guideline 12 (www.nice.org.uk). See BNF section 3.1.1.
- Chlorofluorocarbon (CFC) in metered dose inhalers (MDIs) is gradually being replaced by non-ozone-depleting propellants such as hydrofluorocarbons; doses are not always equivalent.
- Changing the type of inhaler device may affect the effectiveness of therapy and the incidence of adverse effects.
- Generally, manually actuated pressurised metered dose inhalers (MDIs) are the cheapest devices available and should be first choice provided that the patient can use them efficiently. When use is inefficient, alternatives include spacers, dry powder inhalers (DPIs) or breath-actuated MDIs (e.g. Autohaler, Easi-Breathe®). Choice of device should be considered on basis of cost, patient-acceptability and ability to use the inhaler. If a patient elects not to use a prescribed spacer, then an alternative device should be used. All newly diagnosed asthmatics should be given a spacer.
- Inhaler-induced cough by MDI is an indicator for change of device or use of a spacer.
- It is essential to specify inhaler device, strength and dose.
- Not all spacers are compatible with all inhalers; users should seek advice from their local pharmacist regarding the appropriate spacer to be used.
- Older patients may have difficulty using any inhaler device due to reduced hand strength, poor inspiratory effort, or confusion. Individual assessment is required.
3.1 Bronchodilators

3.1.1 Beta_2 agonist bronchodilators

(a) Short-acting beta_2-agonist bronchodilators

First choice: Salbutamol inhaler CFC-free
Second choice: Terbutaline inhaler

Additional Prescribing Advice

• There is virtually no difference in efficacy between salbutamol and terbutaline; currently salbutamol is cheaper and available in a wider range of devices.
• Inhalation is preferred to oral administration because it provides more rapid relief and causes fewer side-effects.
• Short-acting beta_2-agonist bronchodilators should only be prescribed on a "when required" basis for rescue therapy (except for patients with COPD who may use regularly)

(b) Long-acting beta_2-agonist bronchodilators

First choice: Salmeterol or formoterol (eformoterol)

Additional Prescribing Advice

• In patients with asthma, long-acting beta_2-agonists should only be prescribed when they are already receiving inhaled corticosteroids.
• Currently formoterol is slightly cheaper than salmeterol,
3.1.2 Antimuscarinic bronchodilators

*Mild symptoms of COPD*
**First choice:** ipratropium bromide

*Moderate-severe symptoms of COPD*
**First choice:** tiotropium

**Additional Prescribing Advice**

- The principal role of regular inhaled ipratropium is in the management of COPD. Tiotropium is only licensed for COPD.
- For maximum benefit, ipratropium should be administered 4 times daily.
- Generally tiotropium has greater efficacy than ipratropium. It has the advantage of once daily administration but is not available in as wide a range of formulations as ipratropium. Patients who are unable to manage the HandiHaler® device, or who receive no additional benefit, should be trialled with the Respimat device or switched to ipratropium.
- Tiotropium is not suitable for the relief of acute bronchospasm and must not be given in combination with ipratropium. Patients with very severe COPD who are receiving regular home nebulisers should not be prescribed tiotropium in addition.

3.1.3 Theophylline preparations

**First choice:** theophylline (Uniphyllin Continus®)
aminophylline (injection- hospital only)

**Additional Prescribing Advice**

- Theophylline is a bronchodilator used for reversible airways obstruction, which may have an additive effect when used with small doses of beta₂-adrenoceptor stimulants; this combination may increase the risk of side-effects including hypokalaemia.
- Theophylline has a narrow margin between therapeutic and toxic effects; therapy should be monitored.
- Different brands of modified-release theophylline have different bioavailability: the brand to be dispensed must be specified. Uniphyllin Continus® has been selected on the basis of uniformity of drug release and cost; patients maintained on other theophylline preparations need not be changed.
- Intravenous aminophylline is not a recommended drug in primary care having been superseded by nebulised beta₂-agonists.
- Theophylline and aminophylline interact with many drugs; see BNF for details.
- Smoking cessation may increase theophylline levels.
- Older Patients - Theophylline preparations should be used with caution due to increased potential for drug interactions and risk of arrhythmia.

**Medications for hospital use only**

- Caffeine citrate oral solution/injection (unlicensed) - paediatric use only. See Acute Trust Neonatal Drug Monographs
- Aminophylline injection
3.1.4 Compound bronchodilator preparations

Additional Prescribing Advice

• In patients with severe COPD requiring regular nebulised bronchodilators, salbutamol 2.5mg and ipratropium 500micrograms can be prescribed separately or as a combined product (Combivent® nebuliser solution).

3.1.5 Peak flow meters, inhaler devices and nebulisers

Additional Prescribing Advice

• Measurement of peak flow is helpful for patients who are unable to detect deterioration in their asthma, and for those with moderate or severe asthma. Mini-Wright® and Vitalograph® peak flow meters are the most commonly prescribed.

• New peak flow meters (identified by EU or CE marks) give different readings compared to old meters. These readings need to be interpreted using new published predicted equations (see www.airwaysextra.com/AJJune2004-Miller-published.pdf).

• Spacer devices may be useful for patients with poor inhalation technique, children, and for those prone to oral candidiasis with inhaled steroids. They should be prescribed for patients receiving high dose steroids (>800micrograms/day of beclometasone or budesonide; >400micrograms/day fluticasone).

• Spacers should be cleaned no more than monthly with water and washing-up liquid, and allowed to air dry. More frequent cleaning affects their performance due to build up of static.

• Nebulisers are not currently prescribable in general practice; patients should be referred for respiratory assessment. A spacer should be tried before considering a nebuliser – they are more efficient than nebulisers with the only difference being the dose of bronchodilator administered.

• All nebulisers should be serviced regularly. However, difficulties are often encountered in the servicing of privately owned nebulisers.
3.2 Corticosteroids

(a) inhaled corticosteroids

First choice: beclometasone (Clenil modulite®)
Second choice: budesonide
or fluticasone

Additional Prescribing Advice

• Beclometasone inhalers must be prescribed by brand due to the different potencies of available brands.
• Beclometasone is first choice because it is as effective but less expensive than alternative steroid inhalers at standard equivalent doses.
• When considering doses, beclometasone dipropionate and budesonide are equipotent and fluticasone is twice as potent (see BTS guidelines).
• At doses greater than 800 micrograms daily of beclometasone, a spacer device should always be used.
• Second choice corticosteroids could be considered for those patients with sub-optimal control despite doses of 800 micrograms or more daily of beclometasone.
• Patients receiving more than 1500 micrograms daily of beclometasone or budesonide (or 750 micrograms of fluticasone) may have some systemic effects and should be given a steroid card.
• Patients on high doses of inhaled steroids (more than 1000 micrograms/day of beclometasone dipropionate or equivalent) who receive more than three to four courses of oral steroids per year should be considered for bone protection. See section 6.6 (c).
• Asthma guidelines suggest patients may do better with moderate doses of steroid (400-800 micrograms beclometasone dipropionate) plus a long-acting beta₂-adrenoceptor stimulant rather than increasing the steroid dose.
• Inhaled corticosteroids for COPD should only be prescribed for patients who have had two or more exacerbations needing treatment with antibiotics or oral corticosteroids a year. They may be useful in patients whose steroid responsiveness has been demonstrated by either a trial of inhaled or oral steroids.
(b) other corticosteroids

First choice: prednisolone (oral)
or hydrocortisone (intravenous)

Additional Prescribing Advice

• For an exacerbation of COPD, prednisolone 30mg should be prescribed for 7-14 days and then stopped; there is no advantage in prolonged therapy.
• Intravenous hydrocortisone is used in the management of acute severe asthma.
• Hydrocortisone sodium succinate is recommended in preference to hydrocortisone sodium phosphate which has been associated with perineal irritation.

(c) combination products

First choice: Symbicort® (budesonide plus formoterol)
or Seretide® (fluticasone plus salmeterol)

Additional Prescribing Advice

• Ideally, in asthma, Symbicort® (or Seretide®) should only be used when formoterol (or salmeterol) and inhaled steroids have been given separately before, and patients are stable on established doses. They can be a cost-effective alternative to the individual products and are more convenient to use.
• Choice will depend on the selected inhaled steroid and preferred device
• Seretide Accuhaler® is designed to be administered as 1 blister per dose, in contrast to Evohaler® which should be administered as 2 puffs of the appropriate inhaler strength.
• Inhaled corticosteroids for COPD should only be prescribed for patients who have had two or more exacerbations needing treatment with antibiotics or oral corticosteroids a year.

Medications for hospital use only

• Croup - Dexamethasone oral solution 2mg in 5ml – unlicensed special 0.3mg/kg
  or budesonide nebulas 2mg.
  See Acute Trust Paediatric protocols.
3.3.1 Cromoglicate

First choice: sodium cromoglicate (Adults only)
(sodium cromoglycate)

Additional Prescribing Advice

- Sodium cromoglicate has largely been superceded by inhaled corticosteroids but may have a role in some adults as add-on therapy or with exercise-induced asthma.

3.3.2 Leukotriene receptor antagonists

First choice: montelukast

Additional Prescribing Advice

- Montelukast is indicated for add-on therapy in mild-moderate persistent asthma, and to prevent exercise-induced bronchospasm.
- If montelukast is prescribed between steps 2 and 3 of the BTS guidelines (see BNF), symptoms and peak expiratory flow should be monitored and treatment stopped if there is no demonstrative benefit within 4 weeks.
- Leukotriene receptor antagonists should not be used to relieve an attack of acute severe asthma.
3.4 Antihistamines and allergic emergencies

3.4.1 Antihistamines

*Sedating*: chlorphenamine (chlorpheniramine)
*Less-sedating*: cetirizine
*Paediatrics*: Promethazine

Additional Prescribing Advice

- Antihistamines may be of value in the treatment of nasal allergies, especially hay fever, and vasomotor rhinitis. They reduce rhinorrhoea and sneezing but are usually less effective for nasal congestion.
- Oral antihistamines are of value in preventing urticaria and are used to treat urticarial rashes, pruritus, and insect bites and stings; they are also used in drug allergies.
- Cetirizine causes less sedation than chlorphenamine but is more expensive; it is available over-the-counter.
- Acrivastine may be a suitable alternative for patients who develop sedation with cetirizine.
- First choice preparation for allergic rhinitis is beclometasone nasal spray (see section 12.2.1).
- Chlorphenamine is more liable to cause drowsiness in older patients.
- Fexofenadine may be used for chronic idiopathic urticaria.
3.4.3 Allergic emergencies

Adrenaline (epinephrine)
Chlorphenamine (chlorpheniramine)
Hydrocortisone

Additional Prescribing Advice

- Adrenaline should be given immediately for an acute anaphylactic reaction (laryngeal oedema, bronchospasm and hypotension).
- Chlorphenamine injection is a useful adjunctive treatment given after adrenaline injection and continued for 24-48 hours to prevent relapse.
- Hydrocortisone injection is of secondary value in the initial management of anaphylactic shock because the onset of action is delayed for several hours, but should be given to prevent further deterioration in severely affected patients.
- Atopic individuals are particularly at risk of anaphylactic reactions; patients with known severe allergy to insect stings, foods or peanuts should carry, and receive instruction for the use of, prefilled syringes (e.g. EpiPen®) for self-administration. Patients should usually be prescribed two.

Medications for Hospital Use Only

3.5 Respiratory stimulants & pulmonary surfactants

- Doxapram injection/infusion
- Poractant alfa
- See Acute Trust Neonatal Drug monograph
3.6 Oxygen

General considerations

- As from 1 February 2006, the new integrated home oxygen service was introduced, with Air Products providing cylinder, concentrator and ambulatory oxygen service to the North West.
- As recommended in the Royal College of Physicians (RCP) Working Group report on assessing and prescribing oxygen therapy, specialist teams will be able to authorise oxygen therapy in the home, recognising their expertise in assessing patients’ long term and complex oxygen therapy needs. Thus, following specialist assessment or review, a patient does not also need to visit his/her GP surgery for an oxygen prescription.
- GPs can continue to prescribe oxygen - for example for symptomatic relief in palliative care or where a patient has short burst oxygen needs. If a patient requires long term or ambulatory oxygen, the GP can refer patients to the specialist team to assess and prescribe for particular needs.
- Oxygen is a drug and should therefore be prescribed. Inappropriate concentrations may have serious or even lethal effects.
- Patients should be advised of the fire risks with oxygen and they or their contacts must not smoke in the same environment.
- The prescription should include the percentage of oxygen to be administered (24%-100%) by specified mask type and flow rate. For nasal cannulae, the oxygen flow rate in L/minute should be specified.
- Oxygen improves alveolar oxygen tension but this improvement should not occur at the cost of producing a decompensation in the acid-base status of the recipient.
- High concentration oxygen therapy (35%-100%) is used for short periods of time in cases of Type I Respiratory Failure (e.g. asthma, pulmonary embolism, pneumonia, congestive cardiac failure, pulmonary fibrosis) where there is a combination of a low arterial oxygen and normal or low carbon dioxide concentration. If an asthmatic develops acute carbon dioxide retention, high flow oxygen should be continued and mechanical ventilation considered. Humidification should be used routinely with high concentrations.
- Low concentration oxygen therapy (24% - 28%) is used for patients with Ventilatory Failure (Type II Respiratory Failure) [although high concentrations are often used on initial presentation for a short time] and is most commonly prescribed in chronic obstructive pulmonary disease (COPD). The aim is to improve hypoxia without producing acid-base decompensation.
Practical aspects of appropriate oxygen prescription

- Arterial blood gas should be checked 30-60 minutes after starting oxygen therapy (or sooner if the patient deteriorates) to assess oxygenation and acid-base status. Aim for a $P_a O_2 > 8kPa$ with a compensated $P_a CO_2$, $H^+$ and $HCO_3$ status.
- The inspired oxygen concentration must always be documented beside the arterial blood gas result to allow meaningful comparisons between results to be made.
- It is usually necessary to wait at least 20 minutes after any change in inspired oxygen concentration (including administration of a nebuliser) before rechecking a blood gas to allow time for equilibration.
- Oximetry should be used as a means of non-invasively assessing continuous or intermittent oxygen status (aim for $SaO_2 > 92\%$).
- Oxygen therapy should be discontinued at least 24 hours before planned discharge (unless the patient has domiciliary oxygen) and oximetry documented in the case notes.

Long Term Domiciliary Oxygen Therapy (LTOT)

- Patients with stable Type II Respiratory Failure may be candidates for Long Term Domiciliary Oxygen Therapy (LTOT) if they have stopped smoking and have a $P_a O_2 < 7.4 \ kPa$ whilst breathing room air during a period of stability at least one month after any exacerbation of their airways disease.
- Oxygen should be used for at least 15 hours/day.
- The concentrator can deliver 2 - 4L/min. For COPD 2L/min would be standard. A rate of 4L/min would be used under specific circumstances of palliative care or pulmonary fibrosis.
- If a patient is unable to use nasal cannulae, a mask may be provided. Ventimask Mark IV 28% is the appropriate choice.
- Portable oxygen cylinders are available on the NHS.
### Medications for Hospital Use Only

#### 3.7 Mucolytics

**First choice:**
- Dornase alfa for cystic fibrosis
- Nebulised saline for bronchiectasis
- Carbocysteine suspension for spinal unit only

**Additional Prescribing Advice**

- Dornase alfa is used in some patients with cystic fibrosis when they have been shown to respond. See acute trust paediatric guidelines.
- Nebulised saline is commonly used in hospital for patients with bronchiectasis.

Carbocysteine may be considered for a trial in COPD patients who have a chronic productive cough (as per NICE guidance)

#### 3.8 Aromatic Inhalations

**First choice:** Benzoin Compound Tincture inhalation

#### 3.9 Cough preparations

**Not Recommended**

**Additional Prescribing Advice**

- The BNF recommends that cough preparations should be avoided as there is little evidence to support their use.
- For persistent cough lasting 4-6 weeks, the underlying cause should be established.

### Medications for Hospital Use Only

Pleurodesis: Talc or bleomycin

Chapter 4 - Central Nervous System

4.1 Hypnotics and anxiolytics

4.1.1 Hypnotics

First choice: no treatment
Second choice: temazepam

Additional Prescribing Advice
- Non-drug treatments recommended as first-line interventions include sleep hygiene and stimulus control advice.
- Routine prescribing for insomnia is undesirable. Temazepam should be used in short courses only when insomnia is severe, disabling, or subjecting the individual to extreme distress.
- Hypnotic medication should only be initiated in hospital if essential and not continued beyond discharge.
- There is no evidence that newer hypnotics (zaleplon, zolpidem, zopiclone) provide any additional clinical benefit or are free from dependence (see NICE TA77).
- New patients should not be put on a repeat prescription system and existing patients receiving an hypnotic should be reviewed and offered the chance to stop or reduce (see BNF withdrawal protocol).

4.1.2 Drugs used in the treatment of anxiety

(a) acute anxiety state
First choice: diazepam

Additional Prescribing Advice
- Benzodiazepines are indicated for the short-term relief (2-4 weeks only) of anxiety that is severe, disabling or subjecting the individual to unacceptable distress. The use of benzodiazepines to treat short-term "mild" anxiety is inappropriate and unsuitable.
- Treatment should be limited to the lowest possible dose for the shortest possible time.
- Diazepam has a long duration of action and rapid onset. It is the recommended daytime anxiolytic and is used as premedication before surgery and other procedures. See section 15.1.4.1
- Beta-blockers (e.g. propranolol) are useful for reducing autonomic symptoms, such as palpitations and tremor in performance anxiety (e.g. public speaking or a musical performance). See section 2.4.
(b) anxiety disorders

General notes
- Diagnosis and treatment can be difficult and in some cases specialist advice or referral will be necessary.
- Treatment options for panic disorder and generalised anxiety disorder include psychological, pharmacological and self-help approaches. Trauma focused psychological therapy is the first line treatment for PTSD. Choice of treatment in individual cases will usually be determined by patient preference, service availability and the severity of the condition. (see NICE guidance 22)
- There is evidence that SSRIs are effective for anxiety disorders, however the licensed indications are different for each. Paroxetine is licensed for the majority of anxiety disorders whereas fluoxetine is only licensed for obsessive-compulsive disorder.
- The available data for paroxetine does not suggest an increased risk of suicidal behaviour in adults aged 18 or over, however, an increased risk in some young adults cannot be ruled out. Young adults treated with paroxetine should be carefully monitored throughout treatment.
- Due to the risk of withdrawal reactions, patients taking paroxetine should not stop the drug suddenly. Cessation of treatment should involve a very gradual downward titration. If intolerable symptoms develop it may be necessary to reinstate the previously prescribed dose and withdraw more gradually.
- Due to the risk of gastro-intestinal bleeding, SSRIs should be used with caution in patients aged over 80 years, those with prior upper gastro-intestinal bleeding, or in those also taking aspirin or another NSAID.

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<tr>
<th>Older Patients - SSRI s</th>
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<td>SSRIs should be used with caution in patients over 80 years due to the risk of gastro-intestinal bleeding.</td>
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</table>
4.1.3 Barbiturates

Additional Prescribing Advice
- Barbiturates [CD] should only be prescribed to patients already taking them, who have severe intractable insomnia, when attempts to discontinue treatment have been unsuccessful.
- Barbiturates are used in the treatment of epilepsy (section 4.8.1) and anaesthesia (section 15.1.1).
4.2 Drugs used in psychoses and related disorders

4.2.1 Antipsychotic drugs

(a) treatment of acute psychoses by GP

First choice: chlorpromazine
Second choices: haloperidol or sulpiride

Additional Prescribing Advice

- Indications for antipsychotics include schizophrenia and other psychoses, mania and short-term adjunctive management of psychomotor agitation.
- Antipsychotics should be initiated with caution in the first episode (i.e. start with low dose), and monitored carefully due to the risk of adverse effects.
- Haloperidol is a high potency antipsychotic with a high incidence of extrapyramidal side-effects; sulpiride is useful for those who cannot tolerate haloperidol.
- NICE recommend starting an atypical antipsychotic at the earliest opportunity where there are acute symptoms of schizophrenia.

(b) treatment of acute psychoses by specialists in secondary care

As above plus:

amisulpride, olanzapine, quetiapine, risperidone, clozapine (hospital only)

Additional Prescribing Advice

- The above atypical antipsychotics should be initiated by specialists.
- Amisulpride may increase prolactin and cause agitation and anxiety. However, it is less likely to cause hypotension, sedation, weight gain, and anticholinergic and extrapyramidal side-effects.
- Olanzapine can cause weight gain and sedation.
- Quetiapine can be sedative and can cause weight gain but is less likely to cause hyperprolactinaemia
- Risperidone is associated with a dose dependent increase in extrapyramidal side-effects, especially at doses of 6mg daily and above.
- Risperidone orodispersible tablets and olanzapine orodispersible tablets should be reserved for the treatment of acute episodes of schizophrenia in patients who are uncooperative or wary of taking oral medication. They are not intended for long-term use.
- Clozapine should be initiated and maintained by specialists, and dispensed by hospital. Patients must be registered with the Denfleet Clozapine Monitoring Service (DCMS). Clozapine can cause serious side-effects such as agranulocytosis, seizures, cardiomyopathy and myocarditis. Gastro-intestinal obstruction and paralytic ileus may also occur.
Hyperglycaemia has been reported in patients treated with atypical antipsychotics. Patients with diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus who start atypical antipsychotics should undergo fasting blood glucose testing at the beginning of, and during, treatment. Any patient receiving atypical antipsychotics should be monitored for symptoms of hyperglycaemia e.g. polydipsia, polyuria, polyphagia, weakness. Patients who develop symptoms of hyperglycaemia during treatment should undergo fasting blood glucose testing. Hyperglycaemia may resolve when the atypical antipsychotic is discontinued but some patients require continuation of anti-diabetic treatment.

(c) maintenance treatment of psychoses

- Patients should remain on the antipsychotic which controlled their symptoms unless symptoms return or side-effects are intolerable; the dose should be monitored and reviewed regularly with specialist advice.
- Specialist advice should be sought before discontinuing antipsychotics due to the risk of relapse

(d) antipsychotics for older patients

Antipsychotics are frequently prescribed in the management of behavioural disorders associated with dementia. Other forms of management should also be considered before prescribing antipsychotics. It is important to remember that such behaviour can be a temporary phenomenon and that drugs should be prescribed on a short-term basis. In the elderly, antipsychotics should be used with caution because of the side-effect profile, including extrapyramidal symptoms, sedation, anticholinergic effects, cardiovascular effects and tardive dyskinesia.

First choices: haloperidol
sulpiride
olanzapine

Additional Prescribing Advice

- Antipsychotics should be considered when behavioural disorders are accompanied by hallucinations and/or delusions (see SIGN Publication Number 22).
- Haloperidol is an effective drug in the elderly. It can cause extrapyramidal symptoms and should be avoided in those with parkinsonian symptoms or Lewy body dementia. It should be used in small doses e.g. 500micrograms to 3mg, and can be given once daily. Sulpiride is a suitable alternative antipsychotic for the elderly because of a lower incidence of side-effects. It can be started at 100mg once daily and slowly increased according to response.
- MHRA do not recommend risperidone or olanzapine for behavioural symptoms in elderly patients with dementia due to an increased risk of stroke.
4.3 Antidepressant drugs

Drug treatment of major depression

Newly diagnosed depression:

**First choice:** fluoxetine

**Second choice:** citalopram or sertraline in the elderly

Recurrence of depression:

**First choice:** previously successful antidepressant e.g. amitriptyline

Additional Prescribing Advice

- Antidepressants are not recommended for the initial treatment of mild depression because the risk-benefit ratio is poor.
- In general, clinical trials have established little or no difference in efficacy between the various antidepressants. There is some evidence that tricyclic antidepressants (TCAs) are more effective than serotonin re-uptake inhibitors (SSRIs) in severe depression. They all have a delayed onset of action of 2-4 weeks.
- If previous treatment with any antidepressant has been successful it should be considered again for treatment of recurrence.
- Treatment should normally be continued for at least 6 months after response.
- Patients who have had 2 or more previous episodes of depression may benefit from long-term antidepressants at therapeutic doses.
- Fluoxetine is an SSRI; it is better tolerated than TCAs. It is first choice because dose instructions are simpler than with other SSRIs and it is less likely to cause a withdrawal reaction. It is also the most cost-effective SSRI now that a generic is available.
- Fluoxetine is the only SSRI shown to have a favourable balance of risks and benefits for the treatment of depressive illness in under 18’s.
- Citalopram is an SSRI which may be better tolerated and has fewer drug interactions than most other SSRIs and is a useful alternative to fluoxetine when there is concomitant agitation.
- Patients who have had a recent cardiovascular event should be prescribed sertraline, it has less negative effects on the QT interval.
- Traditionally a sedative TCA may have been prescribed for anxious patients and patients with significant insomnia. An alternative strategy may be to prescribe trazodone or a formulary SSRI (plus a benzodiazepine for no longer than 1-2 weeks.)
- Amitriptyline is a sedating TCA which has a high incidence of side-effects and can be lethal in overdose. However, it is well established in general practice and may still be useful for those who have responded to it previously.
- Dosulepin (dothiepin) is not recommended due to its association with ischaemic heart disease, cardiac arrhythmias and fatalities following overdose.
- All antidepressants may be associated with a discontinuation syndrome and, if taken continuously for 6 weeks or longer, should be withdrawn gradually unless a serious adverse effect has occurred.
Due to the risk of gastrointestinal bleeding, SSRIs should be avoided if possible, or used with caution, in patients aged over 80 years, those with prior upper gastrointestinal bleeding, or in those also taking aspirin or another NSAID.

**Antidepressants for treatment of anxiety disorders**

For acute anxiety state, see section 4.1.2(a))

**Older Patients - Hypnotics and anxiolytics**

Hypnotics and anxiolytics should be avoided in older patients if possible. Older patients can become ataxic, confused and are at increased risk of falling and injuring themselves. Trazodone is useful in the management of agitation, irritability and at times aggression in older people. It is relatively safe and the dose can be titrated against the symptoms.

**Older Patients - SSRIs**

SSRIs should be used with caution in patients over 80 years due to the risk of gastrointestinal bleeding. If an SSRI is required, then paroxetine or sertraline should be prescribed. Fluoxetine is not recommended in older patients due to its long half-life and the risk of adverse effects such as agitation.
4.4 Central nervous system stimulants

(a) narcolepsy

First choice: modafinil

Additional Prescribing Advice

- Modafinil is a useful treatment for many patients with narcolepsy and should be initiated by a specialist.
- Supervision should remain the responsibility of the hospital staff for the first 3 months or until objective evidence of effectiveness has been provided.
- Dexamfetamine sulphate or methylphenidate hydrochloride may be prescribed by specialists when modafinil is ineffective.

(a) attention deficit hyperactivity disorder (ADHD)

First choice: methylphenidate

Additional Prescribing Advice

- Methylphenidate is a useful treatment for some children with severe forms of ADHD as part of a comprehensive treatment programme when remedial measures alone prove insufficient. It is licensed for children aged 6 years and above.
- Patient selection is important and therefore initiation and titration of treatment should be carried out by a child/adolescent psychiatrist, or a paediatrician working in a dedicated specialist clinic.
- Because of its substantially greater costs, methylphenidate m/r (Concerta® XL or Equasym® XL) should be restricted to second-line therapy and used only in exceptional circumstances where the supervising clinician has clear evidence of compliance problems with midday dosing. Use of the m/r formulation reduces flexibility of dosage which can be a disadvantage for many children and parents.
- A shared care protocol is available which provides information about prescribing in hospital and general practice.
4.5 Drugs used in obesity

**First choice:** diet and lifestyle changes

**Second choice:** orlistat (GP only)

**Additional Prescribing Advice**

- Diet and lifestyle changes are the mainstay for management of obesity
- Before commencing drug therapy, patients should enter a minimum 3 month structured weight management programme to confirm that they can comply with dietary restriction.
- Drug treatment may be considered in patients as part of an overall treatment plan for managing obesity, who have a BMI > 30kg/m², or BMI > 28kg/m² plus associated risk factors
- Patients should be informed that drug therapy will be discontinued after 3 months if they fail to lose 5% of their initial body weight since starting drug treatment. (Less strict goals may be appropriate for people with type 2 diabetes.) Further courses should only be considered after a suitable period and patients should again demonstrate the ability to lose weight on a suitable diet.
- Continue for longer than 12 months (usually for weight maintenance) only after discussing potential benefits and limitations with the patient.
- Common side-effects with orlistat may be limited by dietary compliance (decreased fat intake).
- Sibutramine may be a suitable alternative to orlistat. The contraindications and side effects of the drug should be carefully considered.
- Patients receiving sibutramine require regular blood pressure and pulse rate monitoring, as it has caused clinically relevant increases in blood pressure in some patients.
  - First 3 months measure BP and pulse every 2 weeks.
  - Second 3 months measure BP and pulse monthly.
  - Thereafter measure regularly at a maximum interval of three months
- Treatment with sibutramine is not recommended beyond the licensed duration of 12 months.
- The European Medicines Agency (EMEA) has recommended the suspension of the marketing authorisation for rimonabant. The EMEA’s Committee for Medicinal Products for Human Use (CHMP) has concluded that the benefits of Accomplia no longer outweigh its risks and the marketing authorisation should be suspended across the European Union (EU).
4.6 Drugs used in nausea and vertigo

(a) Drugs for the treatment of nausea and vomiting

Gastric stasis
First choice: metoclopramide
Second choice: domperidone

Migraine (see section 4.7.4)
First choice: metoclopramide
Second choice: domperidone

Motion sickness
First choice: cyclizine
Second choice: hyoscine (ENT only)

Opioid-induced (not palliative care)
First choices: metoclopramide
or prochlorperazine

Additional Prescribing Advice

- Metoclopramide can cause acute dystonic reactions, usually in the young (especially girls and young women) and the very old. Benzatropine (benztropine) may be given by intramuscular or intravenous injection if acute dystonic reactions occur (dose, 1-2mg repeated if symptoms reappear). If benzatropine is not readily available, then intravenous diazepam may be prescribed.
- Long-term metoclopramide and prochlorperazine may cause tardive dyskinesia in the elderly.
- Domperidone does not cross the blood brain barrier; it is less likely than metoclopramide and prochlorperazine to cause sedation or dystonic reactions.
- Note that cyclizine has potential for abuse.
- Granisetron may be prescribed on specialist advice for postoperative nausea and vomiting for high risk patients.
- Surgical patients receiving morphine should be prescribed prophylactic anti-emetics such as cyclizine or prochlorperazine as required.
- See also Trust PONV guidelines.
(b) drugs for the treatment of labyrinthine vertigo

First choices: cinnarizine
or prochlorperazine

Additional Prescribing Advice
• These products are only effective for labyrinthine vertigo.
• Prochlorperazine buccal tablets may be a suitable alternative for patients who are vomiting.

Older Patients - Prochlorperazine
Prochlorperazine should not be prescribed for "dizziness" in older patients due to the risk of drug-induced parkinsonism, postural hypotension and mental confusion

(c) treatment of Meniere’s disease

Additional Prescribing Advice
• Prochlorperazine or cinnarizine may be used short-term for the acute treatment of Meniere’s disease.
• Betahistine and thiazide diuretics should be reserved for prophylaxis in patients with a proven diagnosis of Meniere’s disease.
4.7 Analgesics

General management of pain

- For dysmenorrhoea, see section 7.0.1 (a).
- For musculoskeletal and joint pain (including gout), see Chapter 10.
- For migraine, see section 4.7.4.
- For palliative care, see separate guidelines.

The treatment of acute and chronic pain follows the general principles developed by the World Health Organisation (WHO):

Step 1 mild pain: use NSAID and/or paracetamol

\[
\text{Pain persisting or increasing}
\]

Step 2 mild to moderate pain: use codeine plus paracetamol and/or NSAID

\[
\text{Pain persisting or increasing}
\]

Step 3 moderate to severe pain: use morphine plus paracetamol and/or NSAID

Step 1 (mild pain)
First choices: paracetamol
ibuprofen

Second choice: naproxen

Additional Prescribing Advice

- Relative contra-indications to NSAIDs include heart failure, hypertension, renal impairment, peptic ulceration; absolute contra-indications include proven hypersensitivity to aspirin or any NSAID.
- NSAIDs may worsen asthma; they are contra-indicated if aspirin or any other NSAID has precipitated attacks of asthma.

Step 2 (mild to moderate pain)
First choice: paracetamol + codeine 30mg
+/- ibuprofen or naproxen

Second choice: dihydrocodeine 30mg + paracetamol 1g
+/- ibuprofen or naproxen
Additional Prescribing Advice

- Compound analgesics containing an opioid may produce opioid side-effects and can complicate treatment of overdosage.
- Codeine is an inefficient analgesic in approximately 10% of patients who are unable to convert it to morphine.
- The Committee on Safety of Medicines has recently concluded that the efficacy of co-proxamol is poorly established and the risk of toxicity in overdose is unacceptable. Co-proxamol products have been withdrawn. For further information and advice see: http://medicines.mhra.gov.uk/aboutagency/regframework/csm/csmhome.htm
- The evidence that tramadol offers any advantage over compound analgesics in patients with moderate acute pain is weak; it should not be considered as a first choice analgesic. It should be reserved for patients in whom constipation poses a major threat (e.g. after bowel surgery) or who experience unacceptable sedation or respiratory depression with other opioids.
- Amitriptyline may be a useful adjunct for chronic pain (unlicensed see sec. 4.7.3).
- Management of postoperative pain should follow hospital acute pain guidelines.
- For greater flexibility, codeine and paracetamol should be prescribed concomitantly as separate drugs (instead of as co-codamol).

Step 3 (moderate to severe pain)

**First choice:** morphine sulphate or diamorphine injection
+ paracetamol
+/- NSAID (ibuprofen or naproxen)

Additional Prescribing Advice

- Morphine should be given parenterally when possible for acute severe pain. The first dose of intravenous morphine should be given slowly, titrated to effect, and respiratory rate monitored. For use of naloxone, see section 15.1.7.
- In chronic non-malignant pain the long-term use of opioids has many implications. Extensive guidance is given on the Pain Society website (www.britishpainsociety.org). Ideally a single practitioner and pharmacy should take primary responsibility for prescribing and dispensing opioids for individual patients; in most cases, day-to-day medical responsibility will lie with a general practitioner. Fixed supplies of these drugs should be prescribed at fixed intervals. Complete analgesia is rarely achievable and then only at the expense of side-effects such as cognitive impairment.
- Chronic pain is not simply a physical problem. It is associated with severe and extensive psychological, social and economic factors. Non-pharmacological treatments are often worthwhile. Consider specialist referral for additional services, e.g. Pain Clinic.
A balance has to be found between the lowest dose of morphine required to improve function versus higher doses required to abolish symptoms. Treatment dose should be discussed with the patient. The initial dose is determined by the age and frailty of the patient, and previous exposure to opioids.

For chronic non-malignant pain, if an opioid is required, treatment may be initiated with low dose modified-release morphine. Treatment with regular opioids should be reviewed regularly. Laxatives should be prescribed.

For postoperative pain refer to relevant acute pain protocols.

Oral oxycodone may be prescribed on specialist advice for patients with severe non-malignant pain in whom morphine is ineffective or not tolerated.

Fentanyl patches should be reserved for patients whose pain is constant and stable, with prior exposure to opioids, who have difficulty swallowing or have problems with compliance or renal impairment.

Paracetamol 1g/100mL infusion (Perfalgan®) may be prescribed by specialists for the short-term treatment of moderate and severe pain following surgery when administration by the intravenous route is clinically justified by an urgent need to treat pain and/or when other routes of administration are not possible.

Older Patients - Opioids

Older patients are particularly susceptible to respiratory depression and constipation secondary to opioids.

MHRA - NSAID guidance

MHRA review of Cardiovascular safety of COX-2 inhibitors and non-selective NSAIDs

Some non-selective NSAIDs may be associated with a small increased risk of thrombotic events such as heart attack or stroke. The lowest effective dose of non-selective NSAID should be prescribed for the shortest possible time. Evidence for diclofenac suggests that it has a thrombotic risk profile similar to that of at least one coxib (etoricoxib) and possibly others. There is some evidence that naproxen may have a lower risk of heart attacks or strokes than selective COX-2 inhibitors.

Ibuprofen is a non-selective NSAID that has been available in low doses for many years as an over-the-counter medicine for short term use. Current evidence does not suggest an increased thrombotic risk for short-term, low dose treatment with ibuprofen; however, high-dose ibuprofen (which is not available over the counter) may be associated with a small increased thrombotic risk.

Less evidence is available for other NSAIDs, but it is possible that they may be associated with a small risk of thrombotic events, especially with long duration of treatment and high doses. The MHRA will continue to monitor closely the safety of all non-selective NSAIDs and coxibs, and will issue updated advice as evidence becomes available.
Opioid Conversion

**Example**

Patient previously taking 180mg MST, orally. Required to be converted to subcutaneous diamorphine.

1) Total Daily Dose = 180 x 2 = 360mg morphine, orally

2) Conversion: oral morphine to subcutaneous diamorphine = ÷ 3 (see chart)

360mg ÷ 3
= 120mg diamorphine subcutaneously via syringe driver.

3) Breakthrough dose of diamorphine as 1/12 to 1/6 of the total daily dose given up to hourly as needed

120mg ÷ 12 = 10mg
120mg ÷ 6 = 20mg

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**Please contact the specialist palliative care services for advice and help e.g. using alfentanil in renal failure, conversion to methadone etc.**

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**Contacts**

<table>
<thead>
<tr>
<th>Person</th>
<th>Umbrella House</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palliative Care Team</td>
<td>01704 704540</td>
</tr>
<tr>
<td>Specialist Pharmacist</td>
<td>01704 517922</td>
</tr>
<tr>
<td>Steven Simpson</td>
<td></td>
</tr>
<tr>
<td>(9am - 5pm Mon—Fri)</td>
<td><a href="http://www.queenscourt.org.uk">www.queenscourt.org.uk</a></td>
</tr>
</tbody>
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Information can also be accessed from carer & patient resource pages of Queenscourt Hospice website.
4.7.3 Adjuvant analgesics for chronic pain

First choice: amitriptyline (unlicensed indication)

Prescribing notes
- There is evidence that tricyclic antidepressants have analgesic efficacy in a variety of chronic pain syndromes and their use should be considered where conventional analgesics are proving of limited benefit in the chronic situation.
- Tricyclic antidepressants (TCAs) appear to be more effective than other classes of antidepressants. Amitriptyline has been the most studied but other TCAs such as imipramine have similar benefits and may be chosen in an attempt to avoid side-effects such as sedation.
- Patients should be warned of likely side-effects and that, unlike conventional analgesics, the medication may have to be taken regularly for 4-6 weeks before the full analgesic effect may be appreciated.
- The analgesic effect of amitriptyline is attained at a lower dose than that required to treat depression.
- Laxatives should be considered for patients receiving regular amitriptyline.
- Amitriptyline should be used with caution in the elderly and patients with glaucoma or prostatic hypertrophy. It should be taken early evening to avoid next day sedation.

Older Patients — Amitriptyline In the older patient, amitriptyline is particularly likely to cause postural hypotension, urinary retention and constipation.

Neuropathic pain

First choice: amitriptyline (unlicensed indication)
Second choice: gabapentin
Cream: capsaicin cream 0.075% (Note - only after lesions healed)

Additional Prescribing Advice
- Neuropathic symptoms are characterised by a description of tingling, burning or shooting pains. There may also be allodynia (pain elicited by a non-noxious stimulus e.g. light touch) and hyperalgesia (pain that is of inappropriate severity to a noxious stimulus)
- Patients should be warned of likely side-effects and that, unlike conventional analgesics, medication may have to be taken regularly for 4-6 weeks before the full analgesic effect is appreciated
- Carbamazepine is first choice for trigeminal neuralgia.
- Consider specialist referral.
• Pregabalin is for use only by specialist pain team due to relative lack of efficacy over gabapentin.

• When prescribing amitriptyline, an initial dose of 10-25mg at night should be increased on a weekly basis up to 75mg if tolerated. A 10mg dosage escalation should be used for the elderly, and 25mg for younger patients. The maximum dose tolerated should be continued for 4 weeks. If no benefit is seen after this time try gabapentin.

• Gabapentin should also be tried for 4 weeks. Patients should be titrated as per BNF. (If patients cannot tolerate 300mg titrations, a 100mg dosage escalation can be tried for 4 weeks).

4.7.4 Antimigraine drugs

4.7.4.1 Treatment of the acute attack

(a) mild to moderate migraine

First choices: aspirin
ibuprofen
paracetamol

use in combination

Additional Prescribing Advice

• Soluble analgesics are absorbed quickly and have a more rapid effect than non-dispersible tablets.

• Aspirin, ibuprofen or paracetamol at full dose (i.e. 600-900mg aspirin, 400-600mg ibuprofen, or 1g paracetamol) are often effective.

• Metoclopramide or domperidone tablets or suppositories may be necessary to relieve nausea, and have the advantage of promoting gastric emptying and normal peristalsis.

• Diclofenac suppositories may be useful for pain relief if vomiting occurs during migraine.

• These analgesics may be useful for tension type or daily headache. However, chronic overuse of aspirin and paracetamol, particularly in combination with codeine, may cause medication overuse headache. Combination analgesics should therefore be avoided.

• Aspirin should not be given to patients under 16 years due to the risk of Reye’s syndrome, unless specifically indicated.

• Metoclopramide can cause acute dystonic reactions especially in patients under 20 years of age. Domperidone may be better tolerated.
(b) moderate to severe migraine

First choice: sumatriptan (oral)
Second choices: zolmitriptan or rizatriptan

Additional Prescribing Advice

- Ensure diagnosis of migraine is correct. Triptans are expensive and ineffective in most other types of headache.
- Medication should be taken as early as possible after migraine headache starts, but not during the aura phase. Headache recurrence within the first 24 hours can be treated with a second dose. If the first dose of a triptan fails to help, alternative (analgesic) medication should be considered.
- Nasal zolmitriptan may be a suitable alternative if oral preparations are ineffective. If this is ineffective, then subcutaneous sumatriptan should be considered, or alternatively intramuscular diclofenac.
- Overuse of triptans (more than 4 doses per week) should be discouraged due to the risk of medication overuse headache.
- Sumatriptan 50mg and 100mg are equally efficacious. Sumatriptan 50mg produces fewer side-effects and is considered the optimum dose.
- Parenteral opioids should be avoided in migraine. Intramuscular diclofenac or ketorolac is preferred if parenteral analgesia is required.

4.7.4.2 Migraine prophylaxis

First choice: propranolol
Second choice: sodium valproate (unlicensed)

Additional Prescribing Advice

- Migraine prophylaxis is justified for attacks occurring more than twice per month, or when less frequent attacks are particularly severe and prolonged.
- Sodium valproate can be a useful alternative in some patients; liver function should be monitored (see BNF section 4.8.1).
- Sodium valproate should not routinely be prescribed to women of child bearing potential. If there is no effective alternative, explain risks during pregnancy and importance of using adequate contraception.
- Other drugs that may be considered are pizotifen and amitriptyline. Amitriptyline may be particularly useful if there is co-existent sleep disturbance and/or tension type headache.
- Prophylaxis should be given for 3-6 months, then consideration given to gradual withdrawal if there has been a good response.
4.7.4.3 Drug treatment of cluster headache

(a) acute attacks

First choice: sumatriptan subcutaneous (or nasal)

Additional Prescribing Advice

- Oral medication is usually ineffective for acute attacks
- High flow oxygen (70-100% at 7L/min for 10-15 minutes at onset of attack) is a useful addition to sumatriptan. The oxygen is administered through a high flow regulator and tight fitting mask. The appropriate mask can be supplied by the hospital clinic. The regulator is available for short-term lease on a trial basis or can be purchased from the Organisation for the Understanding of Cluster Headaches (OUCH). See www.clusterheadaches.org.uk.
- During a cluster, patients may suffer more than one attack daily and require up to 2 doses of sumatriptan in a 24 hour period.

(b) prophylaxis

First choice: verapamil
Second choice: lithium (Priadel®)

Additional Prescribing Advice

- Prophylaxis is indicated during a cluster of attacks (approximately 1-3 months) and should be withdrawn one month after headaches cease.
- Resistant cases may benefit from a short course of prednisolone 60mg daily reducing gradually over 2-3 weeks, then stopped.
- Most patients will require specialist care
4.8 Antiepileptics

4.8.1 Control of epilepsy

First choices: Carbamazepine - for partial seizures and secondary generalised tonic-clonic seizures
sodium valproate - for primary generalised epilepsy (including absences and myoclonus), partial seizures, secondary generalised tonic-clonic seizures
lamotrigine - for primary generalised epilepsy (including absences and myoclonus), partial seizures, secondary generalised tonic-clonic seizures

The above drugs should control approximately 70% of patients singly or in combination. In situations where epilepsy remains poorly controlled, other drugs may have to be used usually on specialist advice.

Additional Prescribing Advice

- Different preparations may vary in bioavailability; it may be prudent to avoid changing the formulation to avoid reduced effect or excessive side-effects.
- The choice of agent is determined by the type of seizure, and age and sex of patient.
- Antiepileptic medication should be commenced after two or more clinically definite seizures or after one seizure in a patient with a clearly epileptiform EEG or causative lesion on brain imaging. Treatment may also be considered after a single attack if the risk of a second seizure is considered to be high.
- If a second fit occurs before the patient is seen by a specialist then start first choice agent. Phone specialist if advice required.
- Antiepileptic drugs which induce hepatic enzymes may impair the efficacy of oral contraceptives; see BNF for details.
- Lamotrigine is now regarded as a first choice agent. However, it may reduce the effectiveness of oral contraceptives. In addition, the dose of lamotrigine may need to be adjusted in women who commence or stop oral contraceptives, or who become pregnant while taking lamotrigine.
- All antiepileptic drugs carry a risk of teratogenicity. Increasing the number of drugs increases the risk; ideally, women planning to conceive should use adequate contraception until on monotherapy. Lamotrigine and sodium valproate should not be taken concomitantly during pregnancy.
- Dose-related side-effects of carbamazepine may be reduced by using the modified-release formulation.
- If first choice agent fails at maximum tolerated dose, gradually change over to another first choice agent. If monotherapy fails, a combination of first choice agents may be tried.
- Routine plasma drug level monitoring is generally unnecessary unless side-effects are a problem, non-compliance is suspected, or phenobarbital or phenytoin are administered. Monitoring is seldom of value for patients on sodium valproate.
• Therapy should be reviewed within the 1st month to assess seizure control, compliance, side-effects (blood tests if required). Therapy should be reviewed at 6 weeks; if seizures are not controlled and there are no unacceptable side-effects, the dose should be increased.

• Gradual withdrawal of antiepileptic drugs can be considered with caution after 2 years free of seizures but note implications for driving. Specialist advice should be sought.

• If patients are established on vigabatrin, the potential for long-term visual side-effects should be considered.

• Primidone is likely to be withdrawn from the market in the future.

4.8.2 Treatment of prolonged seizures and status epilepticus

Status epilepticus is defined as seizures which last for more than 30 minutes or a series of seizures which takes place without the patient regaining consciousness in between them.

In primary care:
First choice: diazepam rectal solution

In hospital:
First choice: lorazepam injection (see trust guidelines)
Second choice: buccal midazolam (Epistatus ®)
                  or phenobarbital (phenobarbitone) inj.
                  or phenytoin injection

Additional Prescribing Advice

Primary care
• Where possible, treatment should be initiated in the community prior to hospital.
• A possible underlying cause (e.g. hypoglycaemia, hypoxia etc) must be considered.
• The first episode of status epilepticus should be treated with rectal diazepam if available, and an ambulance should be called.
• Treatment should be given if convulsion lasts longer than 5 minutes.

Secondary care
• If convulsion continues beyond 30 minutes (status epilepticus), patient will need hospitalisation and preferably admission to ITU.
• Although the BNF recommends lorazepam injection, this requires refrigeration and may therefore not be suitable for GP use.
• Clobazam may be prescribed to prevent status epilepticus in patients with a previous history of status or who are known to be at risk if their seizures accelerate or begin to cluster. It may also be prescribed for those whose seizures occur or accelerate at certain times e.g. during menstruation or intercurrent infections. Prescriptions should be endorsed ‘SLS’.
4.9 Drugs used in parkinsonism and related disorders

People with suspected Parkinson's Disease should be referred quickly and untreated to a specialist with expertise in the differential diagnosis of this condition. They should be reviewed regularly by the specialist - medication should only be changed on the advice of the specialist.

Anti-parkinsonian medication should not be withdrawn abruptly or allowed to fail suddenly due to poor absorption (for example gastroenteritis, abdominal surgery) to avoid the potential for acute akinesia or neuroleptic malignant syndrome. It is extremely important that patients admitted to hospital or a care home have their medication at the correct times which may not coincide with the times of drug rounds.

4.9.1 Dopaminergic drugs used in parkinsonism

**Levodopa**

**First choice:** co-benaldopa or co-careldopa

**Additional Prescribing Advice**
- Evidence suggests that there is no value in using modified-release levodopa preparations to delay the onset of motor complications and these products are therefore not recommended for this purpose.
- In patients who have already developed levodopa induced motor complications, modified-release preparations may be of benefit, but are not drugs of first choice

**Dopamine receptor agonists**

**First choice:** pramipexole or ropinirole

**Additional Prescribing Advice**
- In most cases, ergot-derived dopamine agonists (bromocriptine, cabergoline, lisuride and pergolide) should be avoided because of the extra monitoring required due to the risk of pulmonary, retroperitoneal and pericardial fibrotic reactions
- May be used to reduce motor fluctuations in patients with levodopa induced symptoms

**Monoamine-oxidase-B inhibitors**

Selegiline or rasagiline (consultant only)

**Additional Prescribing Advice**
- May be used to reduce motor fluctuations in patients with levodopa induced symptoms
Catechol-O-methyltransferase inhibitors

First choice: entacapone (consultant only)
Combination product with co-careldopa; Stalevo

Additional Prescribing Advice
• Consider Stalevo® only for patients on a stable dosage of levodopa with dysphagia or other problems affecting compliance

Amantadine
Reserved for patients in whom other drug classes cannot be used. (consultant only)

4.9.2 Antimuscaranic drugs used in parkinsonism

First choice: trihexyphenidyl hydrochloride (benzhexol hydrochloride)

Second choice: Procyclidine

Additional Prescribing Advice
Reserved for patients, typically young with early disease and severe tremor in whom other classes cannot be used.

• Apomorphine - may be initiated by consultant only.
4.10 Drugs used in substance dependence

**Alcohol withdrawal Outpatients and general practice**

**First choice:** chlordiazepoxide

**In-patients**

**First choices:** diazepam
or chlordiazepoxide

**Additional Prescribing Advice**
- For in-patients refer to alcohol withdrawal protocols.
- To gain control of severe symptoms, adjunctive treatment may be necessary. Haloperidol may be considered.
- Benzodiazepines have dependence potential. To minimise risk of dependence, administer short-term only. Benzodiazepines should not be prescribed if the patient is likely to drink alcohol concomitantly.
- Choice of benzodiazepines:
  - (a) Chlordiazepoxide is first choice oral agent for outpatients and general practice alcohol withdrawal, because it has less abuse potential and 'street value' than diazepam.
  - (b) Diazepam or chlordiazepoxide are used for in-patients (refer to local protocol). A reducing course over 2 to 3 days may be prescribed by a hospital clinician on discharge.
  - (c) Diazepam is first choice for in-patients if the parenteral route is required.
  - (d) In liver failure, oxazepam should be considered due to its shorter duration of action and fewer metabolites.

**Older Patients - Benzodiazepines**
Caution needs to be exercised when benzodiazepines are prescribed in older patients since accumulation may result in oversedation

**Maintenance of abstinence**

These treatments are an adjunct to counselling

**First choices:** disulfiram
or acamprosate

**Additional Prescribing Advice**
- Choice of treatment will be influenced by patient acceptability; disulfiram is prescribed for patients who would benefit from a deterrent, particularly if they can nominate a partner who can help them to take it regularly.
• Patients receiving disulfiram suffer unpleasant systemic reactions if alcohol is consumed.
• Disulfiram self-administration should be supervised by, for example, a partner or an appropriate nurse, or at a day hospital.
• Acamprosate should be initiated as soon as possible after alcohol withdrawal and maintained if the patient relapses. Repeated relapsing to heavy drinking indicates non-efficacy. Recommended treatment period is 1 year.

Vitamin supplementation
Prophylaxis of Wernicke-Korsakoff syndrome

First choices: thiamine (vitamin B1)
          or parenteral vitamins B and C (Pabrinex®)

Treatment of patients with Wernicke-Korsakoff syndrome (hospital in-patients)

First choice: parenteral vitamins B and C (Pabrinex®)

Additional Prescribing Advice
• Refer to local alcohol withdrawal protocols.
• Prophylactic doses of parenteral vitamins (Pabrinex®) should be given to patients at risk of Wernicke-Korsakoff syndrome e.g. those with recent diarrhoea, vomiting, poor diet, other physical illness or signs of weight loss or malnutrition. The patient may have been consuming more than 20 units of alcohol per day.
• Oral thiamine is indicated for less severe cases while receiving detoxification treatment for 5 to 7 days. Patients who resume drinking or continue to drink and are at risk of malnourishment should be given oral thiamine 50mg or 300mg daily, according to local protocol, on a long-term basis.
• Patients with any sign of Wernicke-Korsakoff syndrome must be given treatment doses of parenteral vitamins (Pabrinex®) in hospital. Signs include confusion, ataxia, ophthalmoplegia/nystagmus, memory disturbance, hypothermia and hypotension, coma/unconsciousness.
• Pabrinex® should usually be administered in hospitals or health centres where facilities for treating anaphylaxis are available.

Nicotine dependance
Follow NICE guidance TA39 and TA 123.
Varenicline
NRT
Bupropion
4.11 Drugs for dementia

*For Mental Health Team initiation:*

- *donepezil*
- or *galantamine*
- or *rivastigmine*

- Referrals should be made in the usual way to the Mental Health Trust if any doctor considers that a patient may have Alzheimer’s disease and may be suitable for treatment.
- Treatment should not be initiated by GPs.
Chapter 5 - Antimicrobial Prescribing

See Antimicrobial Guidelines 2008
6.0 Endocrine System

6.1 Drugs used in diabetes

6.1.1 Insulins

General notes
- Choice depends on the particular needs of the individual patient, taking into account lifestyle, age, preference and capabilities. Patients should not be changed from the insulin that they are currently receiving without advice from a specialist or a clinician with the appropriate skills and expertise.
- Type of insulin, device and needle size should be specified. Care should be taken to write the brand name in full to avoid errors such as, for example, administration of Humalog® in place of Humalog® Mix25 or Humalog® Mix50.
- Insulin glargine (Lantus®) and detemir (Levemir®) should only be prescribed for those type II diabetics who are at risk of, or experience frequent and/or severe nocturnal hypoglycaemia on attempting to achieve better glycaemic control during treatment with established insulins, or for those who require administration by a carer. Insulin detemir is a long-acting insulin analogue used as a basal insulin. It may be prescribed for patients attempting to minimise the risk of hypoglycaemia as it may cause less intra-individual variation in glycaemic profile than established isophane insulins (see NICE TA 053).
- Insulin is available in 3mL cartridges, 10mL vials, and 3mL disposable pens. Not all insulin cartridges fit all pens.
- The B-D Safe-Clip® device snaps the needle off insulin syringes and stores the needle safely inside the clipper; this device is available on prescription. Sharps bins are also prescribable.

6.1.2 Oral hypoglycaemic agents

**Biguanides**
First choice: metformin

**sulphonylureas**
First choice: gliclazide

**glitazones**
First Choice: pioglitazone (*)

Additional Prescribing Advice
- First-line treatment for management of type 2 diabetes is usually a trial of dietary therapy unless there is intercurrent infection, severe hyperglycaemia or severe osmotic symptoms.
- Patients commencing blood glucose lowering agents should inform the DVLA and their car insurance company.
- Those with type 2 diabetes may require treatment with insulin, either alone or in combination with oral agents.
- Aspirin is recommended for all people with type II diabetes >50 years old and in younger people if had disease >10 years or are hypertensive or have retinopathy/nephropathy.
**Biguanides and sulphonylureas**

- Metformin is the first choice oral hypoglycaemic drug. It is the only oral antidiabetic drug which has a proven survival advantage. It does not need to be limited to overweight patients. There is no proven benefit in prescribing the MR formulation although it can be useful in patients who cannot tolerate therapeutic doses of ordinary metformin.
- Due to the rare but serious risk of lactic acidosis, metformin should be avoided in patients with: significant renal impairment (glomerular filtration rate (GFR) less than 50mL/min or serum creatinine greater than 150micromol/L); alcoholism with previous pancreatitis; severe cardiac/respiratory disease producing tissue hypoxia; severe liver disease with potential for hepatic failure; severe infection (sepsis)
- Metformin may cause gastro-intestinal adverse effects; it should be started at low dose and taken after meals, and the dose gradually increased every 10-15 days if tolerated.
- Hypoglycaemia is not a problem with metformin monotherapy.
- Metformin and sulphonylurea combination therapy is the first treatment choice where monotherapy has failed to achieve adequate glycaemic control. Patients unable to take metformin and sulphonylurea in combination due to an intolerance or contraindication to one of the drugs, may be prescribed a glitazone as an alternative to injected insulin. The glitazone should replace the drug that is poorly tolerated or contraindicated in the combination. In addition, pioglitazone can be used as **triple oral therapy** in combination with metformin and a sulphonylurea, in patients with insufficient glycaemic control despite dual oral therapy - this combination should usually be initiated in secondary care.
- The addition of sitagliptin can be considered if a sulphonylurea is contra-indicated or not tolerated.

**Glitazones and combination treatment**

- Avandamet® is **not recommended** for routine use.
- Liver function should be checked before initiating glitazones and periodically thereafter based on clinical judgement. Glitazones should not be used in patients with hepatic impairment.
- Glitazones can cause weight gain and fluid retention. They must not be used in patients with heart failure or history of heart failure
- Glitazones are substantially more expensive than other hypoglycaemic agents and may take 8 weeks to achieve maximal hypoglycaemic effect.

* Pioglitazone is first line agent. Rosiglitazone is not currently recommended because of the possible increased risk of cardiovascular events. Continuation of existing rosiglitazone therapy can be considered where patients are already stabilised on treatment
6.1.2.3 Incretin mimetic

First choice: Exenatide sc injection (Consultant initiation only for patients with BMI>35)

Additional Prescribing Advice
- Exenatide is a newly licensed incretin mimetic for type II diabetes in combination with metformin/sulphonylureas in patients not controlled on maximum tolerated doses of these. It is not licensed for use in combination with glitazones. It causes a 2-4% weight loss compared to a 2% weight gain with insulin. As morbidity/mortality data are not yet available, its place in therapy is yet to be established. Exenatide might be a viable alternative to insulin/glitazones in patients with a BMI>35 or in patients where insulin/glitazones are not tolerated.
- When transferring a person from a combination of metformin and another oral agent to insulin or exenatide continue the metformin and stop the other oral agents.

6.1.4 Treatment of hypoglycaemia

See Acute trust guidelines
Choice of treatment depends on the clinical situation and includes:
- glucose (oral)
- glucagon injection
- glucose intravenous infusion 50%
- hypostop gel

Additional Prescribing Advice
- Following administration of glucagon, it is important to give supplementary carbohydrate to restore liver glycogen and prevent secondary hypoglycaemia.
- Although intravenous glucose is the more effective treatment where intravenous access is readily available, intramuscular glucagon may be more appropriate.
- Glucagon injection may be repeated once after 10 minutes if necessary, but intravenous glucose is preferable. If there is no response, then hospital admission should be considered.
6.1.6 Glucose monitoring agents in diabetes mellitus

Meters are not available on prescription. Patients may purchase any meter but should do so only following expert advice from a suitably trained person. Strips may be prescribed and can also be bought over-the-counter.

(a) capillary blood glucose monitoring

Additional Prescribing Advice

• Home blood glucose monitoring need not be performed by:
  * those treated by diet alone where HbA1c is <6.5%
  * those who are well controlled on metformin and/or glitazone and stable as indicated by HbA1c <7.5%
In these cases, a six-monthly estimate of HbA1c is adequate to monitor glycaemic control.
• Home blood glucose monitoring in non-insulin treated Type 2 diabetes and steroid-induced diabetes should be undertaken (see chart):
  * where control is poor
  * where treatment change is indicated especially where there is a risk of hypoglycaemia
  * to monitor a treatment change
  * in patients on sulphonylureas with symptoms which may be due to unrecognised hypoglycaemia
In such cases, blood glucose monitoring should not need to be performed routinely on more than 2 days in the week or more than twice in the day although in some cases more frequent testing may be required. The timing of the samples will depend on the particular case but a fasting value is useful. Correct meter care and quality control are essential when meters are used.
• Patients must be aware of how to interpret the results.
• Meters are obtainable from centres with expert advice from a suitably trained person.
• Strips deteriorate rapidly if exposed to the atmosphere.

(b) urine testing for glucose

First Choice: Multistix®

Additional Prescribing Advice

• Urine testing may be appropriate in those with Type 2 diabetes, unless the renal threshold for glucose is high. A 2 hour post-prandial specimen will indicate urinary glucose levels at their highest. A negative result on a first-voided morning sample suggests good glycaemic control overnight. A negative test will not indicate hypoglycaemia, and if this is suspected, blood glucose testing should be performed.
• Patients must be aware of how to interpret the results.
• Strips deteriorate rapidly if exposed to the atmosphere.
(c) urine testing for ketones

Additional Prescribing Advice

- It is important to test for urinary ketones where there is a significant risk of ketoacidosis, such as may occur with significant intercurrent illness.
- Strips deteriorate rapidly if exposed to the atmosphere.

6.2 Thyroid and antithyroid drugs, and parathyroid disease

6.2.1 Hypothyroidism

First choice: levothyroxine (thyroxine)

Additional Prescribing Advice

- Prior to treatment it is important to establish that TSH is elevated thus confirming primary hypothyroidism. A normal or low TSH suggests pituitary or hypothalamic disease for which specialist referral is necessary.
- In elderly patients, especially those with cardiac disease, treatment should be introduced more cautiously.
- Thyroid stimulating hormone should be checked 6 weeks after starting thyroxine or after any change in dose, then annually once stable.
- Dose may need increasing in pregnancy.
- Myxoedema coma is a rare medical emergency and, in a semi-comatose patient, the clue might be a low plasma sodium. Treatment should be specialists using liothyronine (L-try-iodothyronine) by intravenous injection.
6.2.2 Hyperthyroidism

Radioactive iodine is increasingly used as first choice for thyrotoxicosis; its efficacy may be compromised by prior antithyroid drug therapy.

(a) antithyroid drugs

To be initiated on specialist advice

First choice: carbimazole

Additional Prescribing Advice

- Carbimazole 20-40mg daily may be given with levothyroxine 100-125micrograms daily in a block and replace regimen, usually for 18 months.
- Carbimazole has rarely been associated with bone marrow suppression and treatment should be stopped promptly if there is clinical or laboratory evidence of neutropenia. Patients should be asked to report symptoms and signs suggestive of infection, especially sore throat, mouth ulcers or skin rashes. A white blood cell count should be performed if there is any clinical evidence of infection.
- Propylthiouracil may be an alternative for patients who suffer sensitivity reactions to carbimazole.
- Thyrotoxic crisis needs emergency specialist treatment including all, or combinations of, medications such as intravenous fluids, iv propranolol, hydrocortisone sodium succinate (100mg every 6 hours), iodine oral solution, carbimazole.
- Pregnant patients receiving carbimazole must be monitored and administered the lowest effective dose.

(b) beta-blockers

First choice: propranolol

Additional Prescribing Advice

- Beta blockade can be withdrawn once hyperthyroidism is controlled (2-6 weeks), and the patient maintained on carbimazole.
6.2.3 Parathyroid disease

(a) hyperparathyroidism

*Treatment of hyperparathyroidism is surgical although emergency medical therapy is available including intravenous sodium chloride, furosemide (frusemide) and pamidronate. Specialist referral is indicated.*

(b) hypoparathyroidism

First choice: alfacalcidol (1α-hydroxycholecalciferol)

Additional Prescribing Advice

- If hypercalcaemia occurs, alfacalcidol should be stopped and restarted when plasma calcium is normal (usually within a week).
- Supplemental calcium (usual dose 1-2g daily) may be required in addition to alfacalcidol. Care should be taken to avoid hypercalcaemia.

6.3 Corticosteroids

(a) replacement therapy

First choice: hydrocortisone
fludrocortisone

Additional Prescribing Advice

- In Addison’s disease (primary adrenal failure) hydrocortisone (glucocorticoid) and fludrocortisone (mineralocorticoid) are given. In acute adrenocortical insufficiency, intravenous hydrocortisone sodium succinate 100mg is given every 6-8 hours. The extracellular fluid deficit (usually 3-4 litres) should be replaced by: sodium chloride intravenous infusion 0.9% with glucose intravenous infusion 5%; 1litre is given during the first hour, and the remainder over 12-24 hours.
- In secondary adrenal failure (hypopituitarism), hydrocortisone is given alone, there being no mineralocorticoid deficiency.
- Patients deficient in glucocorticoids do not respond adequately to stress and should be advised to double the replacement dose of hydrocortisone for several days if significantly unwell. More serious illnesses or gastro-intestinal disturbances necessitate prompt parenteral hydrocortisone.
(b) pharmacological therapy

First choices: prednisolone
    dexamethasone
    hydrocortisone
    methylprednisolone

Additional Prescribing Advice

• For use of corticosteroids in the treatment of asthma, see section 3.2.
• For use of corticosteroids in the treatment of musculoskeletal and joint disorders see sections 10.1.2 and 10.2.3.
• For use of corticosteroids in dermatology, see section 13.4.
• Patients receiving 7.5mg or more of prednisolone daily (or equivalent; see BNF section 6.3.2) for longer than 3 months should be assessed and where necessary receive osteoporosis prophylaxis. No osteoporosis prophylaxis is indicated when corticosteroids are used as replacement therapy. See section 6.6 (c).
• Care should be taken in reducing pharmacological doses of glucocorticoids if the patient has been treated for longer than 3 weeks to avoid cortisol insufficiency due to prolonged suppression of the hypothalamic-pituitary-adrenal (HPA) axis.
• In terms of their anti-inflammatory properties, approximately 20mg hydrocortisone (oral) is equivalent to 5mg prednisolone or 750micrograms dexamethasone. See BNF section 6.3.2.

6.4 Sex hormones

6.4.1 Hormone replacement therapy (HRT) for menopausal symptoms

General notes

Short-term treatment of menopausal symptoms

• HRT should generally only be prescribed for menopausal symptoms and not for prevention of osteoporosis or cardiovascular disease.
• It is recommended that the lowest dose of HRT based on relieving menopausal symptoms should be prescribed.
• Oral HRT regimens are well tolerated, cheaper than patches and should be considered as first-line therapy in most women.
• Transdermal regimens should be considered in women intolerant of or unable to take oral HRT, or theoretically in those with some gastro-intestinal and liver problems. Transdermal HRT carries less risk of venous thromboembolism and should be used preferentially in women with cardiovascular risk factors.
• There is significant individual variation in response to HRT, and it is often appropriate to try two or three different preparations. Women should be encouraged to persevere with a new preparation for 2-3 months as any side-effects experienced initially may settle with time.
Women should be reviewed three months after commencing therapy. The on-going need for HRT should be reassessed at least annually. Blood pressure should be checked 6-12 monthly, and the woman encouraged to attend cervical and breast screening programmes. Breast awareness should be encouraged.

- HRT is not a method of contraception.
- Mirena® is effective as the progestogen component of HRT (a currently unlicensed indication) in combination with a systemic oestrogen-only preparation. Therefore, perimenopausal women who have had Mirena® previously inserted for contraception and/or to treat heavy bleeding may receive oestrogen if HRT is required.
- Stopping HRT abruptly can cause some women to have hot flushes and it should therefore be withdrawn gradually by decreasing dosages over 3-6 months.
- HRT is contra-indicated in the presence of active venous thromboembolism, unexplained vaginal bleeding, oestrogen dependent tumours (breast and endometrial cancer), current or recent cardiovascular disease and acute porphyria. Women with severe menopausal symptoms following breast or endometrial cancer may occasionally be prescribed HRT after specialist consultation.

**HRT and cardiovascular disease**

- There is no evidence that HRT protects against either ischaemic heart disease or stroke and it should not be commenced for this indication. HRT may be associated with worsening of cardiovascular outcome, particularly in women with pre-existing cardiovascular risk factors. The decision to continue or stop HRT in women with CVD who have been receiving long-term oestrogen therapy should be based on presence of acute menopausal symptoms. If a woman develops an acute CVD event, e.g. heart attack or stroke, or is immobilised while receiving HRT, the risk of thromboembolism is increased and consideration should be given to stopping HRT.

**HRT and breast cancer**

- Risk of breast cancer increases with increasing duration of HRT use (see below) and this should be balanced against the benefits of taking long-term therapy. The risk is significantly greater for combined HRT than for oestrogen only therapy. Tibolone also appears to have an increased risk of breast cancer but to a lesser extent. Women with a significant family history should seek specialist opinion prior to being prescribed HRT.
- The additional risk of breast cancer begins to decline when HRT is stopped and by 5 years reaches the same level as in women who have never taken HRT. The need for HRT should be reassessed at least annually.
- Women with premature menopause have an overall lower risk of breast cancer and in most instances should receive HRT until the age of normal menopause and then should be reassessed.

**HRT and osteoporosis**

- HRT prevents loss of bone density and reduces the risk of osteoporotic fracture. However, in 2003, the Committee on Safety of Medicines in the UK stated that HRT should not be used as first-line therapy for prevention of osteoporosis as the risk: benefit ratio of HRT is unfavourable. See section 6.6.
Summary table of risks and benefits associated with using HRT. *(Taken from Hormone Replacement Therapy (HRT: Latest safety update (updated 3 December 2003). CSM).)*

These numbers are estimates - it is important to remember that not all risks will apply to everyone but will depend on their health, their lifestyle and their family medical history.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Age of woman(yr)</th>
<th>Number of cases/1000 non-HRT users</th>
<th>Extra number of cases in 1000 HRT users over the same period</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cumulative cancer risk with time</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast cancer</td>
<td>50-65</td>
<td>32</td>
<td>1.5 oestrogen-only; 6 (combines HRT)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5 oestrogen-only; 19 (combined HRT)</td>
</tr>
<tr>
<td>Endometrial cancer</td>
<td>50-64</td>
<td>5</td>
<td>4 (oestrogen-only); Data not available (combined HRT)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>10 (oestrogen-only); &lt;2 (combined HRT)</td>
</tr>
<tr>
<td>Ovarian cancer&lt;sup&gt;b&lt;/sup&gt;</td>
<td>50-69</td>
<td>9</td>
<td>1 (oestrogen-only)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 (oestrogen-only)</td>
</tr>
<tr>
<td><strong>Cardiovascular risk over 5 years</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>50-59</td>
<td>3</td>
<td>1 (combined HRT)</td>
</tr>
<tr>
<td></td>
<td>60-69</td>
<td>11</td>
<td>4 (combined HRT)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Data not available</td>
</tr>
<tr>
<td>VTE</td>
<td>50-59</td>
<td>3</td>
<td>4 (combined HRT)</td>
</tr>
<tr>
<td></td>
<td>60-69</td>
<td>8</td>
<td>9 (combined HRT)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Data not available</td>
</tr>
<tr>
<td><strong>Benefits over 5 years</strong></td>
<td></td>
<td></td>
<td>Reduced number of cases in 1000 HRT users over the same period</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>50-59</td>
<td>3</td>
<td>1 (combined HRT)</td>
</tr>
<tr>
<td></td>
<td>60-69</td>
<td>8</td>
<td>3 (combined HRT)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 (combined HRT)</td>
</tr>
<tr>
<td>Fracture of neck of femur</td>
<td>50-59</td>
<td>1-2</td>
<td>0-1 (combined HRT)</td>
</tr>
<tr>
<td></td>
<td>60-69</td>
<td>7-8</td>
<td>2-3 (combined HRT)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>5 (combined HRT)</td>
</tr>
</tbody>
</table>

<sup>b</sup>The risks of ovarian cancer with combined HRT are unknown
(a) Women who have not had a hysterectomy

**Sequential combined (oral):**
- **First choice:** Elleste-Duet®
- **Second choices:** Prempak C® *
  - Femoston®

**Sequential combined (transdermal):**
- **First choice:** Evorel® Sequi
- **Second choice:** FemSeven Sequi®

**Continuous combined (oral):**
- **First choice:** Kliovance®/Kliofem
- **Second choice:** tibolone

**Continuous combined (transdermal):**
- **First choice:** Evorel® Conti

**Additional Prescribing Advice**

- Continuous combined therapy (period-free HRT) should only be used by women who are at least a year past the menopause or over 54 years of age. Both oestrogen and progestogen are taken daily to give a period-free regimen. Erratic bleeding is common in the first few months of use.
- Tibolone (Livial®) may be an alternative period-free HRT for women who develop breast pain with HRT, or who are suffering reduced libido.
- Tibolone appears to increase the risk of breast cancer to a lesser extent than combined HRT but more than oestrogen-only HRT.
- Women with irregular or heavy bleeding with HRT which persists for more than 3 months should be referred to a gynaecology or menopause service.
- Amenorrhoea with HRT is not a risk for endometrial cancer and does not require investigation.
- * Conjugated oestrogens are extracted from pregnant mares' urine and may not be acceptable to some women.

(b) Women who have had a hysterectomy

- **First choice:** Elleste-Solo®
- **Second choice:** Premarin® *

**Unopposed oestrogens (transdermal):**

- **First choice:** Estradot®

(c) Preparations for vaginal atrophy

- see section 7.2
6.4.2 Male sex hormones

**First choice:** testosterone injection (Sustanon®)
**Second choice:** testosterone gel (Testogel®)

**Additional Prescribing Advice**

Intramuscular depot preparations of testosterone esters are preferred for replacement therapy. Gel may be preferred if the patient finds the injection painful.

6.5 Pituitary hormones and anti-oestrogens

6.5.1 Anterior pituitary hormones

**Corticotrophins for testing**

**First choice:** tetracosactide (tetracosactrin)

**Additional Prescribing Advice**

- Reference should be made to local clinical chemistry handbooks or the Southport and Ormskirk hospital NHS trust intranet for interpretation of results.

6.5.2 Posterior pituitary hormones and antagonists

**(a) diabetes insipidus**

**First choice:** desmopressin nasal spray
**Second choice:** desmopressin tablets

**Additional Prescribing Advice**

- A single dose of desmopressin is also used as part of a test following fluid deprivation in the differential diagnosis of diabetes insipidus.
- For nephrogenic diabetes insipidus, the usual treatment is a thiazide diuretic. Caution if due to lithium; refer to endocrinologist.
- Desmopressin injection 4 micrograms/mL may be indicated in unconscious patients (dose 1-4 micrograms daily by subcutaneous, intramuscular or intravenous injection).
(b) antidiuretic hormone antagonists
First choice: demeclocycline

Additional Prescribing Advice
- Demeclocycline is indicated for chronic Syndrome of Inappropriate Secretion of Anti-Diuretic Hormone (SIADH) where fluid deprivation is unsuccessful.
- Higher doses of demeclocycline may be associated with a decline in glomerular filtration. Creatinine should be monitored along with plasma sodium.

(c) oesophageal varices
First choice: terlipressin (hospital use only)

6.6 Drugs affecting bone metabolism

General notes
- The aim of treatment is the prevention of fracture.
- Management should be based on identification of risk factors for osteoporosis and use of bone densitometry scanning.
- An important risk factor is the occurrence of a fragility fracture in patients over 55 years old.
- Before starting treatment, calcium, phosphate, alkaline phosphatase and renal function should be checked.
- Unless clinicians are confident that women who receive osteoporosis treatment have an adequate calcium intake and are vitamin D replete, calcium and/or vitamin D supplementation should be provided. Adcal-D3® and Calfovit D3® may be ineffective in moderate-severe renal disease; alfalcaldiol may be a suitable alternative.
- Long-term therapy is required to treat or prevent osteoporosis. Optimum duration is unknown but there are good safety data over 10 years for bisphosphonates.
- For bisphosphonates used in malignant disease, see section 8.4.
- For treatment of pain, see sections 4.7 and 10.1.

(a) prevention of postmenopausal osteoporosis
Refer to NICE Technology Appraisal Guidance 87 for criteria. A DXA scan is necessary for treatment of women under 75 years.

First choice: alendronate
Additional Prescribing Advice

- Patients with identified risk factors for osteoporosis should be encouraged to perform weight bearing exercise and strength training, give up smoking, and follow a healthy diet with adequate calcium and vitamin D.
- Treatment with oral contraceptives or HRT should be considered for early menopause until around the age of 50 years. The CSM now advises that HRT should not be considered first-line therapy for the long-term prevention of osteoporosis in women who are over 50 years of age and at an increased risk of fractures.
- Calfovit D3® is a suitable second choice calcium and vitamin D supplement for patients with compliance problems or unable to chew Adcal-D3® tablets.
- Calcium and vitamin D supplementation alone may reduce the risk of fracture but it is less effective than other agents. The best evidence supports its use in institutionalized or housebound elderly women.

(b) treatment of postmenopausal osteoporosis

The decision to treat should be tailored to individual requirements depending upon the absolute risk of fracture, the assessment of which should include DXA scanning.

First choice: alendronate + Adcal-D3®
Second choice: strontium ranelate + Adcal-D3®

Older Patients - bisphosphonates

Older patients with osteoporosis, who can comply with administration instructions and have no contraindications, should be given bisphosphonates. Strontium ranelate is a suitable alternative for female patients intolerant of bisphosphonates. Calcium and vitamin D supplementation alone may reduce the risk of fracture but it is less effective than other agents. The best evidence supports its use in institutionalized or housebound older patients.

Additional Prescribing Advice

- Patients receiving daily bisphosphonate should be changed to a weekly formulation.
- Strontium ranelate is an option for those intolerant of bisphosphonates or where there are contraindications, e.g. oesophageal stricture. The evidence suggests greatest benefit in women over 75 years with a t score less than -2.4 and a history of fracture but it can be used in other women with equivalent fracture risk.
- Raloxifene may be considered for patients who are intolerant of bisphosphonates, particularly if there is low density of the spine.
- Teriparatide is for specialist use only, for severe osteoporosis.
- Calfovit D3® is a suitable alternative to Adcal-D3® for patients with compliance problems or unable to chew tablets. See section 9.6.4.
Patients likely to receive 7.5mg or more of prednisolone daily for 3 months or longer (or equivalent dose of other glucocorticoid) should receive prophylaxis against osteoporosis

First choice: alendronate + Adcal-D3®

Additional Prescribing Advice

- Patients over 75 years should receive treatment as above.
- Patients under 75 years should have a DXA scan. Treatment should be offered if they have osteoporosis already with t score less than -2.5, or have osteopenia with t score between -1.5 and -2.5.
- Risedronate is an alternative to alendronate for postmenopausal women receiving steroids. Although the licensed dose is 5mg daily, local expertise suggests that 35mg once weekly is appropriate.
- Although the licensed dose of alendronate for corticosteroid-induced osteoporosis is 5mg or 10mg daily, local expertise suggests that 70mg once weekly is appropriate.
- Calfovit D3® is a suitable alternative to Adcal-D3® for patients with compliance problems or unable to chew tablets. See section 9.6.4.

(d) male osteoporosis

Specialist referral should be considered

First choice: alendronate + Adcal-D3®

Older Patients - bisphosphonates

Older patients with osteoporosis, who can comply with administration instructions and have no contraindications, should be given bisphosphonates. Calcium and vitamin D supplementation alone may reduce the risk of fracture but it is less effective than other agents. The best evidence supports its use in institutionalized or housebound older patients.

Additional Prescribing Advice

- Male osteoporosis is often secondary to other medical conditions; specialist referral is recommended.
- Although the licensed dose of alendronate for osteoporosis in men is 10mg daily, local expertise suggests that 70mg once weekly is appropriate.
- Calfovit D3® is a suitable alternative to Adcal-D3® for patients with compliance problems or unable to chew tablets. See section 9.6.4
6.7 Other endocrine drugs

6.7.1 Dopamine-receptor agonists

Treatment of hyperprolactinaemia

First choice: cabergoline
Second choice: bromocriptine

Additional Prescribing Advice

• Cabergoline is first choice since it may be better tolerated than bromocriptine; however, there is little information on its use in pregnancy; bromocriptine is the drug of choice for hyperprolactinaemia if pregnancy is sought.
• For suppression of lactation, see section 7.1.
• For Parkinson's disease, see section 4.9.1 (b).

6.7.4 Acromegaly

The primary treatment of acromegaly is usually pituitary surgery. Management and treatment requires specialist involvement.

First choices: octreotide or lanreotide

Additional Prescribing Advice

• See section 8.3.4.3 for the use of somatostatin analogues (octreotide and lanreotide) in neuroendocrine tumours.
Treatment of disorders occurring in obstetrics and gynaecology

(a) menorrhagia

Contraception required
First choice: combined oral contraceptive
Second choice: medroxyprogesterone acetate or Mirena®

Contraception not required
First choice: tranexamic acid
Second choice: mefenamic acid

(b) frequent irregular periods

Contraception required
First choice: combined oral contraceptive

Contraception not required
First choice: norethisterone
Second choice: medroxyprogesterone acetate

Additional Prescribing Advice
- norethisterone 5mg tds should be taken from day 5 to 26 of cycle

(c) endometriosis (diagnosis usually made by laparoscopy)
First choices: combined oral contraceptive or medroxyprogesterone acetate
Second choice: GNRH analogue (prostap®) (on specialist advice)

Additional Prescribing Advice
- Symptoms, particularly pelvic pain and abnormal uterine bleeding, may be better controlled if the combined oral contraceptive is taken continuously for at least 6 months.
- Side-effects of gonadorelin analogues related to the inhibition of oestrogen production may be reduced by hormone replacement (e.g. with an oestrogen and a progestogen or with tibolone).
(d) galactorrhoea

**First choice:** no treatment

**Additional Prescribing Advice**

- Most cases of galactorrhoea are mild and resolve spontaneously
- Bromocriptine can be useful for patients with persistent galactorrhoea following specialist referral and investigation. Consider drug causes e.g. chlorpromazine, metoclopramide.

(e) polycystic ovarian syndrome

**Oligomenorrhoea**

**First choice:** combined oral contraceptive

**Second choice:** dianette

**Hirsutism**

**First choice:** Dianette®

**Second choice:** Marvelon®

**Additional Prescribing Advice**

- Polycystic ovarian syndrome consists of a collection of symptoms some or all of which may not require drug treatment; weight reduction is first essential line of management for obese patients.
- For acne, see section 13.6 (a).
- If there are concerns regarding infertility, both the male and female partners should be referred to a clinic. Ovulation induction with anti-oestrogens may be required and should only be prescribed with appropriate monitoring. There is some evidence that metformin may increase the frequency of ovulation but the appropriate dose is uncertain.
- As with Marvelon®, Femodene® and Minulet® contain a less androgenic progestogen and may be used instead of Marvelon® in women with hirsutism or acne.

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FOR HOSPITAL USE ONLY

**Metformin - for polycystic ovaries**
7.1 Drugs used in obstetrics

Hospital Use Only – see department guidelines

7.1.1 Prostaglandins & oxytocics

*Induction of labour*
Dinoprostone vaginal gel, gemeprost pessaries OR Oxytocin injection

**Additional Prescribing Advice**
- See NICE Guidance (induction of labour (June 2001))

*Prevention of post-partum haemorrhage*
Syntometrine® (ergometrine maleate with oxytocin) OR oxytocin

*Suppression of lactation*
**Additional Prescribing Advice**
- No treatment is recommended; bromocriptine should not be prescribed.
- Cabergoline may be used soon after delivery if indicated.

7.1.1.1 Ductus arteriosus

**First choice:** Indometacin injection

**Additional Prescribing Advice**
- Under specialist supervision in neonatal intensive care unit

7.1.2 Mifepristone

to prime the cervix followed by Misoprostol tablets

See RCOG guidelines

7.1.3 Myometrial relaxants

Atosiban injection or nifedipine for pre term labour
Salbutamol or terbutaline iv infusion for uterine relaxation prior to external cephalic version
7.2 Treatment of vaginal and vulval conditions

7.2.1 Preparations for vaginal atrophy

Topical oestrogens

First choice: Estradiol 25mcg m/r vaginal tablets (Vagifem®) or estriol 0.01% vaginal cream/500mcg pessary (Orthogynest®)

Second choice: Estradiol 7.5mcg/24hrs vaginal ring (Estring®)

Prescribing notes

• Local oestrogens can improve local vaginal and bladder symptoms caused by oestrogen deficiency; systemic therapy is necessary for vasomotor symptoms.
• Most women with significant vulvo-vaginal problems will require long-term treatment particularly if sexually active.
• Women without a uterus can use vaginal oestrogens indefinitely.

7.2.2 Vaginal & vulval infections

Candidiasis:

See Chapter 5: Antimicrobial guidelines. Page 26

Additional Prescribing Advice

• With any genital symptoms always consider the possibility of sexually transmitted infection (STI). If an STI is found, there is a strong possibility of others also being present so it is expedient to check. If facilities and skills are available, this can be done by the GP. Otherwise, refer to GUM especially for tests of cure and contact tracing. Candidiasis and bacterial vaginosis are considered non-STIs although they can occur concurrently with STIs.
• Clotrimazole and econazole are available over-the-counter.
• There is no evidence that treating the partner of women suffering from candidiasis is helpful.
• Patients who are inserting intravaginal cream or pessaries into the vagina, may also apply topical clotrimazole or econazole cream to the vulva.

Vaginitis due to candidal, trichomonal, non-specific or mixed infections

See Chapter 5: Antimicrobial guidelines. Page 26

Bacterial vaginosis:

See Chapter 5: Antimicrobial guidelines. Page 26

Additional Prescribing Advice

• Bacterial vaginosis is generally associated with anaerobes; recurrence is frequent but this is not a sexually transmissible condition and treatment of the sexual partner is not necessary.
7.3 Contraceptives

General notes

- Different doses of oestrogen may be associated with different side-effect profiles in individual women.
- For most women a pill containing 30 micrograms oestrogen is recommended.
- The risk of breast cancer appears to be unrelated to the dose of oestrogen.
- The risk of cardiovascular disease (including venous thromboembolism) is higher with pills containing 50 micrograms oestrogen but there is no evidence for a difference in cardiovascular risk between 20 and 30 micrograms.
- The CSM has agreed that while evidence suggests that combined oral contraceptives (COC's) containing gestodene and desogestrel (i.e. third generation pills) have a higher risk of venous thromboembolism, the absolute risk of venous thromboembolism is small. Provided that this is made clear to the user, there is no restriction on prescription of these pills.
- While different progestogens may be associated with different side-effect profiles in individual women, there is no good evidence that there is any difference in cardiovascular or breast cancer risk or cycle control.
- All COC's are associated with metabolic changes, particularly in lipids. While pills containing desogestrel, gestodene and norgestimate are associated with fewer adverse effects on lipids there is no evidence that this has any clinical benefit.
- The androgenicity of different progestogens appears to be related to consistent differences in side-effects. Less androgenic progestogens (e.g. desogestrel) are of benefit to women with acne.
- Most contraceptive failures are due to poor compliance which is strongly influenced by acceptability. It is important therefore to accept that women may prefer one brand to another despite similar or identical composition.
- There is no good evidence that triphasic or biphasic COC's are associated with better cycle control; they are more complicated to use.
- When the pill is used for management of gynaecological conditions, such as menorrhagia or dysmenorrhoea, the risk/benefit ratio changes and it may be prescribed for women who would have relative contraindications if they were using it solely for contraception.
- Some drugs, including enzyme-inducers and antibiotics, may impair the efficacy of oral contraceptives; see BNF for details.
First choices: Microgynon 30® or Cilest®
Second choices: Marvelon® or Femodene®
Low strength option: Loestrin 20® or Mercilon®
Triphasic preparation: Logynon®

Additional Prescribing Advice
• Microgynon 30® and Cilest® are standard low dose COC’s.
• Femodene® is a third generation pill; since the progestogen is different, individual women may experience fewer, or different, side-effects.
• Marvelon® contains a non-androgenic progestogen and may be a suitable alternative second choice for women with acne.
• Mercilon® contains a lower dose of oestrogen and may be associated with a better side-effect profile in women complaining of oestrogenic symptoms such as breast enlargement/mastalgia.
• Dianette® (co-cyprindiol 2000/35 composed of cyproterone acetate 2mg, ethinylestradiol 35micrograms) is a treatment for severe acne that has not responded to oral antibiotics or for moderately severe hirsutism and only in those patients may it also be used as an oral contraceptive (see section 13.6(a)). Most acne improves with any COC; Dianette® is more expensive and recent evidence suggests an increased risk of venous thromboembolism. Some women with acne or hirsutism requiring contraception may benefit from Dianette®. This is a good example of the need to consider a risk-benefit ratio in women with relative contra-indications.
• In accordance with recent CSM guidance, Dianette® should be withdrawn 3-4 cycles after the treated condition has completely resolved. For acne, substitution with another COC is likely to maintain the improvement but for hirsutism, this is likely to recur. A COC containing a less androgenic progestogen e.g. Marvelon®, could be substituted but Dianette® may need to be continued.

Emergency contraception
First choice: Levonelle®-2

Additional Prescribing Advice
• Hormonal emergency contraception (EC) is licensed for use within 72 hours of intercourse. There is evidence to suggest that the sooner it is used, the more likely it is to be effective.
• There is no evidence that hormonal EC is teratogenic. It does not work if a woman is already pregnant. Pregnancy can usually be excluded on the basis of the menstrual history; pelvic examination and/or pregnancy testing is only indicated if pregnancy is suspected on clinical grounds.
• Levonelle®-2 is available over-the-counter as Levonelle®.
7.3.2 Progestogen-only contraceptives

First choices: Micronor®
Second choices: Norgeston®
Restricted Use (see notes below): Cerazette®

Additional Prescribing Advice

- Progestogen-only pills (POPs) are associated with irregular bleeding in up to 40% of users. Bleeding patterns do not tend to improve with time and are not likely to be any different with a different progestogen.
- There is no evidence for any clinical advantage of any one brand of POP; Micronor® is currently less expensive than alternatives.
- Norgeston® contains levonorgestrel, a slightly less androgenic progestogen; it may be the preferred brand for women with oily skin.
- Cerazette® is more expensive but has been shown to inhibit ovulation to a substantially greater extent than other POPs. It should be reserved for women who cannot tolerate oestrogen containing contraceptives or in whom those preparations are contraindicated. It may also be recommended for women with a history of ectopic pregnancy who take a POP.
- Women who are over 70kg should consider taking two progestogen-only pills (POPs) a day, particularly if under 30 years of age, due to a potentially higher failure rate. The dose of Cerazette® does not need to be increased.
Long-acting progestogen-only methods
(a) injectable progestogen-only methods

First choice: medroxyprogesterone acetate (Depo-Provera)

Additional Prescribing Advice
• Depo-Provera® can cause menstrual dysfunction and weight gain. By the end of the first year of use, 80% of women will have become amenorrhoic or have scanty infrequent periods.
• When Depo-Provera® is stopped ovarian activity can take up to a year to recover.
• Depo-Provera® is associated with hypoestrogenism and amenorrhoea; recent data have suggested that this is unlikely to have long-term detrimental effects on bone mineral density.

(b) contraceptive implants

First choice: etonogestral (Implanon®)

Additional Prescribing Advice
• Implanon® insertion requires specialist training.
• Implanon® is a low dose long-acting progestogen sufficient to suppress ovulation in all women. Contraceptive effect lasts for 3 years and there have been no pregnancies reported. Up to 20% of women will experience amenorrhoea; the rest will have irregular and sometimes frequent bleeding. This point should be covered carefully during counselling. Norplant® is no longer marketed in the UK. There is no medical or medico-legal need to remove Norplant® before its five-year life span. Women who still have Norplant® can be offered Implanon® at the time when Norplant® is due for removal if they want to continue using an implant.

(c) hormone releasing intra-uterine systems

First choice: Mirena®

Additional Prescribing Advice
• Mirena® is a highly effective method of contraception. Many women experience quite frequent and prolonged spotting for the first 3-6 months; thereafter amenorrhoea is common. Patients should be counselled accordingly.
• Systemic absorption may cause side-effects e.g. acne or greasy skin.
7.3.3 Spermicidal contraceptives

First choice: Gynol II®
Second choice: Orthoforms®

Additional Prescribing Advice

- Spermicides are not recommended for use as the sole method of contraception but have been traditionally advised for use with the diaphragm and/or for lubrication for male condoms. All currently available spermicides contain nonoxinol 9 (N9) as the active compound. While N9 has been shown to be toxic to HIV in vitro, concerns have been raised regarding its detrimental effect on vaginal integrity and thereby on a possible increase in the risk of HIV/AIDS transmission. Research is ongoing. In the meantime there is no reason to alter the advice that contraceptive diaphragms should be used together with a spermicidal preparation.
- Patient preference determines whether a jelly (Gynol II®) or pessaries (Orthoforms®) is prescribed. Pessaries (Orthoforms®) are less messy and easier to use if intercourse is repeated during the 6 hours when the diaphragm is left in place.
7.3.4 Contraceptive devices

Intra-uterine devices

First choices: T-safe® Cu 380
or Multiload® Cu 375
(or Mirena®)

Additional Prescribing Advice
• IUD insertions should be performed by someone who has been properly trained, regularly updated and performs regular insertions.
• Copper IUDs provide long-acting highly effective contraception for at least 5 years and do not rely on compliance for their efficacy. Devices which contain less than 300mm of copper should no longer be used as they are less effective.
• Multiload® Cu375 and Nova-T® 380 Ag are equally effective with no difference in side-effects.
• GyneFix® is a frameless flexible device which may be associated with a reduction in dysmenorrhoea. Smaller than the framed devices, it is particularly useful for nulliparous women. Since the device is anchored to the myometrium it may be useful for women who have a history of expulsion of a framed device.

Diaphragms

First choice: Ortho®
Second choice: All-flex®

Condoms

Additional Prescribing Advice
• Condoms are available free of charge from Family Planning Services, Brook, C-card outlets and certain GPs.
• Condoms are the only method which protect against sexually transmitted diseases including HIV; condom users should be informed about emergency contraception.
7.4 Drugs for genito-urinary disorders

7.4.1 Drugs for symptoms caused by benign prostatic obstruction
(a) alpha-blockers
First choices: alfuzosin
or tamsulosin MR
Second choice: terazosin (spinal patients)

Additional Prescribing Advice
• Tamsulosin should be prescribed generically as tamsulosin m/r.
• Watchful waiting may be preferable to treatment in men with mild to moderate symptoms.
• Alpha-blockers are the treatment of choice for benign prostatic obstruction, and are likely to provide symptom relief in men with prostates of any size. The effect should be noticed within several days, with full response after 4-6 weeks, and the benefit may be maintained for up to 3 years in those who continue to take the drug. There is a lack of published data on effect beyond 3 years.
• All alpha-blockers are equally effective but there are differences in tolerability. Alfuzosin and tamsulosin are the same in terms of effectiveness and cost.
• Alpha-blockers reduce blood pressure, and first doses may cause drowsiness and dizziness. Patients also receiving antihypertensives may need lower doses and supervision.

(b) 5α -reductase inhibitors
Alternative first-line treatment in patients with large prostates. It may also be recommended when alpha-blockers are ineffective, contra-indicated or not tolerated.

First choice: finasteride

Additional Prescribing Advice
• Finasteride is an appropriate alternative to alpha-blockers. Although there is no clear evidence regarding who should receive which drug, finasteride has been shown to be most effective in men with prostate volumes exceeding 40mL, and has been shown to reduce the risk of acute urinary retention and the need for surgery.
• Treatment with finasteride should be reviewed after 6 months. Several months treatment may be required before benefit is obtained and any observed benefit may be lost after 3-6 months if treatment is discontinued.
• Finasteride decreases plasma levels of PSA by approximately 50%. After 6 months of treatment, PSA values should be doubled for comparison with normal ranges in untreated men.
7.4.2 Drugs for urinary frequency, enuresis and incontinence

(a) Urinary frequency due to bladder instability
First choices: oxybutynin hydrochloride or tolterodine tartrate
Second choice: solifenacin

|Additional Prescribing Advice|
- The use of oxybutynin may be limited by side-effects. These may be reduced by commencing with a low dose and increasing gradually; modified-release oxybutynin is better tolerated. As it is as effective, as well tolerated and substantially less expensive, oxybutynin m/r may be used in preference to standard release tolterodine (1mg, 2mg).
- Tolterodine is substantially more expensive but may be an option for those who do not tolerate oxybutynin.
- Antimuscarinic therapy should be reviewed after 6 months and if symptoms are well-controlled therapy may be reduced or discontinued as symptoms may not recur.
- There is no evidence that oestrogens cause subjective or objective improvement of symptoms of urgency and urge incontinence.

(b) Stress urinary incontinence in women
First choice: pelvic floor muscle exercises
Second choice: duloxetine on specialist advice + pelvic floor muscle exercises

|Additional Prescribing Advice|
- Until further evidence is available on safety, efficacy and cost effectiveness, the prescribing of duloxetine should only be initiated in secondary care by a gynaecologist or urologist.
- Patients should be reviewed after 12 weeks of therapy to assess progress and the treatment discontinued if no improvement is demonstrated.
- See shared care guidelines for further details and ensure arrangements are in place before passing prescribing across to primary care.
7.4.3 Drugs used in dysuria

**Alkalisation of urine**

*First choice:* potassium citrate

**Acidification of urine**

*First choice:* ascorbic acid

**Additional Prescribing Advice**

- Many patients obtain good relief from the symptoms of cystitis with over-the-counter medicines.
- Sodium bicarbonate is used as a urinary alkalinising agent in some metabolic and renal disorders.
- Ascorbic acid is not always reliable for acidification of urine.

7.4.4 Bladder instillations and urological surgery

**Bladder infection, dissolution of blood clots and maintenance of indwelling urinary catheters**

*First choice:* sodium chloride 0.9% or glycine 1.5%
7.4.5 Drugs for erectile failure (impotence)

First choice: sildenafil tablets (Viagra®)
Second choices: tadalafil tablets
or alprostadil injection (Caverject® Dual Chamber)

Additional Prescribing Advice

• NHS Regulations (1999) limit the use of NHS prescriptions by GPs for treatment of erectile dysfunction. NHS prescriptions (endorsed “SLS”) can be issued for sildenafil, alprostadil, tadalafil and certain vacuum tumescence devices to men suffering from erectile dysfunction who have these medical conditions: diabetes, multiple sclerosis, Parkinson’s disease, poliomyelitis, prostate cancer, prostatectomy (including TURP), radical pelvic surgery, renal failure treated by dialysis or transplant, severe pelvic injury, single gene neurological disease, spinal cord injury, and spina bifida.
• GPs can issue private prescriptions for the above drugs and devices for patients on their list but cannot charge patients for issuing a private prescription.
• Treatment should be available from specialist services in cases where erectile dysfunction is causing severe distress.
• Examination of the patient is important to check for anatomical abnormalities and Peyronie's disease which may need referral to Urology. Diabetes needs to be excluded and cardiovascular risk factors addressed because they are commonly present.
• Tadalafil may be a suitable alternative for patients who develop visual disturbances with sildenafil or for whom a longer duration of action is required.
• Sildenafil and tadalafil are contra-indicated in men receiving nitrates in any form, and nicorandil. Consider discontinuing nitrates if no longer needed.
• Cardiovascular disease and multiple antihypertensive drug regimens are not contra-indications to sildenafil or tadalafil therapy provided the man is capable of ordinary daily tasks (and therefore sexual activity) without cardiac symptoms.
• Intracavernosal self-injection with alprostadil is a suitable second choice to sildenafil if treatment with sildenafil fails or is contra-indicated. The recommended alprostadil preparation is Caverject® Dual Chamber, which is supplied with an injector device.
• All patients commencing intracavernosal injection therapy require supervised instruction on its use and advice on action required should a prolonged erection (>6 hours) occur.
Chapter 7 – Obstetrics, gynaecology & urinary-tract disorders

Treatment of disorders occurring in obstetrics and gynaecology

(a) menorrhagia

Contraception required
First choice: combined oral contraceptive
Second choice: medroxyprogesterone acetate or Mirena®

Contraception not required
First choice: tranexamic acid
Second choice: mefenamic acid

Prescribing notes
• Low dose norethisterone is not an effective choice for menorrhagia.

(b) frequent irregular periods

Contraception required
First choice: combined oral contraceptive
Contraception not required
First choice: norethisterone
Second choice: medroxyprogesterone acetate

Prescribing notes
• norethisterone 5mg tds should be taken from day 5 to 26 of cycle

(c) endometriosis (diagnosis usually made by laparoscopy)

First choices: combined oral contraceptive or medroxyprogesterone acetate
Second choice: GNRH analogue (prostap®) (on specialist advice)

Prescribing notes
• Symptoms, particularly pelvic pain and abnormal uterine bleeding, may be better controlled if the combined oral contraceptive is taken continuously for at least 6 months.
• Side-effects of gonadorelin analogues related to the inhibition of oestrogen production may be reduced by hormone replacement (e.g. with an oestrogen and a progestogen or with tibolone).

Urology Products

Short term catheters
Rarely used - not on formulary

Long term catheters
First Choice: Bard Biocath 2 way foley catheter
Silicone catheter: Bard Lubrisil (hydrogel coated)
NB: Use for suprapubic cathererisation
Spinal patients only: Sherwood Argyle All Silicone

Intermittent catheters
First choice: Coloplast Conveen Speedicath
Second choice: Astra LoFric PRIMO catheters

Drainage bags (Night bags)
First choice: Simpla collection bag 2 ltr S2
Second choice: EasiMT urine drainage bags
(where first choice not appropriate)

Leg bags (Day bags)
All sizes and lengths are available and should be chosen according to circumstances
First choice: Simpla (Coloplast) leg bags
Second choice: Bard Uriplan bags

Sheaths
Spinal patients only: Manfred Sauer P SURE. All sizes are available and it is essential that patients are measured accurately.
First choice: Simpla Clear Advantage Aquadry
Second choice: Coloplast Conveen Optima

Thigh Straps
The use of thigh straps is strongly recommended
First choice: Simpla G-strap

Leg Bag Sleeves
First choice: Bard Urisleeve

Catheter Valves
First choice: Flip-flo

Additional Products for Hospital Use Only
100% silicone catheters should be used for all patients
Rusch Brilliant AquaFlate 100% silicone catheter
8.1 Cytotoxic drugs

More than 50 cytotoxic drugs are used in the management of malignant disease, and the recommended doses and schedules vary according to the tumour type and regimen. Anticancer cytotoxic treatment should always be prescribed under the supervision of an oncology specialist. **When oral cytotoxic drugs are used for the treatment of malignant disease, the whole course will be dispensed by the hospital pharmacy. The prescription should not be repeated except on the explicit instruction of a specialist.**

Parenteral cytotoxic drugs should be reconstituted and dispensed by trained oncology pharmacy staff who have access to appropriate equipment. The administration of cytotoxic drugs by all routes other than the oral route should be undertaken only by staff with appropriate training in administration and safe handling, within a designated hospital area which is equipped to deal with drug reactions and emergencies. Extravasation of vesicant cytotoxic drugs may cause severe, permanent tissue damage and functional loss. To avoid extravasation, designated oncology staff are specially trained in the intravenous administration of vesicant drugs. Extravasation is a medical emergency, and expert advice and treatment must be obtained immediately.

In addition to their anti-tumour effects, cytotoxic drugs may damage normal tissues and are a potential hazard to patients, relatives and staff. Protective gloves must be worn when handling cytotoxic agents, and staff, patients and relatives must be advised on the safe handling and disposal of drugs and excreta. Most drugs are teratogenic, and particular care must be taken to avoid the exposure of pregnant women to cytotoxic drugs or contaminated excreta. Men and women receiving chemotherapy should avoid conception during treatment and for up to six months after.

Cytotoxic drugs are also used for their immunosuppressive or anti-proliferative effects in the treatment of auto-immune conditions, rheumatoid arthritis, psoriasis, or prevention of transplant rejection.

Prescribers and pharmacists should be aware of the recent NPSA alert on oral chemotherapy. Retail pharmacists must have access to local protocols.

The prescribing notes for the following sub-sections have been combined and do not follow the structure of chapter 8.1 of the BNF.

*Most of the oncology drugs listed below are for specialist use only and are not suitable for general use in primary care. They are listed here for information only.*
8.1.1 Alkylating drugs
Busulfan (busulphan), carmustine, chlorambucil, cyclophosphamide, estramustine, ifosfamide, lomustine, melphalan, thiotepa.

8.1.2 Cytotoxic antibiotics
Bleomycin, dactinomycin (actinomycin D), daunorubicin, doxorubicin, epirubicin, idarubicin, mitomycin, mitoxantrone (mitozantrone).

8.1.3 Antimetabolites
Capecitabine, cladribine, cytarabine, fludarabine, fluorouracil, gemcitabine, mercaptopurine, methotrexate, raltitrexed, tioguanine (thioguanine).

8.1.3 Vinca alkaloids and etoposide
Etoposide, vinblastine, vincristine, vindesine, vinorelbine.

8.1.4 Other antineoplastic drugs
Altretamine, amsacrine, bexarotene, bortezomib, carboplatin, cisplatin, crisantaspase, dacarbazine, docetaxel, hydroxycarbamide (hydroxyurea), imatinib, irinotecan, oxaliplatin, paclitaxel, pentostatin, procarbazine, temozolomide, topotecan, trastuzumab.
8.2 Drugs affecting the immune response

Following solid organ transplantation, patients are usually managed with a combination of immunosuppressant agents namely: a calcineurin inhibitor (see section 8.2.2(b)) and an antiproliferative agent (see section 8.2.1) and prednisolone (see section 8.2.2(a)). Prednisolone therapy is usually reduced over the initial few months post transplant and patients are maintained on a calcineurin inhibitor and an antiproliferative agent.

8.2.1 Antiproliferative immunosuppressants

First choice: azathioprine
Second choice: mycophenolate mofetil (MMF)

Additional Prescribing Advice
- Azathioprine or mycophenolate are used in combination with a calcineurin inhibitor (tacrolimus or ciclosporin) and prednisolone post transplant.
- Mycophenolate is used when there is an increased risk of rejection and in combined renal/pancreas transplant.
- Azathioprine should not be given in combination with allopurinol due to myelosuppression.
- Patients should be warned to report any signs or symptoms of bone marrow suppression i.e. infection, bruising and bleeding.
- If gastro-intestinal side-effects of mycophenolate are troublesome, then the daily dose may be split into 500mg 3 or 4 times daily.
- Mycophenolate is contra-indicated in pregnancy - seek specialist advice.

8.2.2 Corticosteroids and other immunosuppressants

(a) corticosteroids

First choices: dexamethasone
or prednisolone

Additional Prescribing Advice
- When corticosteroids are prescribed twice daily, the second dose should be taken at 2pm.
- Prednisolone has a marked antitumour effect in many haematological malignancies
Refer to section 6.6 for the treatment and prevention of corticosteroid-induced osteoporosis.

Where corticosteroids are prescribed as premedication or antiemetic, the full course will be supplied by the hospital.

(b) other immunosuppressants
- Ciclosporin
- Tacrolimus
- Thalidomide are calcineurin inhibitors. Both are markedly nephrotoxic.

Additional Prescribing Advice
- Doses are usually administered at 10am and 10pm.
- Trough levels should be sampled prior to drug administration.
- Target trough levels vary depending on indication and time since transplant.

8.2.3 Rituximab (specialist use only)

Additional Prescribing Advice
- Rituximab is recommended for three distinct indications.
- Full resuscitation facilities should be on hand and treatment should only be undertaken with the close supervision of a specialist.
- Rituximab may exacerbate angina, arrhythmia and heart failure; transient hypotension occurs frequently and antihypertensives may need to be withheld for 12 hours before infusion.
- Patients should be given paracetamol and an antihistamine before each dose of rituximab to reduce the incidence of infusion-related side-effects. Pre-medication with a corticosteroid should also be considered. See product literature for treatment of infusion-related side-effects.
- Severe cytokine release syndrome has occurred 1-2 hours after infusion of rituximab. Patients with a high tumour burden as well as those with pulmonary insufficiency or infiltration are at increased risk and should be monitored very closely.
8.2.4 Other immunomodulating drugs

Interferon alpha
Interferon beta (neurology)

Additional Prescribing Advice
- Interferon alpha is used for the treatment of chronic myeloid leukaemia, hairy cell leukaemia, non Hodgkins lymphoma, myeloma, carcinoid tumours, Kaposi's sarcoma, renal carcinoma, adjuvant treatment of malignant melanoma.

BCG bladder instillation
- For hospital use only
8.3 Sex hormones and hormone antagonists in malignant disease

8.3.2 Progestogens

First choices: medroxyprogesterone acetate or megestrol acetate

Additional Prescribing Advice
- Progestogens are rarely used for third-line endocrine therapy in breast cancer and are occasionally used in frail patients with advanced renal cancer or advanced endometrial cancer.
- Progestogens should be used with caution in conditions that may worsen with fluid retention and in those susceptible to thromboembolism.
- Megestrol 40mg daily may also be prescribed for menopausal symptoms for women receiving endocrine therapy.

8.3.4 Hormone antagonists

8.3.4.1 Breast cancer

Drugs for the endocrine therapy of breast cancer

Endocrine therapies are commonly used in the management of patients with estrogen receptor-positive breast cancer. Neo-adjuvant endocrine therapy may be given to postmenopausal women for at least 3 months to down-stage locally advanced tumours before definitive local treatment with surgery or radiotherapy. Adjuvant endocrine therapy is given for 5 to 8 years after local treatment, to reduce the risk of relapse. In metastatic disease, endocrine therapy is continued until the disease progresses. The sequential use of endocrine therapies may control metastatic disease for lengthy periods in estrogen-receptor positive breast cancer.

Anastrozole
Letrozole
Tamoxifen
Exemestane
Fulvestrant
Additional Prescribing Advice

- The aromatase inhibitors letrozole, anastrozole and exemestane are ineffective in premenopausal women unless concomitant goserelin is given to suppress ovarian function.

- Tamoxifen is more effective when ovarian function is suppressed in premenopausal women. Concomitant goserelin may be given for the first two years of adjuvant tamoxifen therapy in this group.

- Oophorectomy is an alternative to goserelin in premenopausal women.

- Tamoxifen increases the risk of venous and arterial thrombosis in postmenopausal women. Letrozole or anastrozole cancer. Abnormal vaginal bleeding should be investigated promptly.

- Letrozole may be initiated by breast cancer specialists, and continued by GPs according to a shared care protocol, for the treatment of invasive early breast cancer in postmenopausal women who have received prior standard adjuvant tamoxifen therapy for 5 years. Letrozole should be initiated within 3 months of completion of tamoxifen and continued for 3 years only or until tumour relapse, whichever occurs first. Extended adjuvant letrozole should not be used in patients completing adjuvant therapy with an aromatase inhibitor.

- Endocrine therapy may cause a transient increase in bone pain in patients with bony metastases.
8.3.4.2 Prostate cancer and gonadorelin analogues

Endocrine therapies are commonly used in the management of patients with prostate cancer. Neo-adjuvant endocrine therapy may be given for up to 3 months to down-stage locally advanced tumours before definitive local treatment with radiotherapy. Locally advanced prostate cancers unsuitable for local therapy may be treated by a gonadorelin analogue, or by bicalutamide alone in younger men who wish to retain potency. Gonadorelin analogues are also used in metastatic prostate cancer, with initial anti-androgen cover to prevent tumour flare, and the combination of a gonadorelin analogue and an anti-androgen is used to provide maximal androgen blockade in second-line treatment of metastatic disease.

Endocrine therapy must only be initiated on the advice of a hospital specialist

Anti-androgen

First choice: bicalutamide
Second choice: flutamide

Gonadorelin analogues

First choice: goserelin
Second choices: leuprorelin acetate

Additional Prescribing Advice

- Triptorelin and leuprorelin are licensed for advanced prostate cancer while goserelin is licensed for all stages of prostate cancer.
- Gonadorelin analogues cause side-effects similar to orchidectomy. Both anti-androgens and gonadorelin analogues may cause gynaecomastia, reduced libido, hot flushes, mood changes and sweats.
- Gonadorelin analogues may cause ‘tumour-flare’ in the first weeks of treatment with a transient worsening of pain or ureteric obstruction. This can be prevented by pre-treatment with an anti-androgen.
- Bicalutamide is the first choice of anti-androgen because of its once daily administration schedule. It should not be used as monotherapy for the treatment of localised prostate cancer, but it is licensed for monotherapy of locally advanced prostate cancer
- Cyproterone 50mg twice daily may be used to treat hot flushes associated with gonadorelin analogues.
8.3.4.3 Somatostatin analogues

Short-acting
First choice: octreotide

Long-acting
First choice: octreotide depot (Sandostatin LAR®)
Second choice: lanreotide

Additional Prescribing Advice
- Somatostatin analogues are used for the relief of symptoms associated with neuroendocrine tumours, particularly carcinoid syndrome.
- Thyroid function should be checked every 12 months
- Treatment may cause diarrhoea.
- See section 6.7.4 for somatostatin analogues used in acromegaly
8.4 Bisphosphonates used in malignant disease

Hypercalcaemia of malignancy

First choice: disodium pamidronate

Prevention of skeletal related events in patients with multiple myeloma

On the advice of an oncologist/haematologist

First choice: zoledronic acid

Second choice: disodium pamidronate

Additional Prescribing Advice

- Zoledronic acid may be given for up to 2 years in patients with breast cancer who have bone metastases.
- Renal function, electrolytes, calcium and phosphate should be monitored during treatment with bisphosphonates.
- Doses of bisphosphonates should be adjusted in renal impairment.
- Osteonecrosis of the jaw has been reported in patients with cancer receiving treatment regimens including bisphosphonates. Many of these patients were also receiving chemotherapy and corticosteroids. A dental examination with appropriate preventive dentistry should be considered prior to treatment with bisphosphonates in patients with concomitant risk factors (e.g. cancer, chemotherapy, corticosteroids, poor oral hygiene). While on treatment, these patients should avoid invasive dental procedures if possible.
- See section 6.6 for bisphosphonates used in osteoporosis.
Chapter 9 — Nutrition and blood

9.1.1 Iron-deficiency anaemias

9.1.1.1 (a) oral iron

First choice: ferrous sulphate  
Second choice: ferrous fumarate

Additional Prescribing Advice
- Iron salts should be given orally unless there are good reasons for using another route.
- Once Haemoglobin levels have reached reference range, treatment should be continued for a further 3 months in order to replenish iron stores, and then stopped.
- Gastro-intestinal side-effects are common. Therefore, although iron preparations are best absorbed on an empty stomach, they may be taken after food to reduce these side-effects. If side-effects are problematic the dose can be reduced or an alternative preparation prescribed.
- Modified-release preparations have no therapeutic advantage and should not be used.

(b) iron and folic acid

Additional Prescribing Advice
- There is no need to routinely prescribe a combined iron/folic acid preparation in pregnancy.
- Folic acid 400 micrograms daily should be recommended for all women attempting to conceive, and continued until the 12th week of pregnancy to reduce the risk of a neural tube defect. Women at high risk (women with epilepsy, and those with a previous affected pregnancy) should take 5mg from pre-conception until 12 weeks.

9.1.1.2 Parenteral iron

First choice: iron dextran (CosmoFer ™)  
Second choice: iron sucrose (Venofer ™)

Additional Prescribing Advice
- The only valid reason for administering iron parenterally is non-tolerance of oral therapy. If oral preparations are taken reliably and are absorbed, the haemoglobin response is not significantly faster with the parenteral route.
● CosmoFer® (iron dextran injection providing iron 50mg/mL) has the advantage of being licensed for administration as a single total dose infusion
● A licensed intramuscular preparation of iron is no longer available.

Iron Overload
The management of established iron overload involves venesection. Desferrioxamine (defereroxamine) is used for prevention in patients receiving regular long-term blood transfusion: this type of management requires specialist input. Desferrioxamine is for hospital use only. Deferasirox is approved for specialist use in patients with rare acquired or inherited anaemias requiring recurrent blood transfusions.

9.1.2 Drugs used in megaloblastic anaemias

Megaloblastic anaemia is usually due to vitamin B12 or folate deficiency; the specific deficiency and underlying cause must be identified. Treatment is usually only begun once a firm diagnosis is made. In emergencies, where delayed treatment may be dangerous, both folate and vitamin B12 may be required initially, until assay results are known. Folate must not be used alone in undiagnosed megaloblastic anaemia due to the risk of B12 deficiency leading to peripheral neuropathy.

(a) vitamin B12 deficiency

First choice: hydroxocobalamin

Additional Prescribing Advice
● Apart from dietary deficiency all other causes of vitamin B12 deficiency are attributable to malabsorption. Vitamin B12 should be given prophylactically after total gastrectomy or total ileal resection.
● There is little place for use of low dose vitamin B12 orally. However, cyanocobalamin tablets can be used in doses of 50-150micrograms daily for vegans or patients who have proven dietary deficiency (prescription must be endorsed SLS).
● Oral cyanocobalamin in larger daily doses of 1-2mg (unlicensed dose) may be effective in patients who experience hypersensitivity reactions to the injection or are unable to receive intramuscular injections.
● There is no evidence that doses larger than those recommended provide any additional benefit in cases with neurological or ocular involvement.
(b) folate deficiency

**First choice**: folic acid

**Additional Prescribing Advice**
- There is no need to routinely prescribe a combined iron/folic acid preparation in pregnancy.
- Folic acid has few indications for long-term therapy since most causes of folate deficiency are self-limiting or will yield to a short course of therapy.
- Folic acid 400 micrograms daily should be recommended for all women attempting to conceive, and continued until the 12th week of pregnancy to reduce the risk of a neural tube defect. Women at high risk (women with epilepsy, and those with a previous affected pregnancy) should take 5mg from pre-conception until 12 weeks.

**9.1.3 Drugs for renal anaemia**

**First choice**: epoetin (recombinant human erythropoietin)

**Second choice**: darbepoetin alfa

**Additional Prescribing Advice**
- Darbepoetin alfa may be prescribed for patients as an alternative to epoetin and for those who would benefit from its once weekly administration instead of the more frequent injections necessary with epoetin.

**9.1.6 Drugs used in neutropenia**

*Hospital use only*

**First choices**: pegfilgrastim

**Second Choice**: lenograstim
9.2 Fluids and electrolytes

9.2.1.1 Oral potassium

**First choices:** Sando-K® effervescent tablets
or Kay-Cee-L® syrup

**Additional Prescribing Advice**
- Potassium-sparing diuretics are recommended instead of potassium supplements for prevention of hypokalaemia due to diuretics such as furosemide (frusemide) or thiazides when these are given to eliminate oedema. See sections 2.2.3 and 2.2.4.

Potassium removal

**First choice:** calcium polystyrene sulphonate

**Additional Prescribing Advice**
- Calcium polystyrene sulphonate may be used to remove excess potassium in mild hyperkalaemia or in moderate hyperkalaemia when there are not ECG changes. Intravenous therapy is required in emergencies; see BNF section 9.2.2.1 and local guidelines for advice.

9.2.1.2 Oral sodium and water

*Sodium depletion (e.g. salt-losing bowel, renal disease)*

**First choice:** sodium chloride m/r

**Oral rehydration therapy**

**First choice:** Dioralyte®

**Additional Prescribing Advice**
- Any unused reconstituted solution of Dioralyte® should be discarded after 1 hour unless stored in a fridge when it may be kept for up to 24 hours.
9.2.1.3 Oral bicarbonate

*Chronic acidotic states*
**First choice:** sodium bicarbonate

*Hyperchloraemic acidosis*
**First choice:** potassium bicarbonate

**Additional Prescribing Advice**
- Sodium bicarbonate is used for chronic acidotic states such as uraemic acidosis or renal tubular acidosis. It should be avoided in respiratory acidosis. The response is unpredictable and must be assessed.
- Potassium bicarbonate is used for hyperchloraemic acidosis associated with K+ deficiency e.g. renal tubular and gastro-intestinal disorders.

9.2.2 Parenteral preparations for fluid and electrolyte imbalance

See BNF
9.4 Oral Nutrition

Oral nutritional supplements should not be regarded as a first line treatment of undernutrition and should always follow dietary intervention.

General notes

- The Advisory Committee on Borderline Substances (ACBS) recommends products on the basis that they may be regarded as drugs for the management of specified conditions. Doctors should satisfy themselves that the products can be safely prescribed, that patients are adequately monitored and where necessary, expert supervision is available.
- Oral Nutritional Supplements should be commenced on the advice of a Registered Dietitian who will advise on the schedule for administration.
- Where appropriate a 1.5kcal/ml supplement rather than a 1.0kcal/ml supplement should be prescribed.
- The Dietitian should advise the patient that the use of ONS will initially be a trial period of up to 3 months.
- The Dietitian should continue to assess the need for patient’s on-going ONS prescription.
- Patients should not receive ONS prescribed for other patients.

9.4.2 Enteral Nutrition

If a patient is unable to meet their nutritional requirements through diet alone or is unable to eat, then enteral feeding may be recommended. This may be nasogastric (NG), gastrostomy e.g.PEG (percutaneous endoscopic gastrostomy) or RIG (radiologically inserted gastrostomy) or jejunal feeding.
9.5 Minerals

9.5.1.1 Calcium supplements

**First choices:** Adcal ®

or Calfovit ®

**Additional Prescribing Advice**

- Calcium supplements are usually only required if dietary calcium intake is deficient.
- Adcal-D3™ is first choice and Calfovit D3™ is second choice calcium and vitamin D supplement for osteoporosis. See section 6.6.

9.5.1.2 Hypercalcaemia and Hypercalciuria

**Additional Prescribing Advice**

- Please see section 6.2.3 for the use of cinacalcet in renal patients with secondary hyperparathyroidism.
9.6 Vitamins

General notes

- The use of vitamins as general "pick-me-ups" is of unproven value and, in the case of preparations containing vitamin A or D, may be harmful if the prescribed dose is exceeded.
- Mega-vitamin therapy with water-soluble vitamins, such as ascorbic acid and pyridoxine, is unscientific and can be harmful.

9.6.2 Vitamin B group

First choice: Vit B co

Additional Prescribing Advice

- Vitamin B deficiency, other than B12, is rare. See section 9.1.2(a)
- pyridoxine (vitamin B6) deficiency may occur during isoniazid treatment. There is evidence to suggest that pyridoxine in doses not exceeding 100mg daily may provide some benefit in premenstrual syndrome.
- For vitamin B supplementation in alcohol dependence, see section 4.10(g).

9.6.3 Vitamin C

First choice: ascorbic acid

Additional Prescribing Advice

- Divided doses are necessary due to the low renal threshold of ascorbic acid

9.6.4 Vitamin D

First choice: alfacalcidol (1-hydroxycholecalciferol)

Additional Prescribing Advice

- Patients with severe renal impairment requiring vitamin D therapy should be prescribed alfacalcidol. Note that AlfaD® capsules contain peanut oil and One-Alpha® capsules contain sesame oil.
Calcium and vitamin D supplements

**First choice:** Adcal-D3® for osteoporosis  
**Second choice:** Calfovit® D3

**Additional Prescribing Advice**
- Adcal-D3® may be prescribed for osteoporosis. See section 6.6.
- Adcal-D3® may be ineffective in moderate-severe renal disease; alfacalcidol may be a suitable alternative; see above.
- Calfovit D3® is a suitable second choice for patients with compliance problems or unable to chew tablets.

9.6.6 Vitamin K

*Malabsorption syndromes (water-soluble preparation required)*  
**First choice:** menadiol sodium phosphate

*Fat soluble formula (not malabsorption)*  
**First choice:** phytomenadione (vitamin K1)
Chapter 10 — Musculoskeletal and joint disorders

10.1 Drugs used in rheumatic diseases and gout

10.1.1 NSAIDs

**First choice:** ibuprofen  
**Second choices:** naproxen  
or cox II - etoricoxib 30mg (gout)

Additional Prescribing Advice
- Consider whether an NSAID is required; regular dosing of paracetamol is often adequate, e.g. for osteoarthritis. (See NICE guidance CG 59)
- Relative contra-indications to NSAIDs include heart failure, hypertension, renal impairment, peptic ulceration; absolute contra-indications include proven hypersensitivity to aspirin or any NSAID
- NSAIDs may worsen asthma; they are contra-indicated if aspirin or any other NSAID has precipitated attacks of asthma
- Intramuscular or intravenous diclofenac must only be used for up to 2 days due to the risk of tissue necrosis.
- Long-term use of ibuprofen has been linked with the interference of cardioprotective effects of low dose aspirin.
- Cox-2 inhibitors are only preferable to NSAIDs when specifically indicated.

*Patients at high risk of serious gastro-intestinal adverse events:*
**First choice:** NSAID  + omeprazole or lansoprazole

10.1.2.1 Systemic corticosteroids

**First choices:**
- Oral: prednisolone (plain)
- Intravenous injection: methylprednisolone sodium succinate (Solu-Medrone®)
- Intramuscular depot injection: methylprednisolone acetate (Depo-Medrone®)
10.1.2.2 Local corticosteroid injections

Intra-articular injections must only be administered by appropriately trained staff.

Soft tissue injection
**hydrocortisone acetate**

Intra-articular injection
**methylprednisolone acetate** (Depo-Medrone ®)
or **triamcinolone acetonide** (Adcortyl ® Intra-articular or Kenalog® Intra-articular)

**Additional Prescribing Advice**
- Corticosteroids should ideally only be commenced after liaison with a rheumatologist, and a steroid card given when appropriate.
- Patients should be provided with written information (e.g. the Arthritis Research Campaign leaflet on steroids) and given the opportunity to discuss the benefits and risks of long-term corticosteroids before treatment is commenced.
- Prophylactic bone protection should be offered to patients anticipated to receive any dose of prednisolone daily for longer than 3 months.
- Bone loss is related to the cumulative dose of glucocorticoids and preventative measures should therefore be considered in patients receiving intermittent courses of prednisolone resulting in a cumulative dose of 250mg or more in 3 months.
- Long-term steroids should be withdrawn gradually.
- Intra-articular steroids should be used judiciously and ideally any one joint should not be injected more than 3 times in 1 year.

10.1.3 Conventional disease-modifying antirheumatic drugs (DMARDs)

**First choice:** sulfasalazine e/c (sulphasalazine e/c)

**Second choices:** (initiated in consultation with a specialist):
- methotrexate
- leflunomide
- sodium aurothiomalate
- penicillamine
- azathioprine
- hydroxychloroquine
- prednisolone
Third choices: *(initiated in consultation with a specialist):*  
ciclosporin (cyclosporin) (Neoral®)  
cyclophosphamide

**Additional Prescribing Advice**

- Risks/benefits of disease-modifying antirheumatic drugs (DMARDs) should be discussed with patients before commencing using a written information sheet available from the Arthritis Research Campaign (arc).
- There are shared care protocols for DMARDs
- The CSM has received reports of prescription and dispensing errors for methotrexate that have resulted in serious and fatal adverse reactions. Methotrexate tablets should be prescribed in 2.5mg strength only. The 10mg strength should not be used since they may be confused with the 2.5mg tablets. (see NPSA alert)
- Providing monitoring procedure is followed, NSAIDs may be prescribed with methotrexate.
- The brand of ciclosporin to be dispensed should be specified since there are differences in bioavailability.

**Tumour necrosis factor (TNF) antagonists (cytokine inhibitors)**

*Cytokine inhibitors may be prescribed by rheumatologists after failure of 2 conventional DMARDs for rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis:*

**First choice:** etanercept

**Additional Prescribing Advice**

- The tumour necrosis factor (TNF) antagonists adalimumab, infliximab and etanercept are reserved for specialist use.
- Adalimumab is an alternative for patients with psoriatic arthritis which is not controlled with two DMARDs or etanercept. Infliximab is an alternative for patients with ankylosing spondylitis who do not respond or do not tolerate etanercept.
10.1.4 Drugs for treatment of gout

Acute Attacks of Gout

**First choice:** indometacin (indomethacin)
**Second choices:** naproxen
or colchicine

**Additional Prescribing Advice**
- Colchicine may be preferable to indometacin in the elderly, patients receiving anticoagulants or in heart failure, or when NSAIDs are contra-indicated.
- The dose of colchicine should be reduced if diarrhoea occurs.

Prophylaxis of gout

**First choice:** allopurinol

**Additional Prescribing Advice**
- Allopurinol should be used to prevent recurrent attacks of gout.
- Allopurinol must not be started during an acute attack of gout since it may exacerbate and prolong it.
- To prevent an acute attack of gout on introduction of allopurinol, low dose colchicine (500micrograms 1-2 times daily) or NSAID should be prescribed concomitantly for 6-8 weeks.
- Allopurinol must be started at low dose.
- If acute gout occurs while the patient is receiving allopurinol, continue the prophylactic agent and add in NSAID or colchicine.
- Allopurinol can be started 2-3 weeks after recovery from the acute attack.
- The dose of allopurinol should be reduced in renal impairment and older patients.
10.2 Drugs used in neuromuscular disorders

10.2.1 Drugs used in myasthenia gravis

**First choice:** pyridostigmine bromide  
**Second choice:** neostigmine

**Additional Prescribing Advice**
- Treatment for myasthenia gravis should only be initiated on specialist advice.
- Edrophonium is used in hospital as a diagnostic test for myasthenia gravis.
- Pyridostigmine bromide has a longer duration of action than neostigmine and is first choice for oral use. Neostigmine is useful in patients requiring parenteral treatment.
- An antimuscarinic (e.g. propantheline) may be required to treat side-effects such as sweating, colic, excessive salivation and diarrhoea.
- In more severe cases, prednisolone – a corticosteroid-sparing agent (azathioprine) may be prescribed under specialist supervision for myasthenia gravis.

10.2.2 Skeletal muscle relaxants

**First choice:** baclofen  
**Second choices:** dantrolene sodium, diazepam

**Additional Prescribing Advice**
- The CSM has advised that serious side-effects can occur following abrupt withdrawal of baclofen; therapy should be discontinued by gradual dose reduction over at least 1-2 weeks (longer if symptoms occur).
- Liver function tests should be performed before commencing dantrolene, then repeated on discharge from hospital (or 6 weeks after starting therapy) and at 3 month intervals thereafter.
- Quinine sulphate is used for nocturnal leg cramps.
10.3 Topical NSAIDs

Additional Prescribing Advice

- Topical NSAIDs are of limited proven benefit. Topical rubefacients may provide symptomatic relief for patients who find massaging the skin helpful. Transvasin® cream may be prescribed and is cheaper than topical NSAIDs.
- NICE guideline CG59 osteoarthritis suggests topical agents may be of benefit in some patients.
Chapter 11 - Eye

11.1 Administration of drugs to the eye

- Drugs administered as eye drops penetrate directly into the globe through the cornea. Absorption may also occur into the general circulation via conjunctival vessels or from the nasal mucosa after drainage of excess preparation down through the tear ducts; this can produce systemic side-effects. Systemic absorption can be reduced by 'punctal occlusion', i.e. pressing tightly with a finger on the inside corner of the eye for about half a minute after instilling the eye drop.

- Eye drops should be instilled by pulling down the lower eyelid and putting one drop into the pocket that is formed. The eye should then be closed tightly for about a minute (or see ‘punctal occlusion’ above). The conjunctival fornix can only accommodate one drop; since any extra will overflow (possibly leading to systemic absorption), only one drop should be used.

- Eye ointments may be applied to the inside of the lower eyelid when a prolonged action is required.

- Eye ointments are applied by starting at the inside corner of the eye and squeezing a thin line (about half a centimetre) along the inside of the lower lid, then blinking the eye.

- Subconjunctival injection may be used to administer anti-infective drugs, mydriatics or corticosteroids for conditions not responding to topical therapy.

- Contact lenses should not generally be worn while using eye drops containing preservatives, or eye ointments. For further information see BNF section 11.9

- If using 2 different eye drops, leave a period of about 5 minutes between the two drops. If using drops and ointment, use the drop first then wait 5 minutes before applying the ointment.

11.2 Control of microbial contamination

- Eye drops in multi-use containers for use in the community should be discarded 4 weeks after opening to avoid contamination. Note: preservative-free preparations may be single-use only or to be discarded 1 week after opening. It is not generally necessary to use separate bottles for each eye (except immediately after eye surgery), but care should be taken to avoid touching the eye(s) during use to avoid contamination. Most drops do not need to be kept in a fridge, unless directed otherwise.
11.3 Anti-infective eye preparations

11.3.1 Antibacterial eye preparations

*Bacterial conjunctivitis*

**First choice:** no treatment

**Second choices:** chloramphenicol eye drops or ointment

*or* gentamicin 0.3% eye drops if allergy or failure to respond to chloramphenicol

*Chlamydia conjunctivitis*

**First choice:** azithromycin (see also Chapter 5(d))

*Blepharitis*

**First choice:** fusidic acid eye drops m/r

*Corneal ulcers (initiated in hospital)*

**First choice:** cefuroxime 50mg/mL eye drops

* + gentamicin 15mg/mL eye drops

**Second choice:** ofloxacin eye drops

*Corneal abrasions*

**First choice:** chloramphenicol eye ointment

**Additional Prescribing Advice**

*Bacterial conjunctivitis*

- Most cases of acute bacterial conjunctivitis are self-limiting. Treatment should be given if the condition has not resolved spontaneously after 5 days.

*Viral conjunctivitis*

- Antibacterials are not helpful in managing viral conjunctivitis.

*Chlamydia conjunctivitis*

- For proven chlamydial infection, appropriate systemic therapy should be prescribed (see also Chapter 5(d)).
Blepharitis
- Bathing eyes and increased hygiene may be all that is necessary to treat blepharitis.
- Fusidic acid eye drops have a narrower spectrum of activity than chloramphenicol, and are more expensive. They should therefore be reserved for blepharitis as they are particularly effective against Staphylococcal infection.

Corneal abrasions
- Corneal abrasions are simply treated with chloramphenicol eye ointment.

Neonatal conjunctivitis
(significant tissue inflammation with purulent discharge)
- Swab for bacteria and chlamydia.
- Initial treatment with chloramphenicol ointment 4 times daily for 1 week.
- If swabs show chlamydia, change treatment to oral erythromycin 62.5mg 4 times daily for 2 weeks. Remember to also manage and treat parents as appropriate (see Chapter 5(d)).

Blocked tear duct
Watery, intermittently sticky eyes in infants are often due to blocked tear ducts and do NOT require topical antibiotic treatment, unless the eye is red. Simple bathing is all that is needed.

11.3.3 Herpes infections - Hospital only

First Choice: Aciclovir 3% ointment

Additional Prescribing Advice
- Topical aciclovir is used for herpes simplex corneal infections, under hospital supervision.
- Oral aciclovir should be prescribed immediately for ophthalmic zoster.
11.4 Corticosteroids and anti-inflammatory preparations

Corticosteroids

**First choices:** betamethasone  
dexamethasone  
prednisolone

**Additional Prescribing Advice**
- Corticosteroid eye preparations should normally only be used under the supervision of an ophthalmologist because (a) their use may mask and worsen infection (especially herpes simplex keratitis), (b) they may cause glaucoma in some patients, and (c) long-term use can cause cataract.
- Betamethasone 0.1% with neomycin 0.5% is used when an antibiotic is also needed. Sometimes neomycin causes allergy in which case chloramphenicol drops may be prescribed along with betamethasone.
- Fluorometholone 0.1% eye drops are weaker and less likely to raise intra-ocular pressure; they are used for patients where a rise in pressure is a known hazard.
- Prednisolone 0.1% is a very weak steroid used by ophthalmologists in patients with low grade chronic corneal inflammatory disease. It is prescribable but must be obtained from Moorfields Eye Hospital, London.
- Preservative-free preparations are available for patients suspected to be intolerant of preservatives, e.g. dexamethasone 0.1% (Moorfields Eye Hospital), prednisolone 0.5% Minims® and prednisolone 0.1% (Moorfields Eye Hospital).
- Dexamethasone eye drops remain longer in the eye and penetrate the eye better than betamethasone eye drops.

Non-steroidal anti-inflammatory drugs

**First choice:** ketorolac 0.5%

**Additional Prescribing Advice**
- Ketaorolac eye drops is the only multi-dose form of a topical NSAID drop. It is licensed for prevention of postoperative inflammation. It is more expensive than steroid preparations. It may have a role in hospital practice where supervision of steroid administration is difficult.
11.4.2 Other anti-inflammatory preparations

First choice: sodium cromoglicate 2% (prophylaxis) (sodium cromoglycate)
Otrivine-Antistin\textsuperscript{©}(acute)

Additional Prescribing Advice
- Sodium cromoglicate is used to treat allergic conjunctivitis. It has a prophylactic action and must be used regularly even when symptoms improve.
- Otrivine-Antistin\textsuperscript{©} eye drops may be used to treat acute allergic conjunctivitis as a short-term measure. Long-term use should be avoided because of rebound hyperaemia.
- Both Otrivine-Antistin\textsuperscript{©} and sodium cromoglicate drops can be bought over-the-counter.

11.5 Mydriatics and cycloplegics

(a) therapeutic uses
Antimuscarinics atropine 1%
cyclopentolate 1%
Sympathomimetic phenylephrine 2.5%

Additional Prescribing Advice
- Antimuscarinics dilate the pupil (mydriasis) and paralyse the ciliary muscle (cycloplegia). They are used in the treatment of anterior uveitis.
- Atropine is the most potent and has the longest duration of action (7 days or more).
- Cyclopentolate is less potent and of shorter duration (up to 24 hours).
- Phenylephrine may be used to supplement the mydriatic effect of these.
- Contact dermatitis occurs relatively frequently when atropine is used in the long term.
(b) diagnostic uses

Antimuscarinic tropicamide

Additional Prescribing Advice

- Tropicamide (with or without phenylephine) is short-acting (up to 3 hours) and is a useful mydriatic prior to examining the eye. It can cause blurred vision and patients should not drive until this has settled.

- The BNF advises caution as mydriasis may precipitate acute angle-closure glaucoma in a very few patients usually aged over 60 years and hypermetropic, who are predisposed to the condition because of a shallow anterior chamber. However, the risk is so minimal that this should not be regarded as a contraindication to its use.

Paediatric uses

- Cyclopentolate 1% drops are used for refraction and fundus examination in children.

- Atropine 1% eye ointment is used for refraction and fundus examination in children with darkly pigmented irises. Ointment is instilled twice on the day before examination and once on the morning of the visit. Systemic absorption may occasionally lead to facial flushing.

- Atropine 1% eye drops or ointment may be used once daily in the "good" eye in patients with a lazy eye (as an alternative to wearing an eye patch).
11.6 Treatment of glaucoma - only initiated by Opthalmologist

**Suggested treatment of glaucoma** At each stage, consideration should be given to withdrawing a drug if there is no significant pressure response.

- **Prostaglandin analogue**
  - First choice: travoprost
  - Second choice: bimatoprost

Open-angle glaucoma and treated angle-closure glaucoma are not contra-indications to the use of oral drugs that have anticholinergic effects.

**(a) prostaglandin analogues**
- First choice: travoprost
- Second choice: bimatoprost
Additional Prescribing Advice

- Latanoprost may cause an increase in brown iris pigment. Following cataract surgery it can cause macular oedema.
- Latanoprost initially causes conjunctival hyperaemia. This should not be painful and wears off as the eye becomes accustomed to it (usually in about 4 weeks).
- Combination products are available as: Ganfort (bimatoprost/timolol) and Duotrav (travoprost/timolol).

(b) beta-blockers

First choice: timolol

Additional Prescribing Advice

- Systemic absorption can follow topical application and contra-indications are therefore asthma, bradycardia and congestive heart failure. This applies to all topical beta-blockers.
- Timolol eye drops are also available in preservative-free units. A long-acting once daily formulation (Timoptol®-LA) is available for patients who have a problem with compliance.
- Timolol 0.5% eye drops have no advantage over 0.25% eye drops.

(c) carbonic anhydrase inhibitors

First choices: dorzolamide (topical)
or acetazolamide (systemic)

Additional Prescribing Advice

- Dorzolamide can cause allergic conjunctivitis.
- Allergy can occur.
- Dorzolamide and acetazolamide are contra-indicated in patients allergic to sulphonamides.
- Acetazolamide can be given orally but long-term use is not advisable because of side-effects. These include metabolic acidosis and electrolyte imbalance; renal calculi; paraesthesia; headache and malaise; gastro-intestinal upset; blood dyscrasias.
- Cosopt® eye drops (dorzolamide 2%, timolol 0.5%) is available as a combination product. Preservative free unit dose eye drops are available for those who have proven sensitivity to the preservative benzalkonium chloride.
(d) alpha2-agonists

First choice: brimonidine

Additional Prescribing Advice
- Brimonidine can cause allergic conjunctivitis. It should not be used with tricyclic antidepressants or MAOIs, or in children under 5 years.

(e) miotics

First choice: pilocarpine

Additional Prescribing Advice
- Pilocarpine causes a small pupil which can compromise visual acuity.
- Headache is a frequent symptom in the first fortnight of treatment.
- Four times a day application can be difficult for elderly people.

(f) drugs used in acute angle-closure glaucoma

Acute angle-closure glaucoma is an emergency and the definitive treatment is laser iridotomy. The pressure of the eye is usually very high and initial treatment is aimed at reducing this.
- Acetazolamide.
- Pilocarpine 2%.
- Timolol 0.25%.
- Mannitol 20% solution may be used if the intra-ocular pressure remains high despite the above measures. It must be given under close supervision because of the danger of volume overload.
11.7 Local anaesthetics

**First choice:** oxybuprocaine  
**Second choice:** tetracaine (amethocaine)

**Additional Prescribing Advice**
- Oxybuprocaine eye drops is the recommended local anaesthetic for use before ophthalmic procedures e.g. tonometry. It has a very rapid onset of action (about 30 seconds).
- Tetracaine (amethocaine) eye drops produce a more profound anaesthesia than oxybuprocaine and are suitable for use before minor surgical procedures. It has a temporary disruptive effect on the corneal epithelium.
- Local anaesthetic drops should never be used for the symptomatic control of pain because of corneal epithelium toxicity.
- Proxymetacaine 0.5% eye drops (Minims®) cause less initial stinging than oxybuprocaine and is useful in children e.g. before the instillation of mydriatic/cycloplegic drops for refraction, which sting on instillation.
11.8 Tear deficiency and diagnostic stains

11.8.1 Preparations for tear deficiency

Eye drops
First choice: hypromellose 0.3%
Second choice: polyvinyl alcohol (Liquifilm Tears®)
or carbomers (Viscotears®)
Eye ointment: Lacri-Lube®

Additional Prescribing Advice
- These preparations are available over-the-counter.
- Chronic soreness of the eyes due to reduced / abnormal tear secretion often responds to tear replacement therapy. The severity of the condition and patient preference will often guide the choice of preparation.
- Frequent instillation of drops (e.g. hourly hypromellose) may cause a sensitivity reaction to the preservative in the drops. There are several preservative-free artificial tear preparations available e.g. Artificial Tears Minims®, Liquifilm Tears® single-dose units, Celluvisc®, Viscotears® single-dose units. There is also a relatively cheap multi-dose hypromellose preservative-free available from Moorfields (bottle keeps for 1 week in the fridge after opening). Hypromellose eye drops is the traditional choice of treatment for tear deficiency. It is the cheapest and the least viscous.
- Acetylcysteine 5% with hypromellose 0.35% (Ilube) drops is useful as a mucolytic agent.

11.8.2 Ocular NSAIDs (see 11.4)

11.8.3 Ocular diagnostic stains

First choice: fluorescein strips

Additional Prescribing Advice
- Fluorescein ophthalmic strips are used to detect corneal abrasions/lesions and foreign bodies. They are also used in tonometry. Fluorescein strips are appropriate in all situations. The solution is rarely required other than to check for leakage of eye wounds.
● Other eye preparations

● **Mydricaine No.1 & No.2** injection is used for rapid dilation of the pupil in iritis and uveitis. *No.1 injection is used in children and No. 2 injection is used for adults.*

● **Sodium chloride** (hypertonic saline) 5% eye drops is used to treat corneal oedema;
Chapter 12 — Ear, nose and oropharynx

12.1 Drugs acting on the ear

12.1.1 Treatment of otitis externa

**First choices:** Otomize® if the eardrum is not perforated
- Betametasone
- or Locorten-Vioform® if perforated eardrum suspected
- or clotrimazole if suspected fungal infection

**Additional Prescribing Advice**
- Many cases of otitis externa recover after thorough cleansing of the external ear canal by suction and dry mopping.
- It is often difficult to differentiate between infection on its own and inflammation, therefore a combined preparation is suitable first choice.
- Otomize® spray is first choice because the delivery system is more effective in getting the drug to the infected site.
- Locorten-Vioform® should not be used for longer than 10 days to prevent fungal overgrowth.
- Recurrent or persistent cases should be swabbed and treated according to sensitivities.
- Otomize® and other products containing aminoglycosides, polymyxin or chlorhexidine should not be used routinely if the eardrum is perforated.
- Eczema of the outer canal and pinna may need treatment with a steroid cream such as Betnovate N

12.1.2 Otitis media

See Chapter 5 (f).

12.1.3 Removal of ear wax

**First choices:** olive oil
- or sodium bicarbonate 5% ear drops
Additional Prescribing Advice

- To soften ear wax the oil should be warmed and a generous amount introduced into the affected ear. The patient should lie with the affected ear uppermost for 5-10 minutes. The treatment should preferably be given for 3-4 days before syringing to ensure maximum softening of the wax.

- Some proprietary preparations contain organic solvents which cause irritation of the meatal skin. In most cases, simple almond or olive oil is just as effective, less likely to cause irritation of the skin and less expensive.

12.2 Drugs acting on the nose

12.2.1 Drugs used in chronic rhinosinusitus (including nasal polyps)

First choice: beclometasone dipropionate
Second choice: mometasone furoate

Additional Prescribing Advice

- for seasonal allergic rhinitis, prophylaxis should begin 1 week before the start of the pollen season and continue throughout. Steroid drops should be prescribed on specialist advice only.

- If symptoms due to nasal polyps are severe, consider a course of oral prednisolone (25mg daily for 2 weeks) followed by topical nasal steroid spray. Steroid drops (Betnesol® drops, Flixonase Nasules ) should be prescribed on specialist advice only.

12.2.2 Topical nasal decongestants

First choice: sodium chloride 0.9%
Second choice: ephedrine

Additional Prescribing Advice

- Inhalation of warm moist air is useful in the treatment of symptoms of acute infective conditions.

- Sodium chloride 0.9% nasal drops may relieve nasal congestion by helping to liquefy mucous secretions.
- Topical nasal decongestants are of limited value because they can give rise to rebound congestion on withdrawal. These products should not be used for more than 7 days.
- Ephedrine nasal drops are the safest sympathomimetic preparation.

12.2.3 Anti-infective nasal preparations

**First choice:** Naseptin®

**Additional Prescribing Advice**
- Elimination of organisms such as staphylococci from the nasal vestibule can be achieved by the use of Naseptin® cream.
- Mupirocin 2% nasal ointment (Bactroban Nasal®) is also available for eradication of staphylococci from the nose but should be reserved for resistant cases only and used for no longer than 10 days to avoid resistance. In hospital, it should be reserved for eradication of methicillin-resistant Staphylococcus aureus (MRSA).

12.3 Drugs acting on the oropharynx

12.3.1 Drugs for oral ulceration and inflammation

**Aphthous ulcers**
- Mouthwash tablets
  **First choice:** benzydamine hydrochloride (Difflam®)
    - chlorhexidine gluconate
  **Second choices:** hydrocortisone sodium succinate lozenge
    or triamcinolone in adhesive basis (Adcortyl in Orabase®)

**Additional Prescribing Advice**
- It is important to consider any possible underlying diagnosis.
- There is some evidence that chlorhexidine gluconate may reduce the duration and severity of each episode of ulceration. Benzydamine mouthwash can be used 10 minutes before meals to relieve pain in patients suffering from aphthous ulcers.
12.3.2 Oropharyngeal anti-infective drugs

Oral thrush
First choice: nystatin suspension

Additional Prescribing Advice
- Nystatin is not absorbed from the gastro-intestinal tract.
- Good denture care is important. Nystatin may be used as a denture soak for the duration of the treatment.

12.3.4 Mouthwashes, gargles and dentifrices

First choices: chlorhexidine gluconate
hydrogen peroxide (for Vincent’s infection)

Additional Prescribing Advice
- There is evidence that chlorhexidine has a specific effect in inhibiting the formation of plaque on teeth. A chlorhexidine mouthwash may be useful as an adjunct to other oral hygiene measures for infection or when toothbrushing is not possible.

12.3.5 Treatment of dry mouth

First choice: Biotene Oralbalance ®
Second choice: Glandosane ®

Additional Prescribing Advice
- Dry mouth can be relieved in many patients by simple measures such as frequent sips of cool drinks or sucking pieces of ice or sugar-free fruit pastilles.
- Biotene Oralbalance ® and glandosane® have ACBS approval for dry mouth due to having (or having undergone) radiotherapy, or sicca syndrome. Prescriptions should be marked ACBS.
Chapter 13 — Skin

13.1 Management of skin conditions

- The vehicle used in topical preparations influences skin hydration, has a mild anti-inflammatory effect and facilitates penetration of the active component.
- Creams are more cosmetically acceptable than ointments. Gels may be used on the face and scalp while lotions are used for moist conditions and hairy areas. Ointments are much less likely to sensitise and are suitable for chronic dry lesions.
- Possible contact sensitivity to preservatives or antiseptics is the reason for the range of topical agents.

<table>
<thead>
<tr>
<th>Body area</th>
<th>Non-corticosteroid cream/ointment</th>
<th>Corticosteroid cream/ointment</th>
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</thead>
<tbody>
<tr>
<td>Face</td>
<td>15 to 30g</td>
<td>15 to 30g</td>
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<td>Face and neck</td>
<td>15 to 30g</td>
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<tr>
<td>Both hands</td>
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<tr>
<td>Scalp</td>
<td>50 to 100g</td>
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<td>Both arms</td>
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<td>30 to 60g</td>
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<tr>
<td>Both legs</td>
<td>100 to 200g</td>
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<tr>
<td>Trunk</td>
<td>400g</td>
<td>100g</td>
</tr>
<tr>
<td>Groins and genitalia</td>
<td>15 to 25g</td>
<td>15 to 30g</td>
</tr>
</tbody>
</table>

Recommended quantities are for twice daily application for 1 week in adults
13.2 Emollient and barrier preparations

13.2.1 Emollients (moisturisers)

First choice: ointment base  
white soft paraffin 50%/liquid paraffin 50%  
(preservative-free)  
Epaderm® oint  
emulsifying ointment (preservative free)

First choice: cream base  
aqueous cream BP  
Diprobase® cream

Additional Prescribing Advice

- The choice of emollient is guided by individual patient tolerance, preference and ease of use.
- Emollients soothe, smooth and hydrate the skin and are indicated for all dry scaling disorders.
- Emollients should be applied regularly to maintain improvement; and are particularly effective applied after a shower or bath.
- These products, apart from white soft paraffin 50%/liquid paraffin 50%, may be used as soap substitutes by firstly wetting the skin, washing with the cream or ointment, then rinsing off.
- If emollients are being applied to the whole body twice daily, children may need 250g per week and adults 500g per week.
- It is more cost-effective to prescribe emollients in large pack sizes.

13.2.1.1 Emollient bath additives

Emollient bath/shower products without antiseptic
First choice: Oilatum®
Second choices: E45®

Emollient bath/shower products with antiseptic
First choices: Oilatum® Plus  
Dermol®

Additional Prescribing Advice

- Bath additives with antiseptic should be used to reduce staphylococcal carriage in eczematous patients.
Soap substitutes

**First choice:** aqueous cream or emulsifying ointment

**Second choices:** Dermol® 500 lotion (with antiseptic)
- or Diprobase® cream
- or Epaderm® oint (preservative-free)

Additional Prescribing Advice

- Most emollients may be used as soap substitutes by firstly wetting the skin, washing with the cream or ointment, then rinsing off.
- White soft paraffin 50%/liquid paraffin 50% is not suitable as a soap substitute.
- A convenient way to apply emulsifying ointment and Epaderm® ointment is as "soap balls", which are made by putting a scoop of the ointment into tubinette or stockinette

13.2.2 Barrier preparations

**First choices:** zinc and castor oil ointment (contains peanut oil)
- or Conotrane® cream

Additional Prescribing Advice

- Urinary (nappy) rash may clear if skin is left exposed to air; if associated with yeast (candida) infection, an antifungal cream such as clotrimazole cream is useful.
13.3 Topical local anaesthetics and antipruritics

(a) topical antipruritics

First choices: calamine cream or lotion
or crotamiton cream
Second choice: 1% menthol in aqueous cream

Additional Prescribing Advice
- 1% menthol in aqueous cream is useful for patients with non-specific itch. The product Arjun® may be most cost effective, other brands are available.
- Crotamiton is useful for pruritus persisting after treatment of scabies.
- Emollient preparations may be useful for pruritus due to dry skin; sedating oral antihistamines may also be helpful for itch (see section 3.4.1).

(b) topical local anaesthetics

First choice: Emla® cream

Additional Prescribing Advice
- Topical local anaesthetics may be absorbed through mucosal surfaces.
- Local anaesthetics may occasionally cause sensitisation.
- Tetracaine 4% gel may be prescribed in infants from 1 month of age.

(c) chronic urticaria

First choice: cetirizine
Second choice: loratadine

Additional Prescribing Advice
- See section 3.4.1 for nasal allergies and vasomotor rhinitis.
- See section 3.4.3 for allergic emergencies.
- Chlorphenamine may be added at night if sleep is disturbed by itching.
- Cimetidine or ranitidine may also be added for resistant cases.
- Fexofenadine may be used when cetirizine and/or loratadine have been ineffective or where sedation is a problem.
- Antihistamines should be taken regularly for best control. However, if urticarial flares occur at specific times, then they may instead be taken 1 hour before the anticipated exacerbation.
- Chlorphenamine may be given by slow intravenous injection for emergency treatment of severe angioedema. See section 3.4.3.
- Chlorphenamine is more liable to cause drowsiness in older patients.

### 13.4 Topical corticosteroids

**Mild corticosteroid**
- **First choice:** hydrocortisone 0.5%, 1%, 2.5%

**Moderately potent corticosteroid**
- **First choice:** clobetasone butyrate 0.05% (Eumovate®)
- **Second choice:** betamethasone valerate 0.025% (Betnovate-RD®)

**Potent corticosteroid**
- **First choice:** betamethasone valerate 0.1% (Betnovate®)
- **Second choice:** fluocinolone acetonide 0.025% (Synalar®)
- mometasone e furoate 0.1% (Elocon®)

**Very potent corticosteroid**
- **First choice:** clobetasol propionate 0.05% (Dermovate®)

**Additional Prescribing Advice**
- Topical corticosteroids are not recommended in urticaria, rosacea, acne or when a primary infective disease is suspected.
- To minimise the risk of side-effects, the smallest effective amount should be used, reducing strength and frequency of application as the condition settles. The risk of systemic side-effects increases with prolonged use on thin, inflamed or raw skin surfaces, use in flexures, or use of more potent corticosteroids. Occlusion increases efficacy and side-effects. Only mild corticosteroids should generally be used on the face.
- Gloves should be worn during, or hands washed after, application of large quantities of steroid preparations.
- The occlusive effect of ointments increases penetration of the corticosteroid.
- Topical corticosteroids should not be used on infected skin unless the infection is being treated.
- Antibacterials and antifungals with corticosteroids may have a role if there is associated infection.
- Palms and soles may require potent or very potent steroids.
● Loss of effect with time (tachyphylaxis) can occur with prolonged use.
● Mometasone 0.1% (Elocon®) cream or ointment may be prescribed once daily in situations where dressings are being used.
● For the use of topical corticosteroids for lichen sclerosus, see section 7.0.1 (e).

13.5 Preparations for eczema and psoriasis

13.5.1 Preparations for atopic eczema

First step: emollients +/- antiseptic (see section 13.2.1) topical corticosteroid (see section 13.4)

Second step: ichthammol 1% + zinc oxide 15% made to 100% with yellow soft paraffin

*Oral immunosuppressants should only be prescribed on specialist advice. See notes below.*

Additional Prescribing Advice

● All patients with eczema should use an emollient and soap substitute and/or bath oil.
● Emollients with antiseptics should be used to reduce staphylococcal carriage in eczematous patients.
● Exacerbation of eczema may represent secondary bacterial or viral infection. Appropriate swabs should be taken, and topical antibacterials applied. Systemic antibiotics may be required in widespread infected eczema.
● Preparations containing coal tar with hydrocortisone may be useful in eczema.
● Tacrolimus ointment 0.03% or 0.1%, or pimecrolimus cream 1%, are usually recommended second-line for patients suffering moderate eczema uncontrolled by topical steroids or those at risk of significant steroid-induced adverse effects.
● Ciclosporin, azathioprine or systemic corticosteroids should be initiated on specialist advice only, with responsibility for monitoring agreed.
● Topical corticosteroids should be tailed off slowly and if possible withdrawn as the condition settles. However, long-term intermittent use may be required in chronic disease.
● Sedating antihistamines may be used short-term for pruritus (see section 3.4.1).
13.5.2 Preparations for psoriasis

**Vitamin D and analogues**

**First choice:** calcipotriol  
**Second choice:** calcitriol

*Other topical preparations for psoriasis used in combination*
- coal tar  
- dithranol  
- emollients (see section 13.2.1)  
- mild/moderate topical corticosteroids (for face or flexures) (see section 13.4)  
- salicylic acid containing preps (for scaling)

**Additional Prescribing Advice**
- Calcitriol may be less irritant than calcipotriol and therefore better tolerated.  
- Topical vitamin D analogues may be alternated with a moderately potent steroid.  
- Treatment choice depends on site, extent of psoriasis and patient preference and tolerance.  
- Guttate psoriasis requires emollients and perhaps a mild tar preparation such as Exorex® lotion; phototherapy may help.  
- Salicylic acid 2% or 3% may enhance loss of scale.  
- "Lotion" should be specified when prescribing Exorex®  
- Coal tar preparations are effective but may stain skin, hair, clothes.  
- Potent and very potent topical corticosteroids should be used on specialist advice only; they may precipitate unstable and pustular psoriasis after stopping.  
- Phototherapy, methotrexate, ciclosporin, acitretin should be initiated on specialist advice only, with responsibility for monitoring agreed.
13.6 Acne and rosacea

(a) acne

Topical treatment:
- benzoyl peroxide
- antibiotics (eg. clindamycin lotion)
- retinoids (adapalene, tretinoin)

Systemic treatment
First choices: oxytetracycline
or erythromycin
Second choice: lymecycline
(an option in women is Dianette®; see prescribing notes)

Under specialist supervision only: isotretinoin

Additional Prescribing Advice
- Topical treatment takes at least 30 days to become effective.
- Topical antibiotics are as effective as oral antibiotics but encourage resistance and are more expensive.
- Topical retinoids are recommended for comedonal acne; they may initially cause redness of the skin.
- Topical combinations products are available and may enhance compliance.
- Oxytetracycline may take up to 6 months of compliant use to achieve maximum benefit.
- Dianette® (cyproterone acetate with ethinylestradiol) is a treatment for severe acne and only in those patients may it also be used as an oral contraceptive (see section 7.3.1). In those who do not require contraception, Dianette® should be withdrawn 3-4 cycles after the treated condition has completely resolved. If ongoing contraception is required, substitution with another COC is likely to maintain the improvement.
- Some drugs, including enzyme-inducers and antibiotics, may impair the efficacy of oral contraceptives; see BNF for details.
- Doxycycline can cause photosensitivity in some patients. Minocycline may be an alternative but prolonged use should be avoided due to the rare risk of liver damage; patients receiving minocycline for longer than 6 months should be monitored at least 3 monthly thereafter for signs and symptoms of hepatitis or SLE.
- Tetracyclines and retinoids (systemic or topical) must be avoided in pregnancy.
- Severe acne requires oral antibiotics and referral for consideration of isotretinoin for treatment failures. Oral isotretinoin (Roaccutane®) is a toxic and teratogenic drug which is only prescribable by a consultant dermatologist.
- Prescription of systemic isotretinoin for women is only possible if adequate contraception is undertaken (Pregnancy prevention programme).

ACNE ALGORITHM

(b) rosacea

**First choices:** metronidazole topical
oxtetracycline oral

**Second choices:** lymecycline
erthromycin (if pregnant)

**Additional Prescribing Advice**
- There is no effective treatment for redness of the skin due to rosacea; camouflage creams may be required (see section 13.8.2).
- Mild rosacea is best treated with a topical agent.
- Pustular rosacea is best treated with systemic antibiotics.
13.7 Preparations for warts and calluses

First choice: salicylic acid
Second choice: formaldehyde

Additional Prescribing Advice
- These preparations are suitable for all cutaneous warts except facial and genital warts.
- Formaldehyde gel may be useful for persistent plantar mosaic warts.
- The wart surface should be rubbed with a file or pumice stone, and the surrounding skin protected, before each application. If application becomes painful, treatment should be withheld for a few days then recommenced.

13.8 Sunscreens and camouflagers

13.8.1 Sunscreening preparations

First choices: Uvistat® cream (SPF 30) (non-fragranced)
E45 Sun® lotion (SPF 50) (non-fragranced)

Additional Prescribing Advice
- The choice of sunscreen depends on individual patient need, tolerance and evidence of sensitivity to excipients.
- Sunscreens with SPF greater than 15 are prescribable for photosensitive skin disorders including genetic disorders, vitiligo, following radio-therapy, photo-aggravated rosacea, or recurrent herpes simplex labialis.
- Tinted preparations are available for darker skins or patients with vitiligo.
- Prescriptions should be endorsed 'ACBS'.
13.8.1.1 Actinic keratosis

(a) Small non tender keratoses

**First choices:** no treatment
or diclofenac gel 3% (Solaraze®)

(b) Extensive thicker keratoses

**First choices:** cryotherapy
or fluorouracil (Efudix ®)

**Additional Prescribing Advice**
- Actinic keratosis are pre-malignant but transformation to squamous cell carcinoma is rare. Patients must be referred if diagnosis is uncertain or if lesions become thickened.

13.8.1.2 Superficial basal cell carcinoma

- Imiquimod cream 5% may be prescribed by dermatologists for the topical treatment of small superficial basal cell carcinoma in adults in whom standard treatment with surgery or cryotherapy is contraindicated.

13.8.2 Camouflagers

**First choice:** Dermablend ®

**Additional Prescribing Advice**
- Camouflagers are prescribable for postoperative scars, other deformities, and as an adjunctive therapy for emotional disturbances due to disfiguring skin disease e.g. vitiligo.
- Prescriptions should be endorsed "ACBS".
13.9 Shampoos and some other scalp preparations

**First choices:** coconut oil containing shampoo (capasal, ccoois ointment)
Polytar® liquid (coal tar)
ketonazole shampoo

**Second choice:** T/Gel® shampoo

**Additional Prescribing Advice**
- Treatment depends on the severity of the condition. Shampoo formulations are preferred for moderate scaly scalp conditions whereas more severe conditions may require an ointment.
- Ketoconazole shampoo is often helpful for seborrhoeic dermatitis of the scalp.

13.10 Anti-infective skin preparations (see also Chapter 5)

**Antiseptics:** silver sulfadiazine (silver sulphadiazine) (for Gram -ve organisms)
silver nitrate solution 0.5% w/v (for exudative leg eczema or ulcers)
potassium permanganate for infected eczema of hands and feet

**Topical antibiotics:** fusidic acid topical (for Gram +ve organisms)
metronidazole topical (for anaerobes)

**Additional Prescribing Advice**
- Topical antibiotics, such as fusidic acid, should only be used for localised infections and short-term to reduce risk of bacterial resistance.

*Burns*
- Silver sulfadiazine cream is used for infected burns and ulcers.

*Exudative eczema*
- See section 13.5.1.

*Fungating tumours*
- Metronidazole gel is helpful for fungating tumours.

*Impetigo*
- Mild impetigo may be treated with topical fusidic acid but resistance may develop if used alone for prolonged periods. Oral flucloxacillin may be prescribed for extensive or bullous impetigo. See Chapter 5(e).

*Leg ulcers*
- See Wound Dressing and Bandages Section 13.13.
13.10.2 Antifungal preparations (see also Chapter 5)

First choice: clotrimazole cream  
Second choice: terbinafine cream

Additional Prescribing Advice
- Both choices can be purchased over-the-counter.
- Selenium sulphide shampoo is useful for pityriasis versicolor; it should be applied once to wet skin, then washed off after 15-20 minutes; repeat after 1 month if necessary. Clotrimazole cream may be prescribed for localised infection.
- Terbinafine cream (but not oral terbinafine) is effective for pityriasis versicolor.

13.10.4 Parasiticidal preparations

(a) scabies

First choice: permethrin

Additional Prescribing Advice
- All members of the household and close contacts should be treated simultaneously, paying particular attention to finger webs and under the nails.
- Clothes and bedlinen should be washed at normal temperatures at time of treatment.
- In pregnancy, malathion in an aqueous basis is recommended (Derbac-M® or Quellada M® liquid).

(b) head lice

First choices: malathion or phenothrin  
Second choice: carbaryl
**Additional Prescribing Advice**

- Head lice should be treated with lotion or liquid. Products with short application times e.g. cream rinse and mousse formulations, are not recommended. Shampoos are diluted too much during use to be effective and should not be used.
- A second application 7 days after the first is needed.
- Aqueous formulations are preferred in severe eczema, asthmatic patients and small children.
- A rotational policy for insecticides is outmoded; a mosaic strategy is suggested whereby if a course of treatment fails then a different insecticide is used for the next course.
- Carbaryl is considered a potential human carcinogen and is available only on prescription. However, the risks from intermittent use of head lice preparations are theoretical and remote.
- Malathion should not be applied at intervals of less than 1 week or for more than 3 consecutive weeks since effectiveness is not increased.
- In pregnancy, malathion in an aqueous basis is preferred.
- Permethrin is not recommended for the treatment of head lice since currently available formulations are diluted too much during use.
- Refer to Public Health guidelines for the treatment of head lice

**(c) pubic lice**

**First choices:** malathion  
or permethrin

**Additional Prescribing Advice**

- An aqueous preparation should be applied to all parts of the head and body for 12 hours or overnight; a second treatment is needed after 7 days to kill lice emerging from surviving eggs.
- Alcoholic lotions are not recommended due to irritation of excoriated skin and genitalia.
- Products should be applied to beards and moustaches but not applied to the face or scalp hair.
- If treatment is not effective, a different insecticide should be used for the second course.
- Aqueous malathion lotion is effective for pubic lice affecting the eye lashes.
13.11 Disinfectants and cleansers

**Cleansers**
*First choice:* sodium chloride 0.9%

**Disinfectants**
*First choices:* chlorhexidine  
or povidone-iodine

**Additional Prescribing Advice**
- Sodium chloride solution 0.9% is suitable for irrigation of skin and wounds.
- Povidone-iodine may produce systemic adverse effects, such as metabolic acidosis, hypernatraemia and renal impairment, if applied to large wounds or severe burns.

13.12 Antiperspirants

**First choice:** aluminium chloride hexahydrate

**Additional Prescribing Advice**
- Glycopyrronium bromide may be prescribed on the recommendation of a specialist as a 0.05% to 2% solution or cream.
- Botulinum toxin may be prescribed and administered by specialists for axillary hyperhidrosis.
13.13 Wound Dressings and Bandages

- The correct dressing for wound management depends both on the type of wound and also on the stage of the healing process.
- The principle stages of healing are:
  - Inflammatory, cleansing, removal of debris;
  - Proliferation, vascularisation, granulation;
  - Epithelialisation, maturation.
- It is now generally accepted that the benefits of managing a moist environment for wound healing has improved the treatment of chronic wounds.
- The ideal dressing needs to ensure that the wound remains:
  - Moist with exudate, but not macerated;
  - Free of clinical infection and excessive slough;
  - Free of toxic chemicals, particles or fibres;
  - At the optimum temperature for healing;
  - Undisturbed by the need for frequent changes;
  - At the optimum pH value.
- As wound healing passes through its different stages, variations in dressing type may be required. See table below.
- The following guidelines are recommended when treating wounds:
  - Always employ an holistic approach to wound care: e.g., investigate any underlying problems
  - Wounds should not be routinely cleansed, but if they require cleansing irrigation should be employed using warm tap water or sodium chloride 0.9%. The decision to cleanse should be based on clinical judgement and consideration of the functions of cleansing. (see box 1)
  - An appropriate timescale for redressing the wound should be decided for each individual patient/wound, taking into account the manufacturer’s instructions.
  - A multidisciplinary approach should be taken in wound care
  - A clear explanation of the action of certain types of dressings must be explained to the patient

13.13.1 See wound formulary for details of products

(a) Alginate dressings
(b) Foam dressings (Polyurethane foam film dressings)
(c) Hydrogel dressings
(d) Hydrocolloid
(e) Vapour-permeable films and membranes
(f) Low adherence dressings and wound contact materials
(g) Odour management dressings
(h) Dressing packs
(i) Surgical absorbent dressings
(j) Maggot (larval) therapy
(k) Antimicrobial Dressing
13.13.2 Bandages

(a) Non-extensible bandages
(b) Light-weight conforming bandages
(c) Tubular bandages
(d) Light support bandages
(e) Light compression bandages (single)
(f) Short stretch compression bandages (single)
(g) High compression bandages (single not mutilayer)
(h) Cohesive bandages (light compression) (single)
(i) High compression multi-layer kits
(j) Light compression multi-layer kits
(k) Orthopaedic wadding
(l) Medicated bandages

13.13.3 Adhesive tapes

13.14 Topical circulatory preparations

Topical circulatory preparations are of little value.

Photodynamic therapy

- Metvix cream
Chapter 14 - Vaccines and immunoglobulins

This section is not included in the formulary
Chapter 15 — anaesthesia

15.1 general anaesthesia

15.1.1 Intravenous anaesthetics
(specialist training required)

**First choices:** propofol
or thiopental (thiopentone)

**Second choice:** etomidate emulsion

**Additional Prescribing Advice**
- Propofol is contra-indicated in patients allergic to eggs and should be used with caution in epileptic patients due to reports of propofol-induced seizures.
- Propofol is used in sub-anaesthetic doses by infusion for sedation.
- Thiopental is used in patients suffering from epilepsy or those who are allergic to propofol. It is contra-indicated in patients allergic to barbiturates or suffering porphyria.

15.1.2 Inhalational anaesthetics
(specialist training required)

**First choice:** isoflurane
+/- nitrous oxide

**Second choice:** sevoflurane
+/- nitrous oxide

**Additional Prescribing Advice**
- Isoflurane is agent of choice for maintenance of anaesthesia since it is less expensive than other agents.
- Sevoflurane is associated with fewer adverse induction effects and can be used for rapid inhalational induction in place of intravenous agents.
- All volatile anaesthetic agents (e.g. isoflurane, sevoflurane) can trigger malignant hyperthermia; nitrous oxide does not trigger malignant hyperthermia.
- Adequate scavenging or external venting should be used.
- Use of absorption breathing systems can permit use of low fresh gas flow techniques which can result in significant economies with these agents.
Inhalational analgesia
(specialist training required)

First choice: nitrous oxide

Additional Prescribing Advice
- Nitrous oxide (maximum dose, 70% in oxygen) is used for sedation or pain relief as:
  1. Entonox® or Equanox® (containing 50% nitrous oxide and 50% oxygen) fixed dose.
  2. Relative analgesia (nitrous oxide 0-70% in oxygen) variable dose.
- Entonox® (or Equanox®) and RA (Relative Analgesia) should be used in well ventilated areas.

15.1.3 Antimuscarinic drugs

First choice: atropine sulphate
Second choice: glycopyrronium bromide

Additional Prescribing Advice
- Atropine and glycopyrronium are both suitable for reducing salivation prior to upper airway endoscopy
- Hyoscine hydrobromide is effective in reducing respiratory secretions

15.1.4 Sedative and analgesic peri-operative drugs

15.1.4.1 Anxiolytics and sedative techniques

Pre-operative sedation
First choices: diazepam
  or temazepam
Second choice: lorazepam

Intravenous sedation (specialist training required)
First choice: midazolam
**Additional Prescribing Advice**

- Temazepam is short-acting and first choice for day case surgery; timing of the dose is important.
- Lorazepam may be preferred for pre-operative sedation because of its amnesic effects.
- Flumazenil can be used to reverse the effect of benzodiazepines.
- Midazolam is drug of choice for intravenous sedation but has no analgesic effect.
- For propofol or Entonox (or Equanox®) sedation see sections 15.1.1 and 15.1.2.

15.1.4.2 Peri-operative analgesics

**General management of pain**
Acute postoperative pain is managed similarly to other pain and usually follows a step down approach. The treatment of acute and chronic pain follows the general principles developed by the World Health Organisation (WHO):

**Step 1: mild pain:** use NSAID and/or paracetamol

\[ \text{Pain persisting or increasing} \]

**Step 2: mild to moderate pain:** use codeine plus paracetamol and/or NSAID

\[ \text{Pain persisting or increasing} \]

**Step 3: moderate to severe pain:** use morphine and paracetamol and/or NSAID

**Note 1:** treatment of postoperative pain will follow a step down approach.
**Note 2:** where appropriate, patients will be offered 3 days supply of analgesics on discharge from day case surgery.

**Step 1 (mild pain)**
**First choices:** ibuprofen
paracetamol

**Second choice:** naproxen

**Additional Prescribing Advice**
- Relative contra-indications to NSAIDs include heart failure, hypertension, renal impairment, peptic ulceration; absolute contra-indications include proven hypersensitivity to aspirin or any NSAID.
● NSAIDs may enhance the effects of warfarin.
● NSAIDs may worsen asthma; they are contra-indicated if aspirin or any other NSAID has precipitated attacks of asthma.

Step 2 (mild to moderate pain)
For greater flexibility, codeine and paracetamol should be prescribed concomitantly as separate drugs (instead of as co-codamol).

**First choice:** paracetamol & codeine 500/30
   +/- NSAID (ibuprofen or naproxen sodium)

**Second choice:** dihydrocodeine

**Additional Prescribing Advice**
● Compound analgesics containing an opioid may produce opioid side-effects and can complicate treatment of overdosage.
● There is no convincing evidence that tramadol offers any advantage over compound analgesics in patients with moderate acute pain; it should not be considered as a first choice analgesic. It may be an alternative to paracetamol/codeine – NSAID in those intolerant to NSAIDs or suffering side-effects, e.g. respiratory depression or constipation.
● Relative contra-indications to NSAIDs include heart failure, hypertension, renal impairment, peptic ulceration; absolute contra-indications include proven hypersensitivity to aspirin or any NSAID.
● NSAIDs may enhance the effects of warfarin.
● NSAIDs may worsen asthma; they are contra-indicated if aspirin or any other NSAID has precipitated attacks of asthma.
● Management of postoperative pain should follow hospital acute pain guidelines where they exist.
● Dihydrocodeine may be prescribed short-term for postoperative pain.
● Codeine is an inefficient analgesic in approximately 10% of patients who are unable to convert it to morphine.
● Co-dydramol is available but is not first choice in the immediate postoperative period.
Step 3 (moderate to severe pain)

First choice: morphine
+ paracetamol
+/- NSAID (ibuprofen or naproxen sodium)

Additional Prescribing Advice
- Morphine should be given parenterally when possible for acute severe pain. The first dose of intravenous morphine should be given slowly, titrated to effect, and respiratory rate monitored. The initial dose is determined by the age and frailty of the patient, and previous exposure to opiates. For use of naloxone, see section 15.1.7.
- A balance has to be found between the lowest dose of morphine required to improve function versus higher doses required to abolish symptoms. Treatment dose should be discussed with the patient.
- Where possible, PCA (Patient Controlled Analgesia) systems should make use of the 1mg/mL (50mL vial) or 2mg/mL (50mL vial) presentation of morphine as it is in a ready to use form.
- Relative contra-indications to NSAIDs include heart failure, hypertension, renal impairment, peptic ulceration; absolute contra-indications include proven hypersensitivity to aspirin or any NSAID.
- NSAIDs may enhance the effects of warfarin.
- NSAIDs may worsen asthma; they are contra-indicated if aspirin or any other NSAID has precipitated attacks of asthma.
- For postoperative pain refer to relevant hospital acute pain protocols.
- Paracetamol 1g/100mL infusion (Perfalgan®) may be prescribed by specialists for the short-term treatment of moderate and severe pain following surgery when administration by the intravenous route is clinically justified by an urgent need to treat pain and/or when other routes of administration are not possible.
15.1.4.3 Opioid analgesics used in anaesthesia

First choices: morphine
or diamorphine

Additional Prescribing Advice
- Fentanyl, alfentanil, remifentanil, morphine and diamorphine are used during anaesthesia under specialist supervision. Since there is a very wide variation in dose requirements, dose should be adjusted to individual patient needs and indication.
- Opioid analgesics given in small doses before or with induction reduce the dose requirement of some drugs used during anaesthesia.
- Where possible, PCA (Patient Controlled Analgesia) systems should make use of the 1mg/mL (50mL vial) presentation of morphine as it is in a ready to use form.
- Alfentanil, fentanyl and remifentanil are useful because of their rapid onset and short duration of action.
- Naloxone may be used to reverse the effects of opioids. See section 15.1.7.
- Older patients are particularly susceptible to respiratory depression and constipation secondary to opiates.

15.1.5 Neuromuscular blocking agents

Specialist training required
First choice: atracurium besilate (atracurium besylate)
Second choice: vecuronium bromide

Rapid sequence induction
First choice: suxamethonium chloride
Second choice: rocuronium bromide

Additional Prescribing Advice
- Repeated suxamethonium doses can cause intense bradycardia or cardiac arrest and patients should be pretreated with an anticholinergic agent.
- Suxamethonium is a depolarising agent causing rapid paralysis. Prolonged paralysis occurs in 1:2400 patients following administration of suxamethonium, as a genetically transmitted defect of metabolism.
- Suxamethonium can trigger malignant hyperthermia.
- Suxamethonium should be used with caution in patients with high potassium levels, such as in renal failure or burns.
15.1.6 Anticholinesterases used in anaesthesia

**First choice:** neostigmine metilsulfate
(neostigmine methylsulphate)

**Additional Prescribing Advice**
- Neostigmine is used for reversal of neuromuscular blocking agents. It requires concurrent antimuscarinic administration to prevent serious bradycardia or cardiac arrest. See section 15.1.3.

15.1.7 Antagonists for central and respiratory depression

**Opioid-induced respiratory depression:**

**First choice:** naloxone

**Reversal of benzodiazepine-induced respiratory depression in anaesthesia:**

**First choice:** flumazenil

Please note that the use and doses of these agents in anaesthesia are different from those given for the treatment of poisoning/overdose.

**Additional Prescribing Advice**
- The antagonist should be matched to the cause of the respiratory depression. All doses should be titrated to the patient’s response.
- Since the duration of action of naloxone may be less than the duration of the opioid causing respiratory depression, repeat doses may be required. Naloxone also antagonises the analgesic effects of opioids.
- Flumazenil is potentially hazardous in patients receiving central nervous system drugs, and may precipitate withdrawal symptoms in patients who are benzodiazepine dependent.
15.1.8 Drugs for malignant hyperthermia due to anaesthesia

**First choice:** dantrolene sodium

**Additional Prescribing Advice**
- Advice regarding the treatment of hyperthermia induced by other drugs, such as MDMA or cocaine, can be obtained from Poisons Information or TOXBASE.
- Patient must be transferred to intensive care as soon as practicable.
- Body temperature may be reduced by surface cooling with ice, or administration of cooled intravenous infusions.
- Treatment of malignant hyperthermia may also include:
  - sodium bicarbonate
  - mannitol
  - furosemide (frusemide)
  - dextrose/insulin infusion
  - intravenous beta-blocker

15.2 Local anaesthesia

*Skin surface application*

**First choices:** Emla®

or tetracaine (amethocaine) (Ametop®)
Skin infiltration
**First choice:** lidocaine (lignocaine)  
+/- adrenaline (epinephrine)

**Second choice:** bupivacaine  
+/- adrenaline (epinephrine)

Biers block
**First choice:** prilocaine 0.5%

Digital nerve block
**First choice:** lidocaine (lignocaine)

**Second choice:** bupivacaine

Intra-articular
**First choice:** bupivacaine

**Second choice:** lidocaine (lignocaine)

Additional Prescribing Advice
- Local anaesthetics can be very toxic and therefore great care should be taken to avoid inadvertent injection into a vein or accidental overdose.
- Vasoconstrictors (adrenaline or octopressin) should not be injected into extremities.
- Choice of local anaesthetic, concentration and the presence of a vasoconstrictor can depend on total dosage required, site of insertion/application and intended surgical procedure.
- Maximum doses of each agent also depend on total dose, site of injection, presence of vasoconstrictor and vascular state of the tissues.
- Emla™ cream is associated with less skin sensitisation than Ametop™ gel. However, Ametop™ gel has a faster onset for situations where speed is important, and causes localised venodilation making cannulation easier.
- Levobupivacaine is less cardiotoxic than bupivacaine and can be used for high dose blocks which have a significant potential for accidental intravenous placement.
- Lower concentrations of anaesthetics cause less stinging on injection; irritation is reduced by warming anaesthetic solutions prior to injection.
- The total dose of adrenaline should not exceed 500micrograms (i.e. 5mL of a 1 in 10,000 solution, or 0.5mL of a 1 in 1000 solution).
• Lidocaine has a faster onset of action and is less toxic than bupivacaine. However, bupivacaine has the advantage of a longer duration of action.

• Major nerve blocks, plexus, epidural and spinal blocks should only be performed by specialists.

• Ethyl chloride spray is occasionally used as a cold stimulus to test the height of epidural or spinal block. It is also used in general practice when rapid topical anaesthesia is required for a short procedure. It is now available in metal cans, which do not explode or shatter when dropped. Its use in glass vial sprays is no longer recommended due to the risk of fire, explosion and serious inhalational overdose for all in the vicinity if dropped or broken.
Absence seizure 73
Acamprosate 77-78
ACBS 127,152,162-3
ACE inhibitors 40-41
Acetazolamide 144-5
Acetylcysteine 147
Aciclovir 139
Acidosis 40,82,126,144,167
Acitretin 159
Acne 98,101-4,157,160-61
Acrivastine 49
Acromegaly 96,120
Actinic keratosis 163
Adalimumab 133
Adapalene 160
Adcal 93-95,128,130
Adcortyl® 132,151
Addisons disease 87
ADHD 61
Adrenaline 31,60,179
ALARM symptoms 9
Alcohol withdrawal 77-8
Alendronate 93-5
Alfacalcidol 87,93,129-30
Alfentanil 176
Alfuzosin 107
Alkylating drugs 113
Allergic emergencies 49-50
Allodynia 69
Allopurinol 114,134
Alpha blockers 107
alpha-2-agonists 145
alprostadil 110
Aluminium chloride 167
Amantadine 76
Amenorrhoea 91,104
Amethocaine 146,178
Amiloride24
Aminophylline 44
Amiodarone 22,25,40
Amisulpride 57
Amisulpiride 59,66,69-71
Amlodipine 29
Anaemia 9,122-24
Anaesthesia 56,146,171,175-7
Analgesics 14,20,65-71,172-76
Anastrozole 117-8
Angina 25-30,34,38,116
Angiotensin II receptor 27,41
Ankylosing spondylitis 133
Antacids 6,14,20
Antimuscarinics 14,44,108,135,141-2,172
Antineoplastics 113
Antiperspirants 167
Antiplatelets 34
<table>
<thead>
<tr>
<th>Antiproliferative agent 114</th>
<th>Bimatoprost 143-4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antipruritics 156</td>
<td>Biotene oralbalance® 152</td>
</tr>
<tr>
<td>Antipsychotics 57-8</td>
<td>bisacodyl 15</td>
</tr>
<tr>
<td>Antispasmodics 7</td>
<td>Bisoprolol 26,40</td>
</tr>
<tr>
<td>Antithyroid 85-6</td>
<td>Bisphosphonates 93-5,121</td>
</tr>
<tr>
<td>Anusol 19</td>
<td>Bleomycin 53,113</td>
</tr>
<tr>
<td>Anxiety 26,54-7,60</td>
<td>Blepharitis 138-9</td>
</tr>
<tr>
<td>Anxiolytics 54-5,60,172</td>
<td>Blood glucose monitoring 58,81,84</td>
</tr>
<tr>
<td>Aphthous ulcers 151</td>
<td>Bortezomib 113</td>
</tr>
<tr>
<td>Aqueous cream 154-56</td>
<td>Botulinum toxin 167</td>
</tr>
<tr>
<td>Arachis oil enema 14-15</td>
<td>Bowel cleansing solutions 16-18</td>
</tr>
<tr>
<td>Arjun® 156</td>
<td>Breast cancer 89-91,101,117-118,121</td>
</tr>
<tr>
<td>Aromatic inhalations 53</td>
<td>Brimonidine 143,145</td>
</tr>
<tr>
<td>Ascorbic acid 109,129</td>
<td>Bromocriptine 75,96-99</td>
</tr>
<tr>
<td>Aspirin 34,38-9,55,60,65,70,81,131,173-5</td>
<td>Bronchiectasis 53</td>
</tr>
<tr>
<td>Atosiban 99</td>
<td>Budesonide 13,45-7</td>
</tr>
<tr>
<td>Atracurium besilate 176</td>
<td>Bumetanide 23,41</td>
</tr>
<tr>
<td>Atropine 25,63,141-2,172</td>
<td>Bupivacaine 179-80</td>
</tr>
<tr>
<td>Atypical antipsychotics 57-8</td>
<td>Bupropion 78</td>
</tr>
<tr>
<td>Aura 71</td>
<td>Busulfan 113</td>
</tr>
<tr>
<td>Avandamet® 82</td>
<td>Cabergoline 96,99</td>
</tr>
<tr>
<td>Azathioprine 13,14,132,135,158</td>
<td>CABG 39</td>
</tr>
<tr>
<td>Azithromycin 138</td>
<td>Caffeine citrate 44</td>
</tr>
<tr>
<td>Baclofen 135</td>
<td>Calamine 156</td>
</tr>
<tr>
<td>Bactroban nasal® 151</td>
<td>Calcineurin inhibitor 114-5</td>
</tr>
<tr>
<td>Bandages 164,168-9</td>
<td>Calcipotriol 159</td>
</tr>
<tr>
<td>Barbiturates 56,171</td>
<td>Calcitriol 159</td>
</tr>
<tr>
<td>Barrier preparations 154-5</td>
<td>Calcium 87,93-5,121,128-30</td>
</tr>
<tr>
<td>Bath additives 154</td>
<td>Calcium channel blockers 28-9,40</td>
</tr>
<tr>
<td>BCG 116</td>
<td>Calcium polystyrene sulphonate 125</td>
</tr>
<tr>
<td>Beclometasone 45-49,150</td>
<td>Calcifvit 94-6,128,130</td>
</tr>
<tr>
<td>Bendroflumethiazide 23</td>
<td>Calluses 162</td>
</tr>
<tr>
<td>Benzatropine (benztropine) 63</td>
<td>Camouflage creams 161-3</td>
</tr>
<tr>
<td>Benzhexol 76</td>
<td>Candesartan 27,41</td>
</tr>
<tr>
<td>Benzodiazepines 54,59,77,173</td>
<td>Candidiasis 45,100,155</td>
</tr>
<tr>
<td>Benzoin compound tincture 53</td>
<td>Capasa® 164</td>
</tr>
<tr>
<td>Benzoyl peroxide 160-1</td>
<td>Capecitabine 113</td>
</tr>
<tr>
<td>Benzydamine 151</td>
<td>Capsaicin cream 69</td>
</tr>
<tr>
<td>Beta blockers 26-9,54,86,143-4,178</td>
<td>Carbamazepine 69,73</td>
</tr>
<tr>
<td>Beta2 agonists 43-4</td>
<td>Carbaryl 165-6</td>
</tr>
<tr>
<td>Betahistine 64</td>
<td>Carbinamazole 96</td>
</tr>
<tr>
<td>Betamethasone 140,157</td>
<td>Carbocysteine 53</td>
</tr>
<tr>
<td>Betnovate 149,157</td>
<td>Carbomers 147</td>
</tr>
<tr>
<td>Bexarotene 113</td>
<td>Carmustine 113</td>
</tr>
<tr>
<td>Bezaflibrate 36</td>
<td>Carvedilol 26,40</td>
</tr>
<tr>
<td>Bicalutamide 119</td>
<td>Caverject 111</td>
</tr>
<tr>
<td>Bicarbonate 109,126,149,178</td>
<td>Cefuroxime 138</td>
</tr>
<tr>
<td>Biers block 179</td>
<td></td>
</tr>
<tr>
<td>Biguanides 81-2</td>
<td></td>
</tr>
<tr>
<td>Celluvisco® 147</td>
<td></td>
</tr>
<tr>
<td>cerazette 103</td>
<td></td>
</tr>
<tr>
<td>Cetirizine 49,156</td>
<td></td>
</tr>
<tr>
<td>CFC-free inhalers 43</td>
<td></td>
</tr>
<tr>
<td>Chlamydia 138-9</td>
<td></td>
</tr>
<tr>
<td>Chlodiazepoxide 77</td>
<td></td>
</tr>
<tr>
<td>Chlorambucil 113</td>
<td></td>
</tr>
<tr>
<td>Chloramphenicol 138-40</td>
<td></td>
</tr>
<tr>
<td>Chlorhexidine 149-52,167</td>
<td></td>
</tr>
<tr>
<td>Chlorphenamine 49-50,156-7</td>
<td></td>
</tr>
<tr>
<td>Chlorpromazine 25,57,98</td>
<td></td>
</tr>
<tr>
<td>Cholesteryamine 12,21</td>
<td></td>
</tr>
<tr>
<td>Chronic myeloid leukaemia 116</td>
<td></td>
</tr>
<tr>
<td>Ciclosporin 114-5,133,158-9</td>
<td></td>
</tr>
<tr>
<td>cilest 102</td>
<td></td>
</tr>
<tr>
<td>Cilostazol 30</td>
<td></td>
</tr>
<tr>
<td>Cimetidine 156</td>
<td></td>
</tr>
<tr>
<td>Cinnarizine 64</td>
<td></td>
</tr>
<tr>
<td>Cisplatin 113</td>
<td></td>
</tr>
<tr>
<td>Citalopram 59</td>
<td></td>
</tr>
<tr>
<td>Cladribine 113</td>
<td></td>
</tr>
<tr>
<td>Clenil modulite® 46</td>
<td></td>
</tr>
<tr>
<td>Clindamycin lotion 160</td>
<td></td>
</tr>
<tr>
<td>Clofazam 74</td>
<td></td>
</tr>
<tr>
<td>Clopbotosol 157</td>
<td></td>
</tr>
<tr>
<td>Clobetasone 157</td>
<td></td>
</tr>
<tr>
<td>Clopidogrel 34,37-9</td>
<td></td>
</tr>
<tr>
<td>Clotrimazole 100,149,155,165</td>
<td></td>
</tr>
<tr>
<td>Clozapine 57</td>
<td></td>
</tr>
<tr>
<td>Cluster headache 72</td>
<td></td>
</tr>
<tr>
<td>Co-amilorfruse 24</td>
<td></td>
</tr>
<tr>
<td>Co-benaldopa 75</td>
<td></td>
</tr>
<tr>
<td>Co-careldopa 75</td>
<td></td>
</tr>
<tr>
<td>Co-codamol 66,174</td>
<td></td>
</tr>
<tr>
<td>Co-danthramer/danthrusate 15</td>
<td></td>
</tr>
<tr>
<td>Co-proxamol 66</td>
<td></td>
</tr>
<tr>
<td>Coal tar 158-9,164</td>
<td></td>
</tr>
<tr>
<td>Cocos ointment 164</td>
<td></td>
</tr>
<tr>
<td>Coconut oil 164</td>
<td></td>
</tr>
<tr>
<td>Codeine 12,20,65-6,70,173-4</td>
<td></td>
</tr>
<tr>
<td>Colchicine 134</td>
<td></td>
</tr>
<tr>
<td>Concerta 61</td>
<td></td>
</tr>
<tr>
<td>Condoms 105-6</td>
<td></td>
</tr>
<tr>
<td>Conjunctivitis 138-145</td>
<td></td>
</tr>
<tr>
<td>Conotrane® 155</td>
<td></td>
</tr>
<tr>
<td>Constipation 6,12-18,66,176</td>
<td></td>
</tr>
<tr>
<td>Contact details 5</td>
<td></td>
</tr>
<tr>
<td>Contact lenses 137</td>
<td></td>
</tr>
<tr>
<td>Contraceptives 73,89,94-8,101-6,160-1</td>
<td></td>
</tr>
<tr>
<td>COPD 26,40,47-52</td>
<td></td>
</tr>
</tbody>
</table>

---

**Contact details**

**Index**
Corneal ulcers 138
Corticosteroids 19,43,46-8,87-9,95,114,131,137,140,153,157-9
Corticotrophins 92
Cosmofer® 122-3
Cosopt 145
Cough preparations 53
Cox-2 inhibitors 67,131
Creon 21
Crotamiton 156
Cryotherapy 163
Cyanocobalamin 123
Cyclizine 63
Cyclopentolate 141-2
Cyclophosphamide 113,133
Cyproterone 102,119,160
Cytokine inhibitors 116,133
Cytotoxics 112-3
Dacarbazine 113
Dactinomycin 113
Dantrolene 135,178
Daunorubicin 113
Deferoxamine 123
Demeclocycline 93
Dementia 58,79
Dependence 17,54,77-8
Depo-medrone® 131-2
Depression 29,59,66,69,145
Derbac-M® 165
Dermablend® 163
Dermatology 167
Dermol® 154-5
Dermovate® 157
Desmopressin 92
Dietary fibres 109
Dietetic advice 109
Dihydrocodeine 65,174
Diabetes insipidus 92
Diabetes mellitus 58,84
Diamorphine 66,176
Dianette 98,102,160-1
diaphragms 105-6
Diarrhoea 6,12-13,20,120,134-5
Diazepam 54,63,74,77,135,172
Diclofenac 67,70-1,131
Diclofenac gel 163
Diffam® 151
Digoxin 23
Dihydrocodeine 65,174
Diltiazem 22,29
Dinoprostone 99
Dioralyte® 125
Diprobase® 154-5
Dipyridamole 34
Disinfectants 167
Disodium pamidronate 121
Disulfiram 77
Dithranol 159
DMARDs 132-3
Dobutamine 31
Docetaxel 113
Docusate sodium 15,18
Dometide 7,63,70
Donepezil 59
Dopamine 59
Doxapram 50
Doxazosin 59
Doxorubicin 113
Dry mouth 152
Ductus arteriosus 99
Duloxetine 108
Duotrov 144
DVLA 81
DVT 32
Dysmenorrhea 65,101,106
Dyspepsia 8
Dystonic reactions 7,63,70
Dysuria 109
E45® 154,162
Ear 149-50
Ear wax 149
Ecstasy 158,164-6
Edrophonium 135
Efomoterol 43
Efudix® 163
Electrolytes 125-6
Elocon® 157
Elocon® 157-8
Emergency contraception 102,106
Emfam® 153-157
Emollients 154-9
Emulsion 154-5
Endometriosis 97
Enoxaparin 32
Entacapone 76
Enteral feeds 127
Entonox® 172-3
Enuresis 108
Epaderm® 154-5
Epilepsy 56,73,122
Epinephrine 31,50,179
Epirubicin 113
Epistatus® 74
Epoptin 124
Equanox® 172-3
Equisym 61
Erectile failure 110
Erythropoetin 124
esradiol 100
Estradot® 91
Estramustine 113
Etanercept 133
Ethyl chloride 180
Etomidine 171
Etonogestrel 104
Etoposide 113
Etoricoxib 67,131
Eumovate® 157
Exemestane 117-8
Exenatide 83
Exorex® 159
Extravasation 112
Eye 137
Ezetimibe 36
Femodene 98,102
Femoston® 91
Fentanyl 67,176
Ferrous fumarate 122
Ferrous sulphate 122
Fexofenadine 49,156
Fibrates 36
Fibrinolytics 35
Finasteride 107
Flecainide 25
Flixonase nasules® 150
Fludarabine 113
Fludrocortisone 87
Fluids 86,125
Flumezenil 173,177-8
Flucinolone 157
Fluorometholone 140
Fluorosceine 147-8
Fluorouracil 113,163
Fluoxetine 55,59-60
Flutamide 119
Fluticasone 45-7
Folate 123-4
Folic acid 122,124
Formaldehyde 162
Formoterol 43,47
Fulvestrant 117
Furosemide 23-4,87,125,178
Fusidic acid 138-9,164
Gabapentin 69-70
galactorrhoea 98
Galantamine 79
Ganfort 144
gargles 152
Gastric stasis 63
Gastro-oesophageal reflux 8
Gastrocote 6
Gaviscon 6
Gemcitabine 113
Gemeprost 99
Gentamicin 138
Glandosane® 152
Glaucoma 69,140-45
Gliclazide 81
Glitazone 81-4
Glucagon 83
Glucose 81-87
glycerol suppositories 15
Glyceryl trinitrate 19,28
glycine 109
Glycopicrylron bromide 167,172
GNRH analogue 97
Gonadorelin analogues 97
Goserelin 118-9
Gout 65,131,134
Granisetron 63
Gynaecology 91,97
Gynol II 105
H. Pylori 8-11
H2 receptor antagonists 9-10
Haemorrhoids 3,19
Hairy cell leukaemia 116
Haloperidol 25,57-8,77
Handihaler 44
Head lice 165-6
Heparin 32-3
Herpes 139-40,162
Hirsutism 98,102
HRT 88-94
Hydrocortisone 13,19,47,50,86-8,132,151,158
Hydrogen peroxide 152
Hydroxocobalamin 123
Hydroxycarbide 113
Hydroxychloroquine 22,132
Hydroxyurea 113
Hyoscine 7,63
Hyperalgesia 69
Hypercalcaemia 87,121,128
Hyperglycaemia 58,81
Hyperkalaemia 24,41,125
Hyperparathyroidism 87,128
Hyperprolactinaemia 57,96
Hyperthyroidism 86
Hypoglycaemia 81
Hypomellose 147
Ibuprofen 65-7,70,131,173-4
Ichthammol & zinc oxide 158
Idarubicin 113
Ifofamide 113
Ilube® 147
Imatinib 113
Imipramine 69
Imiquimod cream 163
Immunoglobulins 170
Immunosuppressants 112-5
Implanon 104
Incontinence 108
Incretin mimetic 83
Indometacin 99,134
Inflammatory bowel disease 13,12
Infliximab 13,133
Inhaler devices 42,43,45,46,47
Insomnia 54,56,59
Insulin 81-4,178
Insulin glargine 81
Interferon alpha 116
Interferon beta 116
Interrmittent catheters 111
Intra-uterine devices 106
Introduction 1
Iodine 86
Ipratropium bromide 44,45
Irbesartan 27
Irinotecan 113
Iron 20,122,124
Iron deficiency anaemia 122
Isoflurane 171
Isoniazid 129
Isosorbide dinitrate 28
Isosorbide mononitrate 28
Isotretinoin 160-1
Ispaghula husk 15
Kaposi’s sarcoma 116
Kay-cee-L 125
Kenalog® 132
Ketoacids 85
Ketoconazole 164
Ketorolac 71,140
Klofem® 91
Kloovance® 91
Labyrinthine disorders 64
Lacri-lube® 147
Lactation 96,99
Lactulose 15,18,20
Lamotrigine 73
Lanreotide 96,120
Lansoprazole 11,131
Lansoprazole 11,131
Lanthus 81
Latanoprost 144
Laxatives 14,15,16,17,18,20,67,69 132
Lefllunamide 111
Leg (day) bags 111
Lenograstim 124
Letrozole 117-8
Leukotriene receptor antagonists 48
Leuprolrelin 119
Levemir insulin 81
Levobupivacaine 179
Levodopa 75
Levonelle-2 102
Levotheroxine 85-6
Lewy body dementia 58
Lidocaine 179-80
Lidocaine ointment 19
Liothyronine 85
Lipid regulating drugs 36
Liquid paraffin 154-5
Liquifilm® 147
Loluside 75
Lithium 25,58,72,92
Livial® 91
Local sclerosants 36
Locorten-vioform® 149
Loestrin 102
Logynon 102
Lomustine 113
long term catheters 111
Long-acting progestogen 104
Loop diuretics 23
Loperamide 12,20
Lorazepam 74,172-3
Lymecycline 160-1
Maalox 6
Magnesium hydroxide 15
Magnesium trisilicate 6
Malathion 165-6
Malignant hyperthermia 171,176,178
Malignant melanoma 116
Mania 57
Mannitol 145,178
Marvelon 98,102
MDIs 42,46
Mebetirene 7
medroxyprogesterone acetate 97,104,117
mefenamic acid 97
Megaloblastic anaemia 123
Megestrol 117
Melphalan 113
Menadiol sodium phosphate 130
Meniere's disease 64
Menopause 88-95,117-8
Menorrhagia 35,97,101
Mental health 79
Menthol in aqueous cream 156
Mercaptopurine 113
Mercilon 102
Mesalazine 13
Metformin 81-84,98
Metotrexate 113,132-3,159
Methylphenidate 61
Methylprednisolone 88,131-2
Metoclopramide 7,63,70,98
Metoprolol 26
Metvix 169
Microgynon 102
Micronor 103
Midazolam 74,172
Mifepristone 99
Migraine 26,63,65,70-1
Minerals 128
Mini-wright® 45
Minocycline 160
Minulet 98
Miotics 145
Mirena® 89,97,104,106
misoprostol 99
Mitomycin 113
Modafenin 61
Moisturisers 154
Mometasone 150,157-8
Montelukast 48
Morphine 63-7,173-6
Motion sickness 63
Mouthwash tablets 151
Mouthwashes 152
Movicol 14-16,18,53
MRSA 151
Mucolytics 53
Mupirocin 151
Musculoskeletal disorders 131
Myasthenia gravis 135
Mycofenolate mofetil 114
Mydriatics 137,141-2,146
Mydricaine 148
Myelosuppression 114
Myoclonus 73
Myxoedema 85
Naloxone 66,175-8
Nappy rash 155
Naproxen 63-7,131,134,173-5
Narcolepsy 61
Nasal polyps 150
Naseptin 151
Nausea 63,70
Nebulised saline 53
Nebulisers 42,44-45
Neomycin 140
Neoral® 133
Neostigmine 135,177
Nerve block 179-80
Neuromuscular disorders 135
Neuropathic pain 69
Neutropenia 86,124
Nicorandil 30,110
Nicotine 78
Nifedipine 29,99
Nitrates 28,41,110
Nitrous oxide 171-2
Non-formulary medicines 3
Non-hodgkins lymphoma 116
Noradrenaline 31
noretosterone 97
Norgeston 103
Nose 149-52
NRT 78
NSAID 8,11,41,55,60,65-8,131-6,140,173
Obesity 62
Obsessive compulsive disorder 55
Obstetrics 97-98
Octopressin 179
Octreotide 96,120
Oesophageal varices 93
Oesophagitis 6,9,11
oestrogens 91-92,98,100,108
Ofloxacin 138
Octoxin® 154
Oily phenol injection
Olanzapine 57
Oligomenorrhoea 98
Olive oil 149-50
Omeprazole 11,38,131
Oncology 112
Opioid 66-7,71,174-8
Opioid conversion 68
Oral nutrition 127
Orlistat 62
Oropharynx 149-51
Orthoforms 105
Osteopenia 95
Osteoporosis 88-9,93-5,115,128-30
Otitis externa 149
Otitis media 149
Otomize® 149
Otrivine-antistin® 141
Oxalplatin 113
Oxazepam 77
Oxybuprocaine 146
Oxybutynin 108
Oxycodeone 67
Oxygen 51-52,72,172
Oxytracycline 160-1
Oxytocics 99
oxytocin 99
Pabrinex® 78
Paclitaxol 113
Paclitaxol 113
Pain 7,65-70,93,97,118,146,172-5
Palliative care 15-16,51-2,63,65
<table>
<thead>
<tr>
<th>Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pamidronate 87,121</td>
</tr>
<tr>
<td>Pancreatin 21</td>
</tr>
<tr>
<td>Pancrex V 21</td>
</tr>
<tr>
<td>Panic disorder 55</td>
</tr>
<tr>
<td>Parathyroid 85,87</td>
</tr>
<tr>
<td>Parkinsons 58,64,75-6,96,110</td>
</tr>
<tr>
<td>Paroxetine 55,60</td>
</tr>
<tr>
<td>Partial seizures 73</td>
</tr>
<tr>
<td>PCA 175-6</td>
</tr>
<tr>
<td>Peak flow meters 45</td>
</tr>
<tr>
<td>Pegfilgrastim 124</td>
</tr>
<tr>
<td>Penicillamine 132</td>
</tr>
<tr>
<td>Peptac6</td>
</tr>
<tr>
<td>Peptic ulcer disease 8,38,65</td>
</tr>
<tr>
<td>Perfalgar® 67,175</td>
</tr>
<tr>
<td>Performance anxiety 54</td>
</tr>
<tr>
<td>Pergolide 75</td>
</tr>
<tr>
<td>Perindopril 27,41</td>
</tr>
<tr>
<td>Permethrin 27,41</td>
</tr>
<tr>
<td>Phenobarbitol 73-4</td>
</tr>
<tr>
<td>Phenolephrine 141-2</td>
</tr>
<tr>
<td>Phenytin 73-4</td>
</tr>
<tr>
<td>Phosphate enema 15</td>
</tr>
<tr>
<td>Phosphodiesterase inhibitors 22</td>
</tr>
<tr>
<td>Phototherapy 159</td>
</tr>
<tr>
<td>Phytomenadione 33,130</td>
</tr>
<tr>
<td>Picolax 16,18</td>
</tr>
<tr>
<td>Pilocarpine 145</td>
</tr>
<tr>
<td>Pimecrolimus 158</td>
</tr>
<tr>
<td>Pioglitazone 81,158</td>
</tr>
<tr>
<td>Pituitary hormones 85,88,92,96</td>
</tr>
<tr>
<td>Pityriasis versicolor 165</td>
</tr>
<tr>
<td>Pizotifen 71</td>
</tr>
<tr>
<td>Pleurodesis 53</td>
</tr>
<tr>
<td>Polycystic ovaries 98</td>
</tr>
<tr>
<td>Polyta® 164</td>
</tr>
<tr>
<td>Polyvinyl alcohol 147</td>
</tr>
<tr>
<td>Poractant 50</td>
</tr>
<tr>
<td>Positive inotropes 22</td>
</tr>
<tr>
<td>Potassium bicarbonate 126</td>
</tr>
<tr>
<td>Potassium channel activators 28,30</td>
</tr>
<tr>
<td>potassium citrate 109</td>
</tr>
<tr>
<td>Sodium bicarbonate 126</td>
</tr>
<tr>
<td>Sodium chloride 87,109,125,148,150,167</td>
</tr>
<tr>
<td>Sodium cromoglicate 48,141</td>
</tr>
<tr>
<td>Sodium picosulphate 18</td>
</tr>
<tr>
<td>Sodium valproate 71,73</td>
</tr>
<tr>
<td>Solaraze® 163</td>
</tr>
<tr>
<td>SLS 74,110,153</td>
</tr>
<tr>
<td>Soap balls 155</td>
</tr>
<tr>
<td>Soap substitutes 154-55,158</td>
</tr>
<tr>
<td>Sotalol 25-26</td>
</tr>
<tr>
<td>Spacers 42,45</td>
</tr>
<tr>
<td>Spironolactone 24,41</td>
</tr>
<tr>
<td>Spermicidal contraceptives 105</td>
</tr>
<tr>
<td>Sildenafil 110</td>
</tr>
<tr>
<td>Selenium sulphide 165</td>
</tr>
<tr>
<td>Silver nitrate 164</td>
</tr>
<tr>
<td>Silver sulfadiazine 164</td>
</tr>
<tr>
<td>Sitagliptin 82</td>
</tr>
<tr>
<td>Skin 153</td>
</tr>
<tr>
<td>SIADH 93</td>
</tr>
<tr>
<td>Sibutramine 62</td>
</tr>
<tr>
<td>Sildenafil 110</td>
</tr>
<tr>
<td>Sildenafil 110</td>
</tr>
<tr>
<td>Sodium bicarbonate 126</td>
</tr>
<tr>
<td>Sodium chloride 87,109,125,148,150,167</td>
</tr>
<tr>
<td>Sodium cromoglicate 48,141</td>
</tr>
<tr>
<td>Sodium picosulphate 18</td>
</tr>
<tr>
<td>Sodium valproate 71,73</td>
</tr>
<tr>
<td>Solaraze® 163</td>
</tr>
<tr>
<td>Solfenacin 108</td>
</tr>
<tr>
<td>Solu-medrone® 131</td>
</tr>
<tr>
<td>Somatostatin analogues 96,120</td>
</tr>
<tr>
<td>Sotalol 25-26</td>
</tr>
<tr>
<td>Spacers 42,45</td>
</tr>
<tr>
<td>Spermicidal contraceptives 105</td>
</tr>
<tr>
<td>Spirone lactone 24,41</td>
</tr>
<tr>
<td>SSRI 55,59,60</td>
</tr>
<tr>
<td>Stalevo® 76</td>
</tr>
</tbody>
</table>
Statins 36
Status epilepticus 74
Stoma appliances 20
Stroke 27, 34, 38-39, 67, 90
Strontium 94
Sucralfate 10
Sulphasalazine 132
Sulphurylurea 81-3
Sulpiride 57-8
Sumatriptan 71-2
Supraventricular arrhythmias 25, 29
Sustanon® 92
Suxamethonium 176
Sympathomimetics 31
Synalar® 157
Syntometrine 99
T/Gel® 164
Tacrolimus 114-5
Tacrolimus ointment 158
Tadalafil 110
Talc 53
Tamoxifen 117-8
Tamsulosin 107
Tardive dyskinesia 58, 63
Tear deficiency 147
Temazepam 54, 172-3
Tenecteplase 35
Tension headache 71
Terazosin 107
Terbinafine 165
Terbutaline 43, 99
Teriparatide 94
Terlipressin 93
Testogel® 92
Testosterone 92
Tetracaine gel 146, 156
Tetracosactide 92
Thalidomide 115
Theophyllin 44
Thiamine 78
Thiazides 23, 27, 125
thigh straps 111
Thiopental 171
Thrombocytopenia 32
Thyroid 85-7
Thyrotoxic crisis 86
Tibilone 89-91, 97
Timolol 143-5
Tioguanine 113
Tiotropium 44
Tirofiban 34
TNF antagonists 133
Tolterodine 108
Tonic-clonic 73
Topical NSAIDs 136, 140
Topotecan 113
TOXBASE 178
Tramadol 66, 174
Tranexamic acid 35, 97
Transdermal HRT 88
Transvasin® 136
Trastuzumab 113
Travoprost 143-4
Trazodone 59-60
Tretinoin 160-1
Triamcinolone 132, 151
Tricyclic antidepressants 59, 69, 145
Trigeminal neuralgia 69
Triamcinolone 132, 151
Trihexyphenidyl hydrochloride 76
Triptorelin 119
Tropicamide 142
TSH 85
Ulcer healing drugs 8
Unlicensed medicines 5, 17
Unstable angina 34, 38
Urinary frequency 108
Urine ketone testing 85
Urology products 111
Ursodeoxycholic acid 21
Urticaria 49, 156-7
Uvistat® 162
Vaccines 170
Vaginal atrophy 91, 100
Vaginitis 100
Vaginositis 100
Vardenicline 78
Vasodilators 30
Vecuronium 176
Venofer® 122
Verapamil 22, 29, 72
Vertigo 63-4
Vigabatrin 74
Vinblastine 113
Vinca alkaloids 113
Vincristine 113
Vincents infection 152
Vinorelbine 113