1. Prescribing should be based on safety, efficacy and cost-effectiveness.

2. Medicines should be prescribed only when they are necessary and, in all cases, the benefit of administering the medicine should be considered in relation to the risk involved.

3. The Highland Formulary should constitute the core of all prescribing. It is based upon current evidence, national guidance, local expertise and patient acceptability.

4. Cost-effectiveness matters. As a guiding principle, the most cost-effective medication should be prescribed for a patient. Specifically, prescribers should not prescribe drugs, medicines or appliances whose cost or quantity, in relation to any patient, is in excess of that which is reasonably necessary for the proper treatment of that patient. Such prescribing denies resource for other essential services.

5. The ‘approved’ (non-proprietary or generic) name of a medicine should be used unless there are important differences in formulation and/or bioavailability. Where a generic product is not considered suitable and it is desirable to recommend a particular brand of a drug, this is specified in the Highland Formulary.

6. Prescribers should always prescribe within their clinical competency.

7. When prescribing, clinicians must avoid making assumptions about people with protected characteristics eg gender, age, black and ethnic minority people, and must be alert to any specific considerations required.

Unnecessary or cost-ineffective prescribing cannot be justified:

- unnecessary prescribing exposes patients to risk without benefit
- cost-ineffective prescribing deprives patients in need of new, effective but expensive medicines with the potential to extend life and/or improve quality of life.

If you require a copy of the Highland Formulary in large print or other format, please contact the Formulary Assistant on nhshighland.highlandformulary@nhs.net
ACKNOWLEDGEMENTS

The ongoing working of the Highland Formulary would not be possible without the hard work and enthusiasm of all those involved. Contributions made via review groups and/or the Formulary Subgroup, comments on draft sections and guidelines, and advice on many different aspects of the Formulary development are invaluable, alongside the support of the NHS Highland Area Drug and Therapeutics Committee.

The Formulary Subgroup of NHS Highland Area Drug and Therapeutics Committee

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Evelyn Cromarty (Professional Secretary) Formulary Pharmacist
Susan Caldwell Senior Pharmacist, Medicines Management & Information
Dr Borja Echavarren GP, Lybster Medical Centre
Findlay Hickey Lead Pharmacist (West), North & West Operational Unit
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Dr Robert Peel Consultant Nephrologist
Johnson Swinton Patient Representative
Dr Simon Thompson Consultant Physician
Dr Jude Watmough GP, Culloden Medical Practice

INTRODUCTION

Background

The Highland Formulary is a limited list of medicines approved for local use in hospitals and primary care. The choice of Formulary medicines is made on the basis of clinical effectiveness, cost-effectiveness, comparative safety and patient acceptability, and covers all prescribers.

Using the Highland Formulary

Formulary medicines are generally presented according to the original BNF classification. Most entries contain relevant Formulary information about the medicine such as dose, place in therapy and additional prescribing guidance. Further product information is available in the BNF and in the Summary of Product Characteristics (SPC), which may be available on www.medicines.org.uk.

The Formulary is updated bimonthly. Changes are notified in the eFormulary Update sent to those on the Formulary distribution list; please email the Formulary Assistant to be added to this list (mailto:nhshighland.highlandformulary@nhs.net). The updated version of the Formulary is available on the Intranet (http://intranet.nhsh.scot.nhs.uk) and website (www.nhshighland.scot.nhs.uk) and as an App for iPhone and iPad. This version contains all updates to the Formulary since the printing of this edition and also includes electronic links to guidelines and other websites.

Formulary management

The Formulary is produced under the auspices of the Formulary Subgroup of the NHS Highland Area Drug and Therapeutics Committee (ADTC). The contents reflect wide consultation with practitioners. Output from the Scottish Medicines Consortium, local and national advice on medicines in relation to clinical effectiveness, cost-effectiveness, comparative safety and patient acceptability together with the work of special interest groups in Highland and clinical networks, are also taken into account. If you wish to request a change or addition to the Formulary refer to the flowchart of the assessment process on page iv. For further information or to provide feedback, which is always welcome, please email the Formulary Pharmacist at nhshighland.highlandformulary@nhs.net.
Guidance
Guidance attached to clinical sections is at the end of each chapter. Those working in Argyll and Bute Health and Social Care Partnership (H&SCP) should follow Greater Glasgow and Clyde (GG&C) adult medicines formulary (http://www.ggcprescribing.org.uk/; for further information see Argyll and Bute pharmacy pages on the Intranet). For emergency sedation, prescribers in Argyll and Bute should follow NHS Highland policies.

Medicines in children
Unless otherwise stated, the doses given are for adults with normal hepatic and renal function. Consult the BNF for Children for advice on prescribing for children and local paediatric drug guidelines on the Children’s Services section of the intranet.

Drug names
ADTC supports a policy of generic prescribing for the majority of medicines. It is noted that in some cases, the generic versions of a medicine may not have the exact same indications listed on the market authorisation as the original branded medicine, but as bioequivalence to the original branded medicine must have been demonstrated as part of the generic market authorisation process, ADTC considers that any additional risks of prescribing and dispensing the medicine generically are negligible. Exceptions to the generic prescribing policy are:
- when the pharmacokinetic profiles of different brands of the same medicine differ widely
- medicines with a narrow therapeutic index, where any variation in the drug concentration in the blood increases the risk of toxicity or treatment failure for the patient.
Where Formulary medicines should be prescribed by brand name, this will be indicated in the prescribing notes of the Highland Formulary. This advice does not override an individual clinician’s decision to prescribe what they believe to be the most appropriate treatment.

Medicines Information
Reference is made throughout the Formulary to information and advice available from Medicines Information. This service can be accessed as follows:

Argyll and Bute H&SCP:
Royal Alexandra Hospital, tel: 0141 887 9111 (switchboard), e-mail: medinfo@ggc.scot.nhs.uk

Highland H&SCP:
Raigmore Hospital, tel: 01463 704000 e-mail: nhshighland.medicineinformation@nhs.net

Unlicensed use of medicines
Medicines included in the Formulary are supported by a valid SPC and the indications and/or dosing information reflect those in the corresponding Market Authorisations (formerly known as Product Licences). Where an unlicensed drug is included in the Formulary, this is indicated. Where the Formulary suggests a use (or route) that is outside the licensed indication of a product (‘off-label’ use), this too is indicated. Unlicensed or off-label use of medicines should only be necessary if the clinical need cannot be met by licensed medicines.

A Highland unlicensed and off-label medicines list providing information on those unlicensed medicines and key off-label uses of licensed medicines can be accessed on the Intranet. This provides links to prescribing data, patient information and shared care protocols, where available. It also outlines the approved indications and any restrictions to use in NHS Highland.

Prescribing medicines outside the terms of their Market Authorisation alters (and may increase) the prescriber’s professional responsibility and potential liability; see advice at www.gov.uk/drug-safety-update. The prescriber should be able to justify, and feel competent in using such medicines. Prescribers have a responsibility to advise patients of the status of the product being provided. Prescribers and those dispensing unlicensed medicines or medicines used off-label are advised to consult the current BNF and/or contact Medicines Information as above for further information.
Adverse drug reactions
All suspected serious adverse drug reactions to any drugs/vaccines/complementary remedies; all adverse reactions (including those considered to be non-serious) suspected to be associated with black triangle (▼) medicines; and all adverse reactions that occur in children associated with either established or new medicines and vaccines should be reported by healthcare professionals and patients to the Medicines and Healthcare Products Regulatory Agency (MHRA). The black triangle symbol ▼ indicates that the MHRA is intensively monitoring the safety of that product. Yellow report cards can be found at the back of the BNF or reports can be submitted online at www.yccscotland.scot.nhs.uk.

NHS Highland Minor Ailments Service Formulary
This Formulary is used within community pharmacies in NHS Highland to support the Minor Ailments Service (MAS) which allows eligible patients to register with and use a community pharmacy as the first port of call for advice and for treatment of common illnesses on the NHS. The Pharmacist advises, prescribes or refers the patient according to their needs. Medicines included in the NHS Highland MAS Formulary are listed in Appendix 5 and the full Formulary is available on the Intranet and website and on the Community Pharmacy website page for Highland.

Disclaimer
While every effort has been made to ensure that the information contained within the Formulary is accurate, no responsibility or liability can be accepted by those involved in its production for any loss, injury or damage which is suffered as a consequence of any errors, omissions or inaccuracies contained within it. In particular, prescribers should always check the suitability of the drug and dosage based on the information provided by the manufacturer.
PROCESS FOR THE ADDITION OF MEDICINES* TO THE HIGHLAND FORMULARY

Senior clinician identifies local need for medicine and requests its inclusion in Highland Formulary

Has SMC advice been issued for this medicine**?

No

Is medicine* in process of being assessed by SMC (on current SMC Work Programme)?

No

Complete ‘Formulary submission form’***

Yes

Await SMC advice before making Formulary decision

Is medicine* accepted for use or restricted use in NHS Scotland?

No

Not included in Highland Formulary

Yes

Senior clinician completes ‘Formulary submission form’**

Formulary Subgroup

Added for general, specialist or restricted use

Decisions disseminated

Not included

Submitting practitioner appeals decision

ADTC

* Includes newly licensed medicines, new formulations of existing medicines, major new indications for established medicines. Excludes high-cost risk-sharing medicines which are handled through other channels.

** Financial arrangements must be in place.

*** Includes medicines not yet assessed by SMC and those licensed prior to January 2002.
ACCESS TO MEDICINES IN NHS HIGHLAND

Is the medicine licensed for the indication?

NO

Is it included in: Highland Unlicensed and Off-label Medicines List or, BNF for Children or, ratified NHS Highland policy?

YES

Prescribe in line with guidance in these documents

NO

Is this likely to be required by more than one patient?

YES

Complete a request form to add to Highland Unlicensed and Off-label Medicines List*

NO

**Complete a request for non-Formulary, unlicensed or off-label medicines supply for individual patient unless SMC did not recommend or awaiting SMC advice when an Individual Patient Treatment Request (IPTR) should be completed.

Has the Scottish Medicines Consortium (SMC) considered this medicine for the indication?

NO

Did SMC recommend its use?

NO

NO

Await guidance from SMC. Go to ** if delay may lead to loss of therapeutic window.

YES

Complete a request form to add to Highland Formulary

YES

NO

Is this likely to be required by more than one patient?

YES

NO

NO

Is it on SMC workplan?

YES

Prescribe in line with Formulary guidance

NO

Complete a formulary request form to add to Highland Formulary

*The Highland Unlicensed and Off-label Medicines List includes both unlicensed medicines and licensed medicines being used in an unlicensed manner, ie ‘off-label’.
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACBS</td>
<td>Advisory Committee on Borderline Substances</td>
</tr>
<tr>
<td>ACE</td>
<td>angiotensin-converting enzyme</td>
</tr>
<tr>
<td>ALT</td>
<td>alanine aminotransferase</td>
</tr>
<tr>
<td>BMI</td>
<td>body mass index</td>
</tr>
<tr>
<td>CD2</td>
<td>preparations subject to prescription requirements of the Misuse of Drugs regulations; see BNF</td>
</tr>
<tr>
<td>CD3</td>
<td>preparations subject to prescription requirements of the Misuse of Drugs regulations; see BNF</td>
</tr>
<tr>
<td>CNS</td>
<td>central nervous system</td>
</tr>
<tr>
<td>COC</td>
<td>combined oral contraceptive</td>
</tr>
<tr>
<td>COPD</td>
<td>chronic obstructive pulmonary disease</td>
</tr>
<tr>
<td>COX-2</td>
<td>cyclo-oxygenase-2</td>
</tr>
<tr>
<td>CSM</td>
<td>Committee on the Safety of Medicines</td>
</tr>
<tr>
<td>CVD</td>
<td>cardiovascular disease</td>
</tr>
<tr>
<td>DPP-4</td>
<td>dipeptidylpeptidase-4</td>
</tr>
<tr>
<td>DVT</td>
<td>deep vein thrombosis</td>
</tr>
<tr>
<td>DXA</td>
<td>dual-energy x-ray absorptiometry</td>
</tr>
<tr>
<td>e/c</td>
<td>enteric-coated</td>
</tr>
<tr>
<td>ECG</td>
<td>electrocardiogram</td>
</tr>
<tr>
<td>eGFR</td>
<td>estimated glomerular filtration rate</td>
</tr>
<tr>
<td>ESR</td>
<td>erythrocyte sedimentation rate</td>
</tr>
<tr>
<td>FBC</td>
<td>full blood count</td>
</tr>
<tr>
<td>FEV</td>
<td>forced expiratory volume</td>
</tr>
<tr>
<td>GI</td>
<td>gastro-intestinal</td>
</tr>
<tr>
<td>GLP-1</td>
<td>glucagon-like peptide-1</td>
</tr>
<tr>
<td>GORD</td>
<td>gastro-oesophageal reflux disease</td>
</tr>
<tr>
<td>Hb</td>
<td>haemoglobin</td>
</tr>
<tr>
<td>HbA1c</td>
<td>glycosylated haemoglobin</td>
</tr>
<tr>
<td>HIS</td>
<td>Health Improvement Scotland</td>
</tr>
<tr>
<td>Hp</td>
<td><em>Helicobacter pylori</em></td>
</tr>
<tr>
<td>HRT</td>
<td>hormone replacement therapy</td>
</tr>
<tr>
<td>IHD</td>
<td>ischaemic heart disease</td>
</tr>
<tr>
<td>INR</td>
<td>international normalised ratio</td>
</tr>
<tr>
<td>IV</td>
<td>intravenous</td>
</tr>
<tr>
<td>LFT</td>
<td>liver function test</td>
</tr>
<tr>
<td>MAS</td>
<td>Minor Ailments Service</td>
</tr>
<tr>
<td>MHRA</td>
<td>Medicines and Healthcare Products Regulatory Agency</td>
</tr>
<tr>
<td>MI</td>
<td>myocardial infarction</td>
</tr>
<tr>
<td>m/r</td>
<td>modified-release</td>
</tr>
<tr>
<td>MRSA</td>
<td>methicillin-resistant <em>Staphylococcus aureus</em></td>
</tr>
<tr>
<td>NICE</td>
<td>National Institute for Health and Care Excellence</td>
</tr>
<tr>
<td>NNT</td>
<td>number needed to treat</td>
</tr>
<tr>
<td>NSAID</td>
<td>non-steroidal anti-inflammatory drug</td>
</tr>
<tr>
<td>OTC</td>
<td>available for purchase in pharmacies; may be available in other retail outlets</td>
</tr>
<tr>
<td>PE</td>
<td>pulmonary embolism</td>
</tr>
<tr>
<td>PPI</td>
<td>proton pump inhibitor</td>
</tr>
<tr>
<td>S</td>
<td>for initiation only on the advice of, or prescription by, a hospital specialist</td>
</tr>
<tr>
<td>SIGN</td>
<td>Scottish Intercollegiate Guidelines Network</td>
</tr>
<tr>
<td>SLS</td>
<td>selected list scheme</td>
</tr>
<tr>
<td>SMC</td>
<td>Scottish Medicines Consortium</td>
</tr>
<tr>
<td>SPC</td>
<td>Summary of Product Characteristics</td>
</tr>
<tr>
<td>TIA</td>
<td>transient ischaemic attack</td>
</tr>
<tr>
<td>TFT</td>
<td>thyroid function test</td>
</tr>
<tr>
<td>TPN</td>
<td>total parenteral nutrition</td>
</tr>
<tr>
<td>U&amp;O</td>
<td>urea and electrolytes</td>
</tr>
<tr>
<td>WCC</td>
<td>white cell count</td>
</tr>
<tr>
<td>▼</td>
<td>newly licensed medicine under intensive monitoring by CSM/MHRA</td>
</tr>
<tr>
<td>&gt;</td>
<td>Greater than</td>
</tr>
<tr>
<td>&lt;</td>
<td>Less than</td>
</tr>
</tbody>
</table>
CHAPTER 1 GASTRO-INTESTINAL SYSTEM

1.1 ANTACIDS AND SIMETICONE

FIRST CHOICE: CO-MAGALDROX

CO-MAGALDROX OTC (Mucogel®) 195/220 suspension
Dose: 10 to 20mL, 20 to 60 minutes after meals and at bedtime or when required.

COMPOUND ALGINATE PREPARATIONS OTC chewable tablets (Gaviscon®); suspension (Peptac®); infant oral powder sachets (Gaviscon® Infant)
Dose: Tablets, 1 to 2 tablets chewed 4 times daily after meals and at bedtime; suspension, 10 to 20mL after meals and at bedtime; infant oral powder sachets, refer to BNF.

Mucogel® is low in sodium (less than 1mmol per 10mL) and is sugar-free. Peptac® is also sugar-free but has a higher content of sodium (6·2mmol per 10mL); avoid where salt restriction is advisable. Peptac® is beneficial in reflux oesophagitis. Antacids reduce the absorption of a number of drugs, eg ciprofloxacin, some tetracyclines. Separate the administration times of these drugs by at least 1 hour to minimise the effect. Similarly, the administration times of an antacid and enteric-coated tablets should be separated so that the pH-sensitive coating is not destroyed in the stomach.

Evidence for the benefit of simeticone in infantile colic is uncertain; see carer information for the management of colic on Intranet. Simeticone is used prior to endoscopy [off-label].

SIMETICONE OTC liquid 40mg/mL

1.2 ANTISPASMODICS AND OTHER DRUGS ALTERING GUT MOTILITY

Antispasmodics

FIRST CHOICE: MEBEVERINE

MEBEVERINE OTC tablets 135mg
Dose: 1 tablet 3 times daily, preferably 20 minutes before meals.

The oral formulation of hyoscine butylbromide is poorly absorbed and therefore is not recommended.

MHRA: hyoscine butylbromide injection (www.gov.uk/drug-safety-update)
- can cause serious adverse effects including tachycardia, hypotension and anaphylaxis
- these adverse effects can result in a fatal outcome in patients with underlying cardiac disease, such as those with heart failure, coronary heart disease, cardiac arrhythmia or hypertension
- use with caution in patients with cardiac disease
- monitor these patients, and ensure that resuscitation equipment, and personnel who are trained how to use this equipment, are readily available
- hyoscine butylbromide remains contraindicated in patients with tachycardia.

HYOSCINE BUTYLBROMIDE injection 20mg/1mL
Dose: By intramuscular or slow intravenous injection, acute spasm and spasm in diagnostic procedures, 20mg repeated after 30 minutes if necessary (may be repeated more frequently in endoscopy).
Motility stimulants

Metoclopramide has both central and peripheral actions. It should only be used after appropriate assessment of gut motility and short-term (up to 5 days). In view of possible extrapyramidal side-effects, do not use metoclopramide for gastro-intestinal motility disorders in patients under 20 years old and in older people. For use in nausea and vertigo refer to section 4.6.

**METOCLOPRAMIDE** tablets 10mg; oral solution 5mg/5mL; injection 10mg/2mL

**Dose:** *By mouth or by intramuscular injection or by slow intravenous injection given over at least 3 minutes: adults up to 60kg* up to 500 micrograms/kg daily in 3 divided doses for up to 5 days, *adults 60kg and above* 10mg up to 3 times daily for up to 5 days.

### 1.3 ANTISECRETORY DRUGS AND MUCOSAL PROTECTANTS

*Helicobacter pylori (H. pylori)* eradication therapy is recommended in patients with *H. pylori*-positive dyspepsia, duodenal and gastric ulcer disease: testing should ideally be by breath test rather than serology. ^13C-urea breath test kits such as ‘Helicobacter Test INFAI’ are available for the diagnosis of gastro-duodenal infection with *H. pylori*. The test should not be performed within 4 weeks of treatment with an antibacterial or within 2 weeks of treatment with an anti-secretory drug.

See guidance on ‘Reflux’ and ‘Indigestion’. For advice on gastroprotection with antiplatelets see section 2.9 and on gastroprotection with a NSAID see guideline.

H\textsubscript{2}-receptor antagonists

**RANITIDINE** tablets 150mg, 300mg; effervescent tablets 150mg, 300mg; oral solution 75mg/5mL; injection 50mg/2mL

**Dose:** *By mouth*, treatment, 150mg twice daily or 300mg at night; maintenance, 150mg at night; *by slow intravenous injection*, 50mg 3 times daily.

Proton pump inhibitors

Proton pump inhibitors have the potential to interact with a range of drugs; refer to BNF for details. Note that proton pump inhibitors have been observed to react with warfarin; this occurs unpredictably and infrequently therefore close monitoring is required. There is no evidence that any of the proton pump inhibitors is safer in this respect.

**Note:** Proton pump inhibitors (PPI):

- **Careful consideration needs to be given to the use of PPIs in vulnerable groups.** Proton pump inhibitors are associated with an increased risk of *Clostridium difficile* infection similar to that with antibiotic therapy, particularly in those aged 65 and over. Patient information leaflets are available on the Intranet.
- There is also an association between long-term high-dose proton pump inhibitors and increased fracture risk.
- Prescribers should advise patients and review continued PPI prescribing annually; refer to ‘Algorithm for the review of patients on proton pump inhibitors’.

For maintenance therapy lansoprazole 15mg once daily is more effective than omeprazole 10mg once daily. Base the choice of formulation on appropriateness for the patient and cost. If co-prescribing for gastroprotection with antiplatelets see section 2.9 and with NSAID see guidance.
Chapter 1  Gastro-Intestinal System

First Choice: Lansoprazole

Note: Lansoprazole orodispersible tablets:
- Lansoprazole orodispersible tablets are preferred first-line in those with swallowing difficulties as they are licensed for use in tube feeding and are lower cost than omeprazole dispersible tablets.
- See ‘Instructions for the administration of lansoprazole orodispersible tablets via an enteral feeding tube’ on Intranet.

Lansoprazole capsules 15mg, 30mg; orodispersible tablets 15mg, 30mg
Dose: Treatment, 30mg once daily for 4 to 8 weeks, maintenance dose, 15mg once daily.

Omeprazole capsules 10mg, 20mg; (for use in children only) dispersible tablets 10mg injection 40mg; intravenous infusion 40mg
Dose: In adults, by mouth, treatment, 20mg once daily for 4 to 8 weeks, in severe cases increase to 40mg once daily; maintenance dose, 20mg once daily; by intravenous infusion, see protocol on Intranet. In children, refer to BNF for Children.

H₂-receptor antagonists and omeprazole (10mg) are available over the counter in pharmacies for short-term (up to 4 weeks) symptomatic relief of heartburn, dyspepsia and hyperacidity. Antacid therapy and lifestyle changes, ie weight loss, smoking cessation and alcohol and caffeine reduction, may often provide sufficient and lasting relief.

1.4 Acute Diarrhoea

Oral rehydration

Note: Seek specialist advice from Consultant Gastroenterologist or Colorectal Surgeon for patients with short bowel syndrome; standard oral rehydration salts are unsuitable.

Oral Rehydration Salts oral powder sachets OTC
Oral powder sachets are recommended for acute diarrhoea, see section 9.2.

Glucodrate® oral powder 39 gram sachets
Glucodrate® oral powder sachets are approved by the Advisory Committee on Borderline Substances (ACBS) for patients with short-bowel-associated intestinal failure and intestinal insufficiency; for specialist initiation, endorse prescriptions ACBS.

Antimotility Drugs

Loperamide is suitable for long-term therapy provided there is an established diagnosis as it has fewer CNS side-effects and less potential for dependence.

First Choice: Loperamide

Loperamide capsules 2mg OTC; orodispersible tablets 2mg; syrup 1mg/5mL
Dose: capsules/syrup, 4mg initially followed by 2mg after each loose stool for up to 5 days, maximum 16mg daily. For faecal incontinence [off-label] initially 500 micrograms daily then increasing the dose until desired stool consistency is reached, maximum 16mg daily in divided doses. Orodispersible tablets are for specialist initiation in patients who have had colectomies and who have either an end ileostomy or have an ileoanal J-pouch.

Codeine tablets 15mg, 30mg
Dose: 30mg 3 to 4 times daily.
Treatment of infective diarrhoea is included in the local Management of Infection guidance, Chapter 5.

1.5 CHRONIC BOWEL DISORDERS

Aminosalicylates

Note:
- Blood disorders: advise patients receiving an aminosalicylate to report any unexplained bleeding, bruising, purpura, sore throat, fever or malaise that occurs during treatment. Perform a blood count and stop the drug immediately if a blood dyscrasia is suspected.
- Check U&Es and renal function 2 weeks after starting therapy due to the risk of nephritis.
- Aminosalicylates are ineffective in Crohn’s disease.

FIRST CHOICE: PENTASA® (mesalazine)

The delivery characteristics of enteric-coated mesalazine preparations vary widely. Specify the brand to be dispensed and continue patients on the same brand. Pentasa® is the preferred mesalazine m/r preparation as it has a once-daily licence and is significantly cheaper than Asacol® MR. Octasa® MR is a lower cost alternative to Asacol® MR.

MESALAZINE (Pentasa®) m/r tablets 500mg, 1 gram; m/r granules 1 gram/sachet, 2 grams/sachet, 4 grams/sachet; suppositories 1 gram; retention enema 1 gram/100mL
Dose: By mouth, 1 to 2 grams twice daily or 4 grams once daily, reducing to maintenance dose depending on response. Suppositories, ulcerative proctitis, acute attack, 1 gram daily for 2 to 4 weeks; maintenance, 1 gram daily. Retention enema, by rectum, one enema at bedtime. Monitor in accordance with ‘Universal requirements for monitoring of conventional DMARDs in primary care’ in Appendix 2.

MESALAZINE (Octasa® MR) m/r tablets 400mg, 800mg
Dose: By mouth, 800mg 3 times daily or 2.4 grams once daily, reducing depending on response, to as low as 400mg twice daily or 800mg once daily. Monitor in accordance with ‘Universal requirements for monitoring of conventional DMARDs in primary care’ in Appendix 2.

MESALAZINE (Asacol® MR) m/r e/c tablets 400mg, 800mg; foam enema (Asacol®) 1 gram/metered application
Dose: By mouth, 800mg 3 times daily reducing, depending on response, to as low as 400mg twice daily. Foam enema, acute attack affecting the rectosigmoid region, 1 metered application (mesalazine 1 gram) into the rectum daily for 4 to 6 weeks; acute attack affecting descending colon, 2 metered applications administered at the same time (mesalazine 2 grams) once daily for 4 to 6 weeks. Monitor in accordance with ‘Universal requirements for monitoring of conventional DMARDs in primary care’ in Appendix 2.

OLSALAZINE tablets 500mg
Dose: Acute attack, 500mg twice daily after meals increased if necessary over 1 week to maximum 1 gram 3 times daily. Maintenance dose, 500mg twice daily after meals. May be useful in distal colitis complicated by constipation. Monitor in accordance with ‘Universal requirements for monitoring of conventional DMARDs in primary care’ in Appendix 2.

SULFASALAZINE e/c tablets 500mg; tablets 500mg; suspension 250mg/5mL
Dose: Acute attack, 3 grams daily in divided doses, reducing to a maintenance dose of 2 grams daily in divided doses.

Sulfasalazine may cause staining of soft contact lenses and may colour urine. Both standard and enteric-coated formulations are licensed in inflammatory bowel disease but only the enteric-coated
version is licensed in rheumatoid arthritis. Sulfasalazine is useful for enteropathic arthritis with colitis. Monitor in accordance with ‘Universal requirements for monitoring of conventional DMARDs in primary care’ in Appendix 2.

Corticosteroids

**Note:** Co-prescribe bone protection for the duration of steroid therapy, refer to section 6.6.

**Note:** Use standard prednisolone tablets instead of enteric-coated tablets in inflammatory bowel disease. For rectal administration, the metasulfobenzoate salt is preferred as it is less absorbed.

**PREDNISOLONE** tablets 1mg, 5mg; soluble tablets 5mg; suppositories 5mg; foam enema 20mg/metered application (as metasulfobenzoate sodium); retention enema 20mg/100mL (as metasulfobenzoate sodium)

**Dose:** Varies depending on condition. Refer to BNF.

**HYDROCORTISONE** rectal foam 10%

**Dose:** Initially 1 metered application inserted into the rectum once or twice daily for 2 to 3 weeks, then once on alternate days; in children, see BNF for Children.

**Immunosuppressants**

Patients uncontrolled on standard therapy may be prescribed azathioprine or other disease modifying agents, initiated by hospital specialists. Regular monitoring is required for all drugs listed, refer to Appendix 2: Universal requirements for monitoring of conventional DMARDs in primary care’.

**Note:** Azathioprine should only be used in combination with allopurinol on Gastroenterology advice. Allopurinol blocks the metabolism of azathioprine leading to increased levels of the active metabolite and potential drug toxicity.

**AZATHIOPRINE** tablets 25mg, 50mg

**Dose:** 2 to 2.5mg/kg daily.

Monitor in accordance with ‘Universal requirements for monitoring of conventional DMARDs in primary care’ in Appendix 2.

**MERCAPTOPURINE** tablets 50mg

**Dose:** 1 to 1.5mg/kg daily when azathioprine is not tolerated [off-label].

Monitor in accordance with ‘Universal requirements for monitoring of conventional DMARDs in primary care’ in Appendix 2.

**CICLOSPORIN** capsules (Neoral®) 25mg, 50mg, 100mg; oral solution (Neoral®) 100mg/1mL; concentrate for intravenous infusion (oily) (Sandimmun®) 50mg/1mL

**Dose:** By mouth, 7mg/kg daily, usual maximum dose for 70kg patient 250mg twice daily [off-label]. Usually only used in acute colitis for 3 months as a bridge to maintenance therapy. Monitor ciclosporin trough blood concentrations (EDTA tube), serum creatinine and blood pressure, especially when the patient is changed to a different formulation or brand. Monitor in accordance with ‘Universal requirements for monitoring of conventional DMARDs in primary care’ in Appendix 2.

**Note:** Methotrexate

- Pay attention to the strength of methotrexate tablets prescribed and the frequency of dosing; methotrexate is always given weekly. Prescribing and dispensing errors have caused fatalities.
- Give methotrexate on day 1 then give folic acid 5mg on day 2 of the same week to reduce
some of the side-effects such as nausea and mouth ulcers [off-label]. If necessary the dose of folic acid can be increased to 5 days per week avoiding the day methotrexate is given.

S METHOTREXATE tablets 2.5mg, injection pre-filled syringe 7.5mg/0.15mL, 10mg/0.2mL, 12.5mg/0.25mL, 15mg/0.3mL, 17.5mg/0.35mL, 20mg/0.4mL, 22.5mg/0.45mL, 25mg/0.5mL
Dose: Maximum dose, 25mg once weekly [off-label].
Monitor in accordance with ‘Universal requirements for monitoring of conventional DMARDs in primary care’ in Appendix 2.

Note: Give patients the infliximab patient information leaflet and the special Patient Alert Card, and advise them appropriately when treatment is administered.

S INFLIXIMAB (Inflectra®, Remicade®) powder for concentrate for solution for infusion 100mg.
Prescribe infliximab by brand name.

S VEDOLIZUMAB® powder for concentrate for solution for infusion 300mg

Adalimumab (section 10.1) is also used under specialist advice, see monitoring advice in Appendix 2.

1.6 LAXATIVES

Refer to guidance at http://cks.nice.org.uk and patient information at www.nhsinform.co.uk.

Osmotic laxatives

FIRST CHOICE: MACROGOL ORAL POWDER COMPOUND

Note: If prescribing the 6.563 gram sachets for children ensure that the brand selected is licensed for and contains appropriate dosing instructions for the age of the child.

MACROGOL 3350 WITH POTASSIUM CLORIDE, SODIUM BICARBONATE AND SODIUM CHLORIDE oral powder 13-125 grams/sachet (Laxido Orange®, 6-563 grams/sachet (Movicol-Half®, Laxido Paediatric Plain®, Movicol Paediatric Chocolate®)
Dose: 13-125 grams/sachet, in adults, chronic constipation, 1 to 3 sachets daily in divided doses usually for up to 2 weeks; maintenance, 1 to 2 sachets daily; faecal impaction, 8 sachets daily dissolved in 1 litre water and drunk within 6 hours, usually for maximum 3 days. Dissolve each sachet in 125mL water. After reconstitution keep the solution in a fridge and discard if unused after 6 hours.

6-563 grams/sachet, in adults, the lower volume with Movicol-Half® may be useful if fluid volume is a problem, refer to SPC; in children, refer to Laxido Paediatric Plain® SPC or Movicol Paediatric Chocolate® SPC.

Note: Lactulose is less effective than macrogol in the treatment of constipation; it takes 2 to 3 days to work, is unsuitable on a ‘when required’ basis and frequently causes bloating.

LACTULOSE OTC solution 3-1 to 3-7 grams/5mL
Dose: Hepatic encephalopathy, 30mL 3 times daily, subsequently adjusted to produce 2 to 3 soft stools daily.

Stimulant laxatives
SENNA <sup>OTC</sup> tablets 7.5mg; syrup 7.5mg/5mL
Dose: 2 to 4 tablets or 10 to 20mL syrup, usually at night, initial dose should be low then gradually increased.

BISACODYL <sup>OTC</sup> e/c tablets 5mg; suppositories 5mg, 10mg
Dose: By mouth, for constipation, 5mg to 10mg at night. By rectum, 10mg in the morning.

DOCUSATE <sup>OTC</sup> capsules 100mg; adult oral solution 50mg/5mL
Dose: Chronic constipation, up to 500mg daily in divided doses.

GLYCEROL <sup>OTC</sup> suppositories 1 gram, 2 grams, 4 grams
Dose: 1 suppository moistened with water before use.

CO-DANTHRAMER suspension 25/200/5mL; strong suspension 75/1000/5mL
Dose: For terminally ill patients only, suspension, 5 to 10mL at night; strong suspension, 5mL at night.

SODIUM PICOSULFATE <sup>OTC</sup> oral solution 5mg/5mL
Dose: 5 to 10mL at night.

**Bulk-forming laxatives**

**Note:** Use ispaghula husk with caution in frail older people to avoid intestinal obstruction.

ISPAGHULA HUSK <sup>OTC</sup> sachets 3.5 grams
Dose: 1 sachet in water, twice daily, preferably after meals.

**Faecal softeners**

PHOSPHATES (RECTAL) enema with standard rectal tube

SODIUM CITRATE (RECTAL) enema with nozzle

**Bowel cleansing preparations**

**FIRST CHOICE:** SODIUM PICOSULFATE WITH MAGNESIUM CITRATE

Avoid bowel cleansing solutions as treatments for constipation. Use with caution in older or debilitated patients; check cautions and contra-indications before prescribing. Patients should stop iron preparations, antidiarrhoea preparations and, when possible, opiates 7 days before the procedure, commence a low residue diet 2 days before the procedure and take copious amounts of water or other clear fluids during treatment.

SODIUM PICOSULFATE oral powder 10mg/sachet with magnesium citrate
Dose: 1 sachet in water in the morning before 8am and a second in the afternoon (2 to 4pm) on day preceding procedure.

MACROGOL 3350 WITH ANHYDROUS SODIUM SULFATE, POTASSIUM CHLORIDE, SODIUM BICARBONATE AND SODIUM CHLORIDE (Klean-Prep<sup>®</sup>) oral powder sachets, 69 grams/sachet
Dose: Reconstitute 4 sachets with 4 litres of water. Drink 250mL (1 tumblerful) of reconstituted solution every 10 to 15 minutes until 4 litres have been consumed or watery stools are free of solid matter. Drink the 4 litres (4 sachets) within 4 to 6 hours. Alternatively the solution from 2 sachets may be taken the night before the procedure and the solution from 2 sachets on the morning of the procedure.
1.7 LOCAL PREPARATIONS FOR ANAL AND RECTAL DISORDERS

Haemorrhoidal preparations

Soothing preparations may provide symptomatic relief. Local anaesthetics are used to relieve pain associated with haemorrhoids and pruritus ani, however good evidence is lacking. Suppositories are suitable for internal haemorrhoids and proctitis whereas creams and ointments are suitable for external haemorrhoids. Xyloproct® contains lidocaine (in addition to hydrocortisone); of the available topical anaesthetics it is least likely to cause irritation. Prolonged use of corticosteroids can cause atrophy of anal skin. Use Anusol-HC®, Xyloproct® and Scheriproct® for a maximum of 7 days.

Soothing preparations

ANUSOL®OTC suppositories; ointment; cream
Dose: Cream or ointment to be applied morning and night and after a bowel movement or insert 1 suppository morning and night and after a bowel movement.

Compound preparations

FIRST CHOICE: XYLOPROCT®

XYLOPROCT® ointment (includes hydrocortisone acetate 0·275%, lidocaine 5%)
Dose: Apply several times daily, short-term use only.

ANUSOL-HC® ointment (includes hydrocortisone acetate 0·25%) (Anusol Plus HC®OTC); suppositories (includes hydrocortisone acetate 10mg) (Anusol Plus HC®OTC)
Dose: Apply ointment/insert 1 suppository morning and night and after a bowel movement, for a maximum of 7 days.

SCHERIPROCT® ointment (includes prednisolone hexanoate 0·19%, cinchocaine 0·5%)
Dose: Apply twice daily for 5 to 7 days.

Anal fissures

GLYCERYL TRINITRATE rectal ointment 0·4%
Dose: Apply a small amount (the size of half a pea) to the site of the anal fissure twice daily. Wash off at night to avoid continuous use.

S DILTIAZEM cream 2% [unlicensed]
Available from special-order manufacturers; for information contact Medicines Information. Diltiazem is useful for patients who cannot tolerate glyceryl trinitrate due to headaches.

1.8 STOMA CARE

See NHS Highland Stoma Accessories Formulary and NHS Highland Policy for the Prescribing of Stoma Appliances.

1.9 DRUGS AFFECTING INTESTINAL SECRETIONS

Drugs affecting biliary composition and flow

URSODEOXYCHOLIC ACID tablets 250mg; capsules 250mg
**Dose:** Primary biliary cirrhosis, 10 to 15mg/kg daily in 2 to 4 divided doses. Tolerance can vary between individual brands; if necessary consider brand name prescribing.

### Bile acid sequestrants

**Note:** Colestyramine: other drugs should be taken at least 1 hour before or 4 to 6 hours after colestyramine to reduce possible interference with absorption.

**COLESTYRAMINE** powder 4 grams/sachet  
**Dose:** Pruritus 4 to 8 grams daily; for bile acid diarrhoea, 4 to 12 grams daily in water or fruit juice.

Colestyramine is also used off-label for the treatment of bile acid diarrhoea post-surgery in patients intolerant of colestyramine.

**COLESEVELAM** tablets 625mg  
**Dose:** Up to 10 tablets daily, under specialist recommendation [off-label]

### Pancreatin

Swallow the recommended dose of pancreatin capsules at intervals during each meal.

**CREON® 10 000** capsules (protease 600 units, lipase 10 000 units, amylase 8000 units)  
**Dose:** Initially 1 to 2 capsule(s) with meals either taken whole or contents mixed with fluid or soft food (then swallowed whole immediately without chewing).

**CREON® 25 000** capsules (protease 1000 units, lipase 25 000 units, amylase 18 000 units)  
**Dose:** Initially 1 capsule with meals either taken whole or contents mixed with fluid or soft food (then swallowed whole immediately without chewing).

**CREON® MICRO** gastro-resistant granules (pork) (protease 200 units, lipase 5000 units, amylase 3600 units)  
**Dose:** Initially 100mg (5000 lipase units) of gastro-resistant granules (one measure) with each feed or meal or immediately after.

**PANCREX V®** capsules (protease 430 units, lipase 8000 units, amylase 9000 units)  
**Dose:** For use in patients with partial or total gastrectomy, 2 to 6 capsules swallowed at intervals during meals, swallowed whole or sprinkled on food.

### 1.10 OTHER DRUGS

**Drugs for bleeding from oesophageal varices**

**TERLIPRESSIN** solution for injection 1mg/8.5mL (Glypressin®)  
**Dose:** For variceal bleeding and hepatorenal syndrome [off-label], by intravenous injection, 2mg followed by 1 or 2mg every 4 to 6 hours until bleeding is controlled, for up to 72 hours.

**Drugs to reduce the risk of recurrence of hepatic encephalopathy**

**RIFAXIMIN** tablets 550mg (Targaxan®)  
**Dose:** 1 tablet twice daily.

**Sealants**

**TISSEEL®** Ready to use Solutions for Sealant
Helicobacter pylori

The role of *H. pylori* in reflux dyspepsia is unclear, as is the efficacy of eradicating *H. Pylori*. If patient also has features of ulcer dyspepsia, test and treat as in the indigestion guidance.
Box 1: Consider risk factors, antacids

- reduce weight
- stop smoking
- reduce caffeine
- reduce alcohol to 14 to 21 (or less) units per week
- regular light meals
- review medication, eg NSAIDs, bisphosphonates, nicorandil.

Box 2: Eradicate Hp

Eradicating Hp prescribe twice daily for 7 days:
- lansoprazole 30mg
- clarithromycin 500mg
- amoxicillin 1 gram or if penicillin sensitive metronidazole 400mg.

Box 3: $^{13}$C-urea breath test

- cheapest commercial test (see BNF 1.3; prescribe on GP10)
- patient must be:
  - off anti-secretory therapy at least 2 weeks before test
  - off antibiotic at least 4 weeks before test.
**ALGORITHM FOR THE REVIEW OF PATIENTS ON PROTON PUMP INHIBITORS (PPIs)**

Has the patient had endoscopically confirmed oesophagitis or ulceration or do they require NSAID/steroid gastroprotection?

- **No**
  - Does the patient take any other medications known to increase the risk of GI bleeds and/or are they of older age with serious comorbidities?
    - **No**
      - Has the patient tried to stop the PPI previously?
        - **No**
          - Advise trial of stopping PPI*
        - **Yes**
          - Discuss re-trial of stopping the PPI* or step-down to lowest effective dose of PPI.
      - **Yes**
        - Advise trial of stopping PPI*
    - **Yes**
      - Continue PPI

- **Yes**
  - Record intervention at each step

---

*Patient advice for stopping a PPI in primary care*

Your GP will advise you how your PPI should be stopped. This is likely to be in 4 stages:

1. If you are on a high dose (more than 20mg) you will reduce to a lower dose for one month. This will be reduced again until you are taking the lowest dose of your PPI.
2. You should then take the low-dose PPI on alternate days for one month. If you have any indigestion or heartburn on the non-medicine days, your GP will give you Peptac®. Peptac® is an antacid: it neutralises the acid but doesn’t interfere with acid production.
3. You should then reduce the dose again to take the PPI once or twice a week for one month, again using Peptac® if needed.
4. Finally, you should stop the PPI. Any symptoms of indigestion or heartburn should clear up within two weeks of stopping the PPI as the level of stomach acid returns to normal. If you still have symptoms after three weeks, consult your doctor.
NHS HIGHLAND STOMA ACCESSORIES FORMULARY

This Formulary should be read in conjunction with the [NHS Highland Policy for the Prescribing of Stoma Appliances](#) on the Intranet. Most available accessories are not normally required however prescriptions for these products may be requested by patients. In general, stoma accessories should only be prescribed on the advice of an NHS Colorectal/Stoma Clinical Nurse Specialist (where available) who will make a decision on an individual patient basis. Seek the advice of an NHS Colorectal/Stoma Clinical Nurse Specialist before initiating a new prescription.

Points to note:
- Do not prescribe deodorants; patients should purchase an ordinary household deodorant/air freshener if required for when changing bags.
- Adhesive removers should only be prescribed following the advice of a Colorectal/Stoma Clinical Nurse Specialist.
- Discharge solidifying agents are not usually needed, unless on the recommendation of a Colorectal/Stoma Clinical Nurse Specialist.

<table>
<thead>
<tr>
<th>Type</th>
<th>Brand</th>
<th>Code</th>
<th>Quantity per box</th>
<th>Cost indication*</th>
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<td>1st choice: WipeAway</td>
<td>WA1</td>
<td>30</td>
<td>29p/wipe</td>
</tr>
<tr>
<td></td>
<td>2nd choice: Appeel</td>
<td>3505</td>
<td>30</td>
<td>49p/wipe</td>
</tr>
<tr>
<td></td>
<td><em>Only for exceptional circumstances when WipeAway is unsuitable</em></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Adhesive remover spray</td>
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<td>WAP</td>
<td>50mL</td>
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<td></td>
<td>2nd choice: Lift</td>
<td>5501</td>
<td>100mL</td>
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</tr>
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</table>

**Barrier products**

Only use barrier products if the skin surrounding the stoma is sore. There is no need to use barrier products all the time. Before prescribing, check that there is still a requirement for prescribing due to sore skin. Wipes are the preferred formulation.

<table>
<thead>
<tr>
<th>Type</th>
<th>Brand</th>
<th>Code</th>
<th>Quantity per tube/box</th>
<th>Cost indication*</th>
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</thead>
<tbody>
<tr>
<td>Barrier film wipes</td>
<td>Salts Peri-Prep sensitive no sting wipes</td>
<td>PPS1</td>
<td>30</td>
<td>50p/wipe</td>
</tr>
</tbody>
</table>

*Cost indication: Prices from ISD Scotland stoma appliances list (Drug Tariff), December 2014*
CHAPTER 2 CARDIOVASCULAR SYSTEM

Refer to:
- Cardiology shared clinical guidelines on Intranet
- SIGN guidance and summary patient guidance:
  - Management of chronic heart failure (SIGN 147)
  - Acute coronary syndrome (SIGN 148)
- NHS Inform Heart Zone (www.nhsinform.co.uk/heart) for patient information
- Also note NICE guidance (www.nice.org.uk).

Note: Be aware when administering parenteral drugs as many preparations share similar containers, eg heparinised saline flush solution and other heparin sodium preparations.

2.1 CARDIAC GLYCOSIDES

DIGOXIN tablets 62.5 micrograms, 125 micrograms, 250 micrograms; oral solution 250 micrograms/5mL; injection 500 micrograms/2mL

**Dose:** By mouth, atrial fibrillation or heart failure, rapid digitalisation, 500 micrograms followed by 500 micrograms 4 hours later; maintenance, 62.5 to 250 micrograms daily (lower doses may be appropriate in older people). Maintenance dose depends on heart rate and renal function. Note NICE CG180 ‘Atrial fibrillation: management’ and ‘Heart Failure Management’ guidance on Intranet.

DIGOXIN-SPECIFIC ANTIBODY FRAGMENTS (F(ab)) (DigiFab®) powder for reconstitution for intravenous infusion 40mg/vial. For the treatment of digoxin overdose.

Hypokalaemia predisposes to digoxin toxicity therefore take care when diuretics are used with a cardiac glycoside. Give potassium supplements if necessary. **Measurements of plasma digoxin concentrations are only usually necessary for confirmation of toxic dosage or where problems occur with maintenance therapy.** Refer to Therapeutic Drug Monitoring summary in Appendix 1.

2.2 DIURETICS

Refer to guidance on diuretic use in: hypertension; post-TIA or ischaemic stroke; heart failure on Intranet. Check urea and electrolytes (U&Es) prior to initiation and within 4 to 7 days of initiation of therapy.

**Thiazides and related diuretics**

BENDROFLUMETHIAZIDE tablets 2.5mg, 5mg

**Dose:** Hypertension, 2.5mg daily in the morning; heart failure, 2.5 to 5mg daily; oedema, initially 5 to 10mg daily in the morning or on alternate days, maintenance 5 to 10mg 1 to 3 times weekly. Bendroflumethiazide 2.5mg daily may be used in many cases of mild to moderate hypertension and higher doses are rarely necessary.

INDAPAMIDE tablets 2.5mg

**Dose:** 2.5mg daily in the morning. Indapamide is the first-line thiazide in NICE CG127 ‘Hypertension in adults; diagnosis and management’. For use post-TIA or ischaemic stroke refer to guidance.

METOLAZONE tablets 5mg [unlicensed]

**Dose:** Initially, 2.5mg to 5mg in the morning for 3 days then review; may be administered on alternate days. Use with caution long-term due to the risk of renal impairment.
Loop diuretics

**FIRST CHOICE: FUROSEMIDE**

**FUROSEMIDE** tablets 20mg, 40mg, 500mg; oral solution 50mg/5mL; injection 20mg/2mL, 50mg/5mL, 250mg/25mL

*Dose:* By mouth, oedema, initially 40mg in the morning, twice daily dosage may be required for nocturnal dyspnoea; maintenance, 20mg to 40mg daily or 40mg on alternate days, higher doses may be required in some patients. Heart failure, refer to Heart Failure Management guidance on Intranet. By slow intravenous injection or intramuscular injection, initially 20 to 50mg; by intravenous infusion, refer to BNF (maximum rate 4mg/minute).

**BUMETANIDE** tablets 1mg, 5mg; oral liquid 1mg/5mL; injection 2mg/4mL [unlicensed]

*Dose:* By mouth, 1mg in the morning, twice daily dosage and higher doses for some patients may be required; by intravenous injection, 1 to 2mg repeated after 20 minutes if necessary; by intravenous infusion, 2 to 5mg over 30 to 60 minutes.

*Note:* Furosemide 40mg is equivalent to bumetanide 1mg.

**Aldosterone antagonists and other potassium-sparing diuretics**

*Note:* Hyperkalaemia is always a risk and is a particular concern for those patients also taking ACE inhibitors or angiotensin-II receptor antagonists.

**SPIRONOLACTONE** tablets 25mg, 100mg; oral suspension 25mg/5mL [unlicensed]

*Dose:* Heart failure, 25mg daily. Spironolactone 25mg daily has been shown to reduce mortality in patients with heart failure (NYHA II to IV) who are already receiving an ACE inhibitor and a diuretic and/or digoxin, refer to Heart Failure Management guidance on Intranet. Spironolactone at higher doses is also indicated for ascites and primary hyperaldosteronism and is used fourth-line for hypertension [off-label]; see guidance and SIGN 147. Check U&Es 1 week after starting. Exercise caution in patients with renal impairment.

*S EPLERENONE* tablets 25mg, 50mg

*Dose:* Heart failure, initially 25mg once daily increased within 4 weeks to 50mg once daily.

Eplerenone can be substituted for spironolactone in patients who develop gynaecomastia. Patients who have suffered a myocardial infarction with left ventricular dysfunction (ejection fraction 40% or less) and either diabetes or clinical signs of heart failure should be considered for eplerenone unless contra-indicated by the presence of renal impairment or high potassium levels, refer to www.sign.ac.uk. Eplerenone should also be considered for patients with NYHA class II (chronic) heart failure and left ventricular dysfunction (ejection fraction 30% or less), refer to SMC 793/12.

**AMILORIDE** tablets 5mg; oral solution 5mg/5mL

*Dose:* With other diuretics, congestive heart failure and hypertension, initially 5 to 10mg daily; cirrhosis with ascites, initially 5mg daily.

Amiloride is rarely prescribed alone; it is more commonly used in combination with a loop or thiazide diuretic. Note that amiloride is an inappropriate substitute for spironolactone in the treatment of heart failure.

**Osmotic diuretics**

*S MANNITOL* infusion 10% (100mg/1mL), 20% (200mg/1mL)
2.3 ANTI-ARRHYTHMIC DRUGS

For permanent atrial fibrillation, beta-blockers, eg bisoprolol (section 2.4) are useful agents for rate control. If contra-indications exist rate limiting calcium-channel blockers eg verapamil, diltiazem [off-label] (section 2.6) or digoxin (section 2.1) may be considered. For paroxysmal atrial fibrillation/supraventricular tachycardias, beta-blockers, eg bisoprolol, are useful first choice agents to prevent paroxysms. Second-line drugs may be used but are limited by adverse and pro-arrhythmic effects; they include flecainide, propafenone, amiodarone and sotalol. Due to potential pro-arrhythmia effects, all require hospital specialist guidance. Digoxin is less useful in these situations providing little preventative effect during paroxysms. Note NICE CG180 ‘Atrial fibrillation: management’ at www.nice.nhs.uk.

S ADENOSINE injection 6mg/2mL (only available via hospital pharmacy); 1mg/mL (in volumes up to 130mL) [unlicensed].

S AMIODARONE tablets 100mg, 200mg; concentrate for dilution and use as an intravenous infusion 150mg/3mL; injection, prefilled syringe 300mg/10mL

Dose: By mouth, 400mg 3 times daily for 10 days, reduced to 200mg once daily or the minimum required to control the arrhythmia for usual maintenance. This loading dose is unlicensed in the UK but is recommended by Highland Consultant Cardiologists based on clinical experience and licensed doses in the US. Alternatively, follow the BNF recommendation of 200mg 3 times daily for 1 week, reduced to 200mg twice daily for a further week, then to 200mg once daily or the minimum required to control the arrhythmia for usual maintenance.

By intravenous infusion, irritant to veins and administration via PICC line preferred, initially 5mg/kg over 20 to 120 minutes with ECG monitoring; subsequent infusion given if necessary according to response up to maximum of 1.2 grams in 24 hours.

Note: Amiodarone
- Only initiate amiodarone following specialist advice.
- Review therapy for patients in permanent atrial fibrillation on amiodarone for rate control only.

Note: Monitoring amiodarone therapy
- A chest x-ray is required prior to initiating therapy. During treatment, if pulmonary toxicity is suspected, repeat chest x-ray and test lung function.
- Test liver and thyroid function (request TSH and FT4 and state patient is on amiodarone) prior to initiating therapy and every 6 months thereafter.
- Development of cough or shortness of breath may indicate presence of serious pulmonary toxicity; new neurological symptoms may indicate development of neuropathy. Withdraw amiodarone immediately until further investigations can be carried out.
- Most patients will develop reversible corneal microdeposits. These tend to be benign, however a small number of patients will develop visual haloes and blurring of vision. Rarely optic neuritis can occur. Recommend ophthalmological examination if blurred or decreased vision occurs.
- Due to the high incidence of phototoxicity advise all patients to avoid exposure to sunlight and use a wide-spectrum sunscreen. Inform patients that photosensitivity may persist for several months after discontinuation of amiodarone.

S DRONEDARONE tablets 400mg
For the prevention of recurrence of atrial fibrillation in patients in whom amiodarone is ineffective, contra-indicated or not tolerated. See dronedarone treatment protocol on Intranet.

S FLECAINIDE tablets 50mg, 100mg; m/r capsules 200mg; injection 150mg/15mL

Dose: By mouth, ventricular arrhythmias, initially 100mg twice daily (maximum 400mg daily usually reserved for rapid control or in heavily-built patients), reduced after 3 to 5 days if possible.
Supraventricular arrhythmias, 50mg twice daily, increased if required to maximum 300mg daily. Initiate only after specialist advice. By slow intravenous injection, cardioversion of haemodynamically stable patients with normal left ventricular function in atrial fibrillation for less than 24 hours to be carried out in hospital with ECG monitoring, bolus of 2mg/kg over 30 minutes maximum 150mg.

**PROPAAFENONE** tablets 150mg
**Dose:** 150mg 3 times daily (maximum 300mg 3 times daily). Reduce dose if less than 70kg. Initiate only after specialist advice.

The management of ventricular and other serious cardiac arrhythmias is best undertaken with specialist cardiological guidance.

### 2.4 Beta-Adrenoceptor Blocking Drugs

Use beta-blockers with caution in patients with asthma or with a history of obstructive airways disease. Combinations with diltiazem or verapamil (section 2.6) may produce excessive bradycardia and should only be used under specialist advice.

Beta-blockers (bisoprolol or carvedilol) for stable heart failure are used under specialist advice. Warn patients that heart failure symptoms may worsen for up to 3 days following dose initiation/titration and consider extra diuretic cover for 3 days.

Beta-blockers appear protective if taken for 1 to 2 years following a myocardial infarction (MI); note NICE CG172 ‘Myocardial infarction: cardiac rehabilitation and prevention of further MI’.

Refer to guidance on the use of beta-blockers in hypertension and as secondary prevention post-MI. Bisoprolol is preferred to atenolol due to a reduced incidence of side-effects.

**FIRST CHOICE: BISOPROLOL**

**BISOPROLOL** tablets 1.25mg, 2.5mg, 3.75mg, 5mg, 7.5mg, 10mg
**Dose:** Adjunct in stable heart failure, initially 1.25mg once daily (in the morning) then if tolerated, double the dose at a minimum of two-weekly intervals to 10mg once daily [off-label]. Hypertension, initially 5mg increased to 10mg once daily.

**ATENOLOL** tablets 25mg, 50mg, 100mg; oral solution 25mg/5mL; injection 5mg/10mL
**Dose:** *By mouth*, hypertension, 50mg daily. Angina, 25 to 100mg daily, in 1 or 2 doses. Arrhythmias, 50 to 100mg daily. Post-myocardial infarction, 25mg initially increasing to 100mg daily.

**CARVEDILOL** tablets 3.125mg, 6.25mg, 12.5mg, 25mg
**Dose:** Adjunct in stable heart failure, initially 3.125mg twice daily (with food), dose increased at intervals of at least 2 weeks to 6.25mg twice daily, then 12.5mg twice daily, then to 25mg twice daily; increase to highest dose tolerated, maximum 25mg twice daily in patients with severe heart failure or bodyweight less than 85kg and 50mg twice daily in patients over 85kg.

**METOPROLOL** tablets 50mg; injection 5mg/5mL
For assuring bradycardia during CT coronary angiography.

**PROPRANOLOL** tablets 10mg, 40mg; m/r capsules 80mg, 160mg
Used for the relief of anxiety (section 4.1), essential tremor (section 4.9), thyrotoxicosis (section 6.2) and the prophylaxis of migraine (section 4.7).

**SOTALOL** tablets 40mg, 80mg
Initiated only under direct hospital advice for the treatment of arrhythmias.
CHAPTER 2   CARDIOVASCULAR SYSTEM

S ESMOLYL injection 100mg/10mL
For use in High Dependency Units only.

S LABETALOL tablets 100mg, 200mg; injection 100mg/20mL
Dose: Hypertension in pregnancy, refer to guidance on Intranet.

2.5 HYPERTENSION AND HEART FAILURE

Vasodilator antihypertensive drugs

S BOSENTAN tablets 62.5mg, 125mg
For the treatment of pulmonary hypertension: initiation and prescribing are restricted to use under the guidance of the Scottish Pulmonary Vascular Unit with funding through the Scottish Board Chief Executive Drug Risk Share Scheme.

S HYDRALAZINE tablets 25mg; injection 20mg
Dose: By mouth, heart failure (initiated in hospital in conjunction with oral nitrates) 25mg 3 to 4 times daily, increased every 2 days if necessary; usual maintenance dose 50 to 75mg 4 times daily. For hypertension in pregnancy, refer to guidance on Intranet.

S SODIUM NITROPRUSSIDE intravenous infusion 50mg [unlicensed]
For use in High Dependency Units only.

Centrally acting antihypertensive drugs

S CLONIDINE injection 150 micrograms/1mL
For use in High Dependency Units only. Oral clonidine is used off-label in Tourette syndrome (Section 4.9).

S METHYLDOPA tablets 250mg
Dose: Initially 250mg 2 to 3 times daily, increased gradually at intervals of 2 or more days, maximum 3 grams daily.

S MOXONIDINE tablets 200 micrograms, 300 micrograms, 400 micrograms
Dose: 200 micrograms once daily in the morning, increased if necessary after 3 weeks to 400 micrograms daily in 1 to 2 divided doses; maximum 600 micrograms daily in 2 divided doses (maximum single dose 400 micrograms).

Alpha-adrenoceptor blocking drugs

DOXAZOSIN tablets 1mg, 2mg, 4mg
Dose: Hypertension, 1mg daily, increased after 1 to 2 weeks to 2mg once daily, and thereafter to 4mg once daily, if necessary; maximum 16mg. For use in urinary retention see section 7.4.

Use of doxazosin m/r tablets is not recommended.

Refer to 'Unlicensed Medicine List' on Intranet for information on the use of prazosin in post traumatic stress disorder [off-label].

For phaeochromocytoma

S PHENOXYBENZAMINE capsules 10mg
Dose: 10mg daily, increased by 10mg daily; usual dose 1 to 2mg/kg daily in 2 divided doses.

S PHENTOLAMINE injection 10mg/1mL [unlicensed]
Angiotensin-converting enzyme (ACE) inhibitors

- ACE inhibitors are recommended in proteinuric renal disease and are the treatment of choice in patients with CKD and albumin:creatinine ratio greater than 30mg/mmol irrespective of blood pressure. Avoid in renal artery stenosis.
- Titrate ACE inhibitor doses up at regular intervals to achieve target blood pressure in hypertension; see guidance. For use in secondary prevention after TIA or ischaemic stroke refer to guidance. In patients with angina, with normal left ventricular function and with neither diabetes nor hypertension, there is little added benefit in adding an ACE inhibitor. On initiation consider issuing a ‘Sick day rule’ card.
- Measure U&Es prior to initiation of ACE inhibitor, repeated 1 to 2 weeks after initiation and after dosage increase. Thereafter, monitor at least annually. Stop ACE inhibitor if potassium greater than 6·0mmol/L, or serum creatinine rises by more than 30% or eGFR falls by more than 25%. Do not increase dosage of ACE inhibitor if potassium greater than 5·0mmol/L. Consider addition of low potassium diet, correction of acidosis and use of thiazide or loop diuretic if strong indication for ACE inhibitor.
- Concomitant treatment with NSAIDs reduces efficacy and increases the risk of renal damage and should, therefore, be avoided. Potassium-sparing diuretics or potassium supplements increase the risk of hyperkalaemia. Refer to guidelines.

**FIRST CHOICE:** LISINOPRIL or PERINDOPRIL ERBUMINE

**LISINOPRIL** tablets 2·5mg, 5mg, 10mg, 20mg
**Dose:** Hypertension, initially 2·5mg to 10mg once daily; maintenance 10 to 20mg once daily, maximum 80mg daily. Heart failure, initially 2·5mg once daily; increasing in steps of up to 10mg at least every 2 weeks; maximum 35mg daily. Prophylaxis after myocardial infarction, systolic blood pressure over 120mmHg, 5mg within 24 hours, followed by further 5mg 24 hours later, then 10mg after a further 24 hours, and continuing with 10mg once daily; systolic blood pressure 100 to 120mmHg, initially 2·5mg daily increased to maintenance dose of 5mg once daily.

**PERINDOPRIL ERBUMINE (= tert-butylamine) tablets** 2mg, 4mg, 8mg
**Dose:** Heart failure, initial dose 2mg in the morning; usual maintenance 4mg once daily (before food). Secondary prevention in ischaemic heart disease, initially 4mg once daily if under 70 years (2mg if over) and increase to 8mg once daily after 2 weeks if tolerated. Hypertension, initially 4mg once daily (before food); in older people or in renal impairment, initially 2mg once daily; usual maintenance dose 4mg once daily; maximum 8mg daily.

Perindopril erbumine (not arginine) is the first choice ACE inhibitor for heart failure and secondary prevention in ischaemic heart disease. It may be particularly useful where difficulties arise with ACE inhibitor initiation over a prolonged period of time and where there is a high risk of first dose hypotension. For use post-TIA and ischaemic stroke refer to guidance.

**RAMIPRIL** capsules 1·25mg, 2·5mg, 5mg, 10mg
**Dose:** Hypertension, initially 1·25mg once daily, usual range 2·5 to 5mg once daily, maximum 10mg once daily. Heart failure, initially 1·25mg once daily, increased gradually, target dose 10mg daily in 1 to 2 divided doses. Prophylaxis after myocardial infarction, initially 2·5mg twice daily, increased after 3 days to 5mg twice daily; maintenance 2·5mg to 5mg twice daily. Prophylaxis of cardiovascular events, initially 2·5mg once daily, increased to 5mg once daily then 10mg once daily.

Prescribe the lower cost ramipril capsules in preference to the higher cost non-Formulary tablets.

**Angiotensin-II receptor antagonists**

**FIRST CHOICE:** CANDESARTAN or LOSARTAN
Candesartan tablets 2mg, 4mg, 8mg, 16mg, 32mg
**Dose:** Hypertension, initially 8mg (hepatic impairment 2mg, renal impairment or intravascular volume depletion 4mg), once daily increased if necessary at intervals of 4 weeks to maximum 32mg once daily; usual maintenance dose 8mg once daily. Heart failure, initially 4mg once daily, increased at intervals of at least 2 weeks to 'target' dose of 32mg once daily or to maximum tolerated dose. Maximum dose 32mg once daily.

Losartan tablets 12.5mg, 25mg, 50mg, 100mg
**Dose:** Hypertension, usually 50mg once daily (older people over 75 years, moderate to severe renal impairment, intravascular volume depletion, initially 25mg once daily); increased to 100mg once daily if needed. Heart failure, initially 12.5mg once daily, increased at weekly intervals to maximum 150mg once daily if tolerated.

Valsartan capsules 40mg, 80mg, 160mg; tablets 40mg
**Dose:** Heart failure post-myocardial infarction, initially 20mg twice daily increased over several weeks to 160mg twice daily if tolerated.

Irbesartan tablets 75mg, 150mg, 300mg
**Dose:** Renal disease in hypertensive type 2 diabetes mellitus, initially 150mg once daily, increased if necessary to 300mg once daily. In haemodialysis or in older people over 75 years, consider initial dose of 75mg once daily.

Angiotensin receptor neprilysin inhibitor

**Note:** Sacubitril/valsartan
If the patient is already on an ACE inhibitor, it should be stopped for 36 hours before initiating sacubitril/valsartan to minimise the risk of angioedema.

SACUBITRIL/VALSARTAN (Entresto®) tablets 24mg/26mg, 49mg/51mg, 97mg/103mg
**Dose:** Patients with heart failure who remain symptomatic despite optimal medical therapy with an ejection fraction less than 40% (equivalence to severe or moderate – severe LV systolic dysfunction), 49mg/51mg twice daily, increased at 2 to 4 weeks to the target dose of 97mg/103mg twice daily as tolerated. Refer to SPC for details of patients for whom a lower starting dose is recommended.

Alpha agonists

Midodrine tablets 2.5mg, 5mg (Bramox®)
**Dose:** Severe orthostatic hypotension, initially 2.5mg three times daily increased weekly according to response up to a maintenance dose of 10mg three times daily. The last dose should be taken at least 4 hours before bedtime.

2.6 NITRATES, CALCIUM-CHANNEL BLOCKERS AND OTHER ANTIANGINAL DRUGS

Refer to the ‘Stable angina management’ shared clinical guideline on Intranet.

Nitrates

**FIRST CHOICE:** GLYCERYL TRINITRATE SPRAY

Glyceryl trinitrate aerosol spray 400 micrograms/metered-dose; injection 5mg/5mL, 50mg/50mL; transdermal patches 5mg, 10mg
Dose: *Sublingually*, 400 to 800 micrograms (1 to 2 sprays) repeated as required. Glycerol trinitrate spray is the formulation of choice. Counsel patients on its prophylactic and therapeutic use. Glycerol trinitrate transdermal patches are only recommended to improve venous patency in hospital [off-label] or to improve compliance in primary care. Nitrate patches may need to be removed for several consecutive hours to produce a nitrate-free period.

**ISOSORBIDE MONONITRATE** tablets 10mg, 20mg, 40mg; m/r capsules 25mg, 50mg; m/r tablets 60mg  
**Dose:** Tablets, initially 20mg 2 to 3 times daily or 40mg twice daily (10mg twice daily in those who have not previously received nitrates), give asymmetrically, ie morning and afternoon (8 am and 2 pm) to prevent nitrate tolerance; m/r capsules/tablets, 25mg in the morning, increasing up to 100mg to 120mg in the morning if necessary.  
Prescribe the standard formulation of isosorbide mononitrate first-line. In primary care, modified-release isosorbide mononitrate preparations are considerably more expensive than the conventional formulations and should be prescribed by generic name.

**Calcium-channel blockers**

**Note:** Combination of beta-blockers ([section 2.4](#)) with diltiazem or verapamil may produce excessive bradycardia and should only be used under specialist advice.

**Note:** Modified-release preparations of diltiazem and nifedipine:
- specify the brand to be dispensed
- select the most cost-effective brand when initiating therapy
- hospitals will only stock some brands; contact Pharmacy to identify brands currently available
- patients should continue on the same brand
- consider once-daily preparations in new patients and when medicine is being changed.

**Rate limiting calcium-channel blockers**

**DILTIAZEM** m/r capsules (twice daily dosing) 60mg, 90mg, 120mg, 180mg; m/r capsules (once-daily dosing) 120mg, 180mg, 200mg, 240mg, 300mg  
**Dose:** Prescribe by brand name; refer to BNF for dosing information of each branded product. When initiating therapy, Zemtard® XL is currently the preferred brand (once daily, m/r capsules 120mg, 180mg, 240mg, 300mg).

**VERAPAMIL** tablets 40mg, 80mg, 120mg; m/r tablets 120mg, 240mg; injection 5mg/2mL  
**Dose:** Supraventricular arrhythmias, 40mg to 120mg 3 times daily; angina, 80mg to 120mg 3 times daily (m/r tablets 240mg twice daily); hypertension 240mg to 480mg daily, in 2 to 3 divided doses (m/r tablets 240mg once or twice daily, new patients initially 120mg). Prophylaxis after myocardial infarction where beta-blockers inappropriate, m/r tablets 360mg daily in divided doses.

**Dihydropyridine calcium-channel blockers**

**FIRST CHOICE:** **AMLODIPINE**

**AMLODIPINE** tablets 5mg, 10mg  
**Dose:** Hypertension or angina, initially 5mg once daily, maximum 10mg once daily.

**NIFEDIPINE** m/r tablets 20mg, 30mg, 40mg, 60mg (once daily dosing), 10mg, 20mg (twice daily dosing)  
**Dose:** Prescribe by brand name; refer to BNF for dosing information of each branded product. Long-acting formulations of nifedipine are recommended for angina or long-term management of hypertension but are [off-label](#) for use in Raynaud's phenomenon.

**NIMODIPINE** tablets 30mg; intravenous infusion 10mg/50mL
Dose: Treatment of aneurysmal subarachnoid haemorrhage, refer to BNF and guidance on Intranet. Prevention, by mouth, 60mg every 4 hours, starting within 4 days of event and continued for 21 days.

Other antianginal drugs

IVABRADINE tablets 5mg, 7.5mg
Dose: Angina, (for people in sinus rhythm) initially 5mg twice daily, increased if necessary after 3 to 4 weeks to 7.5mg twice daily (if not tolerated reduce dose to 2.5 to 5mg twice daily); older people initially 2.5mg twice daily. Chronic heart failure NYHA II to IV class with systolic dysfunction, in patients in sinus rhythm whose resting heart rate remains at 75 or more beats per minute despite optimal standard therapy, initially 5mg twice daily, increased if necessary after 2 weeks to 7.5mg twice daily (if not tolerated reduce dose to 2.5mg twice daily). Ventricular rate at rest should not be allowed to fall below 50 beats per minute.

NICORANDIL tablets 10mg, 20mg
Dose: Initially 10mg twice daily (if susceptible to headache, 5mg twice daily), usual dose 10 to 20mg twice daily; up to 30mg twice daily may be used.

Note: Nicorandil is associated with a risk of gastro-intestinal ulceration including perianal ulceration.

Peripheral vasodilators

NAFTIDROFURYL capsules 100mg
Dose: 200mg 3 times daily. Discontinue after 2 to 4 weeks if no clinical benefit is obtained.

Note: Naftidrofuryl: only for use in peripheral vascular disease, see NICE CG147 'Peripheral arterial disease: diagnosis and management'.

PENTOXIFYLLINE m/r tablets 400mg
Dose: 400mg 3 times daily for up to 6 months to improve healing in patients with chronic venous leg ulcers [off-label]. See ‘Pentoxifylline treatment guidance’ on Intranet.

2.7 SYMPATHOMIMETICS

Inotropic sympathomimetics

DOBUTAMINE concentrate for intravenous infusion 250mg/50mL
DOPAMINE concentrate for intravenous infusion 200mg/5mL
ISOPRENALINE injection 200 micrograms/mL [unlicensed], 2mg/2mL [unlicensed]

Vasoconstrictor sympathomimetics

ADRENALINE/EPINEPHRINE 1 in 1000 injection 5mg/5mL
For use in High Dependency Units only.
EPHEDRINE injection 30mg/10mL
METARAMINOL injection 10mg/1mL
NORADRENALINE/NOREPINEPHRINE 1 in 1000 injection, noradrenaline base 4mg/4mL
2.8 ANTICOAGULANTS AND PROTAMINE

Parenteral anticoagulants

Refer to:
- ‘Policy for extended venous thromboembolism (VTE) prophylaxis on discharge from hospital’ on Intranet.
- ‘Thrombosis and embolism during pregnancy and the puerperium, reducing the risk (Green-top Guideline No 37a)’ at https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg37a/.

HEPARIN SODIUM injection 5000 units/5mL, 20 000 units/20mL, 25 000 units/5mL, subcutaneous injection 5000 units/0.2mL

ENOXAPARIN injection 20mg/0.2mL, 40mg/0.4mL, 60mg/0.6mL, 80mg/0.8mL, 100mg/1mL, 120mg/0.8mL, 150mg/1mL
The low molecular weight heparin (LMWH) enoxaparin is for the initial treatment of thrombotic disease and for thromboprophylaxis. It is given subcutaneously once or twice daily. It can be given in hospital or in the community. Enoxaparin does not require monitoring except in patients with renal impairment, weight greater than 150kg and in pregnancy (factor Xa levels should be taken 3 to 4 hours after the injection). The elimination half-life may be prolonged in older patients and although no dosage adjustment is necessary, monitoring may be advisable where prolonged use is anticipated or if there is significant renal and/or hepatic impairment. A clear management plan must be agreed prior to discharge from hospital to ensure that the patient receives appropriate care. Where indicated enoxaparin and warfarin are given concurrently until a therapeutic INR result is achieved for 48 hours; enoxaparin may then be discontinued. For use in deep venous thrombosis and pulmonary embolism see under ‘Oral anticoagulants’ below. Where an operation is planned, discuss the use of enoxaparin with an Anaesthetist especially if spinal anaesthetic is being considered. Take FBC prior to treatment and 1 week after the start of therapy if heparin is continued; if the platelet count has fallen to below normal levels consider heparin-induced thrombocytopenia and discuss with Haematologist.

Tinzaparin injection, prefilled syringe 2500 units/0.25mL, 3500 units/0.35mL, 4500 units/0.45mL
For Renal Unit use only.

HEPARINISED SALINE flush solution 50 units/5mL

$ DANAPAROID injection 750 units/0.6mL

$ ARGATROBAN concentrate for solution for infusion 250mg/2.5mL

$ BIVALIRUDIN powder for solution for injection 250mg
For use in patients with acute coronary syndrome undergoing percutaneous coronary intervention with a higher bleeding risk.

$ EPOPROSTENOL powder for solution for infusion 500 micrograms
FONDAPARINUX SODIUM injection 2·5mg/0·5mL
Refer to Raigmore Hospital guidance on management of non-ST elevation ACS/Non-STEMI on Intranet.

Oral anticoagulants

Refer to:
• ‘Embolism prophylaxis for patients with non-valvular atrial fibrillation’
• ‘Warfarin anticoagulant advice’
• ‘Anticoagulant switching’
• ‘Management of major haemorrhage and emergency invasive procedures on novel oral anticoagulants (dabigatran and rivaroxaban)’
• ‘Clinical Decision Algorithm for Suspected Leg DVT’ on Intranet.

WARFARIN tablets 500 micrograms, 1mg, 3mg, 5mg*

Dose:
• Venous thromboembolism (VTE) and pulmonary embolism (PE), see warfarin anticoagulant guidance and for in-patients refer to additional guidance on the NHS Highland In-patient Oral Anticoagulant Prescription Chart.
• see ‘Embolism prophylaxis for patients with non-valvular atrial fibrillation’.
• Deep venous thrombosis (DVT) see ‘Clinical Decision Algorithm for Suspected Leg DVT’ on Intranet.
• Metal valves – refer to BCSH ‘Guidelines on oral anticoagulation with warfarin – 4th edition’.

*Use of the warfarin 5mg tablet is no longer recommended for the general population to avoid confusion with the 500 microgram (0·5mg) tablet. There may however be some patients whose risk/benefit is to continue to use the 5mg tablet.

If commencing warfarin for treatment of VTE, low molecular weight heparin (LMWH) is usually administered for at least 5 days AND until adequate oral anticoagulation is established (INR in therapeutic range (>2·0) for 48 hours). Note: warfarin commenced at high dose has an initial pro-coagulant effect, so cover with LMWH is mandatory. Rapid warfarin induction carries potential risks of over-anticoagulation and bleeding. Slow induction is preferable, commencing with 1 to 2mg daily. Refer to ‘Warfarin anticoagulant advice’ for more detailed advice and recommended INR ranges for therapeutic control (usually 2·5, range 2·0 to 3·0 for DVT). Take into account patient circumstances (risk of falls, alcoholism, drug abuse etc) when deciding on appropriate range, and seek advice from Haematology, if unsure. If LMWH is given for more than 5 days, assess renal function and alter dose if impaired. Check baseline platelet count and, if required (see www.bcsghguidelines.com), monitor for up to 14 days for heparin-induced thrombocytopenia. Refer to BNF for contraindications or complications. INR must be monitored at the start of warfarin therapy, frequently in the initiation phase and regularly thereafter.

• There is a wide range of drug and dietary interactions with warfarin which should be carefully considered, refer to BNF.
• Where antibiotics are required, note that many antibiotics interact with warfarin. Ideally patients should be advised and the INR should be checked at baseline and rechecked three days after starting a course of antibiotics, regardless of the length of the antibiotic course.
• On discharge from hospital, to ensure that anticoagulant monitoring can be provided safely, information on the anticipated duration of anticoagulation, target INR, indication and current dose of warfarin must be provided. This information is contained in a form within the Immediate Discharge Document (IDD) system, eg IDL, and should be e-mailed to whoever is responsible for the ongoing management of the patient’s anticoagulation. In Argyll and Bute, until the electronic IDD system, eg IDL, is implemented, this information should be sent to whoever is responsible for the ongoing management of the patient’s anticoagulation by the most expedient and reliable means available, eg fax, mail or copy with patient.
APIXABAN tablets 2.5mg, 5mg
Dose:
- Prophylaxis of venous thromboembolism following knee and hip replacement surgery, 2.5mg twice daily, refer to SPC.
- ‘Embolism prophylaxis for patients with non-valvular atrial fibrillation’.
- Deep venous thrombosis (DVT) and pulmonary embolism (PE): 10mg twice daily for the first 7 days then 5mg twice daily, refer to SPC, also refer to ‘Clinical Decision Algorithm for Suspected Leg DVT’ on Intranet.

DABIGATRAN capsules 110mg, 150mg
Dose:
- Prophylaxis of venous thromboembolism following knee and hip replacement surgery, 220mg once daily, refer to SPC.
- ‘Embolism prophylaxis for patients with non-valvular atrial fibrillation’.
- Deep venous thrombosis (DVT) and pulmonary embolism (PE): 150mg twice daily, refer to SPC, also refer to ‘Clinical Decision Algorithm for Suspected Leg DVT’ on Intranet.

EDOXABAN ▼ tablets 15mg, 30mg, 60mg
Dose:
- ‘Embolism prophylaxis for patients with non-valvular atrial fibrillation’.

RIVAROXABAN ▼ tablets 10mg, 15mg, 20mg
Dose:
- Prophylaxis of venous thromboembolism following knee and hip replacement surgery, 10mg once daily, refer to SPC.
- ‘Embolism prophylaxis for patients with non-valvular atrial fibrillation’.
- Deep venous thrombosis (DVT) and pulmonary embolism (PE):
  - Rivaroxaban is recommended as the first choice oral anticoagulant for treatment of DVT and PE, and the prevention of DVT and PE following an acute DVT in adults. Dose is 15mg twice daily for 21 days followed by 20mg daily thereafter. Refer to SPC for dose adjustments, especially in reduced renal function.
  - If rivaroxaban is contra-indicated: low molecular weight heparin (LMWH) overlapping with warfarin, is the second treatment of choice.
  - If both choices are contra-indicated then discuss further options with the Haematology Department.
  - Active cancer; patients receiving treatment for cancer within the previous 6 months or currently receiving palliative treatment should be treated with LMWH, for at least the first 6 months of therapy. If treatment for longer than 6 months is required, it may be appropriate to switch to an alternative anticoagulant. Discuss with Haematology.
  - Also see ‘Clinical Decision Algorithm for Suspected Leg DVT’ on Intranet.
- Specialist haematology use in patients with multiple myeloma to counteract the prothrombotic effect of immune modulating drugs [off-label], 10mg once daily.

Protamine sulfate

PROTAMINE injection 50mg/5mL
Protamine is capable of partially reversing the anticoagulant activity of unfractionated heparin. It is of limited value in the reversal of low molecular weight heparin (enoxaparin) and of no value in the reversal of warfarin, dabigatran, rivaroxaban or apixaban. It is contra-indicated in patients with fish allergy.

Vitamin K (see section 9.6) is used in patients with high INRs and/or patients on warfarin who are bleeding. It takes 12 to 24 hours to act. It may be given orally using the intravenous preparation or intravenously. The dose is dependent on the INR, the degree of reversal required and whether there is a need for re-anticoagulation in the near future. Vitamin K does not reverse anticoagulation with heparin, dabigatran, apixaban or rivaroxaban.
Dried prothrombin complex (Beriplex®) (section 2.11) is used in addition to vitamin K in patients who are bleeding and on warfarin or in whom surgical intervention is planned imminently and the bleeding risk is thought to be unacceptable (note for certain procedures reversal may not be required; discuss with Haematologist). It provides temporary but immediate reversal of anticoagulation. It can be obtained from the Blood Transfusion Service on the authorisation of a Haematologist. There is limited evidence that rivaroxaban, and probably less so, dabigatran may be reversed using dried prothrombin complex; see ‘Management of major haemorrhage and emergency invasive procedures in patients on direct or novel oral anticoagulants’. Discuss with Haematologists before considering this.

2.9 ANTIPLATELET DRUGS

For advice on initiating warfarin in patients taking antiplatelet agents, see ‘Warfarin anticoagulant advice’.

See guidance on use post-MI, post-TIA or ischaemic stroke and Raigmore Hospital guidance on management of non-ST elevation ACS/Non-STEMI on Intranet. Antiplatelet drugs (aspirin and clopidogrel) are not recommended for primary prevention of cardiovascular disease.

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### Note: Gastroprotection

**Antiplatelet monotherapy** (low dose aspirin or clopidogrel):

- **patients with low gastrointestinal (GI) bleeding risk**: if patients develop dyspepsia whilst on antiplatelet monotherapy consider co-prescription of ranitidine 150mg twice daily initially; if ineffective change to lansoprazole (start on treatment dose but aim to reduce to maintenance dose to minimise *Clostridium difficile* (CDI) risk*).
- **patients with higher GI bleeding risk**: co-prescribe lansoprazole on initiation of antiplatelet monotherapy. Consider the risk of CDI when prescribing antibiotics in the future.

**Antiplatelet dual therapy** (low dose aspirin and clopidogrel/ticagrelor/prasugrel):

- Lansoprazole is indicated in dual therapy if age and co-morbidity confer a significant risk in the event of GI bleeding. Consider the risk of CDI when prescribing antibiotics in the future.

*Patients at high risk of infection with CDI are those with any of the following risk factors:

- a history of previous CDI or known colonisation with CDI (eg glutamate dehydrogenase (GDH) positive)
- age over 65 years
- co-prescription of high risk antibiotics namely clindamycin, cephalosporins, co-amoxiclav and fluoroquinolones (eg ciprofloxacin)
- immunocompromised or severe co-morbidity.

**Patients at high risk of GI adverse effects are those with any of the following risk factors:

- a history of gastroduodenal ulcer, GI bleeding or gastroduodenal perforation
- concomitant use of medications known to increase the risk of GI bleeds (see BNF)
- older age especially if frail, with serious co-morbidities, eg cardiovascular disease, hepatic or renal impairment, diabetes, hypertension.

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### FIRST CHOICE: ASPIRIN DISPERSIBLE TABLETS

**ASPIRIN**

- **OTC** dispersible tablets 75mg, 300mg; suppositories [unlicensed] 150mg, 300mg

**Dose:** 75mg daily for secondary prevention of thrombotic cerebrovascular or cardiovascular disease, and following coronary stenting. Following bypass surgery, aspirin 300mg daily is given initially reducing at a variable interval to 75mg to 150mg daily as defined by the surgeon; if clopidogrel is given concomitantly, only aspirin 75mg daily is given.

For patients with swallowing difficulties, consider rectal aspirin administration. There is no proven additional benefit of using aspirin enteric-coated tablets over the dispersible formulation.
CHAPTER 2 CARDIOVASCULAR SYSTEM

**Note: Clopidogrel**

1. Clopidogrel 75mg daily is a suitable alternative to aspirin if the patient has a further event while on aspirin or where aspirin is contra-indicated or genuinely not tolerated (ie proven hypersensitivity to aspirin-containing medicines or history of severe dyspepsia induced by low-dose aspirin which is unresponsive to PPI co-prescription).
2. See gastroprotection advice above. The risk of gastro-intestinal complications with clopidogrel is as high as with aspirin. Most of the benefit is seen early after starting treatment, however the increased risk of bleeding remains throughout the course; liaise with Cardiologist if appropriate. Combination of aspirin and clopidogrel further increases the risk of GI bleeding.
3. Clopidogrel is contra-indicated in active bleeding.
4. Discontinue 7 days before elective surgery; if in doubt discuss with Consultant Surgeon (if a person with a stent requires clopidogrel this must be discussed with Cardiologist).

**CLOPIDOGREL** tablets 75mg, 300mg

Dose: Secondary prevention of myocardial infarction, cerebrovascular disease or atherosclerotic events in peripheral arterial disease, 75mg daily. Acute coronary syndromes (unstable angina (if new ECG changes), ST elevation MI, non-ST elevation MI), initial loading dose of 300mg then 75mg daily. For cautions, see notes below. Dual antiplatelet therapy with aspirin and clopidogrel (or ticagrelor or prasugrel) is more usually prescribed on the advice of the specialist following acute coronary syndrome. Duration of therapy is decided on an individual basis.

**Note: Ticagrelor:** there is a small risk of episodic breathlessness with ticagrelor which is usually self-limiting.

**TICAGRELOR** tablets 90mg; orodispersible tablets 90mg

Dose: By mouth, initially 180mg as a single dose, then 90mg twice daily. For cardiologist initiation in combination with aspirin for the prevention of atherothrombotic events in patients with acute coronary syndrome.

**PRASUGREL** tablets 5mg, 10mg

Dose: By mouth, initially 60mg as a single dose then, body weight over 60kg, 10mg once daily or body weight under 60kg or over 75 years, 5mg once daily. For cardiologist initiation in combination with aspirin for the prevention of atherothrombotic events in patients with acute coronary syndrome.

**Note: Dipyridamole:** dispense dipyridamole m/r capsules in original container (pack contains a desiccant) and advise patients to follow manufacturer’s directions on discarding after opening.

**DIPYRIDAMOLE** m/r capsules 200mg

Dose: By mouth, 200mg twice daily preferably with food (where there is documented hypersensitivity to the preferred option of clopidogrel 75mg daily monotherapy post-TIA or ischaemic stroke).

**TIROFIBAN** concentrate for intravenous infusion 12.5mg/250mL

Refer to Raigmore Hospital guidance on management of non-ST elevation ACS/Non-STEMI on Intranet.

2.10 STABLE ANGINA, ACUTE CORONARY SYNDROMES, AND FIBRINOLYSIS

Refer to Raigmore Hospital guidance on management of non-ST elevation ACS/Non-STEMI on Intranet.

Fibrinolytic drugs
FIRST CHOICE: TENECTEPLASE

TENECTEPLASE injection 50mg (10 000 units)
Refer to ‘Emergency Thrombolysis’ shared clinical guidance on the intranet and to Raigmore Hospital guidance on management of ST elevation ACS/STEMI on Intranet.

$ ALTEPLASE injection 10mg (5.8 million units/vial); 20mg (11.6 million units/vial); 50mg (29 million units/vial)
Dose: For the management of hyper-acute stroke presenting within 4.5 hours of onset of symptoms refer to the thrombolysis guidance on the intranet. See section 3.4 for use of alteplase in the treatment of pulmonary embolism and of empyema [off-label].

$ UROKINASE injection 10 000 units, 25 000 units, 100 000 units

2.11 ANTIFIBRINOLYTIC DRUGS AND HAEMOSTATICS

TRANEXAMIC ACID tablets 500mg; injection 500mg/5mL
For use in significant haemorrhage following trauma [off-label] see NICE ESUOM1 (www.nice.org.uk). For use in menorrhagia (up to 4 days), see section 6.4.

$ TACHOSIL medicated sponge

Blood products

For further information see blood products table on Formulary webpage on Intranet.

$ DRIED PROTHROMBIN COMPLEX (Beriplex®) injection 500 units
Also see section 2.8 and ‘Warfarin anticoagulant advice’.

$ EPTACOG ALFA (ACTIVATED), FACTOR VIIA (RECOMBINANT) (NovoSeven®) injection 1mg, 2mg

$ FACTOR VIII FRACTION, DRIED (Voncento®, Fanhdi® Factor VIII) injection 1000 units

$ OCTOCOG ALFA, RECOMBINANT FACTOR VIII injection (ReFacto® AF250 units, 1000 units; Advate® 500 units)

$ NONACOG ALFA, FACTOR IX FRACTION, DRIED (BeneFIX®, Dried Factor IX Fraction) injection 1000 units, 2000 units

$ ALBUTREPENONACOG ALFA, FACTOR IX WITH ALBUMIN (Idelvion®) injection 1000 units

2.12 LIPID-REGULATING DRUGS

Statins

Statins are the drugs of first choice for lipid lowering. All currently available statins have long-term evidence of safety.
- Refer to ‘Use of lipid-lowering medication in the prevention of atherosclerosis’. Also note NICE CG181 guidance on Lipid Modification.
- For acute coronary syndromes atorvastatin 80mg daily is the drug of choice. If side-effects occur consider a lower dose or alternative statin. Review the dose annually.
For use following high-risk ischaemic stroke refer to ‘Protocol for acute treatment of ischaemic stroke’ and ‘Protocol for secondary prevention post-ischaemic stroke or immediately post-TIA’.

Only use rosuvastatin if significant interactions or intolerance of low-dose atorvastatin.

MHRA advice: Drug interactions may increase the risk of adverse effects, or reduce the effectiveness of statin treatment. Statins can interact with many drugs, eg diltiazem, verapamil, amiodarone, warfarin, macrolides, antivirals, antifungals; see interaction table and BNF. It is important to check for interactions before prescribing and advise patients to avoid drinking grapefruit juice.

**ATORVASTATIN** tablets 10mg, 20mg, 40mg, 80mg  
**Dose:** Refer to guidance.

**SIMVASTATIN** tablets 10mg<sup>O TC</sup>, 20mg, 40mg, 80mg  
**Dose:** Refer to guidance.

**ROSUVASTATIN** tablets 5mg, 10mg, 20mg, <sup>S</sup>40mg  
**Dose:** Refer to guidance.

**Note (muscle effects):** Rhabdomyolysis associated with lipid-regulating drugs such as the fibrates and statins appears to be rare (approximately 1 case in every 100 000 treatment years) but may be increased in those with renal impairment and possibly in those with hypothyroidism. Concomitant treatment with drugs that increase plasma-statin concentration increases the risk of muscle toxicity; concomitant treatment with a fibrate and a statin may also be associated with an increased risk of serious muscle toxicity. Refer to BNF.

**Fibrates**

Fibrates may be considered first-line therapy in those whose serum-triglyceride concentration is greater than 10mmol/L. Although a fibrate may reduce the risk of coronary heart disease events in those with low HDL-cholesterol or with raised triglycerides, a statin should be used first.

**BEZAFIBRATE** tablets 200mg; m/r tablets 400mg  
**Dose:** Tablets, 200mg 3 times daily after food; m/r tablets, 400mg once daily after food.

**Other**

<sup>S</sup>**ALIROCUMAB** solution for injection, pre-filled pen 75mg/1mL, 150mg/1mL  
**Dose:** By subcutaneous injection, 75 to 150mg every 2 weeks, adjusted according to response, administered into the thigh, abdomen or upper arm, dose adjustments should be made at 4-weekly intervals.

<sup>S</sup>**EVOLOCUMAB** solution for injection, pre-filled pen 140mg/1mL  
**Dose:** By subcutaneous injection, initially 140mg every 2 weeks, alternatively 420mg every month, adjusted according to response, administered into the thigh, abdomen or upper arm.
### STEP UP MANAGEMENT OF ESSENTIAL HYPERTENSION

**BP targets**

- **essential hypertension:** BP less than 140/90 mmHg
- If chronic kidney disease (CKD): BP less than 140/90 mmHg
- If CKD and albuminuria (urine albumin:creatinine ratio greater than 30mg/mmol): BP less than 130/80 mmHg
- If diabetes: BP less than 140/80 mmHg
- If diabetes and eye, cardiovascular or kidney damage including microalbuminuria (2 of 3 morning samples: ACR >2·5mg/mmol for males and >3·5mg/mmol for females) BP less than 130/80 mmHg.

Try to avoid systolic blood pressure below 120 mmHg: [www.nice.org.uk](http://www.nice.org.uk) and [www.renal.org](http://www.renal.org).

If BP is not controlled at each step progress to next step.

Advise all patients on lifestyle measures, eg smoking, physical activity, weight, alcohol, diet (including salt intake).

<table>
<thead>
<tr>
<th>Less than 55 years or with proteinuria</th>
<th>Diabetes</th>
<th>55 years or over and with no proteinuria or of African/Caribbean descent of any age</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitor*</td>
<td>Diuretic</td>
<td>Amlodipine 5 to 10mg daily If heart failure or symptomatic vascular disease consider diuretic</td>
</tr>
<tr>
<td>Use first-line in people with microalbuminuria or overt proteinuria</td>
<td>Bendroflumethazide 2-5mg daily Indapamide 2-5mg daily</td>
<td></td>
</tr>
</tbody>
</table>

**ACE inhibitor* + amlodipine**

Any combination of ACE inhibitor*, amlodipine, diuretic in diabetes

If heart failure/high risk of heart failure or oedema use ACE inhibitor* + diuretic

In those of African/Caribbean descent consider angiotensin-II receptor antagonist in place of ACE inhibitor

**ACE inhibitor* + amlodipine + diuretic**

- Spironolactone 25mg daily if potassium 5-0 or lower [off-label]. Check U&Es 1 week after starting. Consider initiating at 25mg alternate days if CKD.
  - or doxazosin or bisoprolol AND

Consider specialist referral to renal physicians ([High-HB.RaigmoreRenal@nhs.net](mailto:High-HB.RaigmoreRenal@nhs.net)) or diabetes referral.

*ACE inhibitor:

- lisinopril (start at 5mg daily, usual maintenance 20mg) or perindopril erbumine if first dose hypotension an issue (start at 2 to 4mg daily).
- if intolerant of ACE inhibitor consider angiotensin-II receptor antagonist.
- issue ‘Sick Day Rule’ card.
- check U&Es 1 to 2 weeks after starting/dose increase. Monitor annually if stable.
- avoid the combination of ACE inhibitor and angiotensin-II receptor antagonist.
- use caution when combining ACE inhibitors or angiotensin-II receptor antagonists with spironolactone due to risk of hyperkalaemia.

**Beta-blocker therapy:** may be indicated as first-line therapy in ischaemic heart disease.

**Primary prevention:** if diabetes or 10 year risk of CVD is 20% or more, or a strong family history of premature vascular disease recommend lipid-regulating therapies; see guidance and the ASSIGN score at [http://assign-score.com](http://assign-score.com).

**Antiplatelet drugs (aspirin and clopidogrel):** use in secondary prevention only (ensure continued if vascular disease is salt).
EMBOLISM PROPHYLAXIS FOR PATIENTS WITH NON-VALVULAR*, PERSISTENT OR PERMANENT ATRIAL FIBRILLATION (AF)

*non-valvular AF applies to all patients with AF except those with significant mitral stenosis or metal valve replacements.

<table>
<thead>
<tr>
<th>Does the patient with non-valvular AF have one or more non-gender risk factor using CHA2DS2VASc**?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>Is creatinine clearance*** above 15mL/min?</td>
</tr>
<tr>
<td>Yes</td>
</tr>
<tr>
<td>Prescribe (first choice) edoxaban</td>
</tr>
<tr>
<td>or (second choice) either dabigatran or apixaban or rivaroxaban (see below)</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Low risk: patient should not receive long-term thromboprophylaxis</td>
</tr>
</tbody>
</table>

FIRST CHOICE - EDOXABAN
Edoxaban

Dose:
- 60mg once daily
- 30mg once daily if one or more of:
  - creatinine clearance*** less than 30mL/min/m².
  - body weight less than or equal to 60kg
  - concomitant use of erythromycin, ciclosporin, ketoconazole, dronedarone
  - avoid if creatinine clearance*** less than 15mL/min.

SECOND CHOICE
Dabigatran

Dose:
- 150mg every 12 hours (or 110mg every 12 hours following individual assessment when thromboembolic risk is low and bleeding risk is high). Avoid if creatinine clearance*** less than 30mL/min/m².
- 80 years or over, 110mg every 12 hours.
- in patients receiving concomitant verapamil, reduce the dabigatran dose to 110mg every 12 hours.
- patient must be able to swallow capsule whole before prescribing.
- unsuitable for storage in monitored dosage systems (MDS).

SECOND CHOICE
Apixaban

Dose:
- 5mg twice daily
- 2.5mg twice daily if 2 out of (age over 80 years, body weight less than 60kg, creatinine greater than 133micromol/L)
- avoid if creatinine clearance*** less than 15mL/min.

SECOND CHOICE
Rivaroxaban

Dose:
- 20mg once daily (no dosage adjustment required for age)
- if creatinine clearance*** 15 to 49 mL/min reduce dose to 15mg once daily
- avoid if creatinine clearance*** less than 15mL/min
- to be taken with food.

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Approved by: Formulary Subgroup of NHS Highland ADTC
Review date: November 2019
Warning: document uncontrolled when printed
Further prescribing information

Contra-indications: many contra-indications to warfarin therapy will also apply to edoxaban, apixaban, dabigatran and rivaroxaban, eg high bleeding risks, coagulation disorders, non-compliance and, for dabigatran only, liver enzymes 2 or more times the upper limit of normal.

Renal function: monitor renal function before starting edoxaban (see SPC), apixaban (see SPC), dabigatran (see SPC), rivaroxaban (see SPC) and at least annually.

Elderly: take particular caution especially in the frail elderly where adverse events are higher for almost all medication.

Initiating warfarin: LMWH is not usually required to cover slow initiation of warfarin.

Moving from warfarin: stop warfarin and wait until:
- INR is less than or equal to 2·5 prior to starting edoxaban
- INR is less than 2 prior to starting apixaban or dabigatran
- INR is 3 or less prior to starting rivaroxaban.

This will often be between 2 to 3 days depending on initial INR.

For patients who fail to achieve more than 60% time in therapeutic range on warfarin, consider switching to edoxaban or another DOAC if no contra-indication is present.

Cardioversion:
Consider restoration of sinus rhythm in patients in atrial fibrillation for less than 1 year where there is no significant structural heart disease. In asymptomatic patients over 65 years of age there is no justification in restoring sinus rhythm. Elective anticoagulation with edoxaban, apixaban dabigatran, rivaroxaban or for 4 weeks prior to direct current cardioversion is required unless the patient is already well established on warfarin. Continue anticoagulation for at least 1 month after cardioversion as the recurrence rate and embolic risk extend into the period after restoration of sinus rhythm. Patients with risk factors for thromboembolism should remain on an anticoagulant (preferably warfarin) indefinitely even if sinus rhythm is restored. Otherwise, discontinue oral anticoagulant one month post-cardioversion if ECG shows sinus rhythm.

**CHA$_2$DS$_2$VASc scoring**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure (incl. LVD)</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Aged 75 or more</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1</td>
</tr>
<tr>
<td>Stroke/TIA/thromboembolism</td>
<td>2</td>
</tr>
<tr>
<td>Vascular disease (prior MI, PAD or aortic plaque)</td>
<td>1</td>
</tr>
<tr>
<td>Aged 65-74</td>
<td>1</td>
</tr>
<tr>
<td>Sex category: female</td>
<td>1</td>
</tr>
</tbody>
</table>

To assess combined CHA$_2$DS$_2$VASc stroke risk and HAS-BLED bleeding risk see [http://sparctool.com/](http://sparctool.com/).

***see Cockroft and Gault creatinine clearance calculator.***
WARFARIN ANTICOAGULANT ADVICE*

The international normalised ratio (INR) must be monitored at the start of warfarin therapy and regularly thereafter. There is a wide range of drug and dietary interactions which should be carefully considered, refer to the BNF for details or discuss with Haematology Department, Raigmore Hospital (tel: 01463 704000).

Anticoagulant monitoring is provided by GPs and by the Raigmore Hospital Haematology Department. To ensure that this can be provided safely, information on the anticipated duration of anticoagulation, target INR, indication and current dose of warfarin must be submitted to the Haematology Department and to the patient’s GP (see below for use of Immediate Discharge Letter (IDL)).

<table>
<thead>
<tr>
<th>POTENTIAL CONTRA-INDICATIONS/RELATIVE CONTRAINDICATIONS TO ANTICOAGULANT THERAPY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bleeding disorder</strong></td>
</tr>
<tr>
<td>eg                                  liver failure, renal failure, antiplatelet drugs (NSAIDs, aspirin, clopidogrel, prasugrel, ticagrelor), haemophila, von Willbrand’s disease</td>
</tr>
<tr>
<td><strong>Risk of bleeding</strong></td>
</tr>
<tr>
<td>eg                                  cerebral bleed, cerebral infarct in last 2 weeks, active peptic ulcer disease, GI or genito-urinary bleed in last 6 months</td>
</tr>
<tr>
<td><strong>Thrombocytopenia</strong></td>
</tr>
<tr>
<td><strong>Non-compliance/inability to understand therapy</strong></td>
</tr>
<tr>
<td><strong>Pregnancy</strong></td>
</tr>
<tr>
<td><strong>Chronic alcoholism</strong></td>
</tr>
<tr>
<td><strong>Risk of fits or falls</strong></td>
</tr>
<tr>
<td><strong>Severe hypertension</strong></td>
</tr>
<tr>
<td>eg                                  systolic greater than 160mm Hg or diastolic greater than 100mm Hg</td>
</tr>
</tbody>
</table>

Adapted from Pisters R et al. HAS-BLED. Chest. 2010:138:1093-1100

How to initiate warfarin treatment

A. Schedule for slow initiation of prophylactic and therapeutic warfarin therapy for in-patients 1,2

This schedule is intended for use where the need for rapid induction is not necessary, ie in the majority of patients. Slow initiation of warfarin is less likely to lead to bleeding problems and is preferable.

- Determine and record therapeutic indication, target INR (see below) and duration of treatment in the medical notes (and on the In-patient Oral Anticoagulant Prescription Chart if in-patient).
- Obtain pre-treatment INR. NB: INRs are inaccurate if the patient is receiving standard heparin and the APTT ratio is >3-0. Low molecular weight heparin (LMWH) does not affect the INR.
- For VTE patients continue LMWH for at least 5 days and until the INR is above the lower limit of the desired therapeutic range for 24 hours, ie 2 INRs 24 hours apart. Stop the LMWH immediately if INR is greater than the upper limit of the desired therapeutic range.

Commence warfarin 2mg daily

- Check INR on days 3 and 7. (For those with liver failure eg LFTs ≥1·5 times ULN, receiving drugs which interact with warfarin or weighing less than 50kg a smaller starting dose may be appropriate. Discuss with Haematology before initiating therapy.)
- If INR >4-0, then omit for at least 2 days, measuring INR on the first day dose is omitted. Once INR is <3-0 recommence at 1mg daily. Check INR again after 3 days.
- If INR 3-0 to 4-0, reduce 2mg dose to 1·5mg (a 1·5mg dose to 1mg, and a 1mg dose to 0·5mg). Check INR again after 3 days.
- If INR <3-0, continue on current dose until next planned check (day 7 or day 14).
• Recheck INR after 2 weeks of anticoagulation and predict maintenance dose as follows:

<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>INR</td>
<td>Dose (mg/day)</td>
</tr>
<tr>
<td>1·0</td>
<td>6</td>
</tr>
<tr>
<td>1·1 to 1·2</td>
<td>5</td>
</tr>
<tr>
<td>1·3 to 1·5</td>
<td>4</td>
</tr>
<tr>
<td>1·6 to 2·1</td>
<td>3</td>
</tr>
<tr>
<td>2·2 to 3·0</td>
<td>2</td>
</tr>
<tr>
<td>&gt;3·0</td>
<td>1</td>
</tr>
</tbody>
</table>

• Check INR weekly for 6 to 8 weeks. Warfarin dose is only changed when:
  - INR >4·0, but <5·0 then omit for 2 days and recommence daily dose at 20% less than previous dose. Recheck after 3 days.
  - INR >3·5 to 4·0, reduce daily dose by 20%. Recheck after 3 days.
  - INR 3·0 to 3·5, reduce daily dose by 10%. Recheck after 3 days.
  - INR <1·5 for 2 consecutive weeks, then increase daily dose by 25%. Recheck after 1 week.
  - if INR is not stable by week 6, 10% daily dose adjustments can be made weekly.

1 Adapted from Fennerty et al, BMJ 1988; 297: 1285-8.

B. Schedule for the slow initiation of prophylactic and therapeutic warfarin therapy for out-patients and General Practice

• For patients managed via the Haematology Service see ‘GP Referral Form for Anticoagulant Monitoring’ on Blood Sciences Homepage on Intranet.
• For patients managed via the GP follow the local practice guidelines.

C. Schedule for rapid initiation of warfarin therapy – hospital in-patients only

Rapid initiation of oral anticoagulation is potentially hazardous. If required in patients with newly-diagnosed venous thromboembolism discuss this with a Consultant Haematologist before initiating warfarin treatment. The Haematologist will give dosing guidance based on individual patient factors. The initial dosing regimen will vary between patients depending on whether there is increased sensitivity to warfarin, eg aged over 65, low body weight, parenteral feeding, heart failure, liver failure, prolonged baseline prothrombin time or receiving other drugs known to potentiate oral anticoagulants.

• Determine and record therapeutic indication, target INR (see below) and duration of treatment in medical notes and on the In-patient Oral Anticoagulant Prescription Chart.
• Obtain pre-treatment INR. NB: INRs are inaccurate if the patient is receiving standard heparin and the APTT ratio is >3·0. LMWH does not affect the INR.
• Check INR and prescribe warfarin daily as per dose plan agreed with the Haematologist.
• Continue LMWH for at least 5 days and until the INR is above the lower limit of the desired therapeutic range for 24 hours, ie 2 INRs 24 hours apart. Stop the LMWH immediately if INR is greater than the upper limit of the desired therapeutic range.

Using IDL to discharge patients

When completing the IDL for in-patients continuing or starting warfarin therapy, a warning box appears: ‘A tab has been created for completion’. This Anticoagulant Therapy section must be completed prior to sending the IDL to pharmacy. When the IDL has been completed the Anticoagulant Therapy letter created within it should be e-mailed to whoever is responsible for the ongoing management of the patient’s anticoagulation. This information also appears on all copies of the patient’s discharge letter and is emailed to GPs. All patients should receive verbal and written information (Oral Anticoagulant Therapy Booklets are available from Pharmacy). The nurse discharging the patient must ensure that the patient has an up-to-date completed booklet.
GENERAL POINTS

Prior to commencing warfarin:
- counsel patient on warfarin usage; refer to checklist in section 17.2 of SIGN 129.
- measure INR, U&Es, LFTs and FBC.
- fill in In-patient Oral Anticoagulant Prescription Chart.
- patients receiving an anti-platelet agent as primary prophylaxis for cardiovascular disease on developing an indication for warfarin should stop their anti-platelet agent.
- patients with peripheral artery disease or previous ischaemic stroke on antiplatelet therapy should stop this agent if warfarin is commenced.
- patients on aspirin or clopidogrel as secondary prophylaxis with stable ischaemic heart disease (often defined as more than 12 months following acute myocardial infarction) should stop their antiplatelet agent while being treated with warfarin.
- patients on a single antiplatelet agent less than 12 months following an acute coronary syndrome (ACS), who require to start warfarin therapy should continue aspirin therapy until 12 months post-ACS, unless they are regarded as having a high bleeding risk.
- patients on aspirin and clopidogrel/prasugrel/ticagrelor following an ACS or stent placement, who develop an indication for warfarin should be carefully assessed for bleeding risk and discussed with their cardiologist, with a view to introducing warfarin and minimising the duration of triple therapy.
- when combined warfarin and single antiplatelet agent are indicated, consider use of aspirin given the higher bleeding risk associated with clopidogrel (www.bcshguidelines.com (2011)).

On discharge:
- complete IDL including the Anticoagulant Therapy section. Telephone GP regarding INR monitoring. Oral Anticoagulant Therapy booklets can be obtained from Pharmacy. GPs may order booklets from the Supplies Department, Raigmore Hospital (code WMZ 045).

Dose change guidance
Because of the long half-life of oral anticoagulant drugs the full effect of a dose change is not seen for 3 to 4 days in many patients. For those on weekly dosing regimens it will be longer.

Most dose changes should be subtle (ie 10 to 20% of the current average daily dose at a time). The change may well represent less than 0.5mg in patients who only require small doses of warfarin or acenocoumarol and thus an alternate day or weekly dosing regimen may be required to deliver such a change.

There is a wide range of drug and dietary interactions with coumarins which should be carefully considered, refer to BNF. Where antibiotics are required, it should be noted that many antibiotics interact with coumarins and ideally the INR should be rechecked three days after starting a course of antibiotics, regardless of the length of the antibiotic course.

Recommended INR ranges for therapeutic control
This is a guide – patients may require higher or lower levels of anticoagulation depending upon their individual risk factors for bleeding or thrombosis.

Indications for oral anticoagulation, target INR and grade of recommendations

<table>
<thead>
<tr>
<th>Indication</th>
<th>Target INR (range = Target +/-0.5)</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary embolus (PE)</td>
<td>2.5</td>
<td>Anticoagulation for 1 month is inadequate treatment after an episode of venous thromboembolism (grade A, level 1b).</td>
</tr>
<tr>
<td>Proximal deep vein thrombosis (DVT), calf vein thrombus</td>
<td>2.5</td>
<td>At least 6 weeks anticoagulation is recommended after calf vein thrombosis (grade A, level 1b) and at least 3 months after proximal DVT or PE (grade A, level 1b). See also</td>
</tr>
<tr>
<td>Recurrence of venous thromboembolism (VTE) when no longer on warfarin therapy</td>
<td>2.5</td>
<td></td>
</tr>
<tr>
<td>Recurrence of VTE whilst on warfarin therapy</td>
<td>3.5</td>
<td></td>
</tr>
<tr>
<td>Symptomatic inherited thrombophilia</td>
<td>2.5</td>
<td></td>
</tr>
<tr>
<td>Antiphospholipid syndrome</td>
<td>2.5</td>
<td></td>
</tr>
</tbody>
</table>
Atrial fibrillation due to rheumatic heart disease, congenital heart disease and thyrotoxicosis
Cardioversion 2.5
Mural thrombus 2.5

Mechanical prosthetic heart valve – aortic
3 or 2.5 (see section below)
Mechanical prosthetic heart valve – mitral
3.5 or 3 (see section below)

Bioprosthetic valve
2.5 if anticoagulated
Arterial grafts
2.5 if anticoagulated
Coronary artery thrombosis
2.5 if anticoagulated
Ischaemic stroke without atrial fibrillation, retinal vessel occlusion, peripheral arterial thrombosis, coronary artery graft, coronary angioplasty and stents
Not indicated

Indefinite coagulation is indicated for patients with mechanical heart valves and for patients who have had 2 or more proven episodes of VTE. Patients with atrial fibrillation usually require lifelong treatment even if they are successfully cardioverted but still have risk factors for atrial fibrillation. In all cases a risk/benefit balance is required and warfarin should only be given where benefits outweigh risks. If in doubt consult Haematologist or Cardiologist.

Peri-operative anticoagulation

Recommendations for valve-location-specific target international normalised ratios (INRs)

<table>
<thead>
<tr>
<th>Target INR for mechanical prostheses</th>
<th>Prosthesis thrombogenicitya</th>
<th>Patient-related risk factorsb</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low</td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td>Medium</td>
<td>3.0</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>3.5</td>
</tr>
</tbody>
</table>

Prosthesis thrombogenicity:
Low = Carbomedics (aortic position), Medtronic Hall, St Jude Medical (without Silzone); Medium = Bjork-Shiley, other bileaflet valves; High = Lillehei-Kaster, Omnicience, Starr-Edwards.

Patient-related risk factors: mitral, tricuspid, or pulmonary valve replacement; previous thromboembolism; atrial fibrillation; left atrial diameter >50mm; left atrial dense spontaneous contrast; mitral stenosis of any degree; left ventricular ejection fraction <35%; hypercoagulable state.

Strategies for reversal of oral coumarin anticoagulant therapy*

A. Life-threatening bleeding (eg intracranial or major gastro-intestinal bleed)
   1. Stop warfarin.
   2. Intravenous phytoenadione (vitamin K$_1$) by slow intravenous injection 10mg, repeated if necessary 12 hours later.
   3. Prothrombin complex concentrate (Beriplex®). The dose will depend on the current INR and the targeted INR. In the following table approximate doses (mL/kg body weight of the reconstituted product) required for normalisation of INR (≤1·2 within 1 hour) at different initial INR levels are given.

<table>
<thead>
<tr>
<th>Initial INR</th>
<th>2·0 to 3·9</th>
<th>4·0 to 6·0</th>
<th>&gt;6·0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approximate intravenous dose* (units Factor IX/kg body weight)</td>
<td>25</td>
<td>35</td>
<td>50</td>
</tr>
</tbody>
</table>

*The maximum single dose should not exceed 5000 units Factor IX, given at a maximum rate of 200 units/min, ie 8 mL/min of the 25 units/mL reconstituted solution.

The correction of the INR persists for approximately 6 to 8 hours. However, the effects of phytoenadione (vitamin K$_1$) if administered simultaneously, are usually achieved within 4 to 6 hours. Thus, repeated treatment with Beriplex® is not usually required when phytoenadione (vitamin K$_1$) has been administered.

4. If Beriplex® is unavailable, fresh frozen plasma (15mL/kg body weight – approximately 1 litre for adult). Beriplex® and fresh frozen plasma are accessible from the Blood Transfusion Service after discussing with on-call Haematologist.

B. Less severe bleeding (eg haematuria, epistaxis)
   - INR >8·0, minor bleeding – stop warfarin; give phytoenadione (vitamin K$_1$) 1 to 5mg by slow intravenous injection; repeat dose of phytoenadione (vitamin K$_1$) if INR still too high after 24 hours; restart warfarin at 15 to 20% less than previous maintenance dose when INR <5·0, and bleeding has stopped.
   - INR 2·0 to 8·0, minor bleeding – stop warfarin; give phytoenadione (vitamin K$_1$) 1 to 3mg by slow intravenous injection; restart warfarin at 10 to 15% less than previous maintenance dose when INR <5·0 (if target INR range is between 3·0 and 4·0), and when INR <4·0 (if target INR range is between 2·0 and 3·0) and bleeding has stopped.
   - Unexpected bleeding at therapeutic levels – always investigate possibility of underlying cause, eg unsuspected renal or gastro-intestinal tract pathology, and haemorrhagic stroke. Also drug interactions, patient unwell, diet change etc.
   - Discuss with Haematology if more advice required.

C. High INR but no bleeding
   - INR >8·0, no bleeding – stop warfarin; give phytoenadione (vitamin K$_1$) 1 to 3mg by mouth using the intravenous preparation orally [off-label]; repeat dose of phytoenadione (vitamin K$_1$), if INR still too high after 24 hours; restart warfarin at a 15 to 20% less than previous maintenance dose when INR <5·0.
   - INR 5·0 to 8·0, no bleeding – withhold 1 or 2 doses of warfarin and restart warfarin at 10 to 15% less than previous maintenance dose, when INR <5·0 (if target INR range is between 3·0 and 4·0), or when INR <4·0 (if target INR range is between 2·0 and 3·0).
   - Unexpected high INR – always investigate possibility of underlying cause, eg unsuspected renal or gastro-intestinal tract pathology and haemorrhagic stroke. Also drug interactions, patient unwell, diet change etc.
   - Discuss with Haematology if more advice required.

D. Surgical or invasive procedures
   - Seek specialist advice before proceeding. Also see advice on bridging therapy at .

Adapted from:
Guidelines on oral anticoagulation with warfarin – fourth edition, British Committee on Standards in Haematology (2011)
*See guidance for management of haemorrhage with novel oral anticoagulants.

Lead reviewer: Cardiovascular Review Group  Approved by: Formulary Subgroup of NHS Highland ADTC
Date: May 2016  Review date: May 2018
Version: 6  Warning: document uncontrolled when printed
# ANTICOAGULANT SWITCHING

This information is for guidance only. It provides a reasonable starting point for most patients but the clinical background of each patient must be considered before applying the guidance; if unsure, seek specialist advice. The guidance only applies to patients receiving anticoagulation for prophylaxis for stroke and systemic embolism in non-valvular AF or patients treated for DVT and prevention of recurrent DVT and PE. For other indications or for high-risk patients (such as those with artificial heart valves or those with target INRs above 3-0) seek specialist advice.

### Switching to

<table>
<thead>
<tr>
<th>Switching from</th>
<th>Warfarin</th>
<th>Rivaroxaban</th>
<th>Dabigatran</th>
<th>Apixaban</th>
<th>Parenteral anticoagulants*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Warfarin</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Rivaroxaban</strong></td>
<td>Give warfarin concurrently until INR is greater than, or equal to 2 for 2 days. For the first 2 days use standard initial dosing of warfarin, followed by warfarin dosing guided by INR testing. While patients are on both rivaroxaban and warfarin test INR just prior to the next dose of rivaroxaban.</td>
<td>For stroke and systemic embolism prophylaxis stop warfarin and initiate rivaroxaban when INR is less than or equal to 3-0. For patients treated for DVT, PE and prevention of recurrence, stop warfarin and initiate rivaroxaban once INR is less than or equal to 2-5.</td>
<td>Stop warfarin. Dabigatran can be given as soon as INR is less than 2-0. Patient must be able to swallow capsule whole, as opening or chewing the capsule increases oral bioavailability and bleeding risk.</td>
<td>Stop warfarin. Start apixaban at the time the next rivaroxaban dose would have been due.</td>
<td>Stop warfarin therapy. Give first dose of parenteral anticoagulant when INR is less than 2-0.</td>
</tr>
<tr>
<td><strong>Dabigatran</strong></td>
<td>Adjust the starting time of the warfarin based on CrCL:  - CrCL greater than or equal to 50mL/min, start warfarin 3 days before stopping dabigatran.  - CrCL 30 to 49mL/min, start warfarin 2 days before stopping dabigatran.  - INR testing is unreliable until dabigatran has been stopped for at least 2 days.</td>
<td>If CrCL greater than or equal to 50mL/min start rivaroxaban 24 hours after last dose of dabigatran.</td>
<td>If CrCL 30 to 49mL/min start rivaroxaban 48 hours after last dose of dabigatran.</td>
<td>If CrCL less than 30mL/min commence rivaroxaban 3 to 4 days after last dose of dabigatran.</td>
<td>Stop dabigatran. Start apixaban at the time the next dabigatran dose would have been due.</td>
</tr>
<tr>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

*It is recommended to wait at least 12 hours after the last dose before switching from dabigatran to parenteral anticoagulant.*
<table>
<thead>
<tr>
<th></th>
<th>Warfarin</th>
<th>Rivaroxaban</th>
<th>Dabigatran</th>
<th>Apixaban</th>
<th>Parenteral anticoagulants*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Switching from Apixaban</strong></td>
<td>Give warfarin concurrently using standard initial dosing for at least 2 days. After 2 days of co-administration obtain INR prior to next dose of apixaban. Continue co-administration of apixaban and warfarin until INR is greater than or equal to 2.</td>
<td>Stop apixaban. Start rivaroxaban when the next dose of apixaban would have been due.</td>
<td>Stop apixaban. Start dabigatran at the time the next apixaban dose would have been due.</td>
<td></td>
<td>Stop apixaban. Start parenteral anticoagulant at the time the next dose of apixaban would have been due. These agents should not be administered together.</td>
</tr>
<tr>
<td><strong>Parenteral anticoagulants</strong>*</td>
<td>Continue parenteral anticoagulant for at least 5 days and until the INR is above the lower limit of the desired therapeutic range for 24 hours, ie 2 INRs 24 hours apart. Stop the parenteral anticoagulant immediately if INR is greater than the upper limit of the desired therapeutic range.</td>
<td>Start rivaroxaban 0 to 2 hours before the time of the next scheduled dose of LMWH or fondaparinux or at the same time of discontinuation of a continuous infusion of UH**.</td>
<td>Start dabigatran 0 to 2 hours before the time of the next scheduled dose of LMWH or fondaparinux or at the same time of discontinuation of a continuous infusion of UH**.</td>
<td>Start apixaban at the next scheduled dose of LMWH or fondaparinux or at the same time of discontinuation of a continuous infusion of UH**.</td>
<td></td>
</tr>
</tbody>
</table>

*includes low molecular weight heparins (LMWH) and fondaparinux ** UH = unfractionated heparin.

*** usually no need of parenteral anticoagulants when initiating oral anticoagulants in patients with atrial fibrillation only.
MANAGEMENT OF MAJOR HAEMORRHAGE AND EMERGENCY INVASIVE PROCEDURES IN PATIENTS ON DIRECT OR NOVEL ORAL ANTICOAGULANTS (DABIGATRAN, RIVAROXABAN AND APIXABAN)

There is no specific antidote available yet for dabigatran, rivaroxaban or apixaban. The key principles in managing these situations are:

- Assess coagulation screen and renal function, bearing in mind the limited prolongation of prothrombin time (PT) and activated partial thromboplastin time (APTT) induced by therapeutic doses of dabigatran, rivaroxaban and apixaban.

- Ascertain time of the most recent dose of anticoagulant, and administer no further doses. If very recent ingestion (<2h) consider administration of oral activated charcoal to inhibit absorption.

- If significant dabigatran effect, as assessed by coagulation screen (eg APPT >50s) consider feasibility of urgent haemodialysis to remove anticoagulant. Discuss with on-call renal consultant.

- Consider possibility of delaying major surgery until the anticoagulant effect has sufficiently dissipated.

- If major surgery has to proceed in the face of significant anticoagulant effect:
  - ensure haemostatic platelet count and fibrinogen level and satisfactory pre-operative Hb
  - treat any additional causes of coagulopathy
  - consider general haemostatic measures (eg intravenous tranexamic acid)
  - if despite the above measures there is significant peri- or post-operative bleeding discuss with Haematologist and consider administration of prothrombin complex concentrate (Beriplex 25 to 50mg/kg).

- In the presence of major bleeding:
  - follow general major haemorrhage protocol – see separate algorithms for dabigatran-treated and rivaroxaban/apixaban-treated patients (Appendices 1 and 2).

- once haemostasis is secured and/or the invasive procedure completed introduce thromboprophylaxis with low molecular weight heparin (LMWH) when appropriate. If dabigatran or rivaroxaban/apixaban is to be re-introduced this should be deferred until 24 hours after the last dose of LMWH.
APPENDIX 1: PATIENT RECEIVING DABIGATRAN THERAPY: HAEMORRHAGE PROTOCOL

STOP: Dabigatran

1. Coagulation screen [important to document time of last dose of dabigatran].
2. Full blood count and renal function/eGFR.

APTT prolonged

APTT normal

Dabigatran anticoagulant effect may be present – if normal APTT consider timing of last dose, and renal function (consider oral charcoal if dabigatran ingestion <2 hours)

MILD BLEED

- mechanical compression
- tranexamic acid
  - oral 25mg/kg
  - or IV 10mg/kg
- delay next dabigatran dose or discontinue treatment.

MAJOR BLEED

Maintain BP and urine output (dabigatran 80% renal excretion)

- optimise tissue oxygenation
- control haemorrhage
  - mechanical compression
  - surgical/radiological intervention
- tranexamic acid (1gram IV)
- red cell transfusion
  - aim Hb >70g/L
- platelet transfusion
  - aim Plt >50x10^9/L or
  - if CNS bleed aim Plt >100x10^9/L.

LIFE-THREATENING BLEED

Contact Haematologist

Consider haemodialysis

*Beriplex 25 to 50 units/kg

*NB: rFVIIa or FEIBA can be considered as an option if available. The choice of haemostatic agent is currently based on limited published evidence and advice from Haematologist.
APPENDIX 2: PATIENT RECEIVING RIVAROXABAN OR APIXABAN THERAPY: HAEMORRHAGE PROTOCOL

STOP: Rivaroxaban

1. Coagulation screen [important to document time of last dose of rivaroxaban].
2. Full blood count and renal function/eGFR.

PT prolonged

Likely LOW level rivaroxaban anticoagulant effect present

Mild Bleed
- mechanical compression
- tranexamic acid
  - oral 25mg/kg
  - or IV 10mg/kg
- delay next rivaroxaban dose or discontinue treatment.

MAJOR BLEED
- Contact Haematologist
- Maintain BP and urine output

LIFE-THREATENING BLEED
- Contact Haematologist

Continues to bleed

Major bleed: symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intra-articular, pericardial or intramuscular with compartment syndrome. (Schulman et al: J Thromb Haemost 2010; 3:692-694)

MAJOR BLEED
- optimise tissue oxygenation
- control haemorrhage
  - mechanical compression
  - surgical/radiological intervention
- tranexamic acid (1gram IV)
- red cell transfusion
  - aim Hb >70g/L
- platelet transfusion
  - aim Plt >50x10^9/L or
  - if CNS bleed aim Plt >100x10^9/L.

*NB: rFVIIa can be considered as an option. The choice of haemostatic agent is currently based on limited published evidence and advice from Haematologist.
### DRUG USE IN SECONDARY PREVENTION FOLLOWING MYOCARDIAL INFARCTION

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Immediate</th>
<th>Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antiplatelet therapy</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| a. aspirin (or clopidogrel if true intolerance to aspirin) | Initiate on suspecting a myocardial infarction.                              | a. continue aspirin or clopidogrel indefinitely  
  b. aspirin and clopidogrel (or ticagrelor or prasugrel) | b. continue single antiplatelet indefinitely and stop second antiplatelet agent after duration advised by local specialist. |
| **Beta-blocker**            |                                                                           |                                                                                                  |
| eg bisoprolol               | Initiate unless patient:  
  • remains hypotensive  
  • remains bradycardic  
  • is receiving verapamil  
  • has heart block or unstable cardiac failure  
  • has proven bronchospasm. | If not started immediately, initiate as soon as possible (up to 28 days post-MI) if patient is no longer bradycardic or hypotensive and has no other contra-indications. |
| **ACE inhibitors**          |                                                                           |                                                                                                  |
| eg perindopril erbumine     | Initiate within 24 hours of MI. Monitor U&Es.                             | Avoid with potassium-sparing diuretics or potassium supplements.  
  Measure U&Es 1 to 2 weeks after initiation, after dosage increase and at least annually thereafter. |
| **Lipid-lowering therapy**  |                                                                           |                                                                                                  |
| eg atorvastatin 80mg daily  | Indicated in all patients, irrespective of cholesterol level.  
  Consider drug interactions, see BNF. | Follow up in accordance with the lipid-lowering guidance.  
  If side-effects occur consider a lower dose or alternative statin. Review dose annually. |
| **Eplerenone or spironolactone** | Initiate if left ventricular dysfunction.  
  Monitor U&Es.                                           | Continue lifelong.  
  Monitor U&Es 1 week after starting and annually thereafter if stable. |

*In normotensive, non-diabetic, NSTEMI patients with preserved LV function, the potential benefit of beta-blockers and ACE inhibitors is small with a high NNT and therefore it may be decided by the cardiologist not to prescribe these treatments in such patients.*

<table>
<thead>
<tr>
<th>Patient group/treatment</th>
<th>Immediate</th>
<th>Maintenance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus or if blood glucose greater than 11mmol/L on admission.</td>
<td>If type 2 diabetes discontinue oral hypoglycaemic agents and for all patient groups give 24 hours of intravenous insulin according to Integrated Care guidance (opposite), aiming for a blood glucose of 7 to 10mmol/L.</td>
<td>Better control of blood glucose indefinitely. Refer to Management of Hyperglycaemia in Acute MI guidance in the Raigmore Hospital Integrated Care Pathway for Acute Coronary Syndromes.</td>
</tr>
<tr>
<td>Hypertension following myocardial infarction.</td>
<td>Initiate antihypertensive treatment.</td>
<td>Follow up, monitor and adjust therapy to obtain target BP.</td>
</tr>
</tbody>
</table>
PROTOCOL FOR ACUTE TREATMENT OF ISCHAEMIC STROKE (DAY 1-14 POST-ISCHAEMIC STROKE)

- Post-TIA refer to the ‘Protocol for secondary prevention post-TIA or ischaemic stroke’.
- Information for patients is available at www.SelfHelp4Stroke.org.

<table>
<thead>
<tr>
<th>ANTIPLATELETS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin 300mg once daily started within 24 hours of the event for 14 days.</td>
</tr>
<tr>
<td>- If the patient is already on clopidogrel, eg for coronary artery stent, seek stroke specialist advice before switching to aspirin.</td>
</tr>
<tr>
<td>- If already on aspirin 75mg daily then increase dose to 300mg daily for 14 days then refer to ‘Protocol for secondary prevention starting 2 weeks post-ischaemic stroke’.</td>
</tr>
<tr>
<td>- If already on warfarin, see anticoagulant advice below.</td>
</tr>
<tr>
<td>- If thrombolysed, initiate aspirin 24 hours after thrombolysis.</td>
</tr>
</tbody>
</table>

**Prescribing information**

- Only for use in confirmed non-haemorrhagic stroke after a CT scan.
- For patients with dysphagia, aspirin 300mg once daily should be administered rectally as a suppository, or as the dispersible tablet via an enteral tube if this route is available.
- In documented aspirin intolerance or allergy prescribe clopidogrel 75mg daily.
- For patients at risk of gastrointestinal complications with aspirin (known peptic ulcer or dyspepsia) co-prescribe gastroprotection (see Highland Formulary section 2.9).
- Discontinue NSAIDs as they antagonise the antiplatelet effect of aspirin.

<table>
<thead>
<tr>
<th>ANTIHYPERTENSIVES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Withhold prescribing of NEW antihypertensives for 14 days post-ischaemic stroke.</td>
</tr>
</tbody>
</table>

**Prescribing information**

- Consider patients with more than one event in seven days as high-risk and initiate antihypertensives immediately, as per secondary intervention protocol.
- Regular antihypertensive medication should be continued as before in the post-stroke period if the blood pressure is permissible (refer to the table below).

<table>
<thead>
<tr>
<th>Blood pressure</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consistently less than 120/80mmHg</td>
<td>Withhold any regular antihypertensive medication.</td>
</tr>
<tr>
<td>Consistently 120/80mmHg or greater but less than 220 systolic BP OR less than 130 mean arterial pressure</td>
<td>Continue regular antihypertensive medication if no other acute contra-indications.</td>
</tr>
<tr>
<td>Consistently 220 or greater systolic BP OR greater than 130 mean arterial pressure</td>
<td>Continue regular antihypertensive medication if no other acute contra-indications. Seek specialist advice from a physician experienced in stroke.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ANTICOAGULANTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Withhold for 3 days post-ischaemic stroke to decrease the risk of haemorrhagic transformation.</td>
</tr>
</tbody>
</table>

**Prescribing information**

- For patients presenting with stroke in atrial fibrillation (AF) while on oral anticoagulants, in most circumstances consider withholding the oral anticoagulant for 3 days and prescribe aspirin 300mg daily until Stroke Team review.
- There is no evidence of benefit in co-prescribing antiplatelets and anticoagulants for the prevention of further strokes.
- In patients with atrial fibrillation assess stroke risk using CHA2DS2-VASc and bleeding risk using HAS-BLED: see http://sparctool.com/.
### STATINS

**Atorvastatin 80mg daily**

**Prescribing information**

- Prior to prescribing a statin, check non-fasting total cholesterol (TC), high-density lipoprotein (HDL) and triglyceride (TG) levels, as well as liver function tests (LFTs) and thyroid function tests (TFTs).
- For further information refer to ‘Use of lipid-lowering medication in the prevention of atherosclerosis’.
- Consider drug interactions; refer to table in above lipid-lowering guidance or to BNF.
- If a person is not able to tolerate atorvastatin 80mg consider a lower dose or alternative statin. Refer to BNF for common side-effects.

**Note**: patients post-haemorrhagic stroke should not normally be prescribed a statin unless the risks of further vascular events outweigh the risk of further haemorrhage.
PROTOCOL FOR SECONDARY PREVENTION POST-TIA OR ISCHAEMIC STROKE (STARTING 2 WEEKS POST-ISCHAEMIC STROKE OR IMMEDIATELY POST-TIA)

- Days 1-14 post-ischaemic stroke see ‘Protocol for acute treatment of ischaemic stroke’.
- Information for patients is available at www.SelfHelp4Stroke.org

### ANTIPLATELETS

**Clopidogrel 75mg once daily (monotherapy)**

**Prescribing information**

- The efficacy of clopidogrel monotherapy is equivalent to a combination of aspirin and dipyridamole.
- Clopidogrel may be associated with fewer side-effects, has once-daily dosing and is the preferred choice for better compliance.
- Patients with documented hypersensitivity to clopidogrel should receive aspirin 75mg daily.
- For patients at risk of gastro-intestinal complications with aspirin (known peptic ulcer or dyspepsia) co-prescribe gastroprotection (see Highland Formulary section 2.9).
- There is currently no evidence base for dual therapy with aspirin and clopidogrel or with dipyridamole and clopidogrel.

### ANTIHYPERTENSIVES

**Perindopril erbumine 2mg daily titrating to 4mg AND Indapamide 2.5mg daily**

**Prescribing information**

- All stroke types, haemorrhagic, ischaemic and TIA, derive risk reduction in secondary events from tight blood pressure control, even in the normotensive patient though caution should be exercised in the frail elderly whose diastolic BP is below 70mmHg, and the combination withheld if below 60mmHg.
- Initiate treatment with the combination of perindopril 2mg daily and indapamide 2.5mg daily, then after 2 weeks titrate perindopril to 4mg daily if tolerated, U&Es are stable and blood pressure is permissible.
- Check U&Es prior to initiation and then within 4 to 7 days of initiation and at each dose titration.
- If intolerant of perindopril, eg ACE-induced cough, stop both perindopril and indapamide and consider losartan monotherapy (there is no evidence base to support the combination of losartan and indapamide as a means to offset the risk of future stroke/TIA). Thereafter refer to 'Step up management of essential hypertension'.
- Once stabilised on treatment, recheck U&Es annually.
- Once the above treatment has been maximised refer to ‘Step up management of essential hypertension’ for further advice regarding blood pressure control and treat to target.

**Blood pressure target post-stroke/TIA: 140/85mmHg (if diabetic, 130/80mmHg or less)**
## ANTICOAGULANTS

### Oral anticoagulants

**Prescribing information**

- Consider patients with ischaemic stroke or TIA in atrial fibrillation (AF) for anticoagulant treatment. Refer to ‘Embolism prophylaxis for patients with non-valvular, persistent or permanent atrial fibrillation (AF)’.
- There is no evidence of benefit in co-prescribing antiplatelets and anticoagulants for the prevention of further strokes.
- In days following a TIA assess risk for stroke using ABCD² score.

---

### STATINS

**Atorvastatin 80mg daily**

**Prescribing information**

- Prior to prescribing a statin, check non-fasting total cholesterol (TC), high-density lipoprotein (HDL) and triglyceride (TG) levels, as well as liver function tests (LFTs) and thyroid function tests (TFTs).
- For further information refer to ‘Use of lipid-lowering medication in the prevention of atherosclerosis’.
- Consider drug interactions; refer to table in above lipid-lowering guidance or to BNF.
- Refer to BNF for common side-effects. If a person is not able to tolerate atorvastatin 80mg consider a lower dose or alternative statin.

**Note:** patients post-haemorrhagic stroke should not normally be prescribed a statin unless the risks of further vascular events outweigh the risk of further haemorrhage.
**USE OF LIPID-LOWERING MEDICATION IN THE PREVENTION OF ATHEROSCLEROSIS**

**Patients without established cardiovascular disease (CVD)**

For primary prevention, therapy with a statin should be discussed with patients whose predicted cardiovascular disease risk over 10 years is 20% or more using ASSIGN or JBS3 risk calculators.

Patients with diabetes and/or ischaemic stroke should be treated as per the pathway for Patients with Established Vascular Disease and/or Diabetes and/or Ischaemic Stroke.


Patients with rheumatological disease (RA/SLE): estimate the risk using ASSIGN, ticking the box for RA.

Screen for potential candidates for treatment. These are adults who:
- smoke – stopping smoking will dramatically reduce cardiovascular risk (more than any other intervention) and improve quality of life. Appropriate measures to support stopping smoking should therefore be considered first-line in all patients who smoke.
- are hypertensive.
- have a family history of premature coronary artery disease (ie MI or CABG in first degree relative under 60).

Discuss treatment options with the patient taking into consideration that the benefits of therapy, eg absolute reductions in risk of heart attack and stroke are small and may be outweighed by the risk of side-effects, eg muscle pain and development of diabetes mellitus.

### Key

- TC = total cholesterol
- LDL = low density lipo-protein cholesterol
- HDL = high density lipo-protein cholesterol
- TG = triglyceride
- LFTs = liver function tests
- FH = familial hypercholesterolaemia

#### Request lipid test for TC, HDL and TG, and test LFTs

- If TC greater than 7.5 mmol/L consider secondary causes and FH (see Simon Broome criteria).*

#### Calculate patient’s cardiovascular risk using **ASSIGN** or **JBS3** risk calculator

- If 10 year cardiovascular disease risk less than 20%, repeat risk prediction calculation at least every 5 years.*

### Treat patient, if 10 year cardiovascular disease risk 20% or greater, with either:

- **ATORVASTATIN 20mg** or **SIMVASTATIN 40mg DAILY**
  
  - see BNF for cautions, contra-indications and interactions (see also interactions table)
  - initially prescribe no more than 1 month of treatment
  - advise patient to report muscle symptoms (pain, tenderness, soreness) without delay
  - before issuing further supply, ensure patient tolerating therapy
  - if side-effects occur or there are potential drug interactions (see interactions table) consider a lower dose or alternative statin
  - always give dietary and lifestyle advice eg smoking, alcohol, diet, physical activity in addition to statin.

#### Check LFTs and cholesterol at 3 months and at 1 year

#### Review annually* to ensure continued adherence to therapy

---

*SUPPLEMENTARY INFORMATION*

Prevention of atherosclerotic arterial disease in patients with or without established cardiovascular disease requires control of all risk factors. No single risk factor, including cholesterol concentration, should be viewed in isolation.

- consider all other risk factors, including hypertension and diabetic control (see appropriate separate guidelines)
- antplatelet drugs (aspirin and clopidogrel) are no longer recommended for primary prevention.

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Lead reviewer: Cardiovascular Review Group
Date: May 2016 (amended October 2016)
Version: 6

Approved by: Formulary Subgroup of NHS Highland ADTC
Review date: May 2018

Warning: document uncontrolled when printed
Patients with established vascular disease and/or ischaemic stroke** and/or diabetes

- Patients with established occlusive arterial disease are at high risk and should be treated with a statin regardless of total cholesterol concentration, ie:
  
<table>
<thead>
<tr>
<th>Previous MI</th>
<th>Pre- or post-CABG</th>
<th>Pre- or post-angiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite angina*</td>
<td>Angiographic coronary artery disease</td>
<td>Definite peripheral artery disease*</td>
</tr>
<tr>
<td>Previous TIA or ischaemic stroke**</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Definite’ indicates diagnosis confirmed by investigation or firm (not suspected) clinical diagnosis.

- Patients aged over 40 years with diabetes but without established CVD should be treated with a statin regardless of total cholesterol concentration.

- Patients under 40 years with diabetes should be considered for treatment with a statin if at least one of the following is present:
  - Previous MI
  - Pre- or post-CABG
  - Pre- or post-angiography
  - Definite angina*
  - Angiographic coronary artery disease
  - Definite peripheral artery disease*
  - Angiographic coronary artery disease
  - Definite peripheral artery disease*
  - Previous TIA or ischaemic stroke**

- Patients with established occlusive arterial disease are at high risk and should be treated with a statin regardless of total cholesterol concentration.

- Additional secondary prevention measures, eg antiplatelet therapy (Highland Formulary Section 2.9) should also be considered for all patients.

Request lipid test for TC, HDL and TG and test LFTs. Repeat fasting test if TGs raised. Check fasting blood glucose.

If TC greater than 7.5 mmol/L consider secondary causes and FH (see Simon Broome criteria).

Treat all patients**, regardless of baseline cholesterol concentration, with either:

**ATARVASTATIN 20mg or SIMVASTATIN 40mg DAILY**

- see BNF for cautions, contra-indications and interactions (see also interaction table overleaf)
- initially prescribe no more than 1 month of treatment
- advise patient to report muscle symptoms (pain, tenderness, soreness) without delay
- before issuing further supply, ensure patient tolerating therapy
- if not tolerated/side-effects occur consider a lower dose or alternative statin
- always give dietary and lifestyle advice, eg smoking cessation, alcohol, diet, physical activity etc.

Re-test at 12 weeks: request lipid test for TC, HDL and TG and test LFTs (fasting TG if random TG greater than 4mmol/L)

**Therapeutic target: TC less than 5mmol/L**

If target not achieved:

- ensure compliance
- consider increasing dose or an alternative statin
- if not tolerated/side-effects occur consider a lower dose or alternative statin.

**SUPPLEMENTARY INFORMATION**

Patients diagnosed with high risk acute coronary syndrome or ischaemic stroke will be treated with

**ATARVASTATIN 80mg DAILY**

(If not tolerated/side-effects try lower dose or different statin. Review dose annually.)

(Also see stroke guidance)
Monitoring requirements for statin efficacy

**BASELINE**
- lipid test for TC, HDL and TG (fasting TG if random TG greater than 4mmol/L). Also check fasting blood sugar.
- liver function test.
- exclude hypothyroidism as a secondary cause – thyroid stimulating hormone (TSH).
- if TC greater than 7.5 mmol/L consider FH (see Simon Broome criteria).

**Primary prevention** (high risk without CVD)

**3 MONTHS AND 1 YEAR AFTER STARTING STATIN AND THEREAFTER ONLY IF CONCERNS:**
- lipid test for TC, HDL and TG (fasting TG if random TG greater than 4mmol/L)
- liver function test.

**Secondary prevention or diabetes** (established vascular disease and/or ischaemic stroke)

**3 MONTHS AFTER STARTING STATIN OR FOLLOWING INCREASE IN DOSE/CHANGE IN THERAPY AND AT 1 YEAR**
- lipid test for TC, HDL and TG (fasting TG if random TG greater than 4mmol/L).
- liver function test.

**ANNUALLY ONCE TREATMENT STABLE**
- lipid test for TC, HDL and TG (fasting TG if random TG greater than 4mmol/L).

**AT ANY TIME IF GENUINE MUSCLE SYMPTOMS SUSPECTED**
- creatine kinase (always advise patients being started on a statin to report any muscle symptoms (pain, tenderness, soreness) without delay).
- if statin not tolerated and/or side-effects consider a lower dose or alternative statin.

---

**Summary of common statin interactions** (this list is not exhaustive; refer to BNF for full information on interactions)

<table>
<thead>
<tr>
<th>Interacting drug</th>
<th>Simvastatin prescribing advice</th>
<th>Atorvastatin prescribing advice</th>
<th>Rosuvastatin prescribing advice*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clarithromycin</td>
<td>Contra-indicated with simvastatin</td>
<td>Use lowest necessary dose of atorvastatin. Close monitoring advised for atorvastatin doses above 20mg daily. Avoid clarithromycin if possible.</td>
<td>No information of interaction</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Contra-indicated with simvastatin</td>
<td>Use lowest necessary dose of atorvastatin***</td>
<td>Possible reduction in rosuvastatin levels – not clinically relevant in short courses of erythromycin.</td>
</tr>
<tr>
<td>Verapamil Amlodipine Amiodarone Diltiazem</td>
<td>Do not exceed 20mg simvastatin daily</td>
<td>Use lowest necessary dose of atorvastatin (monitor lipid levels)***</td>
<td>No information of interaction</td>
</tr>
<tr>
<td>Amlodipine</td>
<td>Do not exceed 20mg simvastatin daily</td>
<td>No clinically significant interaction expected***</td>
<td>No information of interaction</td>
</tr>
<tr>
<td>Warfarin</td>
<td>Monitor INR</td>
<td>Monitor INR</td>
<td>Monitor INR</td>
</tr>
<tr>
<td>Ciclosporin</td>
<td>Contra-indicated with simvastatin</td>
<td>Do not exceed 10mg atorvastatin daily.*** Avoid if possible.</td>
<td>Contra-indicated with rosuvastatin</td>
</tr>
<tr>
<td>Grapefruit juice</td>
<td>Avoid grapefruit juice</td>
<td>Limit or avoid grapefruit juice intake</td>
<td>No information of interaction</td>
</tr>
<tr>
<td>HIV protease inhibitors**</td>
<td>Contra-indicated with simvastatin</td>
<td>Use lowest necessary dose of atorvastatin (monitor lipid levels). Consult manufacturers’ literature for maximum recommended doses. Avoid if possible.</td>
<td>Not recommended for combination use. Consult manufacturers’ literature for maximum recommended doses.</td>
</tr>
<tr>
<td>Itraconazole</td>
<td>Contra-indicated with simvastatin</td>
<td>Contra-indicated with atorvastatin</td>
<td>Increased level of rosuvastatin – not expected to be clinically significant.***</td>
</tr>
<tr>
<td>Posaconazole</td>
<td>Contra-indicated with simvastatin</td>
<td>Contra-indicated with atorvastatin</td>
<td>No information of interaction</td>
</tr>
<tr>
<td>Drug</td>
<td>Interaction Note</td>
<td></td>
<td></td>
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<tr>
<td>--------------</td>
<td>-------------------------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simvastatin</td>
<td>Use lowest necessary dose of simvastatin***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluconazole</td>
<td>Use lowest necessary dose of atorvastatin***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miconazole oral gel</td>
<td>Contra-indicated with simvastatin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium fusidate</td>
<td>Not recommended for combination use***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ticagrelor</td>
<td>Do not exceed 40mg simvastatin daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No clinically significant interaction expected***</td>
<td></td>
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<tr>
<td></td>
<td>No clinically significant interaction expected***</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No clinically significant interaction expected***</td>
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</tr>
</tbody>
</table>

*If changing to rosuvastatin, start at 5 or 10mg daily and titrate up to 20mg daily if necessary (patients of asian origin start at 5mg and do not exceed 20mg)

**See summary of product characteristics (SPC) for advice regarding specific drugs

***Monitor closely for signs of side-effects (eg myopathy, rhabdomyolysis)
CHAPTER 3 RESPIRATORY SYSTEM

Refer to SIGN guidance on the Management of Asthma produced in conjunction with the British Thoracic Society. For the management of chronic obstructive pulmonary disease (COPD) refer to Respiratory Shared Clinical Guidelines, NICE CG101 and the ‘Global initiative for chronic obstructive lung disease (GOLD)’. Also refer to local guidance on inhaler devices on NHS Highland Intranet.

Patients should receive regular face-to-face review to ensure correct inhaler technique, self-management (where appropriate) and concordance with agreed treatment. Information for patients is available at http://mylungsmylife.org/. Consider referring patients with COPD to pulmonary rehabilitation.

To achieve optimal compliance with inhaled therapy consider the following:
- base the choice of inhaler device on patient acceptability, suitability and cost.
- patients should only be given a device they can demonstrate they can use; many adults struggle to use metered dose inhalers (MDI) therefore dry powder inhalers (DPI) or other breath activated devices should be considered.
- always take appropriate time to teach and check inhaler technique.
- where possible use the same inhaler device if a patient requires a number of different inhaled medicines.
- reduce the number of inhalers by use of appropriate combination products.

Note: Nebulisers

In hospital:
- Nebulised bronchodilator solutions should always be driven by oxygen when administered to a patient with asthma and by air when administered to a patient with COPD or any other diagnosis.

In primary care:
- In both COPD and asthma, only prescribe nebulisers in primary care following a formal assessment through the Respiratory Clinic; evidence suggests that maximising inhaled therapy through a spacer device is the preferred choice.
- For chronic domiciliary use electric compressors should be used to deliver nebulised therapy as the flow rate from an oxygen concentrator is insufficient to nebulise solutions effectively.
- In acute asthma in primary care, nebulisers should be driven by oxygen provided a minimum flow rate of at least 6 litres/min is available. As an alternative to air-driven nebulised therapy, high-dose salbutamol may be delivered by a large volume spacer (Volumatic®) to children aged over 2 years and adults.

There is no place for nebulised sodium chloride 0·9% solution in either COPD or asthma.

3.1 BRONCHODILATORS

Inhaled beta₂ agonists

Short-acting beta₂ agonists (SABA)

FIRST CHOICE: SALBUTAMOL

SALBUTAMOL aerosol inhalation 100 micrograms/metered inhalation; breath-actuated aerosol inhalation (Salamol Easi-Breathe®) 100 micrograms/metered inhalation; dry powder for inhalation (Ventolin Accuhaler®) disk containing blisters of salbutamol 200 micrograms/blister; nebuliser solution 2·5mg/2·5mL, 5mg/2·5mL
Dose: By aerosol inhalation, 100 to 200 micrograms (1 to 2 puffs), or by inhalation of powder, 200 to 400 micrograms (1 to 2 blisters), when required to relieve breathlessness; by inhalation of nebulised solution, 2·5mg, repeated up to 4 times daily (also see nebuliser note box above).

**TERBUTALINE** dry powder inhaler (Bricanyl Turbohaler®) 500 micrograms/metered inhalation

Dose: By inhalation of powder, 500 micrograms (1 inhalation) when required to relieve breathlessness.

**Long-acting beta\(_2\) agonists (LABA)**

Consider use of combination inhalers with inhaled steroids (section 3.2); in asthma, LABAs should only be given in a combination inhaler; in COPD use as per NICE.

**FIRST CHOICE: FORMOTEROL**

FORMOTEROL dry powder inhaler (Oxis Turbohaler®) 6 micrograms, 12 micrograms per metered inhalation.

Dose: By inhalation of powder, 6 to 12 micrograms once or twice daily.

SALMETEROL aerosol inhalation (Serevent Evohaler®) 25 micrograms/metered inhalation; dry powder for inhalation (Serevent Accuhaler®) disk containing blisters of salmeterol 50 micrograms /blister

Dose: By inhalation, 50 micrograms (2 puffs or 1 blister) twice daily.

**Oral beta\(_2\) agonists**

Note: Prescribe oral salbutamol in line with SIGN guidance on asthma management.

SALBUTAMOL m/r tablets 8mg [unlicensed]; oral solution 2mg/5mL

**Parenteral beta\(_2\) agonists**

S SALBUTAMOL injection 500 micrograms/1mL; solution for intravenous infusion 5mg/5mL

S TERBUTALINE injection 500 micrograms/1mL, 2·5mg/5mL

For respiratory physician use only, in severe asthma [off-label].

**Antimuscarinic bronchodilators**

Note: Acute angle-closure glaucoma reported with antimuscarinic bronchodilators:
- Ideally nebulise solution through a mouthpiece.
- Advise patients to avoid getting powder or spray into their eyes; this may result in precipitation or worsening of angle-closure glaucoma, eye pain or discomfort, temporary blurring of vision, visual halos or coloured images in association with red eyes from conjunctival congestion and corneal oedema. If any combination of these eye symptoms develops, advise patients to stop treatment and consult their GP immediately.

**Short-acting antimuscarinic bronchodilators (SAMA)**

IPRATROPIUM BROMIDE nebuliser solution 250 micrograms/1mL, 500 micrograms/2mL; S aerosol inhalation 20 micrograms/metered inhalation

Dose: By inhalation of nebuliser solution, 250 to 500 micrograms 3 to 4 times daily (also see nebuliser note box). The aerosol inhaler is for specialist use on ITU.
Long-acting antimuscarinic bronchodilators (LAMA) in COPD

Consider umeclidinium as first choice for patients with moderate or severe COPD (FEV\(_1\) 60% or less and frequent exacerbations and breathlessness). Stop ipratropium if a long-acting antimuscarinic bronchodilator is started. Assess after 2 months and discontinue if no improvement. Advise patients that dry mouth is a frequent side-effect.

**FIRST CHOICE: UMECLIDINIUM**

UMECLIDINIUM (Incurs Ellipta®) dry powder inhaler 55 micrograms/inhalation

**Dose:** COPD, by *inhalation of powder*, 1 inhalation once daily.

TIOTROPIUM inhalation powder capsules (Spiriva®) (for use with HandiHaler® device) 18 micrograms, capsule pack with HandiHaler® device, capsule refill; solution for inhalation cartridge (Spiriva® Respimat®) 2·5 micrograms/metered inhalation

**Dose:** COPD, by *inhalation of powder*, 18 micrograms (1 capsule) once daily; by *inhalation of aerosol* (Spiriva® Respimat®), 5 micrograms (2 puffs) once daily.

ACLIDINIUM dry powder inhaler (Eklira Genuair®) 322 micrograms/inhalation

**Dose:** COPD, by *inhalation of powder*, 1 inhalation twice daily.

Long-acting antimuscarinic bronchodilator (LAMA) in asthma

Tiotropium solution for inhalation (Spiriva® Respimat®) has been accepted by SMC as add-on maintenance bronchodilator treatment in adult patients with asthma at Step 4 who are currently treated with the maintenance combination of inhaled corticosteroids (800 micrograms or more of budesonide per day or equivalent) and long-acting beta\(_2\) agonists and who experienced one or more severe exacerbations in the previous year.

**Dose:** Asthma at Step 4, *by inhalation*, 5 micrograms (2 puffs) once daily.

Theophylline

**Note: Theophylline**

- Keep patients on the same brand of modified-release theophylline as there are differences in bioavailability between brands; the same dose of different brands may not be therapeutically equivalent.
- Theophylline has a narrow therapeutic range therefore therapeutic drug monitoring is advised when initiating therapy and thereafter as clinically indicated (eg dose changes, introduction of long-term interacting drug).
- Monitor plasma theophylline concentration at least 5 days after initiation or changing the oral dose or immediately after an intravenous aminophylline loading dose. Sample 4 to 6 hours after an oral dose (not critical). See advice on therapeutic monitoring in Appendix 1.
- Theophylline can cause arrhythmias; check plasma concentration in the event of any new cardiac symptoms.
- Important interactions exist with other drugs; some may produce theophylline toxicity (eg erythromycin, ciprofloxacin), others may decrease plasma levels (eg antiepileptics, rifampicin). Refer to BNF for further information.

Oral theophyllines are weak bronchodilators with a high incidence of side-effects and are now less commonly used. Uniphyllin Continus® is the recommended preparation and should be used for all patients who are being commenced on theophylline for the first time. For advice on therapeutic monitoring of theophylline/aminophylline, refer to Appendix 1.
**FIRST CHOICE: UNIPHYLLIN CONTINUS®**

**UNIPHYLLIN CONTINUS®** (theophylline) m/r tablets 200mg, 300mg, 400mg  
**Dose:** 200mg every 12 hours, increased according to response and therapeutic drug levels.

**SLO-PHYLLIN®** (theophylline) m/r capsules 60mg, 125mg, 250mg  
**Dose:** 250 to 500mg every 12 hours. For use in patients with difficulties in swallowing. Capsules can be opened and taken with soft food.

**AMINOPHYLLINE** injection 250mg/10mL (hospital use only, after consultation with senior medical staff)  
**Dose:** In hospital only, by slow intravenous infusion, deteriorating acute severe asthma **NOT** previously treated with theophylline, over at least 20 minutes (with close monitoring), 250mg to 500mg (5mg/kg) then as for severe acute asthma. **Severe acute asthma, by intravenous infusion** (with close monitoring), 500 micrograms/kg/hour, adjusted according to plasma theophylline concentration. If the patient's body weight is 20% or more over ideal body weight (IBW*) then use IBW to calculate the dose. Patients taking oral theophylline should not normally receive intravenous aminophylline unless plasma theophylline concentration is available to guide dosage.  
*IBW (male) = 50kg plus 0·9kg for every cm above 150cm, IBW (female) = 45·5kg plus 0·9kg for every cm above 150cm.

**Compound bronchodilator preparations in COPD (LAMA/LABA)**

Consider combination umeclidinium with vilanterol (Anoro Ellipta®) as first choice in patients with moderate to very severe COPD who are breathless but not prone to exacerbations or not suitable/unwilling to take inhaled corticosteroid. The Spiolto Respimat® and the Duaklir Genuair® offer alternative devices.

**FIRST CHOICE: UMECLIDINIUM WITH VILANTEROL**

**UMECLIDINIUM WITH VILANTEROL** (Anoro Ellipta®) (umeclidinium 55 micrograms and vilanterol 22 micrograms per dose) dry powder inhaler  
**Dose:** COPD, by inhalation of powder, 1 puff once daily.

**TIOTROPIUM WITH OLODATEROL** (Spiolto Respimat®) (tiotropium 2·5 micrograms and olodaterol 2·5 micrograms per dose) solution for inhalation cartridge  
**Dose:** COPD, by inhalation of aerosol, 2 puffs once daily.

**ACLIDINIUM WITH FORMOTEROL** (Duaklir Genuair®) (aclidinium 340 micrograms and formoterol 12 micrograms per dose) inhalation powder  
**Dose:** COPD, by inhalation of powder, 1 puff twice daily.

**Acute asthma (severe/life-threatening)**

Refer to SIGN asthma guidance. Patients with severe asthma may be helped by magnesium sulfate (section 9.5), [off-label]. After consultation with senior medical staff, magnesium sulfate 1·2 to 2 grams may be given by intravenous infusion over 20 minutes.

**Peak flow meters and drug delivery devices**

**Peak flow meters** (standard and low range) are available on prescription in the community and in hospital via PECOS.

**Spacer devices** improve lung deposition and reduce oropharyngeal deposition of drugs delivered via a metered-dose inhaler; lung deposition data is superior for the Volumatic® as compared to the AeroChamber® Plus. A spacer device is recommended for all patients inhaling high-dose steroids.
(greater than beclometasone 800 micrograms per day or equivalent) via a pressurised, metered-dose inhaler and when inhaler technique is sub-optimal:
- if the Volumatic® device is available for a particular product (see below), consider it first choice
- where a number of different inhalers are prescribed for the same patient they should be compatible if possible with the selected spacer device.

Advise patients to clean devices no more often than once a month and replace every 6 to 12 months. After cleaning spacers should be air-dried, not dried with a towel.

FIRST CHOICE: VOLUMATIC® (in adults)

VOLUMATIC®
For use only with Clenil Modulite®, Flixotide®, Serevent® and Ventolin® pressurised, metered-dose inhalers. Paediatric mask available.

AEROCHAMBER® PLUS standard, child, infant
For use with all pressurised, metered-dose inhalers. Masks are available with all sizes.

The Haleraid®-120, -200 device is placed over Flixotide®, Serevent® and Ventolin® pressurised, metered-dose inhalers to aid when strength in hands is impaired. It is not available in the community.

The In-Check DIAL® is a useful guide for inhaler use checking as part of inhaler assessment.

3.2 INHALED CORTICOSTEROIDS (ICS)

A spacer device is recommended for all patients using high-dose inhaled steroids via a metered-dose inhaler, see section 3.1. Drug choice should be determined partly by the patient’s ability to use the device and by patient acceptability.

Bone mineral density may be reduced following long-term high-dose inhaled steroids; assess the patient holistically and if other risk factors are present, refer for a DXA scan.

If compliance is good, most patients with asthma will have adequate control of their symptoms with doses less than 800 micrograms of inhaled beclometasone or budesonide or equivalent.

FIRST CHOICE: BUDESONIDE

BUDESONIDE dry powder for inhalation (Easyhaler® Budesonide, Pulmicort® Turbohaler®) 100 micrograms, 200 micrograms, 400 micrograms/metered inhalation; nebuliser suspension 500 micrograms/2mL, 1mg/2mL

Dose: By inhalation of powder, 200 micrograms to 1·6mg daily in 2 divided doses, in less severe cases 200 to 400 micrograms daily. Specify brand when prescribing to ensure correct device is dispensed.

Reserve budesonide nebuliser solution for the treatment of croup in children who are unable to swallow dexamethasone tablets; refer to Paediatric Handbook and BNF for Children.

MHRA advice: The 2 CFC-free beclometasone aerosol inhalers available at present (Clenil Modulite® and Qvar®) are not interchangeable; prescribe by brand name.

BECLOMETASONE aerosol inhalation (Clenil Modulite®) 50 micrograms, 100 micrograms, 200 micrograms, 250 micrograms/metered inhalation; aerosol inhalation (Qvar®) 50 micrograms, 100 micrograms/ metered inhalation; breath-actuated aerosol inhalation (Qvar Easi-Breathe®) 50 micrograms, 100 micrograms/metered inhalation
**Dose:** By aerosol inhalation, Clenil Modulite®, 200 micrograms twice daily, (in more severe cases initially 300 to 400 micrograms twice daily); may give up to 1mg twice daily as per SIGN guidance. Qvar®, 50 to 200 micrograms twice daily. For a patient with stable symptoms the equivalent dose of Qvar® is half that of Clenil Modulite® and other CFC-containing beclometasone inhalers, ie 100 micrograms aerosol inhalation of Qvar® is equivalent to 200 micrograms aerosol inhalation of Clenil Modulite® and other CFC-containing beclometasone inhalers.

**Note:** Increasing the dose of fluticasone propionate above 1mg/day is unlikely to confer extra clinical benefit and will increase the risk of systemic side-effects. Counsel patients on systemic side-effects, step down where appropriate and review regularly.

**FLUTICASONE PROPIONATE** aerosol inhalation 50 micrograms, 125 micrograms, 250 micrograms/metered inhalation; dry powder for inhalation (Flixtotide® Accuhaler®) disk containing blisters of fluticasone propionate 50 micrograms, 100 micrograms, 250 micrograms, 500 micrograms/blister

**Dose:** By aerosol inhalation or inhalation of powder, 100 to 250 micrograms twice daily, increased according to severity of asthma; doses above 500 micrograms twice daily initiated by a specialist.

**Compound preparations with corticosteroid and long acting beta_2 agonist (ICS/LABA)**

**Combination inhalers (ICS/LABA) in asthma**

<table>
<thead>
<tr>
<th>FIRST CHOICE:</th>
<th>SYMBICORT® TURBOHALER</th>
</tr>
</thead>
<tbody>
<tr>
<td>SECOND CHOICE:</td>
<td>FOSTAIR® NEXTHALER</td>
</tr>
<tr>
<td>THIRD CHOICE:</td>
<td>RELVAR® ELLIPTA®</td>
</tr>
</tbody>
</table>

- In asthma always use combination inhalers when an inhaled corticosteroid and long-acting beta_2 agonist (LABA) are indicated; there is no difference in efficacy in giving inhaled steroid and LABA in combination or in separate devices but there are risks associated with patients receiving a LABA on its own.
- Use Symbicort® Turbohaler® first-line. Alternative, easy to use, cost-effective options are Fostair® NEXThaler and Relvar® Ellipta®. If an MDI is preferred, consider Flutiform® or Fostair®.
- Doubling the dose in an exacerbation is of unproven value and is no longer recommended.
- Maintain patients at the lowest possible dose of steroid; stepping down therapy once asthma is controlled is recommended; reduction in the steroid dose should be slow as patients deteriorate at different rates; consider a dose reduction every 3 months, decreasing the dose by approximately 25 to 50% each time.
- In adult patients at step 3 of SIGN 153 whose symptoms are poorly controlled, the use of budesonide/formoterol in a single inhaler as rescue medication instead of a short-acting beta_2 agonist, in addition to its regular use as a controller treatment, has been shown to be an effective treatment option. Fostair® is also licensed for maintenance and reliever therapy. This management technique has not been investigated with other combination inhalers. Careful patient education is required before instituting this management.

**BUDESONIDE WITH FORMOTEROL** dry powder for inhalation (Symbicort® Turbohaler®) 100/6, 200/6, 400/12 (in micrograms)

**Dose:** Asthma, by inhalation of powder, 100/6 and 200/6 inhaler, 1 to 2 puffs twice daily, reduced in well-controlled asthma to once daily; 400/12 inhaler, 1 puff twice daily reduced to 1 puff once daily if control maintained.

**BECLOMETASONE WITH FORMOTEROL** dry powder inhaler (Fostair® NEXThaler) 100/6 (in micrograms); aerosol inhalation (Fostair®) 100/6 (in micrograms)
Dose: Asthma, by dry powder inhalation (Fostair® NEXThaler), 1 to 2 puffs twice daily, maximum 4 puffs daily; by aerosol inhalation (Fostair®), 1 to 2 puffs twice daily; maximum 4 puffs daily.

FLUTICASONE WITH VILANTEROL dry powder inhaler (Relvar Ellipta®) 92/22, 184/22 (in micrograms)
Dose: Asthma, by inhalation of powder, 92/22, 184/22 inhaler, 1 puff once daily.

FLUTICASONE WITH FORMOTEROL aerosol inhalation (Flutiform®) 50/5, 125/5, 250/10 (in micrograms)
Dose: Asthma, by aerosol inhalation, 2 puffs twice daily. Titrate to the lowest dose at which effective control of symptoms is maintained. The 50/5 and 125/5 inhalers are licensed for use in adults and adolescents aged 12 years and above, the 250/10 inhaler is licensed for adults only.

FLUTICASONE WITH SALMETEROL dry powder for inhalation (Seretide® Accuhaler®) disk containing blisters of 100/50, 250/50, 500/50 (in micrograms)/blister
Dose: Asthma, by inhalation of powder, 1 blister twice daily.

Steroid potency of combination inhalers in asthma: equivalent beclometasone dose per day

<table>
<thead>
<tr>
<th>Equivalent beclometasone dose per day (micrograms)</th>
<th>Combination inhaler (in micrograms)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greater than 1000 micrograms</td>
<td>Relvar Ellipta 184/22 (1 inhalation daily)</td>
</tr>
<tr>
<td></td>
<td>Seretide Accuhaler 500/50 (2 inhalations daily)</td>
</tr>
<tr>
<td></td>
<td>Flutiform inhaler 250/10 (4 inhalations daily)</td>
</tr>
<tr>
<td></td>
<td>Symbicort Turbohaler 400/12 (4 inhalations daily)</td>
</tr>
<tr>
<td>1000 micrograms or less</td>
<td>Flutiform inhaler 125/5 (4 inhalations daily)</td>
</tr>
<tr>
<td></td>
<td>Fostair NEXThaler 100/6 (4 inhalations daily)</td>
</tr>
<tr>
<td></td>
<td>Fostair inhaler 100/6 (4 inhalations daily)</td>
</tr>
<tr>
<td></td>
<td>Relvar Ellipta 92/22 (1 inhalation daily)</td>
</tr>
<tr>
<td></td>
<td>Seretide Accuhaler 250/50 (2 inhalations daily)</td>
</tr>
<tr>
<td>800 micrograms or less</td>
<td>Fostair NEXThaler 100/6 (2 inhalations daily)</td>
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<td></td>
<td>Fostair inhaler 100/6 (2 inhalations daily)</td>
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<td></td>
<td>Symbicort Turbohaler 200/6 (4 inhalations daily)</td>
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<tr>
<td></td>
<td>Symbicort Turbohaler 400/12 (2 inhalations daily)</td>
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<tr>
<td>400 micrograms or less</td>
<td>Symbicort Turbohaler 100/6 (1 inhalation daily)</td>
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<tr>
<td></td>
<td>Symbicort Turbohaler 100/6 (4 inhalations daily)</td>
</tr>
</tbody>
</table>

*Consider giving a ‘steroid card’ to patients using greater than maximum licensed doses of inhaled corticosteroids.

Combination inhalers in COPD (ICS/LABA)

**Note:** Review the need for inhaled steroids in patients with COPD if an episode of pneumonia has occurred. High doses of inhaled corticosteroid have been associated with lower respiratory tract infections, including pneumonia, in older patients with COPD.

- Inhaled corticosteroids, in combination with a long-acting bronchodilator, should be prescribed for patients with an FEV₁ of 50% or less of predicted, who are having 2 or more exacerbations requiring treatment with antibiotics or oral corticosteroid in a 12-month period. Refer to NICE guidance on the management of COPD in adults in primary and secondary care.
Fluticasone with vilanterol (Relvar® Ellipta® 92/22) is cost-effective and offers the advantage of once-daily dosing.

In patients with moderate to very severe COPD who are unsuitable for inhaled corticosteroid and in those who remain breathless or have exacerbations despite taking long-acting beta agonist plus inhaled corticosteroid consider combination bronchodilator inhaler (LAMA/LABA).

**FIRST CHOICE: FLUTICASONE WITH VILANTEROL**

**FLUTICASONE WITH VILANTEROL** dry powder inhaler (Relvar Ellipta®) 92/22 (in micrograms)

**Dose:** COPD, by inhalation of powder, 92/22 inhaler, 1 puff once daily.

**BECLOMETASONE WITH FORMOTEROL** dry powder inhaler (Fostair® NEXThaler) 100/6 (in micrograms); aerosol inhalation (Fostair®) 100/6 (in micrograms)

**Dose:** COPD, by inhalation of powder (Fostair® NEXThaler), 2 puffs twice daily; by aerosol inhalation (Fostair®), 2 puffs twice daily.

**FLUTICASONE WITH SALMETEROL** dry powder for inhalation (Seretide® Accuhaler®) disk containing blisters of 500/50 (in micrograms)/blister

**Dose:** COPD, by inhalation of powder 500/50/blister, 1 blister twice daily.

**Other corticosteroids**

**Acute attack of asthma:** treat with short course of 40 to 50mg oral prednisolone* (section 6.3) daily for at least 5 days; longer courses may be required for more severe or recurrent cases.

**Acute exacerbation of COPD:** consider oral prednisolone* 30mg daily for 7 to 14 days in all patients who are admitted to hospital and in those in the community with a significant increase in breathlessness which interferes with daily activities; there is no advantage in treating for longer than 14 days.

**Dose tapering:** usually doses of up to 40mg daily taken for less than 3 weeks do not need to be tapered and can be stopped abruptly provided the patient is receiving inhaled steroids, however in certain cases they should be tapered; see BNF for more information.

**Bone protection:** for advice on the need for Bone protection refer to osteoporosis guidance on the Rheumatology webpage on NHS Highland Intranet.

*If possible, avoid use of the high-cost prednisolone tablets 25mg and soluble tablets 5mg.

### 3.3 LEUKOTRIENE RECEPTOR ANTAGONISTS

Leukotriene receptor antagonists are non-steroidal anti-inflammatory agents that can be used as add-on therapy in persistent asthma or in exercise-induced asthma. The efficacy is variable therefore review patients after a 4 to 8 week period of therapy. Do not start during pregnancy. Advise patients that montelukast is most effective if taken in the evening.

**MONTELUKAST** chewable tablets 4mg, 5mg; tablets 10mg; sugar-free granules 4mg

**Dose:** Prophylaxis of asthma, child 6 months-6 years 4mg daily in the evening, 6-15 years 5mg daily in the evening, adult and child over 15 years, 10mg daily in the evening.
3.4 ANTIHISTAMINES AND ALLERGIC EMERGENCIES

Non-sedating antihistamines

Non-sedating antihistamines are useful in urticaria and angioedema, refer to ‘Management of chronic urticaria and angioedema’.

**FIRST CHOICE: CETIRIZINE**

**CETIRIZINE**<sup>O</sup> tablets 10mg; oral solution 5mg/5mL
Dose: Adults, 10mg daily. Children, refer to BNF for Children.

**LORATADINE**<sup>O</sup> tablets 10mg
Dose: Adults, 10mg once daily. Children, refer to BNF for Children.

Sedating antihistamines

**FIRST CHOICE: HYDROXYZINE**

Hydroxyzine is useful in pruritus; refer to ‘Management of pruritus’.

**MHRA:** Hydroxyzine should not be prescribed to people with a prolonged QT interval or risk factors for QT interval prolongation ([www.gov.uk](http://www.gov.uk)).

**HYDROXYZINE** tablets 10mg, 25mg; syrup 10mg/5mL
Dose: Pruritus, initially 25mg at night, increased if necessary to 25mg 3 to 4 times daily.

**CHLORPHENAMINE** tablets<sup>O</sup> 4mg; oral solution<sup>O</sup> 2mg/5mL; injection 10mg/1mL
Dose: Adults, by mouth, 4mg every 4 to 6 hours, maximum 24mg daily; by subcutaneous or intramuscular injection or by intravenous injection over 1 minute, 10mg; max 40mg in 24 hours. Children, refer to BNF for Children.

**PROMETHAZINE** tablets 10mg, 25mg; elixir 5mg/5mL
For sedation or pre-medication.

Omalizumab

**OMALIZUMAB** solution for injection prefilled syringe 75mg/0.5mL, 150mg/1mL
Dose: By subcutaneous injection, adults and children over 6 years, according to immunoglobulin E concentration and body-weight, refer to SPC.

Allergic emergencies

**ADRENALINE/EPINEPHRINE** injection 1 in 1000, ampoule 500 micrograms/0.5mL, 1mg/1mL; disposable syringe 1mg/1mL (Minijet®)

**ADRENALINE/EPINEPHRINE** injection 1 in 10 000 DILUTE; 1mg/10mL ampoules

For guidance on management of anaphylaxis in adults see [www.resus.org.uk](http://www.resus.org.uk).
Self-administration of adrenaline (epinephrine)

**Note:**
- Injection technique for the self-administration of adrenaline is device-specific.
- EpiPen® is the recommended device in NHS Highland; training on anaphylaxis recognition and use of the EpiPen® is essential; prescribe all new patients 2 EpiPens® on diagnosis; add note onto Key Information Summary.
- Advise all sufferers of anaphylaxis of the benefits of wearing some device such as a bracelet (available from allergy charities) to inform bystanders at the time of any future attack.
- MHRA advice for healthcare professionals and for patients on adrenaline auto-injectors is available at [www.gov.uk](http://www.gov.uk).

**ADRENALINE/EPINEPHRINE** (EpiPen® Auto-injector 0·3mg) intramuscular injection
- 300 micrograms

**ADRENALINE/EPINEPHRINE** (EpiPen® Junior Auto-injector 0·15mg) intramuscular injection
- 150 micrograms

**Other respiratory emergencies**

S **ALTEPLASE** injection 10mg (5·8 million units/vial), 50mg (29 million units/vial)

**Dose:** *By intravenous injection*, for the treatment of pulmonary embolism following specialist advice, 10mg over 1 to 2 minutes, followed by intravenous infusion of 90mg over 2 hours; max 1·5mg/kg in patients less than 65kg. *By intrapleural injection*, for the treatment of empyema [off-label] 10mg every 12 hours for three days (followed by 5mg intrapleural dornase alfa (section 3.7) [off-label] one hour after each alteplase injection and subsequent free drainage); refer to guidance in respiratory handbook on Ward 7a, Raigmore Hospital. For use in the management of hyper-acute stroke refer to section 2.10.

3.5 **RESPIRATORY STIMULANTS AND PULMONARY SURFACTANTS**

S **DOXAPRAM** injection 100mg/5mL; infusion 1 gram/500mL

S **PORACTANT ALFA** suspension 120mg/1·5mL, 240mg/3mL

For use in the Specialist Care Baby Unit only.

3.6 **OXYGEN**

In the community an oxygen prescription falls into 2 categories:
1. Long-term oxygen therapy (LTOT) for patients with defined chronic respiratory failure.
2. Ambulatory oxygen therapy.

**General considerations**

Oxygen is a medicine and has to be prescribed. Inappropriate concentrations may have serious or even lethal effects. Advise patients and their families of the risks of burns and fire with oxygen. Oxygen can be delivered either nasally or by mask.

**Long-term domiciliary oxygen therapy (LTOT)**

Home oxygen services, previously delivered from local community pharmacies, have been transferred over to a nationally coordinated service provided by Dolby Vivisol.
Only specific consultants (eg Respiratory, Palliative Care, Cardiology) will be authorised to prescribe home oxygen, any new patient believed to require home oxygen must be referred to the appropriate consultant for their assessment and the production of a Scottish Home Oxygen Order Form (SHOOF) for transmission to the provider Dolby Vivisol.

The National Advisory Group for Respiratory Managed Clinical Networks ‘Domiciliary oxygen service - national guidance/best practice’ (http://guidelines.nhshighland.scot.nhs.uk) emphasises that:

- oxygen therapy is only indicated for patients with persistent hypoxaemia at rest
- oxygen has no effect on breathlessness
- palliative patients alone may get some symptomatic relief.

Patients who meet the criteria should be referred via the SCI Store to the local Respiratory Team. See also LTOT shared clinical guideline on Intranet.

Ambulatory oxygen for intermittent symptom control

The respiratory teams at Raigmore Hospital and Lorn and Islands District General Hospital are available to formally assess patients for ambulatory oxygen therapy as specified in HDL (2004) 01.

Oxygen use in palliative care

Refer to national palliative care guideline on palliation of breathlessness available at: www.palliativecareguidelines.scot.nhs.uk or seek specialist advice.

Emergency oxygen use

Guidelines for emergency oxygen use in adult patients are available at www.brit-thoracic.org.uk.

3.7 MUCOLYTICS

Consider carbocisteine in patients with COPD and chronic cough productive of sputum. Continue if there is symptomatic improvement. If there is no benefit after a 4-week trial, stop therapy. Nebulised sodium chloride 0·9% solution has no place as a mucolytic in either COPD or asthma.

CARBOCISTEINE capsules 375mg, oral liquid 250mg/5mL
Dose: 750mg 3 times daily initially, then 375mg 4 times daily as condition improves.

DORNASE ALFA nebuliser solution 2·5mg (2500 units)/2·5mL
For use in patients with cystic fibrosis. Also used with alteplase in the management of empyema [off-label]; see section 3.4.

3.9 COUGH PREPARATIONS

Note:
- There is little evidence to support the use of cough suppressants.
- For persistent cough lasting 4 to 6 weeks establish the underlying cause.
- For the treatment of cough in palliative care, seek specialist advice.
- Many cough preparations contain opiates; their use is discouraged because they are a respiratory depressant and can be particularly dangerous in COPD. The same applies to analgesics containing codeine and other opiates.
- Demulcent cough preparations, such as simple linctus, should not be prescribed.
3.11 ANTIFIBROTICS

Pirfenidone and nintedanib are only available in hospital on the prescription of a respiratory specialist.

**SPIRFENIDONE** capsules 267mg
*Dose*: Idiopathic pulmonary fibrosis, initially 1 capsule 3 times daily for 7 days, then 2 capsules 3 times daily for 7 days, then 3 capsules 3 times daily. If treatment is interrupted for 14 consecutive days or more, the initial 2-week titration regimen should be repeated; if treatment is interrupted for less than 14 consecutive days, the dose can be resumed at the previous daily dose without titration.

**SNINTEDANIB** (Ofev®) capsules 100mg, 150mg
*Dose*: Idiopathic pulmonary fibrosis, 150mg twice daily 12 hours apart. The 100mg twice daily dose is only recommended to be used in patients who do not tolerate the 150mg twice daily dose. Dose reduction or interruption to manage adverse events is detailed in the SPC. The capsules should be taken with food, swallowed whole with water, and should not be chewed or crushed.
## GUIDE TO INHALER DEVICES
(see full listing in sections 3.1 and 3.2)

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<th>ACTIVE DRUG(S)</th>
<th>INHALATION DEVICE</th>
<th>DEVICE NAME FOR PRESCRIBING</th>
<th>DOSE PER INHALATION</th>
<th>DOSES PER PACK</th>
<th>SPACER DEVICE</th>
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<tr>
<td>Salbutamol</td>
<td>aerosol</td>
<td>inhaler</td>
<td>100 micrograms</td>
<td>200 doses</td>
<td>See brand</td>
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<td>Salamol Easi-Breathe®</td>
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<td>dry powder</td>
<td>Ventolin® Accuhaler®</td>
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<td>dry powder</td>
<td>Bricanyl® Turbohaler®</td>
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<td>Formoterol</td>
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<td>Oxis® Turbohaler®</td>
<td>6, 12 micrograms</td>
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<td>Salmeterol</td>
<td>aerosol</td>
<td>Serevent® Evohaler®</td>
<td>25 micrograms</td>
<td>120 doses</td>
<td>Volumatic®</td>
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<tr>
<td></td>
<td>dry powder</td>
<td>Serevent® Accuhaler®</td>
<td>50 micrograms</td>
<td>60 doses</td>
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<tr>
<td>Umeclidinium</td>
<td>dry powder inhalation</td>
<td>Incruse Ellipta®</td>
<td>55 micrograms</td>
<td>30 doses</td>
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<tr>
<td>Tiotropium</td>
<td>dry powder inhalation</td>
<td>Spiriva® inhalation capsules (+/- HandiHaler® device)</td>
<td>18 micrograms</td>
<td>30 caps</td>
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<td></td>
<td>solution for inhalation</td>
<td>Spiriva® Respimat®</td>
<td>2.5 micrograms</td>
<td>60 doses</td>
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<tr>
<td>Aclidinium</td>
<td>dry powder inhalation</td>
<td>Eklira Genuair®</td>
<td>322 micrograms</td>
<td>60 doses</td>
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<tr>
<td><strong>COMPOUND BRONCHODILATORS (LAMA/LABA)</strong></td>
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<tr>
<td>Umeclidinium with vilanterol</td>
<td>dry powder</td>
<td>Anoro Ellipta®</td>
<td>55/22 micrograms</td>
<td>30 doses</td>
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<tr>
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<td>dry powder</td>
<td>Spiolto Respimat®</td>
<td>2.5/2.5 micrograms</td>
<td>60 doses</td>
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<tr>
<td>Aclidinium with formoterol</td>
<td>dry powder</td>
<td>Duaklir Genuair®</td>
<td>340/12 micrograms</td>
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<td><strong>CORTICOSTEROIDS (ICS)</strong></td>
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<td>Budesonide</td>
<td>dry powder inhalation</td>
<td>Pulmicort® Turbohaler®</td>
<td>100, 200, 400 micrograms</td>
<td>200, 100, 50 doses</td>
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<td>dry powder inhalation</td>
<td>Easyhaler® Budesonide</td>
<td>100, 200, 400 micrograms</td>
<td>200, 200, 100 doses</td>
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<td>Beclometasone</td>
<td>aerosol</td>
<td>prescribe as Clenil Modulite® inhaler*</td>
<td>50, 100, 200, 250 micrograms</td>
<td>200 doses</td>
<td>Volumatic®</td>
</tr>
<tr>
<td></td>
<td>aerosol</td>
<td>prescribe as Qvar® inhaler*</td>
<td>50, 100 micrograms</td>
<td>200 doses</td>
<td>Aerochamber Plus®</td>
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<tr>
<td></td>
<td>breath-actuated aerosol</td>
<td>prescribe as Qvar Easi-Breathe® inhaler*</td>
<td>50, 100 micrograms</td>
<td>200 doses</td>
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<tr>
<td>Fluticasone propionate</td>
<td>aerosol</td>
<td>Flixotide® Evohaler®</td>
<td>50, 125, 250 micrograms</td>
<td>120 doses</td>
<td>Volumatic®</td>
</tr>
<tr>
<td></td>
<td>dry powder</td>
<td>Flixotide® Accuhaler®</td>
<td>50, 100, 250, 500 micrograms</td>
<td>60 doses</td>
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</tbody>
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*Note Clenil Modulite® and Qvar® doses are not interchangeable.
<table>
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<tr>
<th>COMPOUND PREPARATIONS WITH CORTICOSTEROID (ICS/LABA)</th>
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<tr>
<td><strong>Budesonide/formoterol</strong></td>
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<tr>
<td><strong>Beclometasone/formoterol</strong></td>
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<td></td>
<td>aerosol</td>
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<tr>
<td><strong>Fluticasone propionate/formoterol</strong></td>
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<td><strong>Fluticasone furoate/vilanterol</strong></td>
<td>dry powder</td>
</tr>
<tr>
<td><strong>Fluticasone propionate/salmeterol</strong></td>
<td>dry powder</td>
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</tbody>
</table>
CHAPTER 4  CENTRAL NERVOUS SYSTEM

Information on mental health conditions, treatments and medicines is available at: http://www.choiceandmedication.org/nhs24/. For further information on medicines listed in sections 4.1, 4.2, 4.3 and 4.11 contact Pharmacy Department, New Craigs, tel: 01463 704000 (Raigmore Hospital switchboard) or, for Argyll and Bute, contact Pharmacy Department, Mid Argyll Community Hospital, tel: 01546 462000.

User-friendly patient advice leaflets on a range of topics including ‘Weight gain and medicines used for mental health’ are available on the Mental Health and Learning Disabilities webpage on the Intranet or from Pharmacy Department, New Craigs. For advice on psychotropic prescribing in pregnancy and breast-feeding refer to SIGN 127 ‘Management of perinatal mood disorders’.

4.1 HYPNOTICS AND ANXIOLYTICS

Hypnotics

If, after consideration of the use of non-pharmacological measures, hypnotics are considered necessary, limit their use to short periods of time only (1 to 4 weeks). Establish cause of insomnia. Be aware of drug and alcohol use and educate on realistic sleep patterns. Patient information leaflets are available from www.rcpsych.ac.uk and www.moodjuice.scot.nhs.uk. In most cases, hospital patients should only be discharged home with a supply of hypnotics if they were admitted on them and there is good reason to continue. This is particularly important for older patients. The use of hypnotics with a long half-life such as nitrazepam (non-Formulary) is not recommended as they often result in a hangover effect and may lead to accumulation, particularly in older people. Sedative antihistamines are not recommended.

Long-term hypnotic use is associated with falls, road traffic accidents and hip fractures. For advice on managing long-term hypnotic use refer to ‘Prescribing of Hypnotics’ GMS prescribing protocol on Intranet and to BNF.

Be aware or gain reassurance that the person being prescribed benzodiazepines is not diverting or purchasing/acquiring medicines privately.

NICE guidance April 2004 (www.nice.org.uk) recommends that switching from one hypnotic to another should only occur if a patient experiences adverse effects thought to be directly related to a specific agent. Patients who have not responded to one hypnotic should not be prescribed any of the others.

For information on the use of melatonin in children and adolescents see shared care protocol and ‘Unlicensed medicines list’ on Intranet.

FIRST CHOICE: ZOLPIDEM

ZOLPIDEM tablets 5mg, 10mg
Dose: 10mg at bedtime. Older or debilitated patients 5mg at bedtime.

ZOPICLONE tablets 3.75mg, 7.5mg
Dose: 7.5mg at bedtime. Older or debilitated patients initially 3.75mg at bedtime increased if necessary.

TEMAZEPAM CD tablets 10mg; oral solution 10mg/5mL
Dose: 10 to 20mg at bedtime, exceptional circumstances 30 to 40mg. Older or debilitated patients 10mg at bedtime, exceptional circumstances 20mg.
Anxiolytics


Benzodiazepines

Limit the use of benzodiazepines as anxiolytics to the lowest possible dose for the shortest possible time.

Diazepam has a long half-life (24 to 48 hours) and, in addition to its short-term use in severe anxiety, is suitable for withdrawal regimens:

- for further guidance on dose conversions to diazepam refer to http://cks.nice.org.uk
- for advice on use in alcohol withdrawal (abstinence from alcohol must be assured) refer to BNF, NICE guidance January 2011 on anxiety (www.nice.org.uk) and to section 4.10.

Lorazepam is recommended for patients with evidence of grossly impaired liver function. See policies on emergency sedation in specialist psychiatric hospitals including a local policy for Argyll and Bute, District and Rural General Hospitals, and for use in the Community including use in Community Hospitals. For information refer to ‘Guidance for the use of psychotropics in older adults’.

**FIRST CHOICE: DIAZEPAM**

**DIAZEPAM** tablets 2mg, 5mg; oral solution 2mg/5mL

Dose: *By mouth*, anxiety, 2mg 3 times daily increased if necessary to 15 to 30mg daily in divided doses.

**LORAZEPAM** tablets 1mg; injection 4mg/1mL [licensed and unlicensed]

Dose: *By mouth*, 1 to 4mg daily in divided doses. Older or debilitated patients, half the adult dose. The tablets are used for the management of agitation associated with severe and enduring mental illness. Use of the injection is limited to acute panic attacks, emergency sedation (see links above) and status epilepticus (refer to section 4.8).

**CHLORDIAZEPOXIDE** capsules 5mg, 10mg

Restricted to attenuating alcohol withdrawal symptoms; refer to section 4.10.

**CLONAZEPAM** tablets 500 micrograms, 2mg

Indicated for specialist treatment of chronic anxiety and disturbed behaviour associated with severe and enduring mental illness [off-label].

**Other drugs used in the management of anxiety**

Propranolol may be used to reduce the autonomic symptoms of situational anxiety but is potentially harmful and is not recommended for long-term management. Other drugs for anxiety, in the longer term, are more appropriate first-line in most patients; refer to guidance.

**PROPRANOLOL** tablets 10mg, 40mg; m/r capsules 80mg

Dose: Initially 10mg 3 times daily, increased to 40mg 3 times daily if necessary. Monitor blood pressure as appropriate; refer to BNF.

Pregabalin has become a drug of misuse and caution is advised when prescribing. Be aware or gain reassurance that the person being prescribed pregabalin is not purchasing/acquiring medicines privately.
Pregabalin can be used third-line after specialist initiation only, in treatment-resistant generalised anxiety disorder but other options are recommended in preference; refer to anxiety guidance. Pregabalin is licensed for the treatment of generalised anxiety disorder however the manufacturer has not made a submission to SMC regarding pregabalin in this indication and it has consequently not received a recommendation for this use in NHS Scotland.

S PREGABALIN capsules 25mg, 50mg, 75mg, 100mg, 150mg, 200mg, 225mg, 300mg; oral solution 100mg/5mL

Dose: initially 75mg twice daily, increased if necessary, at 7-day intervals in steps of 75mg twice daily; maximum dose 300mg twice daily. Minimise the number of capsules to be taken by use of higher strength capsules as appropriate.

For patient information on the use of prazosin in post-traumatic stress disorder [off-label] refer to Intranet.

4.2 DRUGS USED IN PSYCHOSES AND RELATED DISORDERS

Antipsychotic drugs

All drugs (except clozapine) have similar antipsychotic efficacy, however the side-effect profile varies greatly; refer to ‘Antipsychotics – relative side-effects’. Select drugs on an individual basis and take into account the indication:

- psychosis/schizophrenia – consider oral atypical antipsychotics first-line (see below). Keep the patient on a typical antipsychotic if they are stable.
- short-term sedation – typicals can be used at a sufficiently low dose to avoid side-effects.
- mania/hypomania – patients may be particularly sensitive to developing tardive dyskinesia, so atypical antipsychotics are considered first-line in the longer term, usually as an adjunct to a mood stabiliser. Typical antipsychotics can be used short-term and typical depots are occasionally used in the longer term where compliance has been poor.
- bipolar depression – quetiapine is an effective treatment for bipolar depression and does not appear to be associated with a switch to mania.
- dementia – antipsychotic medication should be reserved for severe non-cognitive symptoms or behaviour that challenges, where other approaches have failed or would be inappropriate. Refer to ‘Guidelines for the use of psychotropics in older adults’.

Introduce clozapine if schizophrenia is inadequately controlled despite the sequential use of 2 or more antipsychotics (one of which should be an atypical antipsychotic) each for at least 4 to 6 weeks.

Note:

- There is a clear increased risk of stroke and a small increased risk of death when antipsychotics (typical or atypical) are used in older people with dementia (www.gov.uk/drug-safety-update 2012).
- Antipsychotics may also have adverse effects on cognition.

Atypical (second generation) antipsychotics

Atypical antipsychotics may be better tolerated than typical antipsychotics and cause fewer extrapyramidal side-effects. Advise patients on possible weight gain; refer to ‘Weight gain and medicines used in mental health’ patient information leaflet on Intranet or request a copy from Pharmacy Department, New Craigs, tel: 01463 704000 (Raigmore Hospital switchboard).
Note: Only use orodispersible tablets where there is swallowing difficulty or where consumption can be supervised. Place the orodispersible tablet in the mouth, where it will rapidly disperse with saliva and can be easily swallowed. Removal of intact orodispersible tablets from the mouth is difficult. As the orodispersible tablet is fragile administer immediately on opening the blister. Alternatively, disperse in a full glass of water or other suitable beverage (orange juice, apple juice, milk or coffee) immediately before administration.

AMISULPRIDE tablets 50mg, 100mg, 200mg, 400mg; oral solution 100mg/1mL
Dose: Acute psychotic episode, 400 to 800mg daily in 2 divided doses, adjusted according to response; maximum 1200mg daily. Predominantly negative symptoms, 50 to 300mg daily.

ARIPIPRAZOLE tablets 5mg, 10mg, 15mg, 30mg; orodispersible tablets 10mg, 15mg (see administration advice in note box); oral solution 5mg/5mL; solution for injection vials 7.5mg/1mL
Dose: Tablets and oral solution, for schizophrenia, 10 to 15mg once daily, usual maintenance 15mg once daily, maximum 30mg once daily, for mania, 15mg once daily, increased if necessary, maximum 30mg once daily. By intramuscular injection, for rapid control of agitation and disturbed behaviours in patients with schizophrenia when oral therapy is not appropriate, initially 5-25 to 15mg for 1 dose, alternatively usual dose 9-75mg for 1 dose, followed by 5-25 to 15mg after 2 hours if required, maximum 3 injections daily, maximum daily combined oral and parenteral dose 30mg.

Note: Olanzapine: when one or more factors are present that might result in slower metabolism of olanzapine (eg female, older person, non-smoker) consider lower initial dose and more gradual dose increase.

OLANZAPINE tablets 2.5mg, 5mg, 7.5mg, 10mg, 15mg, 20mg; orodispersible tablets 5mg, 10mg, 15mg, 20mg (see administration advice in note box)
Dose: Schizophrenia, combination therapy for mania, preventing recurrence in bipolar disorder, 10mg daily adjusted to usual range of 5 to 20mg daily; doses greater than 10mg daily only after reassessment; maximum 20mg daily. Monotherapy for mania, 15mg daily adjusted to usual range of 5 to 20mg daily; doses greater than 15mg only after reassessment; maximum 20mg daily.

Note: Quetiapine: where possible use the immediate-release tablets. Only use the higher cost modified-release (m/r) tablets where there is a particular clinical advantage.

QUETIAPINE tablets 25mg, 100mg, 150mg, 200mg, 300mg; m/r tablets 50mg, 150mg, 200mg, 300mg, 400mg
Dose: Schizophrenia, 25mg twice daily on day 1, 50mg twice daily on day 2, 100mg twice daily on day 3, 150mg twice daily on day 4, then adjusted according to response, usual range 300 to 450mg daily in 2 divided doses; maximum 750mg daily. Older people, initially 25mg daily as a single dose, increased in steps of 25 to 50mg daily in 2 divided doses. Mania, 50mg twice daily on day 1, 100mg twice daily on day 2, 150mg twice daily on day 3, 200mg twice daily on day 4, then adjusted according to response in steps of up to 200mg daily to maximum 800mg daily; usual range 400 to 800mg daily in 2 divided doses. Older people, initially 25mg daily as a single dose, increased in steps of 25 to 50mg daily in 2 divided doses. Treatment of depression in bipolar disorder, 50mg daily on day 1, 100mg daily on day 2, 200mg daily on day 3, 300mg daily on day 4, then adjusted according to response, usual dose 300mg daily, maximum 600mg daily; licensed for once daily administration for this indication however local experience suggests a lesser risk of hypotension with a twice daily split dose, or use of the m/r tablets. Prevention of mania and depression in bipolar disorder, continue at the dose effective for treatment of bipolar disorder and adjust to lowest effective dose, usual range 300 to 800mg daily in 2 divided doses.

RISPERIDONE tablets 500 micrograms, 1mg, 2mg, 3mg, 4mg, 6mg; orodispersible tablets 500 micrograms, 1mg, 2mg, 3mg, 4mg (see administration advice in note box); liquid 1mg/1mL
Dose: Psychoses, 2mg in 1 to 2 divided doses on first day then 4mg in 1 to 2 divided doses on second day (slower titration appropriate in some patients); usual dose range 4 to 6mg daily; doses
above 10mg daily only if benefit considered to outweigh risk (maximum 16mg daily). Older people, or in hepatic or renal impairment, initially 500 micrograms twice daily increased in steps of 500 micrograms twice daily to 1 to 2mg twice daily. Mania, initially 2mg once daily, increased if necessary in steps of 1mg daily; usual dose range 1 to 6mg daily. Older people, initially 500 micrograms twice daily increased in steps of 500 micrograms twice daily to 1 to 2mg twice daily.

**Note:** Clozapine has been associated with varying degrees of intestinal obstruction, faecal impaction and paralytic ileus. On rare occasions these cases have been fatal. Clozapine should be used cautiously with drugs which cause constipation (eg antimuscarinic drugs) or in history of colonic disease or bowel surgery. Monitor for constipation and prescribe laxative if required.

**CLOZAPINE** tablets 25mg, 100mg; oral suspension 50mg/1mL
Clozapine is indicated for treatment-resistant schizophrenia (including psychosis in Parkinson’s disease) in patients unresponsive to, or intolerant of, conventional antipsychotic drugs. It can cause agranulocytosis. Clozapine is initiated by secondary care and restricted to patients registered with a Clozapine Patient Monitoring Service. For further information contact Pharmacy Department, New Craigs, tel: 01463 704000 (Raigmore Hospital switchboard) or, for Argyll and Bute, contact Pharmacy Department, Mid Argyll Community Hospital, tel: 01546 602323.

**Typical (first generation) antipsychotics**

As a group these vary in their side-effect profiles, eg the likelihood of causing extrapyramidal side-effects or cardiotoxicity. Some are more sedative than others and may be used primarily for this purpose, eg chlorpromazine and levomepromazine.

**CHLORPROMAZINE** tablets 25mg, 50mg, 100mg; oral solution 25mg/5mL
**Dose:** Schizophrenia and other psychoses, mania, short-term adjunctive management of severe anxiety, psychomotor agitation, excitement, and violent or dangerously impulsive behaviour initially 25mg 3 times daily (or 75mg at night), adjusted according to response, to usual maintenance dose of 75 to 300mg daily (but up to 1 gram daily may be required in psychoses). Older or debilitated patients, third to half adult dose.

**Note:** Flupentixol is used in schizophrenia and other psychoses, particularly with apathy and withdrawal, but should be avoided in mania or psychomotor hyperactivity.

**FLUPENTIXOL** tablets 500 micrograms, 1mg, 3mg
**Dose:** Psychosis, initially 3 to 9mg twice daily adjusted according to the response; maximum 18mg daily. Older or debilitated patients, initially quarter to half adult dose. The 500 micrograms and 1mg tablets are off-label for this indication.

**HALOPERIDOL** tablets 1·5mg, 5mg, 10mg; capsules 500 micrograms; oral liquid 2mg/1mL; injection 5mg/1mL
**Dose:** Schizophrenia and other psychoses, mania, short-term adjunctive management of psychomotor agitation, excitement, and violent or dangerously impulsive behaviour, by mouth, initially 500 micrograms to 3mg 2 to 3 times daily or 3 to 5mg 2 to 3 times daily in severely affected or resistant patients; in resistant schizophrenia up to 30mg daily may be needed; adjusted according to response to lowest effective maintenance dose (as low as 5 to 10mg daily). Older or debilitated patients, initially half adult dose. By intramuscular injection, initially 2 to 10mg then every 4 to 8 hours according to response to total maximum 18mg daily; severely disturbed patients may require initial dose of up to 18mg; older or debilitated patients, initially half adult dose. Agitation and restlessness in older people, by mouth, initially 500 micrograms to 1·5mg once or twice daily.
Note: Older people and risk of postural hypotension; levomepromazine is not recommended for ambulant patients over 50 years unless the risk of hypotensive reaction is assessed.

LEVOMEPRAMZINE tablets 25mg
Dose: Schizophrenia, initially 25 to 50mg daily in divided doses increased as necessary; bedpatients initially 100 to 200mg daily usually in 3 divided doses, increased if necessary to 1 gram daily.

SULPIRIDE tablets 200mg, 400mg
Dose: 200 to 400mg twice daily; maximum 800mg daily in predominantly negative symptoms, and 2400mg daily in mainly positive symptoms. Older people, lower initial dose, increased gradually according to response.

TRIFLUOPERAZINE tablets 1mg, 5mg; oral solution 1mg/5mL
Dose: Schizophrenia and other psychoses, short-term adjunctive management of psychomotor agitation, excitement, and violent or dangerously impulsive behaviour, initially 5mg twice daily, increased by 5mg daily after 1 week, then at intervals of 3 days, according to the response. Older people, reduce initial dose by at least half.

ZUCLOPENTHIXOL tablets 2mg, 10mg, 25mg
Dose: Schizophrenia and other psychoses, particularly when associated with agitated, aggressive, or hostile behaviour, initially 20 to 30mg daily in divided doses, increasing to a maximum of 150mg daily if necessary; usual maintenance dose 20 to 50mg daily. Older or debilitated patients, initially quarter to half adult dose.

Note: Following treatment with zuclopenthixol acetate (Clopixol Acuphase®), if maintenance treatment is necessary, change to an oral antipsychotic 2 to 3 days after last injection, or to a longer-acting antipsychotic depot injection given concomitantly with last injection of zuclopenthixol acetate. For further guidance on the use of zuclopenthixol acetate injection see policies on emergency sedation in specialist psychiatric, Community and District and Rural General Hospitals on intranet.

ZUCLOPENTHIXOL ACETATE (Clopixol Acuphase®) solution for injection (oily) 50mg/1mL
Dose: By deep intramuscular injection into the gluteal muscle or lateral thigh, 50 to 150mg (older people 50 to 100mg), if necessary repeated after 2 to 3 days (1 additional dose may be needed 1 to 2 days after the first injection); maximum cumulative dose 400mg per course and maximum 4 injections; maximum duration of treatment 2 weeks. Avoid use in neuroleptic-naïve patients.

Antipsychotic depot injections

Long-acting depot injections are used for the patient’s convenience or to improve compliance. They may produce more extrapyramidal reactions than oral preparations. For traditional depot preparations (flupentixol, fluphenazine, haloperidol and zuclopenthixol decanoate) the BNF recommends giving a test dose as some side-effects are prolonged. The drug is dissolved in oil and, when injected into muscle, it slowly comes out of the oil and into the bloodstream over a period of up to 6 weeks. Peak levels are achieved within 10 days. Steady blood levels are achieved by 6 to 12 weeks, depending on which drug is used.

FLUPENTIXOL DECANOATE solution for injection (oily) 20mg/1mL, 40mg/2mL, 100mg/1mL, 200mg/1mL
Dose: By deep intramuscular injection into the upper outer buttock or lateral thigh, test dose 20mg, then after at least 7 days 20 to 40mg repeated at intervals of 2 to 4 weeks, adjusted according to response; maximum 400mg weekly; usual maintenance dose 50mg every 4 weeks to 300mg every 2 weeks. Older people, initially quarter to half adult dose.
FLUPHENAZINE DECANOATE solution for injection (oily) 12.5mg/0.5mL, 25mg/1mL, 100mg/1mL
Dose: By deep intramuscular injection into the gluteal muscle, test dose 12.5mg (6.25mg in older patients), then after 4 to 7 days 12.5 to 100mg repeated at intervals of 14 to 35 days, adjusted according to response.

**Note:** If fortnightly administration of haloperidol decanoate is preferred, halve the dose.

HALOPERIDOL DECANOATE solution for injection (oily) 50mg/1mL, 100mg/1mL
Dose: By deep intramuscular injection into the gluteal muscle, initially 50mg every 4 weeks, if necessary increasing by 50mg increments to 300mg every 4 weeks; higher doses may be needed in some patients. Older people, initially 12.5 to 25mg every 4 weeks.

ZUCLOPENTHIXOL DECANOATE (Clopixol®) solution for injection (oily) 200mg/1mL, 500mg/1mL
Dose: By deep intramuscular injection into the upper outer buttock or lateral thigh, test dose 100mg, followed after at least 7 days by 200 to 500mg or more, repeated at intervals of 1 to 4 weeks, adjusted according to response; maximum 600mg weekly. Older people, quarter to half usual starting dose.

**Note:** Aripiprazole: a trial of oral aripiprazole is recommended before initiation of aripiprazole depot injection because no test dose is given.

^ ARIPIPRAZOLE (Abilify Maintena®) powder and solvent for prolonged-release suspension for injection vial 400mg, pre-filled syringe 400mg
Dose: By deep intramuscular injection into the gluteal muscle, 400mg repeated at monthly intervals (minimum 26 days between injections). Continue treatment with 10 to 20mg of oral aripiprazole for 14 consecutive days after the first injection. For dose adjustments due to side-effects, concomitant use of interacting drugs or missed depot doses, consult SPC.

**Note:** Risperidone depot injection differs from other depot formulations. A trial of oral risperidone is recommended before initiation of risperidone depot injection because no test dose is given. During initiation there is a lag time of 3 weeks before significant blood levels are reached; continue oral risperidone if necessary for a minimum of 4 to 6 weeks (often longer); oral risperidone may be continued during dose adjustment of the depot injection. Peak levels are reached 4 to 6 weeks after depot injection and steady state blood levels by 8 to 10 weeks. Store the injection in a fridge (only stable for 7 days if unrefrigerated). The whole vial must be administered (due to the nature of the suspension) giving limited flexibility in dosing.

^ RISPERIDONE (Risperdal Consta®) powder and solvent for suspension for injection 25mg, 37.5mg, 50mg
Dose: By deep intramuscular injection into the deltoid or gluteal muscle, patients taking oral risperidone up to 4mg daily, initially 25mg every 2 weeks; patients taking oral risperidone over 4mg daily, initially 37.5mg every 2 weeks; dose adjusted at intervals of at least 4 weeks in steps of 12.5mg to maximum 50mg (older people 25mg) every 2 weeks.

^ PALIPERIDONE (Xeplion®) suspension for injection, pre-filled syringe 50mg, 75mg, 100mg, 150mg
Dose: By deep intramuscular injection into the deltoid muscle, 150mg on day 1, then 100mg on day 8, then adjusted at monthly intervals according to response; recommended maintenance dose 75mg (range 25 to 150mg) monthly.

^ PALIPERIDONE (Trevicta®) prolonged-release suspension for injection, pre-filled syringe 175mg, 263mg, 350mg, 525mg
Dose: By deep intramuscular injection into the deltoid muscle, for three-monthly maintenance treatment in patients who are clinically stable on one-monthly paliperidone injection; refer to SPC.
Antimuscarinic drugs used to treat extrapyramidal side-effects

Antimuscarinic drugs reduce the symptoms of drug-induced Parkinsonism, although tardive dyskinesia is not improved and may be worsened. They do not improve akathisia unless associated with stiffness. Assess the need for antimuscarinic drugs after 3 months of treatment. These drugs have the potential for misuse and careful review of some patients’ motivation in asking for them is required. Antimuscarinic drugs are known to have an effect on cognition, particularly in the elderly.

PROCYCLIDINE tablets 5mg; syrup 2.5mg/5mL; solution for injection 10mg/2mL

Dose: By mouth, 2.5mg 3 times daily, increased gradually if necessary; usual maximum 30mg daily. Older people, preferably lower end of range. Acute dystonia, by intramuscular or intravenous injection, 5 to 10mg (occasionally more than 10mg), usually effective in 5 to 10 minutes but may need 30 minutes for relief. Older people, preferably lower end of range. When stopping reduce stepwise to the minimum effective dose.

Drugs used in bipolar disorder

See NICE guidance on ‘Bipolar Disorder’ (www.nice.org.uk). For advice on antidepressant drug use in bipolar disorder refer to section 4.3.

Lithium, antipsychotics and antiepileptics are used in bipolar disorder to control acute attacks and to prevent their recurrence. In the long-term treatment of bipolar disorder the choice of drug depends upon:

- response to previous treatments
- the relative risk, and known precipitants, of manic versus depressive relapse
- physical risk factors, particularly renal disease, obesity and diabetes
- the patient’s preference and history of adherence
- gender – see note below regarding use in women of child-bearing age
- a brief assessment of cognitive state (such as the Mini-Mental State Examination) if appropriate, for example, for older people.

For monitoring requirements for lithium, antipsychotics and antiepileptics refer to:

- ‘Physical Monitoring Requirements for Patients with enduring mental illness’
- local ‘Therapeutic drug monitoring’ guidance in Appendix 1.

Withdraw all prophylactic drugs gradually over at least 4 weeks. In particular, abrupt withdrawal of lithium may cause mania; withdraw over a 3-month period.

Reproductive health issues: see SIGN 127 (www.sign.ac.uk).

- Discuss pregnancy planning and the role of contraception.
- Discuss specific risks in relation to postnatal relapse of illness for women with bipolar disorder.
- When planning a pregnancy, discuss the risks and benefits of changing or stopping medication and emphasise the need to continue contraception where appropriate.
- Valproate should only be used in women of child-bearing potential if there is no alternative and adequate contraception is in place; see MHRA advice at www.gov.uk/drug-safety-update.

Lithium

Lithium has a narrow therapeutic index and regular monitoring is required – see Appendix 1. If lithium toxicity develops seek specialist advice. Early features include an exacerbation of existing side-effects: nausea, vomiting and tremor. As toxicity develops further, disorientation and dysarthria appear, followed by convulsions, coma and eventually death from cardiac effects or pulmonary complications.
Note: Lithium

- Always prescribe the same brand of lithium to avoid differences in bioavailability.
- All patients starting lithium should be offered written information; ensure your patient has a copy of the lithium patient information booklet (www.npsa.nhs.uk).
- In long-term use lithium has been associated with thyroid disorders and mild cognitive and memory impairment.
- Avoid abrupt cessation of lithium. NICE recommends titrating down over 3 months routinely.

*S LITHIUM CARBONATE* (Priadel®) m/r tablets 200mg (5·4mmol lithium/tablet), 400mg (10·8mmol lithium/tablet)

*S LITHIUM CITRATE* (Priadel®) oral solution 520mg/5mL (5·5mmol lithium/5mL)

**Valproate**

Valproate is the first choice of the antiepileptics used to treat bipolar disorder. In acute mania valproic acid is licensed; sodium valproate is a cost-effective alternative to valproic acid but is off-label for this indication. Both drugs are used for maintenance treatment but both are off-label for this indication.

**MHRA: valproate:** risk of abnormal pregnancy outcomes, see www.gov.uk/drug-safety-update.
- Children exposed *in utero* to valproate are at a high risk of serious developmental disorders (in up to 30-40% of cases) and/or congenital malformations (in approximately 10% of cases).
- Valproate should not be prescribed to female children, female adolescents, women of childbearing potential or pregnant women unless other treatments are ineffective or not tolerated and adequate contraception is in place.

*S SODIUM VALPROATE*▼ e/c tablets 200mg, 500mg; crushable tablets 100mg; m/r tablets 200mg, 300mg, 500mg; oral solution 200mg/5mL

*S VALPROIC ACID*▼ e/c tablets 250mg, 500mg

### 4.3 ANTIDEPRESSANT DRUGS

- For guidance on the non-pharmaceutical management of depression refer to SIGN 114.
- Refer to antidepressant guidelines.
- Use antidepressants with caution in children and adolescents; refer to BNF for details.
- The following patient information leaflets are available:
  - ‘Breast-feeding and antidepressant medication’ on the Mental Health and Learning Disabilities webpage on Intranet or from Pharmacy Department, New Craigs, tel: 01463 704663

**Note:** Hyponatraemia (usually in older people and possibly due to inappropriate secretion of antidiuretic hormone) has been associated with all types of antidepressants and should be considered in the differential diagnosis of all patients who develop drowsiness, confusion or convulsions while taking an antidepressant.

**Antidepressant use in bipolar disorder**

Although antidepressants are needed to treat bipolar depression their use may carry the risk of switching to manic states and may cause mood destabilisation:
• at the onset of a manic episode, stop the antidepressant; abrupt withdrawal may be justified in this situation.
• an antidepressant drug in combination with an antimanic drug is recommended for the treatment of acute bipolar depression.
• after successful treatment for acute depression, avoid maintenance antidepressant treatment.

Lamotrigine (section 4.8) may be used after specialist initiation for the prevention of depressive episodes in bipolar disorder. Because of the risk of Stevens-Johnson syndrome/toxic epidermal necrolysis, the initial dose and subsequent slow dose escalation should not be exceeded; refer to SPC for further information. Quetiapine (section 4.2) may also be used after specialist initiation.

Selective serotonin re-uptake inhibitors (SSRIs)

For most patients fluoxetine or sertraline are the first choice SSRIs. Sertraline is preferred in older people and those with a recent myocardial infarction or unstable angina. Citalopram should not be initiated due to the potential risk of co-prescribing contra-indicated medicines. Paroxetine is not recommended for initiation in new patients.

**FIRST CHOICE:** FLUOXETINE

SERTRALINE

**FLUOXETINE** capsules 20mg; liquid 20mg/5mL

**Dose:** Depressive illness, 20mg once daily. Refer to BNF for other indications.

**SERTRALINE** tablets 50mg, 100mg

**Dose:** Depressive illness, initially 50mg daily, increased if necessary by increments of 50mg over several weeks to maximum 200mg daily; usual maintenance dose 50mg daily. Refer to BNF for other indications.

**Note: Citalopram:**

• Citalopram should not be initiated due to the potential risk of co-prescribing contra-indicated medicines.
• Citalopram is associated with dose-dependent QT interval prolongation; it is contra-indicated when co-prescribed with all other medicines that prolong the QT interval – see www.gov.uk/drug-safety-update.
• 8mg (4 drops) oral drops may be considered to be equivalent in therapeutic effect to 10mg citalopram tablet. Mix with water, orange juice, or apple juice before taking.

**CITALOPRAM** tablets 10mg, 20mg, 40mg; oral drops 40mg/mL

**Dose:** Depressive illness, tablets 20mg once daily as a single dose in the morning or evening increased if necessary to maximum 40mg daily. Older people, maximum 20mg daily. Oral drops, 16mg daily as a single dose in the morning or evening increased if necessary to maximum 32mg daily. Older people maximum 16mg daily. Refer to BNF for other indications.

**Note: Paroxetine**

• There is no evidence that paroxetine doses higher than licensed doses are more effective.
• Paroxetine is not recommended for initiation in new patients.

**PAROXETINE** tablets 20mg, 30mg; oral suspension 10mg/5mL

**Dose:** Depressive illness, 20mg each morning. Refer to BNF for other indications.
Other antidepressant drugs

Choice of therapy is influenced by side-effect profiles; mirtazapine is associated with weight gain and sedative effects whilst the use of venlafaxine is associated with cardiovascular side-effects and requires monitoring. See section 6.1 for the use of duloxetine in the treatment of painful diabetic neuropathy.

**MIRTAZAPINE** tablets 15mg, 30mg, 45mg  
**Dose:** Initially 15mg daily at bedtime increased according to response to 45mg daily as a single dose at bedtime or in 2 divided doses.

**Note:** Venlafaxine: screen all patients carefully for high blood pressure. Pre-existing hypertension should be controlled before initiation of treatment. Review blood pressure periodically, after initiation of treatment and after dose increases.

**VENLAFAXINE** tablets 37.5mg, 75mg; m/r capsules 75mg, 150mg  
**Dose:** *Immediate-release tablets*, depressive illness, initially 75mg daily in 2 divided doses increased if necessary after several weeks to 150mg daily in 2 divided doses. In severely depressed or hospitalised patients, maximum 375mg daily. *Modified-release capsules,* depression, 75mg daily increased if necessary after at least 3 to 4 weeks to 150mg once daily; maximum 375mg once daily. Refer to BNF for other indications.

The immediate-release twice-daily tablets are the more cost-effective option and should be considered first choice unless once-daily dosing is an advantage for individual patients.

**Monoamine-oxidase inhibitors (MAOIs)**

**S PHENELZINE** tablets 15mg  
**Dose:** 15mg 3 times daily, increased if necessary to 4 times daily after 2 weeks (hospital patients, maximum 30mg 3 times daily), then reduced gradually to lowest possible maintenance dose (15mg on alternate days may be adequate). A patient information pack is available from the Pharmacy Departments in New Craigs and Mid Argyll Community Hospital.

**Tricyclic antidepressants**

Dispense limited quantities of tricyclic antidepressants at any one time because their cardiovascular effects are dangerous in overdosage. Clomipramine is predominantly serotonergic and is preferred when there are significant symptoms of anxiety. Refer to section 4.7 for use of tricyclic antidepressants in neuropathic pain and migraine prophylaxis.

**CLOMIPRAMINE** capsules 10mg, 25mg, 50mg  
**Dose:** Depression, initially 10mg daily, increased gradually as necessary to 30 to 150mg daily in divided doses or as a single dose at bedtime; maximum 250mg daily. Older people, initially 10mg daily increased carefully over approximately 10 days to 30 to 75mg daily.

**S AMITRIPTYLINE** tablets 10mg, 25mg, 50mg; oral solution 25mg/5mL, 50mg/5mL  
**Dose:** depressive illness, initially 30 to 75mg daily in divided doses, alternatively initially 30 to 75mg once daily, dose to be taken at bedtime, increased gradually if necessary to 150 to 200mg.

### 4.4 CNS STIMULANTS AND DRUGS USED FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER

CNS stimulant medication (methylphenidate, lisdexamfetamine) is only indicated for the treatment of attention deficit hyperactivity disorder (ADHD) under specialist supervision. Initiation,
stabilisation and ongoing supervision are provided by the relevant specialist. Unacceptable side-effects or a poor response to first-line treatment can be discussed with the specialist. When response to stimulants is inadequate or when stimulants are unsuitable or not tolerated, use of the non-stimulant guanfacine may be considered.

For information on prescribing in ADHD and the characteristics and release profiles of immediate and modified-release formulations of methylphenidate, refer to SIGN guidance (www.sign.ac.uk) and to the shared-care protocol on Intranet. In a small minority of patients response to methylphenidate therapy may differ if the formulation changes; brand name prescribing may be required as per BNF advice.

**S METHYLPHENIDATE CD2**
- tablets 5mg, 10mg, 20mg; m/r tablets (Xenidate® XL (equivalent to Concerta® XL)) 18mg, 27mg, 36mg, 54mg; m/r capsules (Equasym XL®) 10mg, 20mg, 30mg; m/r capsules (Medikinet XL®) 5mg, 10mg, 20mg, 30mg, 40mg

**S LISDEXAMFETAMINE CD2**
- capsules 20mg, 30mg, 40mg, 50mg, 60mg, 70mg

**S GUANFACINE m/r**
- tablets 1mg, 2mg, 3mg, 4mg

### 4.5 DRUGS USED IN THE TREATMENT OF OBESITY

Drug treatment is not a long-term solution in weight management but can be considered as an adjunct to lifestyle interventions where weight loss would lead to significant health benefit: refer to algorithm ‘Orlistat in the management of obesity’.

**Note:** If a meal is missed or contains no fat, omit the dose of orlistat.

**ORLISTAT**
- capsules 120mg

**Dose:** Refer to algorithm ‘Orlistat in the management of obesity’.

### 4.6 DRUGS USED IN NAUSEA AND VERTIGO

**Assessment**

Accurate diagnosis of the aetiology of both nausea and vomiting as separate symptoms is important; reversal of any cause is preferential to simply treating the symptom and should include a review of medication. Consider the possibility of withdrawing any causative agent from the patient’s drug profile.

**Treatment**

Base selection of an antiemetic on the likely cause, mechanism of action of the drugs available, the side-effect profile of each drug, interactions and concomitant conditions. Refer to guidance below and/or to BNF:
- ‘Aid to antiemetic selection’
- Scottish Palliative Care Guideline on ‘Nausea and vomiting’
- Cancer Centre ‘Guidelines for the Management of Chemotherapy-induced Nausea and Vomiting in Adult Patients’ on Intranet
- Raigmore Hospital guidance on ‘Surgical Ward Management of Post Operative Nausea and Vomiting in Adults’ on Intranet.

Use metoclopramide and prochlorperazine with caution in the young, the very old and the debilitated, due to extrapyramidal side-effects. Domperidone does not readily cross the blood-
brain barrier and is less likely to exhibit these side-effects. See section 4.7 for the use of antiemetics in the treatment of migraine.

**Antihistamines**

**CYCLIZINE** tablets 50mg; injection 50mg/1mL  
**Dose:** 50mg up to 3 times daily.  
Use cyclizine with caution in severe heart failure or acute myocardial infarction; it may counteract the beneficial haemodynamic effects of opioids.

**PROMETHAZINE HYDROCHLORIDE** OTC tablets 10mg, 25mg; elixir 5mg/5mL  
**Dose:** Motion sickness prevention, 20 to 25mg at bedtime on night before travel, repeat on the following morning if necessary. In severe vomiting in pregnancy seek specialist advice.

**Phenothiazines and related drugs**

**PROCHLORPERAZINE** tablets 5mg; syrup 5mg/5mL; injection 12.5mg/1mL; buccal tablets OTC 3mg  
**Dose:** Nausea and vomiting, *by mouth, tablets*, acute attack 20mg initially then 10mg after 2 hours; prevention 5 to 10mg 2 to 3 times daily; *buccal tablets*, 3 to 6mg twice daily, placed high between upper lip and gum and left to dissolve; *by deep intramuscular injection*, nausea and vomiting, 12.5mg when required followed if necessary after 6 hours by an oral dose, as above.

Avoid prochlorperazine in balance disturbances in older people as it may often lead to drug-induced Parkinson’s disease, postural hypotension and mental confusion. Prochlorperazine injection is considered inappropriate for patients with reduced consciousness due to its tendency to deepen any state of sedation.

**LEVOMEepromazine** tablets 25mg; injection 25mg/1mL  
**Dose:** In palliative care, 5 to 25mg daily *[off-label]*, refer to Scottish Palliative Care Guidelines on ‘Nausea and vomiting’. Unlicensed 6mg tablets are also used within Palliative Care; see Unlicensed Medicine List on Intranet.

Levomepromazine carries a risk of postural hypotension; avoid in ambulant patients over 50 years, unless risk of hypotensive reaction has been assessed.

**S DROPERIDOL** injection 2.5mg/1mL

**Domperidone and metoclopramide**

MHRA:  

**DOMPERIDONE** tablets 10mg; suspension 5mg/5mL  
**Dose:** *By mouth*, 10mg up to 3 times daily for up to 1 week.

**METOCLOPRAMIDE** tablets 10mg; oral solution 5mg/5mL; injection 10mg/2mL  
**Dose:** Tablets, 10mg up to 3 times daily, 5mg in young adults 15-19 years, body weight under 60kg.

Metoclopramide is a prokinetic. It is contra-indicated in gastro-intestinal obstruction, perforation or haemorrhage. Avoid where haematemesis or melaena are present. Caution in Parkinson’s disease.
5HT₃-receptor antagonists

5HT₃-receptor antagonists increase large bowel transit time; constipation can be a problem.


ONDANSETRON tablets 4mg, 8mg; oral lyophilisates 4mg, 8mg; oral solution (sugar-free) 4mg/5mL; injection 4mg/2mL, 8mg/4mL

Dose: Prevention of post-operative nausea and vomiting, by mouth, 16mg 1 hour before anaesthesia or 8mg 1 hour before anaesthesia followed by a further 2 doses of 8mg every 8 hours; by intramuscular or slow intravenous injection, 4mg at induction of anaesthesia. Treatment of post-operative nausea and vomiting, by intramuscular or slow intravenous injection, 4mg. In oncology, refer to ‘Guidelines for the Management of Chemotherapy-induced Nausea and Vomiting in Adult Patients’ on Intranet.

Oral lyophilisates are useful in primary care for the immediate treatment of nausea and vomiting; place on the tongue, allow to disperse and swallow. Change to non-dispersible formulations at the earliest opportunity.

GRANISETRON tablets 1mg, 2mg; injection 3mg/3mL

Only for nausea and vomiting induced by cytotoxic chemotherapy or radiotherapy.

PALONOSETRON WITH NETUPITANT* (palonosetron 500 micrograms, netupitant 300mg) capsules (Akynezo®)

Dose: Moderately emetogenic chemotherapy and highly emetogenic cisplatin-based chemotherapy, 1 capsule approximately 1 hour before the start of each chemotherapy cycle.

Neurokinin-receptor antagonists

APREPIANT capsules 80mg, 125mg; powder for oral suspension 125mg

FOSAPREPIANT injection 150mg

Hyoscine

HYOSCINE HYDROBROMIDE chewable tabletsOTC 150 micrograms, 300 micrograms; transdermal patchesOTC 1mg/72 hours; injection 400 micrograms/1mL

Dose: Motion sickness, by mouth, 150 to 300 micrograms up to 30 minutes before start of journey, repeat every 6 hours as required, up to 3 doses in 24 hours. The patch may be used as an alternative, 1 patch placed behind the ear 5 to 6 hours before journey may remain in place for up to 72 hours. Place replacement patch behind other ear. Sedation can be a problematic side-effect if driving or operating machinery is required.

For the use of hyoscine in palliative care refer to Scottish Palliative Care Guidelines on ‘Nausea and vomiting’.

Other antiemetics

Refer to ‘Aid to antiemetic selection’ and to Scottish Palliative Care Guidelines on ‘Nausea and vomiting’.

DEXAMETHASONE tablets 500 micrograms, 2mg, 4mg; oral solution (as sodium phosphate) 2mg/5mL; injection 3·3mg/1mL, 6·6mg/2mL

Dose: For chemotherapy-induced nausea and vomiting, by mouth, 8 to 16mg in the morning, or in 2 divided doses before 2pm to reduce sleep disturbance; by intravenous injection, as monotherapy
or with 5HT₃ antagonist, 8 to 16mg daily. For post-operative nausea and vomiting, by intravenous injection, in resistant cases 8mg as a single dose. Most patients can either take the tablets as they are or dispersed in a little water prior to use [off-label].

**Note:** The haloperidol SPC (www.medicines.org.uk/emc) requires a baseline ECG prior to treatment with haloperidol and consideration of the need for ongoing ECG monitoring.

**HALOPERIDOL** tablets 1.5mg, 5mg, 10mg; capsules 500 micrograms; oral liquid 10mg/5mL; injection 5mg/1mL

**Dose:** Refer to Scottish Palliative Care Guidelines on ‘Nausea and vomiting’ [off-label].

**S OCTREOTIDE** injection 50 micrograms/1mL, 100 micrograms/1mL, 500 micrograms/1mL

Only for intractable nausea and vomiting in palliative care [off-label].

In anticipatory nausea and vomiting, lorazepam (section 4.1) can be useful.

**Other drugs for Ménière's disease and other labyrinthine disorders**

Ménière’s is a disease causing attacks of disabling dizziness associated with transient loss of hearing and tinnitus. Betahistine is used specifically for Ménière’s however is of no benefit in other types of imbalance. For further information refer to ‘Dizziness’ guidance on Intranet.

**BETAHISTINE** tablets 8mg, 16mg

**Dose:** Vertigo, tinnitus and hearing loss associated with Ménière’s disease, initially 16mg 3 times daily, maintenance 24 to 48mg daily in divided doses.

**CINNARIZINE** OTC tablets 15mg

**Dose:** Vestibular disorders, 30mg 3 times daily. Motion sickness, 30mg 2 hours before travel then 15mg every 8 hours during journey if necessary.

### 4.7 ANALGESICS

Refer to:

- Acute pain:
  - ‘Acute Pain Manual’ on Intranet
  - ‘Acute pain adult oral and rectal analgesic step ladder’ on Intranet
  - ‘Acute pain management in adults with renal impairment’ on Intranet

- Scottish Palliative Care Guidelines on Pain

- Chronic non-malignant pain:
  - opioid guidelines for Highland Health & Social Care Partnership on Intranet
  - neuropathic pain guidelines for Highland Health & Social Care Partnership on Intranet
  - guidance is also available under ‘Chronic Pain’ on the Shared Clinical Guidelines Intranet site

- Non-steroidal anti-inflammatory drugs (NSAIDs) listed in section 10.1 and guidance.

**Non-opioid analgesics**

**Note:** The salt content of dispersible formulations of paracetamol and co-codamol may be unsuitable for some patients.
**Note: Paracetamol infusion:**
- Is 100% bioavailable and there is a greater risk of toxicity so should only be prescribed where clinically indicated. Review the prescription regularly.
- Should only be used when the patient is ‘nil by mouth’, or has swallowing difficulty which is not overcome by the use of suspension.
- **Must be given in smaller doses to patients under 50kg (see dose below).**
- Maximum daily dose must not exceed 3 grams in patient with renal/hepatic impairment, chronic malnutrition, chronic alcoholism.
- Increase the minimum interval between each dose to 6 hours if creatinine clearance is less than 30mL/min.
- Is more effective than paracetamol suppositories.

### Paracetamol

**Dose:** By mouth/by rectum, 1 gram up to 4 times daily. Consider dose reduction in patients with low body weight (less than 50kg), renal/hepatic impairment, chronic malnutrition, or chronic alcoholism to 15mg/kg/dose up to 4 times daily (to a maximum of 3 grams/day). **By intravenous infusion:** adults 50kg and over 1 gram up to 4 times daily, adults less than 50kg 15mg/kg/dose up to 4 times daily.

Paracetamol caplets may be easier to swallow than standard tablets and are preferred by many patients. Caplets may be supplied on a prescription for paracetamol tablets.

**NEFOPAM** tablets 30mg

**Dose:** By mouth, in patients with renal impairment as an alternative to opioids and NSAIDs, start at 30mg up to 3 times daily. Can cause sympathomimetic and anticholinergic side-effects and is increasingly expensive.

### Weak opioid analgesics

**DIHYDROCODEINE** tablets 30mg; oral solution 10mg/5mL

**Dose:** 30mg every 4 to 6 hours when necessary. For advice on prescribing dihydrocodeine to drug misusers see section 4.10.

**Note: Codeine:**
- The capacity to metabolise codeine can vary considerably and lead to either reduced therapeutic effect or marked increase in side-effects; refer to [www.gov.uk/drug-safety-update](http://www.gov.uk/drug-safety-update).
- Codeine should not be used by breast-feeding mothers because it can pass to the baby through breast milk and potentially cause harm.
- Codeine should be avoided in paediatric care.

**CODEINE** tablets 15mg, 30mg; syrup 25mg/5mL

**Dose:** By mouth, 30 to 60mg every 4 hours when necessary.

**CO-CODAMOL** (codeine/paracetamol) tablets 30/500; effervescent tablets 30/500

**Dose:** 1 to 2 tablets every 4 hours; maximum 8 tablets daily (see low-body weight dose reduction under paracetamol).

### Strong opioid analgesics

Follow local guidance on pain control:
- **Acute pain:**
  - ‘Acute Pain Manual’ on [Intranet](http://Intranet)
• Chronic non-malignant pain opioid prescribing guidelines for Highland Health & Social Care Partnership on Intranet.
• Guidance on pain management in patients on long-term methadone in section 4.10. Also refer to:
  • Scottish Palliative Care Guidelines on Pain
  • SIGN guidance 106 ‘Control of pain in adults with cancer’ (www.sign.ac.uk)
  • SIGN guidance 136 ‘Management of chronic pain’ (www.sign.ac.uk)
  • ‘Recommendations for the Appropriate Use of Opioids for Persistent Non-Cancer Pain’ (www.britishpainsociety.org)

**Note:** Chronic non-malignant pain

- In osteoarthritis the side-effects of strong opioids (oral and transdermal) outweigh any minimal benefits achieved*; local rheumatologists consider that this applies even more so to use in inflammatory joint disease.
  
  *Oral or transdermal opioids for osteoarthritis of the knee or hip’, Cochrane Database of Systematic Reviews (http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD003115/frame.html).

- There is no clinical evidence for the long-term effectiveness of strong opioids in fibromyalgia, non-specific low back pain, unexplained persistent pain or headaches; avoid use of strong opioids in the treatment of these conditions.

<table>
<thead>
<tr>
<th>Opioid conversions – refer to guidance on ‘Choosing and changing opioids’ at <a href="http://www.palliativecareguidelines.scot.nhs.uk">www.palliativecareguidelines.scot.nhs.uk</a>. If in doubt, seek specialist palliative care advice.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid tolerance – if an individual is taking opioids for a chronic non-malignant pain condition, and cannot achieve effective pain relief despite increases in dose, they may be experiencing opioid tolerance; seek specialist advice.</td>
</tr>
</tbody>
</table>

**Opioid-induced hyperalgesia (OIH)** is a paradoxical response whereby opioid administration induces an increase in pain sensitivity rather than an analgesic effect. The three features felt to be most suggestive of OIH are escalating pain despite increasing opioids, demonstrable hyperalgesia or allodynia and a more diffuse pain distribution away from pre-existing pain sites. Other symptoms of opioid toxicity such as myoclonus, subtle hallucinations may or may not accompany this presentation. Management can involve different approaches including temporary withholding of opioid, dose reduction and/or opioid switching alongside measures to increase elimination of opioid and alternative approaches for breakthrough analgesia. Seek palliative care advice either from PCAS, tel: 01463 705405 or Highland Hospice 24 hour advice line, tel: 01463 243132 or 1333 from Raigmore.

**Antiemetics and laxatives** – an antiemetic (dopamine antagonist) may be required on initiation of an opioid or on dose increase, however tolerance to nausea occurs within 7 to 10 days. Co-prescribe a combination of a regular stimulant and softening laxative with regular opioid therapy (including weak opioid therapy) for prophylaxis of opioid-induced constipation; refer to Scottish Palliative Care Guidelines on Constipation and ‘Aid to antiemetic selection’.
Table summarising strong opioid analgesic oral and transdermal preparations listed below

<table>
<thead>
<tr>
<th></th>
<th>Short-acting (immediate-release)</th>
<th>Long-acting (modified-release)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Morphine</strong></td>
<td>Sevredol® tablets 10mg, 20mg, 50mg</td>
<td>MXL® m/r capsules (once daily) 30mg, 60mg, 90mg, 120mg, 150mg, 200mg</td>
</tr>
<tr>
<td></td>
<td>Oral solution 10mg/5mL, 100mg/5mL</td>
<td>MST Continus® m/r tablets (twice daily) 5mg, 10mg, 15mg, 30mg, 60mg, 100mg, 200mg</td>
</tr>
<tr>
<td><strong>Oxycodone</strong></td>
<td>Shortec® capsules 5mg, 10mg, 20mg,</td>
<td>Longtec® m/r tablets (twice daily) 5mg, 10mg, 15mg, 20mg, 30mg, 40mg, 60mg, 80mg, 120mg</td>
</tr>
<tr>
<td></td>
<td>Oral solution 5mg/5mL, 50mg/5mL</td>
<td></td>
</tr>
<tr>
<td><strong>Fentanyl</strong></td>
<td>Abstral® sublingual tablets 100 micrograms, 200 micrograms, 300 micrograms, 400 micrograms, 600 micrograms, 800 micrograms</td>
<td>Matrifen® transdermal patches (72 hour release) 12 micrograms/hour, 25 micrograms/hour, 50 micrograms/hour, 75 micrograms/hour, 100 micrograms/hour</td>
</tr>
<tr>
<td></td>
<td>PecFent® nasal spray 100 micrograms/metered spray, 400 micrograms/metered spray</td>
<td></td>
</tr>
<tr>
<td><strong>Tramadol</strong></td>
<td>Capsules 50mg; soluble tablets 50mg</td>
<td>m/r capsules (twice daily) 50mg, 100mg, 150mg, 200mg</td>
</tr>
</tbody>
</table>

**FIRST CHOICE:** MORPHINE or DIAMORPHINE

**MORPHINE** CD2:
- tablets (immediate-release, Sevredol®) 10mg, 20mg, 50mg;
- m/r tablets (twice daily, MST Continus®) 5mg, 10mg, 15mg, 30mg, 60mg, 100mg, 200mg;
- m/r capsules (once daily, MXL®) 30mg, 60mg, 90mg, 120mg, 150mg, 200mg;
- oral solution 10mg/5mL, 100mg/5mL;
- injection 10mg/1mL;
- intravenous infusion 50mg/50mL

**Dose:** By mouth, initially 5 to 15mg in opioid-naïve individuals. Dose will vary according to individual patient requirements.

- in acute pain, see guidance on Intranet
- for palliative care, breakthrough pain, refer to Scottish Palliative Care Guidelines on Pain
- for chronic non-malignant pain, see chronic non-malignant pain opioid prescribing guidelines for Highland Health & Social Care Partnership on Intranet and SIGN 136 ‘Management of chronic pain’.

**DIAMORPHINE** CD2 injection 5mg, 10mg, 30mg, 100mg

**Dose:** Refer to local guidance. Dose should be one third of the corresponding oral morphine dose, eg for a total daily dose of oral morphine 30mg, change to continuous subcutaneous infusion of diamorphine 10mg daily. For doses above 100 to 120mg consider specialist advice. See guidance on epidural use on Intranet.

Diamorphine is administered by subcutaneous injection or continuous subcutaneous infusion in chronic cancer pain. Diamorphine is more soluble than morphine and reduces the volume of administration of the injection. The subcutaneous route is less invasive, more comfortable and less painful than other parenteral routes and has 100% bioavailability.
### Note: Oxycodone:
- Oxycodone may be considered as an alternative in patients unable to tolerate morphine; refer to SIGN 106 guidance on cancer pain (www.sign.ac.uk).
- For patients with renal or hepatic impairment, refer to guidance on ‘Acute pain management in adults with renal impairment’ on Intranet and/or discuss oxycodone use with a specialist.
- Take care with the form of preparation as brand names are similar and easily confused; **brand name prescribing of Shortec® and Longtec® is recommended for advantageous release characteristics and cost-effectiveness.**

**OXYCODONE CD2:**
- capsules (immediate-release, Shortec®) 5mg, 10mg, 20mg;
- m/r tablets (twice daily, Longtec®) 5mg, 10mg, 15mg, 20mg, 30mg, 40mg, 60mg, 80mg, 120mg;
- oral solution 5mg/5mL, 50mg/5mL;
- injection 10mg/1mL, 20mg/2mL, 50mg/1mL

**Dose:** *By mouth,* (oral solution/Shortec®) 2mg to 5mg every 4 hours as required, (Longtec®) 10mg to 20mg every 12 hours.
- for palliative care, refer to Scottish Palliative Care Guidelines on Pain.
- for chronic non-malignant pain, see chronic non-malignant pain opioid prescribing guidelines for Highland Health & Social Care Partnership on Intranet.

### Note: Fentanyl:
**Nasal spray/sublingual tablets:**
- PecFent® and Abstral® are rapid acting preparations to be used for the management of breakthrough pain in patients using opioid therapy for chronic cancer pain only. Their prescription should only be initiated by a specialist in palliative care.

**Transdermal:**
- should only be used if oral opioid/analgesic requirements are stable.
- accidental transfer of transdermal fentanyl can lead to unintended exposure which can be especially hazardous to children – see www.gov.uk/drug-safety-update.
- in chronic non-malignant pain, if patch requirements are above 50 micrograms/hour, refer the patient for a specialist opinion as unlikely to benefit beyond this dose.

**FENTANYL CD2:**
- $^S$sublingual tablets (immediate-release, $^S$Abstral®) 100 micrograms, 200 micrograms, 300 micrograms, 400 micrograms, 600 micrograms, 800 micrograms;
- $^S$nasal spray (immediate-release, $^S$PecFent®) 100 micrograms/metered spray, 400 micrograms/metered spray;
- transdermal patches (72-hour release, Matrifen®) 12 micrograms/hour, 25 micrograms/hour, 50 micrograms/hour, 75 micrograms/hour, 100 micrograms/hour;
- injection 100 micrograms/2mL, 500 micrograms/10mL

**Dose:**
- for palliative care see Scottish Palliative Care Guidelines medicines information sheets on the use of fentanyl sublingual tablets, nasal spray and transdermal patches.
- for chronic non-malignant pain see chronic non-malignant pain opioid prescribing guidelines for Highland Health & Social Care Partnership on Intranet.

### Note: Tramadol has a mixed mode of action but still displays some of the opioid side-effects.
- It can still cause respiratory depression.
- It reduces the seizure threshold; take care with patients who abuse alcohol and those with epilepsy.
- There is a risk of serotonin syndrome when tramadol is used in combination with other serotonergic drugs like antidepressants. Take particular care with MAOIs to avoid concomitant use and for 2 weeks after stopping; refer to BNF for full list of interactions.
- Avoid concomitant use with other opioids.
- To avoid withdrawal symptoms following treatment for longer than 1 month, gradual dose reduction is recommended. Seek specialist advice.
- M/r capsules and soluble tablets are considerably more expensive than the 50mg capsules.

**TRAMADOL CD³:**
- capsules 50mg;
- soluble tablets 50mg;
- m/r capsules (twice daily) 50mg, 100mg, 150mg, 200mg;
- $^1$ Injection 100mg/2mL (for use by anaesthetists only)

**Dose:** capsules/soluble tablets, 50 to 100mg no more often than every 4 hours, maximum 400mg daily; m/r capsules 50 to 200mg twice daily, maximum 400mg daily.
- for chronic non-malignant pain, see chronic non-malignant pain opioid prescribing guidelines for Highland Health & Social Care Partnership on Intranet.

**Note:** Tapentadol: for initiation by or on the advice of a chronic pain consultant only.

**S TAPENTADOL CD²** m/r tablets (twice daily, Palexia® SR) 50mg, 100mg, 150mg, 200mg, 250mg

**Note:** Pethidine: for specialist use for management of rigors in patients receiving treatment with monoclonal antibodies [off-label].

**S PETHIDINE CD²** injection 50mg/1mL

**Note:** Methadone: only for initiation under the guidance of a palliative care or chronic pain specialist.

**S METHADONE CD²** tablets 5mg, injection 10mg/1mL

**Neuropathic pain**

Refer to local management guidance:
- chronic non-malignant neuropathic pain guidelines for Highland Health & Social Care Partnership on Intranet

Also refer to:
- Scottish Palliative Care Guidelines on ‘Neuropathic pain’.
- SIGN 136 ‘Management of chronic pain’ at www.sign.ac.uk.

**FIRST CHOICE:** **AMITRIPTYLINE**

**AMITRIPTYLINE** tablets 10mg, 25mg, 50mg; oral solution 25mg/5mL, 50mg/5mL

**Dose:** Neuropathic pain [off-label], refer to chronic non-malignant neuropathic pain guidelines for Highland Health & Social Care Partnership on Intranet and Scottish Palliative Care Guidelines.

**NORTRIPTYLINE** tablets 10mg, 25mg

**Dose:** Neuropathic pain if amitriptyline is poorly tolerated [off-label], refer to chronic non-malignant neuropathic pain guidelines for Highland Health & Social Care Partnership on Intranet and Scottish Palliative Care Guidelines.

**GABAPENTIN** capsules 100mg, 300mg, 400mg, tablets 600mg

**Dose:** Neuropathic pain, refer to chronic non-malignant neuropathic pain guidelines for Highland Health & Social Care Partnership on Intranet and Scottish Palliative Care Guidelines. See section 4.8 for antiepileptic use.
Painful diabetic neuropathy: after failure of simple analgesics and local measures, and where treatment with amitriptyline (uptitrated) and then with gabapentin has been ineffective or unsuitable, consider the use of duloxetine. For further guidance refer to: http://www.nhshighland.scot.nhs.uk/YourHealth/Diabetes/Pages/DiabeticNeuropathy.aspx.

**DULOXETINE** capsules 30mg, 60mg
**Dose:** Diabetic peripheral neuropathic pain, 60mg once daily; if ineffective, some patients may benefit from 60mg twice daily maximum. Discontinue if inadequate response after 2 months; review treatment at least every 3 months

**Capsaicin cream (section 10.3)** is used in post-herpetic neuralgia, **carbamazepine (section 4.8)** in trigeminal neuralgia and **pregabalin (section 4.8)** in neuropathic pain – see note box below.

**Dose:** Diabetic peripheral neuropathic pain, 60mg once daily; if ineffective, some patients may benefit from 60mg twice daily maximum. Discontinue if inadequate response after 2 months; review treatment at least every 3 months

**Capsaicin cream (section 10.3)** is used in post-herpetic neuralgia, **carbamazepine (section 4.8)** in trigeminal neuralgia and **pregabalin (section 4.8)** in neuropathic pain – see note box below.

**Note:**
- **Pregabalin** should be restricted to use for peripheral neuropathic pain in adults who have not responded to or tolerated conventional first and second-line treatments. Discontinue treatment if the patient has not shown sufficient benefit within 8 weeks of reaching the maximally tolerated therapeutic dose. Optimise tablet strength and use twice-daily dosing to minimise cost. Restrict use of the oral solution to those patients who find it difficult to or are unable to swallow tablets. See section 4.8 for antiepileptic use.
- **Gabapentin** and **pregabalin** have the potential for misuse and careful review of some patients’ motivation in asking for them is required; refer to SIGN 136 ‘Management of chronic pain’ (www.sign.ac.uk).

**Chronic widespread pain/fibromyalgia**

Many of the principles involved in the management of neuropathic pain are used with fibromyalgia, however medication is not always required: refer to guidance on ‘Management of chronic widespread pain (fibromyalgia)’ on Intranet and to SIGN 136 ‘Management of chronic pain’ (www.sign.ac.uk).

**Antimigraine drugs**

**Prophylaxis of episodic migraine**

Base selection of migraine prophylaxis on age, gender and co-morbidity:
- propranolol is first-line unless contra-indicated by asthma, COPD, peripheral vascular disease, heart failure or depression.
- amitriptyline is first-line when migraine coexists with troublesome tension-type headache, another chronic pain condition, disturbed sleep or depression.
- sodium valproate should not be used in women of child-bearing age (teratogenic potential) and those who are overweight.

Titrated over several weeks and continue for a further 3 months, then assess and discontinue if ineffective.

**FIRST CHOICE:** PROPRANOLOL or AMITRIPTYLINE

**PROPRANOLOL** tablets 10mg, 40mg; m/r capsules 80mg, 160mg
**Dose:** 40mg 2 to 3 times daily; maintenance 80 to 160mg daily.

**AMITRIPTYLINE** tablets 10mg, 25mg, 50mg
**Dose:** Migraine prophylaxis, [off-label], initially 10mg at night, increased if necessary to maintenance of 50 to 75mg at night. If amitriptyline is poorly tolerated consider nortriptyline.
NORTRIPTYLINE tablets 10mg, 25mg  
**Dose:** Migraine prophylaxis if amitriptyline is poorly tolerated [off-label], initially 10mg at night, increased if necessary to maintenance of 50 to 75mg at night.

TOPIRAMATE tablets 25mg, 50mg, 100mg  
**Dose:** Migraine prophylaxis, initially 25mg at night for 1 week, increased in increments of 25mg/day to weekly intervals up to 50mg twice daily. Some patients may experience a benefit at 25mg twice daily. See SPC for dosing in renal impairment.

SODIUM VALPROATE crushable tablets 100mg; e/c tablets 200mg, 500mg  
**Dose:** Migraine prophylaxis, [off-label], initially 200mg twice daily; doses up to 500mg twice daily are effective in most patients. Avoid in women of child-bearing age and those who are overweight; refer to MHRA advice at www.gov.uk/drug-safety-update.

Other antiepileptic drugs for migraine prophylaxis, the use of which should be discussed with a specialist, include gabapentin (section 4.8) [off-label]: refer to BNF for dosing instructions.

Pizotifen is of limited value in prophylaxis of migraine (refer to SIGN 107). It may cause increased appetite and weight gain. It can also cause drowsiness and so night-time dosing may help prevent day-time sedation. Use with caution in patients with a history of epilepsy.

PIZOTIFEN tablets 500 micrograms, 1·5mg  
**Dose:** Initially 500 micrograms at night increased gradually to usual dose of 1·5mg at night or in 3 divided doses; may be further increased up to maximum daily dose of 4·5mg (but rarely necessary), maximum single dose 3mg.

Flunarizine [unlicensed] is used under specialist advice in patients with episodic migraine with failure to, or side-effects from, classical preventative migraine therapy.

**Treatment**

**Note:** Advise all patients starting on any acute headache treatment:
- of the risk of developing medication-overuse headache
- to take any acute headache treatment on no more than 2 days per week
- to avoid opioids (including codeine and dihydrocodeine).

For the treatment of migraine, soluble simple analgesics (eg paracetamol 1 gram for mild to moderate migraine, or for all severities of migraine ibuprofen 400mg or soluble aspirin 900mg), if necessary with an antiemetic, eg metoclopramide 10mg (section 4.6), are often effective if taken early in the attack. Diclofenac or paracetamol suppositories may be an option.

Reserve triptans for patients resistant to simple analgesics and antiemetic therapy; if the headache always progresses to a moderate to severe attack despite patients taking acute therapy when symptoms are still mild, then consider triptans. Use during the established headache phase and not during the aura phase of an attack. In triptan responders, approximately one in four attacks do not respond to triptans. Refer to guidance on the diagnosis and management of headache at www.sign.ac.uk and www.nice.org.uk. Continue triptan treatment for 3 months and only discontinue at that point if ineffective. If one triptan is ineffective then consider trial of another.

**Note: Triptans:**
- Triptans should **not** be used in ischaemic heart disease or coronary vasospasm (including Prinzmetal's angina), uncontrolled hypertension and previous myocardial infarction (refer to BNF), or with ergotamine.
- Advise patients that triptans should be taken on no more than 2 days per week due to the risk of developing medication overuse headache.
**SUMATRIPTAN** tablets 50mg<sup>OTC</sup>, 100mg; solution for injection 6mg/0.5mL; nasal spray 10mg/0.1mL unit-dose spray, 20mg/0.1mL unit-dose spray

**Dose:** By mouth, 50mg to 100mg; dose may be repeated after at least 2 hours if migraine recurs, maximum 300mg in 24 hours; by subcutaneous injection, 6mg; dose may be repeated once after at least 1 hour if migraine recurs, maximum 12mg in 24 hours; intranasally, 10mg to 20mg into one nostril; dose may be repeated once after at least 2 hours if migraine recurs; maximum 40mg in 24 hours.

**RIZATRIPTAN** tablets 5mg, 10mg; orodispersible tablets 10mg

**Dose:** 10mg as soon as possible after onset, repeated after 2 hours if migraine recurs (patient not responding should not take second dose for same attack); maximum 20mg in 24 hours. Place the orodispersible tablet on the tongue and allow to dissolve.

Rizatriptan is a useful alternative to sumatriptan where a more potent and rapidly acting treatment is required. The metabolism of rizatriptan is affected by propranolol. Avoid rizatriptan completely within 2 hours of taking propranolol. At other times patients taking propranolol should take only 5mg rizatriptan.

**ZOLMITRIPTAN** tablets 2.5mg; orodispersible tablets 2.5mg, 5mg; nasal spray 5mg/0.1mL unit-dose spray

**Dose:** By mouth, 2.5mg repeated after at least 2 hours if migraine recurs (increase to 5mg for subsequent attacks in patients not achieving satisfactory relief with 2.5mg dose); maximum 10mg in 24 hours (place the orodispersible tablet on the tongue and allow to dissolve); intranasally, 5mg into one nostril as soon as possible after onset repeated after at least 2 hours if migraine recurs; maximum 10mg in 24 hours.

Other triptans, eg naratriptan, almotriptan and frovatriptan, may be considered for the treatment of non-responsive episodic migraine; refer to BNF. For chronic migraine which has failed to respond to 3 or more preventative treatments, botulinum toxin (Botox<sup>®</sup>) (section 4.9) may be used under specialist advice.

### 4.8 ANTIEPILEPTICS

For further information on the management of epilepsy and choice of antiepileptic drug therapy refer to:
- SIGN guideline ‘Diagnosis and Management of Epilepsy in Adults’ ([www.sign.ac.uk](http://www.sign.ac.uk))
- NICE CG137 guidance on the epilepsies ([www.nice.org.uk](http://www.nice.org.uk))
- Royal College of Psychiatrists CR206 guidance ‘Prescribing antiepileptic drugs for people with epilepsy and intellectual disability’ ([www.rcpsych.ac.uk](http://www.rcpsych.ac.uk)).

**Note:** The effectiveness of hormonal contraceptives may be considerably reduced by some antiepileptics; consider this when discussing choice of contraception. Refer to SIGN guidance and to section 7.3 for further information. Women wishing to become pregnant and those who conceive should be counselled by a specialist about possible risks and changes in antiepileptic medication.

**MHRA:** Brand switching of antiepileptics for seizure control ([www.mhra.gov.uk](http://www.mhra.gov.uk)):
- Carbamazepine, phenobarbital, phenytoin, primidone: all use should be brand or manufacturer-specific.
- Valproate, lamotrigine, perampanel, clobazam, clonazepam, oxcarbazepine, eslicarbazepine, zonisamide, topiramate: for most patients, switching between brands or manufacturers of these medicines should not pose a significant risk. However, any patient...
who has experienced loss of effect or adverse effects on switching brands of one of these medicines should be managed using specific medicine brand or manufacturer.

- **Levetiracetam, lacosamide, tiagabine, gabapentin, pregabalin, ethosuximide:** may be prescribed, supplied and administered generically unless there are specific circumstances dictating otherwise.

- In addition to the 3 risk-based categories of antiepileptic drugs, patient-related factors should be considered when deciding whether it is necessary to maintain continuity of supply for a specific product ([www.gov.uk](http://www.gov.uk)).

For indications other than seizure control (eg trigeminal neuralgia) all antiepileptics may be used generically.

### Choice of antiepileptic drug monotherapy (from SIGN Guideline 143)

<table>
<thead>
<tr>
<th>Partial and secondary generalised seizures</th>
<th>Primary generalised seizures</th>
<th>Uncertain seizure type</th>
</tr>
</thead>
<tbody>
<tr>
<td>- carbamazepine</td>
<td>- lamotrigine</td>
<td>As recommended by specialist</td>
</tr>
<tr>
<td>- sodium valproate</td>
<td>- levetiracetam</td>
<td></td>
</tr>
<tr>
<td>- lamotrigine</td>
<td>- sodium valproate</td>
<td></td>
</tr>
<tr>
<td>- oxcarbazepine</td>
<td></td>
<td></td>
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<tr>
<td>- levetiracetam</td>
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</tbody>
</table>

- Side-effect and interaction profiles should direct the choice of drug for the individual patient. Refer to the [BNF](https://www.gov.uk) for the wide range of interactions with this group of drugs.
- It is acceptable to titrate up the antiepileptic drug dose more slowly in certain patient groups, eg older people, patients with learning disabilities.
- Some antiepileptic drugs can exacerbate myoclonus, notably gabapentin, carbamazepine, oxcarbazepine and tiagabine.

### CARBAMAZEPINE

tablets 100mg, 200mg, 400mg; m/r tablets (Tegretol® Prolonged Release) 200mg, 400mg; liquid 100mg/5mL; suppositories 125mg, 250mg

**Dose:** Epilepsy, by mouth, initially 100 to 200mg once or twice daily, increased slowly in increments of 100 to 200mg every 2 weeks to usual dose of 400mg to 1·2 grams daily in divided doses. In some cases 1·6 to 2 grams daily may be needed.

### SODIUM VALPROATE

e/c tablets 200mg, 500mg; crushable tablets 100mg; m/r tablets (Epilim Chrono®) 200mg, 300mg, 500mg; m/r granules (Epilim Chronosphere® MR) 50mg, 100mg, 250mg, 500mg, 750mg, 1 gram; m/r granules (Episenta®) 500mg, 1 gram; oral solution 200mg/5mL; solution for injection 300mg/3mL

**Dose:** By mouth, initially 600mg daily given in 2 divided doses, preferably after food, increasing by 200mg daily at 3 day intervals to a maximum of 2·5 grams daily in divided doses; usual maintenance 1 to 2 grams daily. Sampling is only useful if toxicity or poor compliance suspected.

**Note:** Lamotrigine: serious skin reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis have developed, especially in children. Most rashes occur in the first 8 weeks. Factors associated include concomitant use of valproate, initial lamotrigine dosing higher than recommended and more rapid dose escalation than recommended. Aplastic anaemia, bone marrow depression and pancytopenia have been associated rarely with lamotrigine. If suspected stop drug immediately.
LAMOTRIGINE tablets 25mg, 50mg, 100mg, 200mg; dispersible tablets 5mg, 25mg, 100mg

**Dose:** Monotherapy, initially 25mg daily for 14 days, increased to 50mg daily for further 14 days, then increased by a maximum of 50 to 100mg every 7 to 14 days, usual maintenance 100 to 200mg daily in 1 to 2 divided doses. Adjunctive therapy with valproate, initially 25mg every other day for 14 days, then 25mg daily for further 14 days, thereafter increased by a maximum of 25 to 50mg every 7 to 14 days, usual maintenance as above for monotherapy. Adjunctive therapy (with enzyme inducing drugs) without valproate, initially 50mg daily for 14 days then 50mg twice daily for a further 14 days, thereafter increased by maximum of 100mg every 7 to 14 days, usual maintenance 200 to 400mg daily in 2 divided doses.

Advise women on lamotrigine monotherapy that due to the risk of reduced seizure control whilst on combined hormonal contraception (CHC), and the potential for toxicity in the CHC-free week, the risks of using CHC may outweigh the benefits.

**Note:** For older or immobile patients on long-term phenytoin therapy, consider their increased risk of osteoporosis.

PHENYTOIN capsules 25mg, 50mg, 100mg, 300mg; suspension 30mg(base)/5mL; solution for injection 250mg/5mL

**Dose:** By mouth, initially 3 to 4mg/kg daily or 150 to 300mg daily (as a single dose or in 2 divided doses) increased gradually as necessary, usual dose 200 to 500mg daily.

**Therapeutic drug monitoring**
Phenytoin is the only antiepileptic where regular monitoring is helpful. Sampling for carbamazepine and sodium valproate is usually only used to confirm toxicity or poor compliance (see also local therapeutic drug monitoring guidance in Appendix 1).

- **Phenytoin:** has a narrow therapeutic index and the relationship between dose and plasma concentration is non-linear; small changes in dose may result in significant changes in plasma concentration. Measure plasma phenytoin concentration 3 days after initiating treatment to confirm the patient’s metabolism is not remarkably different from the norm, and then 7 days after initiation with subsequent doses of phenytoin adjusted accordingly. Within or around the therapeutic level, dose changes should be no larger than 25mg. If plasma concentrations are unchanged over a 3 to 5 day period, the monitoring interval may be increased to once weekly in the acute clinical setting. In stable patients requiring long-term therapy, generally monitor levels every 6 months. Take care when converting from the oral phenytoin (sodium) capsules to the phenytoin (base) suspension (90mg in 15mL is considered to be approximately equivalent to 100mg phenytoin sodium).

- **Carbamazepine:** has a wider therapeutic range than phenytoin. Start doses low and increase every 1 to 2 weeks.

- **Sodium valproate:** plasma concentrations do not always correlate with efficacy, hence routine monitoring is usually unhelpful.

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. Refer to the BNF for doses of the preparations below.

- **CLOBAZAM** tablets 10mg
  Clobazam 10mg is useful in catamenial epilepsy and for the prevention of further seizures in patients who tend to have seizure clusters. It should only be prescribed for epilepsy and the prescription must be endorsed ‘SLS’.

- **CLONAZEPAM** tablets 500 micrograms, 2mg; oral solution 500 micrograms/5mL

- **ESLICARBAZEPINE** tablets 800mg

- **ETHOSUXIMIDE** capsules 250mg
**GABAPENTIN** capsules 100mg, 300mg, 400mg; tablets 600mg

**LACOSAMIDE** tablets 50mg, 100mg, 150mg, 200mg

**Note:** Levetiracetam oral solution 100mg/mL; risk of medication errors associated with overdose

- always prescribe the dose in mg with mL equivalence based on the correct age and body weight
- advise the patient and/or caregiver on how to measure the prescribed dose
- see full advice at https://assets.publishing.service.gov.uk/

**LEVETIRACETAM** tablets 250mg, 500mg, 750mg, 1 gram; oral solution 100mg/1mL

**BRIVARACETAM** tablets 10mg, 25mg, 50mg, 75mg, 100mg; oral solution 50mg/5mL; solution for infusion 50mg/5mL

**OXCARBAZEPINE** tablets 150mg, 300mg, 600mg

**PERAMPANEL** tablets 2mg, 4mg, 6mg, 8mg, 10mg, 12mg

**PHENOBARBITAL** tablets 15mg, 30mg, 60mg; oral solution 50mg/5mL (sugar- and alcohol-free) [unlicensed]; solution for injection 30mg/1mL, 200mg/1mL. Use of alcohol-free solution is recommended for children. Maintain patients on a specific generic tablet/unlicensed oral solution.

**PREGABALIN** capsules 25mg, 50mg, 75mg, 100mg, 150mg, 200mg, 225mg, 300mg; oral solution 100mg/5mL

**PRIMIDONE** tablets 250mg

**TOPIRAMATE** tablets 25mg, 50mg, 100mg, 200mg; sprinkle capsules 15mg, 25mg, 50mg

**ZONISAMIDE** capsules 25mg, 50mg, 100mg

### For rescue medication

Midazolam (or in occasional circumstances rectal diazepam) is used for clusters or prolonged generalised seizures.

**Note:** Plasma midazolam concentrations are markedly increased by co-administration of CYP3A4 inhibitors eg **antibacterials** (erythromycin, clarithromycin) and **antifungals** (ketoconazole, itraconazole, and fluconazole). After a single dose of oromucosal midazolam in patients on these drugs, careful monitoring of the clinical effects and vital signs is recommended; for further information see Epistatus SPC.

**MIDAZOLAM** (Epistatus®) pre-filled oral syringe 10mg/1mL; pre-filled oral syringes [unlicensed] 2.5mg/0.25mL, 5mg/0.5mL, 7.5mg/0.75mL; oromucosal solution 50mg/5mL [unlicensed]

**Dose:** Intranasal or buccal midazolam is used in accordance with Highland guidelines for staff administering and providing training in the use of buccal (or nasal) midazolam, available on Intranet, and ‘Guidelines for staff administering and providing training in the use of buccal midazolam’, also on Intranet. Midazolam should be initiated by specialist epilepsy services only. Refer to specialist for advice. Brand name prescribing is recommended to ensure carers receive the brand they have been trained to use.

**Note:** Intramuscular diazepam is not recommended for rescue medication.
For status epilepticus

Refer to guidance on ‘Management of prolonged seizures’.

**Note:** Complex partial status epilepticus with loss of awareness is treated as for convulsive status epilepticus.

**MIDAZOLAM**<sup>CD3</sup> (Epistatus®) pre-filled oral syringe 10mg/1mL; oromucosal solution 50mg/5mL [unlicensed]; *solution for injection 5mg/5mL, 50mg/50mL

**Dose:** *Intranasally or buccally*, 10mg.

**LORAZEPAM** solution for injection 4mg/1mL

**Dose:** *By slow intravenous injection* (into large vein), 4mg.

Lorazepam as a bolus is preferable to diazepam because of its long duration of antiepileptic action.

**DIAZEPAM** rectal solution tubes 2·5mg/1·25mL, 5mg/2·5mL, 10mg/2·5mL; emulsion for injection 10mg/2mL

**Dose:** Adult and child over 12 years, *by rectum*, 10mg, repeated once after 10 to 15 minutes if necessary. *By intravenous injection*, 10mg at a rate of 0·5mL (2·5mg) per 30 seconds, repeated once after 10 minutes if necessary. Intravenous infusion of diazepam is potentially hazardous (especially if prolonged) calling for close and constant observation and best carried out in a hospital with intensive care facilities. Diazemuls® injection is licensed for intravenous administration only.

**PHENYTOIN** solution for injection 250mg/5mL

**Dose:** Refer to ‘Guideline for phenytoin dose calculation’

**SODIUM VALPROATE**<sup>S</sup> solution for injection 300mg/3mL

For emergency use only. Note risk of abnormal pregnancy outcomes, liver dysfunction and contraindication in patients with certain mitochondrial disorders.

**LEVETIRACETAM** concentrate for solution for infusion 500mg/5mL

For use where other medicines are contra-indicated.

**PARALDEHYDE** enema 50% in olive oil [unlicensed]

Use in Paediatrics in accordance with Children’s BNF (BNFC). Available from special-order manufacturers; for information contact Medicines Information.

**4.9 DRUGS USED IN PARKINSONISM AND RELATED DISORDERS**

Refer patients with suspected Parkinson’s disease (PD) early, before beginning treatment, to a clinician with relevant expertise, who should be involved in both initiation and ongoing monitoring of drug therapy. Therapy for PD should be multi-disciplinary; drug treatment is only one aspect. Refer to:

- ‘Parkinson’s disease guideline’
- ‘Alternative methods of administration for Parkinson’s disease medicines’
- ‘Inpatient management of Parkinson’s including nil by mouth guidance’
- Patient information leaflet, ‘Dopamine agonist medication used to treat Parkinson’s and restless legs’.
- SIGN 113 ‘Diagnosis and pharmacological management of Parkinson’s disease’.
Note: Excessive daytime sleepiness and sudden onset of sleep can occur with dopamine agonists, co-careldopa and co-beneldopa. Warn patients starting treatment with these drugs of the possibility of these effects and of the need for caution when driving or operating machinery.

Levodopa and dopa-decarboxylase inhibitors

**FIRST CHOICE:** CO-BENELDOPA  
**SECOND CHOICE:** CO-CARELDOPA

___

CO-BENELDOPA (benserazide/levodopa) capsules (Madopar®) 12.5/50, 25/100, 50/200 (in mg); dispersible tablets 12.5/50, 25/100 (in mg); (Madopar® CR) m/r capsules 25/100 (in mg)

**Dose:** Initially 62.5mg 3 to 4 times daily, increase according to response.

Note: When using co-careldopa, the total daily dose of carbidopa should be at least 70mg. A lower dose may not achieve full inhibition of peripheral dopa-decarboxylase, with a resultant increase in side-effects. Therefore, Sinemet-110® is not usually recommended for initiation of therapy.

CO-CARELDOPA (carbidopa/levodopa) tablets (Sinemet®) 12.5/50, 10/100, 25/100, 25/250 (in mg); m/r tablets (Half Sinemet® CR) 25/100, (Sinemet® CR) 50/200 (in mg)

**Dose:** Initially 62.5mg 3 to 4 times daily, increased according to response.

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**Available preparations containing levodopa and dopa-decarboxylase inhibitors**

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Brand name</th>
<th>Drug components</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co-beneldopa</td>
<td>Madopar® 62.5 caps</td>
<td></td>
<td>A generic product is not available, but, generic prescribing is preferred.</td>
</tr>
<tr>
<td></td>
<td>50mg 12.5mg</td>
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<td>Prescribers should take care with what they prescribe.</td>
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<tr>
<td></td>
<td>Madopar® 125 caps</td>
<td>100mg 25mg</td>
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<tr>
<td></td>
<td>Madopar® 250 caps</td>
<td>200mg 50mg</td>
<td></td>
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<tr>
<td></td>
<td>Madopar® dispersible tabs</td>
<td>50mg 12.5mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Madopar® CR</td>
<td>100mg 25mg</td>
<td></td>
</tr>
<tr>
<td>Co-careldopa</td>
<td>Co-careldopa 10/100 tabs</td>
<td>100mg -</td>
<td>The total daily dose of carbidopa should be at least 70mg. A lower dose may not achieve full inhibition of extracerebral dopa-decarboxylase, with a resultant increase in adverse effects.</td>
</tr>
<tr>
<td></td>
<td>25/100 tabs</td>
<td>100mg 25mg</td>
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<tr>
<td>Sinemet®-62.5 tabs</td>
<td>50mg 12.5mg</td>
<td>-</td>
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</tr>
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<td>Sinemet®-Plus tabs</td>
<td>100mg 25mg</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Sinemet®-275 tabs</td>
<td>250mg 25mg</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Half Sinemet® CR tabs</td>
<td>100mg 25mg</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>
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Sinemet® CR tabs 200mg - 50mg -

Carbidopa with entacapone and levo-dopa

| Stanek® | 50/12.5/200 | 50mg | - | 12.5mg | 200mg |
| Stanek® | 100/25/200 | 100mg | - | 25mg | 200mg |
| Stanek® | 150/37.5/200 | 150mg | - | 37.5mg | 200mg |
| Stanek® | 200/50/200, 75/18.75/200, 125/31.25/200, 175/43.75/200 | 200mg | - | 50mg | 200mg |

(Stanek® is equivalent to Stalevo®)

Only 1 tablet of Stanek® for each dose, to limit the amount of entacapone taken. Maximum 10 tablets daily.

Dopamine-receptor agonists

Note: Dopamine agonists

- **Impulse control:** all dopamine agonists and levodopa can lead to a problem with impulse control which can lead to gambling, hypersexuality, overeating and excessive shopping. If these develop after the initiation of dopamine agonists seek urgent specialist review: patients will often not recognise these as medicine side-effects and so will need to be asked specifically. Provide a patient information leaflet to all patients on initiation with a dopamine agonist and remind them on a dose increase and when adding in other levodopa therapies.

- Nausea and vomiting can be a particular problem when uptitrating dopamine agonists. Consider co-prescription of domperidone.

- All dopamine agonists require careful dose titration.

- All dopamine agonists can cause postural hypotension, neuropsychiatric adverse effects including psychosis, and leg oedema.

- For use in the management of restless legs syndrome see guidance.

**FIRST CHOICE:** ROPINIROLE

**SECOND CHOICE:** PRAMIPEXOLE

**ROPINIROLE** tablets 250 micrograms, 500 micrograms, 1mg, 2mg, 5mg; m/r tablets 2mg, 4mg, 8mg

**Dose:** Initially 750 micrograms daily in 3 divided doses, increased by increments of 750 micrograms at weekly intervals to 3mg daily; further increased by increments of up to 3mg at weekly intervals according to response; usual range 3 to 9mg daily; maximum 24mg daily.

**PRAMIPEXOLE** tablets 88 micrograms, 180 micrograms, 350 micrograms, 700 micrograms; m/r tablets 260 micrograms, 520 micrograms, 1·05mg, 2·1mg, 3·15mg

**Dose:** tablets, initially 88 micrograms 3 times daily, doubled every 7 days if tolerated to 350 micrograms 3 times daily; further increased if necessary by 180 micrograms 3 times daily at weekly intervals; maximum 3·3mg daily in 3 divided doses; m/r tablets, initially 260 micrograms once daily, doubling the dose every 7 days to 1·05mg once daily; if necessary, increase further by 520 micrograms at weekly intervals; maximum 3·15mg once daily. Note dosage reduction in renal impairment.

**Note:** Rotigotine: If switching patients to transdermal rotigotine from oral levodopa/dopamine agonists, refer to advice in ‘Impaired oral intake advice for patients with Parkinson’s’.

**ROTIGOTINE** transdermal patches 1mg/24 hours, 2mg/24 hours, 3mg/24 hours, 4mg/24 hours, 6mg/24 hours, 8mg/24 hours
Dose: Parkinson’s disease, initially apply 2mg/24 hours patch, increased in steps of 2mg/24 hours at weekly intervals if required; maximum as monotherapy 8mg/24 hours, maximum as adjunctive therapy with levodopa 16mg/24 hours.

**APOMORPHINE** solution for injection 20mg/2mL, 50mg/5mL; solution for injection, pen injector 30mg/3mL; solution for infusion, pre-filled syringe 50mg/10mL

**Dose:** Under specialist advice only, by subcutaneous injection, usual range (after initial titration) 3 to 30mg daily in divided doses; can be given by subcutaneous infusion if requiring more than 10 injections daily; maximum total daily dose 100mg.

**Other dopaminergic drugs**

**Note:** Entacapone may cause:
- urine to be coloured reddish-brown
- gastro-intestinal upset, particularly diarrhoea.

**ENTACAPONE** tablets 200mg

**Dose:** 200mg at the same time as each dose of co-beneldopa or co-careldopa, maximum 2 grams daily.

**STANEK®** (levodopa, carbidopa, entacapone) tablets 50/12.5/200, 75/18.75/200, 100/25/200, 125/31.25/200, 150/37.5/200, 175/43.75/200, 200/50/200 (in mg) (equivalent to Stalevo®)

**AMANTADINE** capsules 100mg, syrup 50mg/5mL

**Dose:** Peak dose dyskinesia, 100mg daily increased after 1 week to 100mg twice daily, (morning dose and second dose no later than 4pm) usually in conjunction with other treatment; some patients may require higher doses, maximum 400mg daily. Older patients, 65 years and over, 100mg daily adjusted according to response.

**SELEGILINE** tablets 5mg, 10mg; oral lyophilisates (Zelapar®) 1.25mg

**Dose:** Tablets, 5mg at breakfast and midday, oral lyophilisates, initially 1.25mg before breakfast, place tablets on tongue and allow to dissolve.

**RASAGILINE** tablets 1mg

**Dose:** 1mg daily.

Refer to section 4.2 for antimuscarinic drugs used in Parkinsonism.

Drugs used in postural tremor, chorea, tics, Huntington's chorea and related disorders

**Note:** The drugs in this section are unsuitable for the management of Parkinson’s disease.

**Chorea and tics**

**HALOPERIDOL** tablets 1.5mg, 5mg, 10mg; capsules 500 micrograms; oral liquid 10mg/5mL; solution for injection 5mg/1mL

**Dose:** By mouth, 500 micrograms to 1.5mg 3 times daily adjusted according to response. 10mg daily may occasionally be required in Tourette syndrome.

**TETRABENAZINE** tablets 25mg

**Dose:** Movement disorders, initially 12.5mg twice daily (older patients 12.5mg daily) gradually increased to 12.5mg to 25mg 3 times daily; maximum 200mg daily. Moderate to severe tardive dyskinesia, initially 12.5mg daily; gradually increased according to response.
TRIHEXYPHENIDYL tablets 2mg, 5mg
Anticholinergic.

CLONIDINE tablets 25 micrograms
Used for Tourette syndrome [off-label].

Essential tremor

PROPRANOLOL tablets 10mg, 40mg; m/r capsules 80mg, 160mg
**Dose:** Essential tremor or tremors associated with anxiety or thyrotoxicosis, 40mg 2 or 3 times daily, increased if necessary; 80 to 160mg daily is usually required for maintenance.

PRIMIDONE tablets 50mg
**Dose:** For patients intolerant to propranolol, but only under specialist advice, initiate at 12.5 to 25mg daily then adjust dose according to response.

Motor neurone disease

RILUZOLE tablets 50mg, oral suspension 25mg/5mL
Used for motor neurone disease under specialist supervision. Monitor liver function as per SPC.

Torsion dystonias and other involuntary movements

**FIRST CHOICE:** BOTULINUM TOXIN TYPE A (XEOMIN®)

BOTULINUM TOXIN TYPE A powder for solution for injection vial 50 units, 100 units (Xeomin®), powder for solution for injection vial 50 units, 100 units (Botox®), powder for solution for injection vial 300 units, 500 units (Dysport®)
Also used under specialist advice for migraine (Section 4.7), bladder dysfunction and urinary incontinence, spasticity (Section 10.2), blepharospasm (Section 11.8).

**Note:** Botulinum toxin type B is not interchangeable with other botulinum toxin preparations.

BOTULINUM TOXIN TYPE B solution for injection vial 2500units/0.5mL, 5000 units/1mL, 10 000units/2mL (NeuroBloc®)

Management of primary (idiopathic) restless legs syndrome (RLS)

Refer to guidance on the management of RLS, cautions in dopamine agonist use and patient information leaflet on dopamine agonists.

PRAMIPEXOLE tablets 88 micrograms, 180 micrograms, 350 micrograms
**Dose:** RLS, initially 88 micrograms once daily 2 to 3 hours before bedtime, dose doubled every 7 days if necessary; maximum dose 540 micrograms daily. Repeat dose titration if restarting treatment after an interval of more than a few days.

ROPINIROLE tablets 250 micrograms, 500 micrograms, 1mg, 2mg
**Dose:** RLS, initially 250 micrograms at night for 7 days, increased if tolerated to 500 micrograms at night for 7 days and then to 1mg at night for 7 days; further increased at weekly intervals in steps of 500 micrograms daily according to response; usual dose 2mg at night; maximum dose 4mg daily. Repeat dose titration if restarting treatment after an interval of more than a few days.
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Note: Rotigotine is accepted for use within NHS Scotland for the symptomatic treatment of moderate to severe idiopathic RLS in adults. It should only be used in patients with a baseline score of 15 points or more on the International Restless Legs Syndrome Rating Scale.

Rotigotine transdermal patches 1mg/24 hours, 2mg/24 hours, 3mg/24 hours
Dose: RLS, initially apply 1mg/24 hours patch, increased in steps of 1mg/24 hours at weekly intervals if required; maximum 3mg/24 hours.

4.10 Drugs Used in Substance Dependence

Alcohol Dependence

For further information refer to:
- NICE CG115 ‘Alcohol-use disorders’ at www.nice.org.uk.

Acamprosate, disulfiram and naltrexone are licensed for maintenance of abstinence after alcohol withdrawal. Baclofen is also used [off-label] in the treatment of alcohol dependency – see http://www.choiceandmedication.org.

Acamprosate e/c tablets 333mg
Dose: 18 to 65 years, 60kg and over, 666mg 3 times daily; less than 60kg, 666mg at breakfast, 333mg at midday and 333mg at night.
Acamprosate treatment, in combination with counselling, should be initiated during or immediately after the alcohol withdrawal period. Maintain treatment during relapse, unless clinical judgement is that acamprosate has led to no change in pattern of substance use. The recommended period of treatment is one year.

Note: Warn those taking disulfiram, and their families and carers, about:
- The interaction between disulfiram and alcohol (which may also be found in food, perfume, aerosol sprays etc), the symptoms of which may include flushing, nausea, palpitations and, more seriously, arrhythmias, hypotension and collapse.
- The rapid and unpredictable onset of the rare complication of hepatotoxicity; advise patients that if they feel unwell or develop a fever or jaundice that they should stop taking disulfiram and seek urgent medical attention.

Disulfiram tablets 200mg
Dose: 200mg daily, should not be continued for longer than 6 months without review.
Only use a loading dose with specialist advice. Ensure that alcohol is not consumed for at least 24 hours before initiating treatment. In the initial stages of treatment, Community Nurse (Addictions) involvement is desirable. Follow specialist advice on monitoring and during treatment: monitor patients at least every 2 weeks for the first 2 months, then each month for the following 4 months, and at least every 6 months thereafter.

In order for this treatment to be successful the patient must be motivated; offer the information leaflet available at http://www.choiceandmedication.org. Maximum benefit is achieved with supervised treatment.

Naltrexone tablets 50mg
Dose: Relapse prevention in alcohol dependence in patients free of opioids, 50mg daily as a maintenance dose. Check liver function before starting naltrexone and at 3-monthly intervals for one year. Warn patients against use of opioids, eg in OTC cough medication and analgesics.

Alcohol withdrawal: seek specialist advice:
- Vitamin supplementation: alcohol dependent individuals requiring detoxification should be offered Pabrinex® in addition to oral thiamine. Patients detoxifying in the community should be given Pabrinex® if they present with features which put them at risk of Wernicke’s
encephalopathy (those with diarrhoea, vomiting, physical illness, weight loss, poor diet). Refer to section 9.6, ‘Guidelines for administration of Pabrinex®/thiamine in alcohol detoxification’. There is a PGD for the administration of Pabrinex® in primary care settings on the Intranet.

- **consider choice of drug for alcohol withdrawal** (see section 4.2):
  - chlordiazepoxide is preferred for alcohol withdrawal in the community because of lesser toxicity in overdose and a lower street resale value. Also see Patient Group Direction (PGD) on Intranet for the supply of chlordiazepoxide 10mg capsules.
  - diazepam is recommended if there is a risk of seizures; it should be used in secondary care facilities only.

- **consider choice of medication regimen**: there are two approaches to alcohol withdrawal: symptom trigger (ST) or fixed dose (FD) regimens. ST is the 'gold standard' (shorter ‘detox’ and less benzodiazepine use) but requires staff to be trained in the assessment of the symptoms, the administration of medication and to consider whether they have sufficient time in their jobs to be able to do this and use the scoring sheets (without this level of training and time then there is a risk of a paradoxical increase in the length of ‘detox’ and the amount of benzodiazepines used). The following medication regimens are available on the intranet:
  - ST scoring sheets for chlordiazepoxide and diazepam
  - FD chlordiazepoxide protocol.

### Nicotine dependence

Refer to the BNF and guidance on ‘Smoking cessation interventions’. Smoking cessation interventions are a cost-effective way of reducing ill health and prolonging life. Advise smokers to stop and offer help, with follow-up when appropriate. When possible, smokers should have access to a smoking cessation advisor and/or a pharmacist for behavioural support. Encourage smokers who are not ready to stop smoking or are unable to stop in one step to reduce tobacco use in preparation for a future quit attempt.

NICE guidance (www.nice.org.uk) recommends that NRT or varenicline should be prescribed:
- along with advice, encouragement and support as part of the smoking cessation programme.
- taking into account the person’s intention and motivation to quit and how likely it is they will follow the course of treatment.

Use NRT or varenicline as a component of a smoking cessation support programme in accordance with SMC advice. Do not offer any combination of varenicline and NRT.

**NICOTINE OTC**: see formulations and brands listed in table below.

**Dose**: Refer to BNF and ‘Smoking cessation interventions’.

<table>
<thead>
<tr>
<th>NICOTINE formulations</th>
<th>First choice</th>
<th>Alternative choices</th>
</tr>
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<tbody>
<tr>
<td><strong>Transdermal patches</strong></td>
<td></td>
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<tr>
<td>7mg/24 hours</td>
<td>Nicotinell® patch</td>
<td>Niquitin® clear patches</td>
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<tr>
<td>14mg/24 hours</td>
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<td>21mg/24 hours</td>
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<td>10mg/16 hours</td>
<td>Nicorette Invisipatch®</td>
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<td>15mg/16 hours</td>
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<td>recommended for pregnant women and those who suffer sleep disturbance with the 24-hour patch</td>
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<tr>
<td>25mg/16 hours</td>
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<td><strong>Lozenges</strong></td>
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<tr>
<td>'Mini' lozenges 1.5mg, 4mg</td>
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<td>Niquitin Minis Lozenge®</td>
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<tr>
<td>Sublingual tablets 2mg</td>
<td></td>
<td>Nicorette Microtab®</td>
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<tr>
<td><strong>Chewing gum</strong></td>
<td>Nicotinell Gum®</td>
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</tr>
<tr>
<td>Chewing gum 2mg, 4mg</td>
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</table>
VARENICLINE tablets 500 microgram, 1mg, starter pack

**Dose:** Start 1 to 2 weeks before target stop date, initially 500 micrograms once daily for 3 days, increased to 500 micrograms twice daily for 4 days, then 1mg twice daily for 11 weeks. Reduce to 500 micrograms twice daily if not tolerated. Avoid abrupt withdrawal except where significant adverse drug reactions occur (see BNF); there is a risk of relapse, irritability, depression and insomnia on discontinuation (consider dose tapering on completion of the 12 week course). The benefits of an additional treatment course in those who have stopped smoking after the initial 12 weeks of therapy appear modest.

**Opioid dependence**

For further information refer to the 2007 guidance ‘Drug misuse and dependence: UK guidelines on clinical management’ (www.gov.uk) and ‘Prescribing guidelines for the management of opiate misuse using methadone or buprenorphine’ on Intranet. National guidance recommends daily supervised consumption of methadone or buprenorphine or buprenorphine with naloxone for the first 3 months of treatment.

**Pain management:** for guidance on pain management in patients on long-term methadone, buprenorphine or buprenorphine with naloxone seek specialist advice. The Maudsley Prescribing Guidelines recommend that, for methadone prescribed patients requiring analgesia, non-opioid analgesia (eg paracetamol, NSAIDs) should be used in preference. If opioid analgesia is indicated (eg codeine, dihydrocodeine, morphine), the drug should be titrated accordingly against pain relief, with the methadone dose remaining constant to alleviate withdrawal symptoms. Titrating the methadone dose to provide analgesia may be used in certain circumstances but should only be carried out by experienced specialists. For further information see also ‘Pain and substance misuse; improving the patient experience’ at www.britishpainsociety.org.


**Opioid conversions:** for advice on conversions from opioids to methadone or buprenorphine contact Drug and Alcohol Services at Osprey House, Inverness tel: 01463 704000 (Raigmore Hospital Switchboard) or Argyll and Bute Addiction Team, Argyll and Bute Hospital, Lochgilphead, tel: 01546 602323.

**Note: Methadone**

- in patients with recognised risk factors for QT-prolongation, or in case of concomitant treatment with drugs that have a potential for QT-prolongation, ECG monitoring is recommended prior to methadone treatment, with review on dose stabilisation. In patients without recognised risk factors for QT-prolongation, ECG monitoring is recommended before dose titration above 100mg/day.
- in methadone overdose when using naloxone be aware of its short duration of action.

**METHADONE CD2** oral solution 1mg/mL

**Dose:** Initially 10 to 30mg daily, increased by 10mg daily until no signs of withdrawal or intoxication, usual dose 60 to 120mg daily. Higher doses may be used in consultation with specialist units. Usual maximum weekly increase should not exceed 30mg.
Note: Buprenorphine: In those who have not undergone opioid withdrawal, administer buprenorphine at least 12 hours after last use of opioid or when signs of withdrawal appear. For those receiving methadone, reduce the dose of methadone to maximum 30mg daily before starting buprenorphine. Start buprenorphine at least 24 hours after methadone.

**BUPRENORPHINE** CD³ sublingual tablets 400 micrograms, 2mg, 8mg

**Dose:** By sublingual administration, initially, 800 micrograms to 8mg daily (dividing the daily dose may be useful), adjusted according to response; maximum 32mg daily; withdraw gradually.

**BUPRENORPHINE WITH NALOXONE** CD³ sublingual tablets 2mg/500 micrograms, 8mg/2mg

**Dose:** By sublingual administration, expressed as buprenorphine, initially 2 to 8mg once daily; maximum 24mg daily.

Dihydrocodeine (section 4.7) should only be prescribed to drug misusers by clinicians with appropriate specialist competencies. There is a small evidence base that dihydrocodeine can be used effectively for maintenance although none that it is superior to other opioid medicines. Dihydrocodeine tablets are difficult to supervise, are short-acting (so need frequent dosing) and can be easily diverted (www.nta.nhs.uk).

Note: Lofexidine: monitor blood pressure and pulse rate on lofexidine initiation, for at least 72 hours or until a stable dose is achieved, and on discontinuation; discontinue treatment gradually over 2 to 4 days to reduce the risk of rebound hypertension.

**LOFEXIDINE** tablets 200 micrograms

**Dose:** Adjunctive treatment in opiate detoxification or precipitated withdrawal, initially 200 micrograms 4 times daily, increased as necessary in steps of 400 to 800 micrograms daily to maximum 2-4mg daily; recommended duration of treatment 7 to 10 days if no opioid use (but longer may be required). Higher doses may be used in specialist units.

Note: Naltrexone: warn patients taking naltrexone that an attempt to overcome the block could result in potentially fatal opioid intoxication.

**NALTREXONE** tablets 50mg

**Dose:** Commence under specialist supervision, Day 1, test urine to confirm patient is opioid and methadone-negative, give 25mg then observe for an hour. If tolerated, subsequent doses can be increased to 50mg daily as a maintenance dose. Check liver function before starting naltrexone and at 3-monthly intervals for one year.

Benzodiazepine dependence

Benzodiazepines should only be prescribed to drug misusers by clinicians with appropriate specialist competencies.

4.11 DRUGS FOR DEMENTIA

The 3 cholinesterase inhibitors donepezil, galantamine, rivastigmine and the NMDA partial antagonist memantine should only be initiated in dementia according to the shared care guidance on Intranet. For further information refer to NICE CG42, NICE TA217. For guidance on the use of psychotropics in older adults refer to guidance. The cholinesterase inhibitors are licensed in mild to moderate dementia.

**DONEPEZIL** tablets 5mg, 10mg; orodispersible tablets 5mg, 10mg

**Dose:** Initially 5mg once daily, increased if necessary after 1 month to 10mg once daily. Place the orodispersible tablet on the tongue, allow to disperse and swallow.
GALANTAMINE m/r capsules 8mg, 16mg, 24mg; oral solution 4mg/1mL
Dose: m/r capsules, initially 8mg once daily for 4 weeks increased to 16mg once daily for 4 weeks; maintenance 16 to 24mg daily.

RIVASTIGMINE capsules 1.5mg, 3mg, 4.5mg, 6mg; oral solution 2mg/mL; transdermal patch 4.6mg/24hours, 9.5mg/24 hours
Dose: By mouth, initially 1.5mg twice daily, increased in steps of 1.5mg twice daily at intervals of at least 2 weeks according to response and tolerance; usual range 3 to 6mg twice daily; maximum 6mg twice daily; transdermal patch, initially apply 4.6mg/24 hours patch daily, if well tolerated increase to 9.5mg/24 hours patch daily after no less than 4 weeks. If switching a patient from oral to transdermal therapy refer to BNF.

Memantine is an alternative treatment recommended in moderate Alzheimer’s disease where the cholinesterase inhibitors cannot be used. It is also recommended as an option in severe Alzheimer’s disease.

MEMANTINE tablets 10mg, 20mg; oral solution 5mg/actuation (10mg/mL)
Dose: initially 5mg once daily, increased in steps of 5mg at weekly intervals to maximum of 20mg daily. Reduced dose in renal impairment, refer to BNF.
## ANXIETY SPECTRUM DISORDERS

*(see also ‘Generalised anxiety disorder (GAD)’ guidance on next page)*

<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>Generalised anxiety disorder (GAD)</th>
<th>Panic disorder</th>
<th>Post-traumatic stress disorder (PTSD)</th>
<th>Obsessive-compulsive disorder</th>
<th>Social phobia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irrational worries</td>
<td>sudden unpredictable episodes of severe anxiety</td>
<td>history of a traumatic life event (as perceived by the sufferer)</td>
<td>obsessional thinking (eg constantly thinking that the door has been left unlocked)</td>
<td>extreme fear of social situations (eg eating in public places or public speaking)</td>
<td></td>
</tr>
<tr>
<td>Motor tension</td>
<td>Shortness of breath</td>
<td>Emotional numbness or detachment</td>
<td>Compulsive behaviour (eg constantly going back to check)</td>
<td>fear of humiliation or embarrassment</td>
<td></td>
</tr>
<tr>
<td>Hypervigilance</td>
<td>Fear of suffocation/dying</td>
<td>Intrusive flashbacks or vivid dreams</td>
<td>Avoidant behaviour (eg never eating in restaurants)</td>
<td>Avoidant behaviour (eg never eating in restaurants)</td>
<td></td>
</tr>
<tr>
<td>Somatic symptoms (eg hyperventilation, tachycardia and sweating)</td>
<td>Urgent desire to flee</td>
<td>Disabling fear of re-exposure, causing avoidance of perceived similar situations</td>
<td>Anxious anticipation (eg feeling sick on entering a restaurant)</td>
<td>Anxious anticipation (eg feeling sick on entering a restaurant)</td>
<td></td>
</tr>
<tr>
<td>Present all/most of time.</td>
<td>Short-lived episodes of sudden unpredictable severe anxiety</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Emergency management**

- Benzodiazepines (normally for short-term use only: max 2 to 4 weeks, very rarely long-term).
- Benzodiazepines (have a rapid effect, although panic symptoms return quickly if the drug is withdrawn).
- Not usually appropriate.
- Not usually appropriate.
- Benzodiazepines (have a rapid effect and may be useful on a 'when required' basis).

**Non-drug treatments**

- These are equally as effective as drug treatment.

**Drug treatment**

- Treatment of anxiety may prevent the subsequent development of depression. See section 4.1 and ‘Guidance for the treatment of GAD’.
- For moderate panic disorder consider individual CBT* which can be augmented with bibliotherapy, internet/computer packages and/or group CBT*.
- In more severe cases, individual CBT* (up to 20 sessions) supplemented with written material.
- Best evidence is for guided self-help and group psychoeducation (eg Stresspac/www.lttf.com) for mild cases.
- CBT* for moderate or severe cases.
- First choice: sertraline or alternative SSRIs** (although may initially exacerbate symptoms. A lower starting dose of 25mg sertraline is often required).
- Second-line antidepressant: venlafaxine or mirtazapine.
- Referral for specialist advice (options include alternative antidepressants, pregabalin***, duloxetine*** or antipsychotic).
- NICE do not recommend benzodiazepines.
- SSRIs** (therapeutic effect can be delayed and patients can experience an initial exacerbation of panic symptoms).
- Referral for specialist advice.
- Best evidence is for brief trauma-focussed CBT* if presentation is mild (although this should not be offered to asymptomatic patients as a preventative measure).
- Beyond mild presentations, trauma-focussed CBT or Eye Movement Desensitisation and Reprocessing (EMDR) are both well supported.
- Best evidence is for CBT*, which should incorporate Exposure and Response Prevention (Ex/RP). This holds across all levels of severity.
- Combined drug and psychological therapy may be the most effective option.
- Best evidence is for guided self-help for mild cases (bibliotherapy or via internet).
- For moderate and severe cases, consider either behavioural therapy (incorporating exposure) or CBT* (incorporating exposure and cognitive restructuring).
- If presentation is severe enough to meet criteria for avoidant personality disorder, consider CBT (20 sessions).

---

*Cognitive behavioural therapy (CBT): GP referral for CBT via SCI gateway or free telephone service, GP or self-referral, to NHS Living Life (tel: 0800 328 9655)

** If using citalopram note cautions on its use: see www.gov.uk/drug-safety-update

*** For specialist initiation only: pregabalin and duloxetine are licensed for the treatment of GAD however the manufacturers have not made a submission to SMC in this indication and consequently neither has received a recommendation for this use in NHS Scotland. For pregabalin: use twice daily dosing and higher strength capsules as appropriate, to minimise capsule burden.

---

**Lead reviewer:** Mental Health Review Group  
**Date:** January 2017  
**Version:** 4  
**Approved by:** Formulary Subgroup of NHS Highland ADTC  
**Review date:** January 2019  
**Warning:** document uncontrolled when printed
**GENERALISED ANXIETY DISORDER (GAD): TREATMENT GUIDANCE**

(see also ‘Anxiety spectrum disorders’ table on previous page)

**Introduction**
Before treating anxiety, first establish whether it is pathological or non-pathological. Anxiety is a normal human emotion which should not require treatment unless disproportionate to the context in which it occurs by either degree or duration. Explanation of this may be reassuring. For example, anxiety associated with bereavement/loss should not be treated with medication unless it fulfills these criteria even if it causes acute distress and/or dysfunction. Benzodiazepines in particular should be avoided in these situations as they are associated with poor long-term outcomes and an increased risk of psychological processing difficulties including post-traumatic stress disorders.

If anxiety is assessed as pathological, cognitive behavioural therapy (CBT) is a non-drug therapy which may be an appropriate first-line treatment for many patients (GP referral for CBT via SCI gateway or free telephone-based service, GP or self-referral, to NHS Living Life tel: 0800 328 9655). Drug treatments alone may be appropriate first-line for others, and there is some evidence that optimal outcome is achieved by combining psychological and drug therapies. Self-help CBT-based approaches may be useful for less severe presentations.

The Highland Formulary recommends both antidepressants and pregabalin as a number of drug treatments for GAD. This guidance provides additional information on how these drugs should be used.

Where drug treatment is considered appropriate use SSRIs first-line. People with anxiety disorders may be particularly prone to the activating side-effects of antidepressants, therefore start the dose low and increase slowly. Inform the patient that the anxiolytic effect of antidepressants may be delayed (over 1 week or more) and that they may initially feel an increase in anxiety or agitation. Response is usually seen within 6 weeks and continues to increase over time.

Benzodiazepines should only be used as a short-term measure for a maximum of 2 to 4 weeks. They should be prescribed only with informed consent following discussion; this should include the association of benzodiazepines with the following:

- poor long-term outcomes in anxiety disorders
- risk of dependence
- impaired psychological processing
- impaired ability to drive
- disinhibition
- mood disturbance.

Propranolol treats physical symptoms of anxiety only. It has little effect on cognitive symptoms and will prevent any exposure process occurring. It appears to cause depression of mood in some patients. It is not recommended in the treatment of anxiety disorders.

Pregabalin and antipsychotics: pregabalin has evidence of benefit in the treatment of GAD and low-dose antipsychotics may also be of some value. These drugs should only be started by a psychiatrist in treatment-resistant anxiety; and neither pregabalin nor antipsychotics should be initiated in primary care.

**Treatment flowchart**

![Treatment flowchart](chart_image)

*see Highland Formulary section 4.1 and ’Anxiety Spectrum Disorders’ guidance.*

**Lead reviewer:** Mental Health Review Group
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## Antipsychotics – Relative Side-Effects
- see also section 4.2

### Typicals

<table>
<thead>
<tr>
<th>Drug</th>
<th>Anti-cholinergic</th>
<th>Cardiac</th>
<th>QT interval</th>
<th>EPSE</th>
<th>Hypotension</th>
<th>Sedation</th>
<th>Minor O/D</th>
<th>Weight gain*</th>
<th>Prolactin</th>
<th>Pro-convulsant</th>
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### Atypical

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<th>Hypotension</th>
<th>Sedation</th>
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<th>Weight gain*</th>
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<td>Aripiprazole</td>
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<td>Amisulpride</td>
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</tbody>
</table>

### Side-effects:
- •••• = marked effect
- ••• = moderate effect
- • = mild/transient effect
- O = little or no effect
- ? = no information

D = depot available
EPSE = extrapyrdamidal side-effects

* Local experience suggests quetiapine may have a moderate sedative effect and moderate to marked weight gain effect.
** Offer patient information leaflet ‘Weight gain and medicines used in mental health’ available on Intranet or from Pharmacy Department, New Craigs, tel: 01463 704000 (Raigmore Hospital Switchboard).

GUIDELINES FOR THE USE OF PSYCHOTROPICS IN OLDER ADULTS (GENERALLY OVER 65 YEARS OF AGE)

GENERAL
- Start with the lowest appropriate dose and titrate slowly upwards if necessary.
- **When the oral route (preferable) is unavailable use intramuscular (IM) route with caution.**
- Avoid the intravenous (IV) route.
- Avoid the use of Clopixol Acuphase®, chlorpromazine and long-acting benzodiazepines such as diazepam.
- Always check for possible interactions, cautions and contra-indications for individual patients.
- The bioavailability of drugs varies according to the route of administration. Adjust the dose accordingly.
- Do not routinely prescribe anticholinergics and avoid their use if possible.
- It is advised a pre-treatment ECG, specifically QT interval, is performed prior to commencing antipsychotic treatment.
- Avoid concurrent use of more than one antipsychotic/sedative where possible.
- **If in doubt seek specialist/liaison psychiatry advice.**

DEMENTIA

Features
Dementia is a gradually progressive, chronic and irreversible reduction in the previously attained level of intellectual, emotional and practical functioning. Features include memory impairment, disorientation, impoverished thought, language problems, loss of skills and socially inappropriate behaviour.

Management of challenging behaviour and agitation
Refer to NICE Guidance No 42 Dementia 2011 (www.nice.org.uk).

1. Establish and treat any physical exacerbating factors.
2. Consider depression (see over for treatment options).
3. Nursing intervention:
   a) reality orientation
   b) environmental modifications
   c) behavioural intervention
   d) occupational activities and distractions
   e) sensory stimulation.
4. If symptoms are **severe** consider the cautious use of medication (often **off-label**).

**Note 1:** The possibility of an increased risk of stroke and worsening cognitive decline should be considered in this population when prescribed antipsychotics. Prescriptions for antipsychotics should be reviewed regularly (minimum every 3 months) and stopped as soon as possible. Please refer to p12 of *Polypharmacy: Guidance for Prescribing In Frail Adults* for advice on the rationalisation of antipsychotics in patients with dementia.

Pharmacological options

a) Quetiapine (**off-label**), orally 25mg, dose adjusted as necessary; maximum dose in 24 hours is 100mg.

b) Lorazepam, orally 500 micrograms to 1mg; maximum dose in 24 hours is 2mg.

c) Cholinesterase inhibitors if not already prescribed for cognitive impairment.

**Note 2:** In Lewy Body type dementia and Parkinsonism there is marked sensitivity to antipsychotics and they should be avoided.
Challenging behaviours requiring urgent treatment (refer to the NHS Highland specialist emergency sedation policy for advice and physical monitoring requirements).

a) Haloperidol, orally 500 micrograms to 1mg repeated after 1 to 2 hours if necessary; maximum dose in 24 hours is 10mg. If oral route not available by intramuscular injection, 500 micrograms to 1mg repeated after 1 hour if necessary; maximum dose in 24 hours is 5mg.

and/or

b) Lorazepam 500 micrograms to 1mg orally or if not available by intramuscular injection. Leave at least 1 hour between doses. Maximum dose in 24 hours is 2mg.

For night time disturbance consider

a) Simple, short-acting hypnotic, eg zolpidem 5mg at night.

DELIRIUM (ACUTE CONFUSIONAL STATE)

Features

Associated with a precipitating illness, eg infection, delirium develops over hours or days. Common characteristics include confusion, deterioration in pre-existing cognitive function, fear, persecutory ideas, hallucinations and autonomic features such as sweating and tachycardia. It is usually fluctuating in course, often worse at night and resolves once the underlying condition is resolved.

Note 3: Remember delirium tremens, the management of which is different, specific and a medical emergency.

Management

Refer to NICE Guidance No 103 Delirium 2010 (www.nice.org.uk) and Scottish Delirium Association pathway.

1. Appropriate investigation, medication review and treatment of precipitating condition.
2. Maintain good physical condition, eg hydration, nutrition.
3. Nursing intervention:
   a) aid interpretation of the environment, eg adequate lighting
   b) avoid conflict and misinterpretations.
4. Cautious use of psychotropic medications for symptomatic relief of severe agitation, as they can exacerbate the confusional state.

Pharmacological options

a) Consider giving short-term (usually for 1 week or less) haloperidol or olanzapine (both off-label). Start at the lowest clinically appropriate dose and titrate cautiously according to symptoms.

If antipsychotics are contra-indicated (see note 2) seek specialist advice.
DEPRESSION

Refer to NICE Guidance 90 & 91 Depression in adults and in those with a chronic physical health problem 2009 (www.nice.org.uk).

Features

Persistent morbidly lowered mood (may present as unexplained physical symptoms) with associated biological (sleep and appetite disturbance) and cognitive (diminished concentration, memory impairment and agitation) symptoms. Depression may co-exist with dementia and physical illness.

Management

1. Assessment of aetiological factors and severity, including suicide risk.
2. Appropriate interventions with respect to contributing factors and physical illness.
3. Start an antidepressant for moderate to severe symptoms:
   a) Serotonin specific reuptake inhibitor (SSRI) eg sertraline 50mg once daily.

   **Note 4: Citalopram and escitalopram are associated with dose-dependent QT prolongation. Citalopram dose limited to 20mg and escitalopram dose limited to 10mg in over 65 year olds. Both medications are contra-indicated in combination with other drugs that prolong the QT interval, eg antipsychotics, domperidone.**

   b) Mirtazapine 15mg at night increased after 1 week to 30mg. (May be useful in patients who cannot tolerate an SSRI due to increased anxiety/agitation or GI upset.)

4. Evaluate effectiveness after 6 weeks of treatment or 9 weeks after a partial response and titrate dose accordingly. The length of treatment required in older adults may be considerably longer than in the general adult population.

5. Be aware of withdrawal/washout period when switching antidepressants.

If depression is severe then seek specialist psychiatric opinion early. If in doubt seek advice.
## PHYSICAL MONITORING REQUIREMENTS FOR PATIENTS WITH ENDURING MENTAL ILLNESS

<table>
<thead>
<tr>
<th>Test or measurement</th>
<th>Monitoring for all patients</th>
<th>Monitoring for specific drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Throat function</td>
<td>Yes</td>
<td>At start and every 6 months; more often if evidence of deterioration.</td>
</tr>
<tr>
<td>Liver function</td>
<td>Yes</td>
<td>At start and at 6 months.</td>
</tr>
<tr>
<td>Renal function</td>
<td>Yes</td>
<td>At start and every 6 months; more often if there is evidence of deterioration or the patient starts taking drugs such as ACE inhibitors, diuretics or NSAIDs.</td>
</tr>
<tr>
<td>Thyroid function</td>
<td>Yes</td>
<td>Urea and electrolytes every 6 months.</td>
</tr>
<tr>
<td>Blood (plasma) glucose</td>
<td>Yes</td>
<td>At start and at 6 months.</td>
</tr>
<tr>
<td>Lipid profile</td>
<td>Yes</td>
<td>At start and at 6 months; more often if evidence of elevated levels.</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Yes</td>
<td>At start and at 6 months.</td>
</tr>
<tr>
<td>Prolactin</td>
<td>Children and adolescents only.</td>
<td>At start and if symptoms of raised prolactin develop.</td>
</tr>
<tr>
<td>ECG</td>
<td>If indicated by history or clinical picture.</td>
<td>At start of treatment.</td>
</tr>
<tr>
<td>Weight and height</td>
<td>Yes</td>
<td>At start and when needed if the patient gains weight rapidly.</td>
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<tr>
<td>Drug screening and chest x-ray</td>
<td>If suggested by the history or clinical picture.</td>
<td>1 week after initiation and 1 week after every dose change until levels stable, then every 3 months.</td>
</tr>
<tr>
<td>EEG, MRI, CT scans</td>
<td>If organic aetiology or comorbidity suspected.</td>
<td>Only if there is evidence of ineffective-ness, poor adherence or toxicity.</td>
</tr>
<tr>
<td>Smoking/ alcohol</td>
<td>Yes</td>
<td>Every 6 months.</td>
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</table>

For patients on lamotrigine, do an annual health check, but no special monitoring tests are needed.

- a Every 6 months for people with rapid-cycling bipolar disorder, plus thyroid antibody levels if indicated, eg by thyroid function tests.
- b For children and adolescents, monthly for 6 months, then every 6 months.
- c Note that therapeutic levels and toxic levels of carbamazepine are close.

CG38 Bipolar Disorder. Adapted from NICE CG185 2014.
**ANTIDEPRESSANT GUIDANCE**
- see also section 4.3, ‘Antidepressant selection’ and ‘Antidepressant switching’ guidance

### Treatment

- **First choice** - antidepressant with best-fit profile. In the absence of special factors consider **fluoxetine** or **sertraline**. Where there is a risk of overdose, SSRIs and mirtazapine are safest, venlafaxine is of intermediate risk and tricyclics are the most toxic.
- Counsel patient following the bullet points below in achieving the best use of medicines.
- Review at 1 to 2 weeks for side-effects.
- Review again at 4 to 6 weeks to check response. Consider an earlier review in the 18 to 30 year age group. An adequate trial is a therapeutic dose for 4 weeks in adults and 6 weeks in older people. For a partial response obtained after 4 or 6 weeks, continue for 2 more weeks in the adult population (3 in older people) in an effort to convert to a full response.
- If a full response is not obtained, check compliance, reassess clinical condition, consider increased dose where appropriate or change to a different class of antidepressant. See **Antidepressant switching**.
- After remission of symptoms, continue treatment at the dose the patient responded to for a minimum of 6 months in adults (1 year in older people) to reduce the risk of relapse by up to 50%.
- Consider maintenance treatment for patients with:
  - 3 or more episodes in 5 years
  - more than 5 episodes
  - fewer episodes but with persistent risk factors present.

- Gradually reduce and stop antidepressants to avoid discontinuation reactions. Aim to achieve this over a period of at least 4 weeks. **Venlafaxine** and **paroxetine** tend to be most problematic due to their short half-lives. Offer patient information leaflet ‘A handy fact sheet on coming off antidepressants’, available at [www.choiceandmedication.org/nhs24](http://www.choiceandmedication.org/nhs24).

### Achieving the best use of medicines

- Give positive advice regarding the benefits of treatment.
- Reinforce that antidepressants are not addictive.
- Inform patients about the potential side-effects.
- Inform patients about probable lack of initial benefit.
- Advise on timing of dosage.
- Advise that treatment is likely to be continued for at least 6 months (12 months in older people).
- Reinforce the importance of not discontinuing treatment too early.
- Reassure regarding the low risk of discontinuation reactions provided a planned gradual approach is taken.
- Be aware of increased risk of suicidal behaviour in patients under 25 years old particularly at the beginning of treatment or if the dose changes.
## ANTIDEPRESSANT SELECTION

- see also section 4.3, ‘Antidepressant guidance’ and ‘Antidepressant switching’ guidance

<table>
<thead>
<tr>
<th>Drug group</th>
<th>Description</th>
<th>Suggested drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selective serotonin re-uptake inhibitors (SSRIs)</td>
<td>Recommended for first-line use, especially in older or physically ill patients (more susceptible to side-effects). Better-tolerated than TCAs and more likely to be prescribed at adequate doses for an adequate period. Fewer anticholinergic and cardiovascular side-effects than TCAs. Not without side-effects. These are mainly gastrointestinal e.g. nausea, diarrhoea.</td>
<td>Fluoxetine or sertraline</td>
</tr>
<tr>
<td>Norepinephrine and serotonin specific antidepressants (NASSAs)</td>
<td>Not for first-line use. Weight gain can be a problem. Low incidence of sexual dysfunction. May potentiate other centrally acting sedatives. Suitable for patients who require sedation but for whom a TCA is unsuitable.</td>
<td>Mirtazapine</td>
</tr>
<tr>
<td>Serotonin norepinephrine re-uptake inhibitor (SNRI)</td>
<td>Not for first-line use. May have greater efficacy than SSRIs at doses of 150mg or greater. Dose-responsive so can titrate dose for further effect. Side-effect profile similar to SSRIs but can lower/elevate blood pressure.</td>
<td>Venlafaxine</td>
</tr>
<tr>
<td>Tricyclic antidepressants (TCAs)</td>
<td>May be used first-line in certain circumstances. Use at adequate dosage, often limited by side-effects. Anticholinergic side-effects, e.g. constipation, blurred vision and dry mouth are common. Cardiovascular effects such as arrhythmias and hypotension can also occur. TCAs can prolong the QT interval. Sedation can be problematic but may also be useful in some patients. Tolerance to some side-effects can develop but may necessitate gradual dosage increases.</td>
<td>Clomipramine or Amitriptyline (specialist use only)</td>
</tr>
<tr>
<td>Norepinephrine re-uptake inhibitor (NARI)</td>
<td>Normally used after consultation with specialist services. Not sedating but insomnia can be a problem, as can anticholinergic side-effects.</td>
<td>There is no NARI in the formulary.</td>
</tr>
<tr>
<td>Monoamine-oxidase inhibitor (MAOI)</td>
<td>Always used after consultation with specialist services.</td>
<td>Phenelzine (specialist use only)</td>
</tr>
</tbody>
</table>
ANTIDEPRESSANT SWITCHING: ADVICE FROM NEW CRAIGS PHARMACY

When switching between selective serotonin reuptake inhibitors (SSRIs), tricyclic (TCAs) and related antidepressants (see section 4.3), it is safer to reduce the dose of the first antidepressant and discontinue it before starting the second antidepressant. This is not always possible. Cross-tapering is an option for some switches but should always be done cautiously. Cross-tapering with mirtazapine is usually low risk.

Fluoxetine and paroxetine are inhibitors of cytochrome P450 isoenzymes; concomitant use with TCAs may result in a 2 to 3-fold increase in plasma levels of these TCAs.

Assess patients on an individual basis to determine how quickly the switch can be done, taking into account the following factors:

- urgency of the switch.
- the patient’s physical condition. Caution is required in older patients and those with co-morbidities.
- the potential for close monitoring.
- the risk that the switching regimen will confuse the patient and result in medication error.
- the risk of discontinuation reactions which can be unpleasant (see PIL on Intranet)
  - higher risk with higher doses, longer duration of therapy (more than 6 weeks) and with antidepressants with a short half-life, eg venlafaxine and paroxetine.
  - lower risk with antidepressants with a long half-life, fluoxetine, and short duration of antidepressant therapy.
- the risk of serotonin syndrome which can be dangerous
  - serotonin syndrome is more likely to occur if the patient is on other drug therapy with serotonergic activity, for example triptans, tramadol, pethidine, selegiline, lithium and tricyclic antidepressants for neuropathic pain.

Table 1: Switching antidepressants: use this table in conjunction with the previous notes

<table>
<thead>
<tr>
<th>From</th>
<th>SSRI</th>
<th>TCA *</th>
<th>Venlafaxine</th>
<th>Mirtazapine</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSRI except fluoxetine</td>
<td>Reduce first SSRI gradually and stop. Leave 2 to 3 days then start second SSRI.</td>
<td>Reduce SSRI gradually and stop. Leave 2 to 3 days then start low dose TCA.</td>
<td>Reduce SSRI gradually and stop. Leave 2 to 3 days then start venlafaxine 37.5mg twice daily and increase as necessary.</td>
<td>Reduce SSRI dose and cross-taper cautiously.</td>
</tr>
<tr>
<td>Fluoxetine 20mg daily§</td>
<td>Stop fluoxetine abruptly. Start low-dose SSRI 4 to 7 days later and increase slowly.</td>
<td>Stop fluoxetine abruptly. Start low-dose TCA 4 to 7 days later and increase slowly.</td>
<td>Stop fluoxetine abruptly. Start venlafaxine 37.5mg twice daily 4 to 7 days later and increase slowly.</td>
<td>Stop fluoxetine abruptly. Start mirtazapine 15mg the following day and increase dose slowly.</td>
</tr>
<tr>
<td>TCA *</td>
<td>Reduce the dose of TCA to 25 to 50mg daily then stop. Leave 2 to 3 days then start SSRI.</td>
<td>Reduce the dose of TCA to 25 to 50mg daily then stop. Leave 2 to 3 days then start second TCA.</td>
<td>Reduce the dose of TCA to 25 to 50mg daily then stop. Leave 2 to 3 days then start venlafaxine 37.5mg twice daily and increase as necessary.</td>
<td>Reduce the dose of TCA and cross-taper cautiously.</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>Reduce venlafaxine gradually and stop. Leave 2 to 3 days then start SSRI.</td>
<td>Reduce venlafaxine gradually and stop. Leave 2 to 3 days then start low dose TCA.</td>
<td></td>
<td>Reduce venlafaxine dose and cross-taper cautiously.</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>Reduce mirtazapine dose and cross-taper cautiously.</td>
<td>Reduce mirtazapine dose and cross-taper cautiously.</td>
<td></td>
<td>Reduce mirtazapine dose and cross-taper cautiously.</td>
</tr>
</tbody>
</table>

* Cross-tapering clomipramine with venlafaxine or a SSRI is not recommended.
§ Fluoxetine at doses greater than 20mg may need to be withdrawn gradually rather than stopping abruptly.
ORLISTAT IN THE MANAGEMENT OF OBESITY

Drug treatment is not a long-term solution in weight management and is not part of local weight management pathways but can be considered as an adjunct to lifestyle interventions as per NICE CG189 where weight loss would lead to significant health benefit.

- Refer to shared care Adult Weight Management guidance on the Intranet.
- Never use orlistat as the sole element of treatment; only use where diet, physical activity and behavioural change are supported.
- Discontinue at 3-monthly reviews if weight loss targets not met. Not indicated for weight maintenance.
- Consider patients on an individual case basis following assessment of risk and benefit.
- Monitor regularly and offer support. Given that most adults gain weight, weight maintenance is the first goal of any intervention, with a focus on lifestyle changes to improve health.

Inadequate response to at least 3 months of supervised diet, exercise and behaviour modification, ie weight gain.

If BMI 30kg/m² or more

(or BMI 28 kg/m² or more with other risk factors such as type 2 diabetes, hypertension or hypercholesterolaemia (also consider ethnic group)).

Consider ORLISTAT* 120mg up to 3 times daily for 12 weeks + continued support for diet, physical activity and behavioural change.

Review at 12 weeks

Is weight loss at least 5% of body weight? (target may be lower in patients with type 2 diabetes).

Yes

Continue treatment (review every 3 months) + support for diet, physical activity and behaviour change.

No

Withdraw treatment: leave door open for behaviour change and continue support as appropriate.

At any stage between 4 and 12 months treatment discuss potential benefits and risks with the patient.

Is weight loss continued?

Yes

No

Withdraw orlistat: focus on maintenance of weight loss achieved. Continue structured support.

Orlistat (section 4.5)

- Take immediately before, during or up to 1 hour after each main meal.
- Advise patients to omit the dose of orlistat if a meal is missed or contains no fat.
- The most commonly reported side-effects are oily spotting with flatus, faecal urgency and anal leakage.
- May impair the absorption of other medicines (for further information see SPC):
  - fat-soluble vitamins: advise patients to take a diet rich in fruit and vegetables; if a multi-vitamin supplement is required, take at least 2 hours after the orlistat dose, or at bedtime.
  - levothyroxine: separate the administration of levothyroxine and orlistat by at least 4 hours and monitor thyroid hormone levels.
  - antiepileptics, warfarin, ciclosporin: monitor for possible effect on their absorption.
  - antiretroviral HIV medicines: consider possible negative impact on antiretroviral efficacy.
- Severe diarrhoea may cause oral contraceptive failure; recommend additional contraceptive methods.
- There is no requirement in the orlistat SPC for routine monitoring of LFTs, but be aware orlistat is listed as potentially causing an increase in transaminases and alkaline phosphatase, cholelithiasis and hepatitis.
# AID TO ANTIEMETIC SELECTION

Base selection on the likely cause, mechanism of action of the drugs available, the side-effect profile of each drug, interactions and concomitant conditions. The information table is not fully comprehensive, for further information refer to guidance below and/or BNF/manufacturers Summary of Product Characteristics:

- Section 4.6 ‘Drugs used in nausea and vertigo’
- Cancer Centre ‘Guidelines for the Management of Chemotherapy-induced Nausea in Adult Patients’ on Intranet.
- Raigmore Hospital guidance on ‘Surgical Ward Management of Post Operative Nausea and Vomiting in Adults’ on Intranet.
- See section 4.7 for the use of antiemetics in the treatment of migraine.

### DRUG CLASS/ANTIEMETIC

<table>
<thead>
<tr>
<th>ANTINISTAMINES</th>
<th>CAUTION/ CONTRA-INDICATIONS</th>
<th>GOOD FOR NAUSEA CAUSED BY/OTHER USES</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYCLIZINE</td>
<td>Caution Severe heart failure or acute myocardial infarction; may counteract the beneficial haemodynamic effects of opioids. Anticholinergic**</td>
<td>Movement, ↑ intracranial pressure, mechanical bowel obstruction, post-operative.</td>
</tr>
<tr>
<td>PROMETHAZINE**</td>
<td>Caution Strongly anticholinergic**</td>
<td>Movement</td>
</tr>
<tr>
<td>PHENOTHIAZINES AND RELATED DRUGS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PROCHLORPERAZINE**</td>
<td>Caution Balance disturbances in older people; may often lead to drug-induced Parkinson’s disease, postural hypotension and mental confusion. Strongly anticholinergic**</td>
<td>Contra-indication Prochlorperazine injection is considered inappropriate for patients with reduced consciousness due to its tendency to deepen any state of sedation.</td>
</tr>
<tr>
<td>LEVOMEPROMAZINE**</td>
<td>Caution Risk of postural hypotension; avoid in ambulant patients over 50 years, unless a risk of hypotensive reaction has been assessed. Anticholinergic**</td>
<td>Palliative care.</td>
</tr>
<tr>
<td>DOMPERIDONE AND METOCLOPRAMIDE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DOMPERIDONE**</td>
<td>Caution Does not readily cross the blood brain barrier and less likely to exhibit extra-pyramidal effects and sedation compared with metoclopramide, however caution is still recommended in the young, very old and debilitated. Risk of cardiac side-effects; for short term use only (up to 7 days).</td>
<td>Contra-indication Cardiac conduction is, or could be impaired, or where there is underlying cardiac disease, when administered concomitantly with drugs that prolong the QT interval or potent CYP3A4 inhibitors, and in severe impairment. Gastro-intestinal obstruction.</td>
</tr>
<tr>
<td>METOCLOPRAMIDE**</td>
<td>Caution in young, very old and debilitated, due to extrapyramidal effects. Risk of neurological side-effects (up to 5 days only). Anticholinergic**</td>
<td>Contra-indicated in gastro-intestinal obstruction, post bowel surgery and in Parkinson’s disease. Avoid where emesis and melana are present.</td>
</tr>
<tr>
<td>SHT3 RECEPTOR ANTAGONIST</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ONDANSETRON**</td>
<td>Caution Increased large bowel transit time; constipation can be a problem.</td>
<td>Post-operative, radiotherapy and chemotherapy, palliative care.</td>
</tr>
<tr>
<td>HYOSCINE</td>
<td>Caution Sedation can be a problematic side-effect if driving or operating machinery. Strongly anticholinergic**</td>
<td>Motion sickness, bowel obstruction, palliative care.</td>
</tr>
<tr>
<td>OTHER</td>
<td>Caution Requires a baseline ECG prior to treatment and consider the need for ongoing ECG monitoring. Anticholinergic**</td>
<td>For palliative care (opioid-induced and metabolic causes).</td>
</tr>
<tr>
<td>LORAZEPAM</td>
<td>Caution Addictive potential.</td>
<td>Short-term use in anticipatory nausea and vomiting.</td>
</tr>
</tbody>
</table>

** Consider the cumulative anticholinergic burden of all medicines. Anticholinergic side-effects include increased risk of urinary retention, falls, BP reduction, confusion, sedation, dementia, glaucoma etc.

(see [http://www.uea.ac.uk/mac/comm/media/press/2011/June/Anticholinergics+study+drug+list](http://www.uea.ac.uk/mac/comm/media/press/2011/June/Anticholinergics+study+drug+list)).
MANAGEMENT OF PROLONGED SEIZURES

Intervention should occur after **5 minutes** of seizure activity.

**Patients with prolonged tonic clonic seizures that have lasted 5 minutes or more should be given:**

Midazolam (Epistatus®) 10mg buccally or intranasally.

OR

Lorazepam 4mg intravenously if midazolam is unavailable.

OR

Diazepam 10mg intravenously or rectally if midazolam and lorazepam unavailable.

If there is no response after **10 minutes**, administer a repeat dose of benzodiazepine.

Establish aetiology – (50mL 50% glucose if hypoglycaemia, Pabrinex® 2 pairs of ampoules (section 9.6) if alcohol misuse or impaired nutritional status).

Measure blood gases to assess extent of acidosis.

FBC, U+E, LFT, Ca, Gluc, Clot, AED levels.

Administer usual antiepileptic medication in patients with established epilepsy.

Within **30 minutes** if seizures continue:

Intravenous sodium valproate 20 to 30mg/kg rate 40mg/min

OR

Intravenous phenytoin 18 to 20mg/kg rate 50mg/min with ECG monitoring (reduce rate if hypotension or arrhythmia), maximum per dose 2 grams. Refer to ‘Guideline for phenytoin dose calculations’.

If *status* persists, then within **60 minutes**:

- admit the patient to an intensive treatment unit and administer general anaesthesia
- refer for specialist advice. Midazolam, pentobarbital (unlicensed), propofol or thiopentone are most commonly used in these circumstances
- EEG should be used to determine response to treatment.

For further information refer to:

Section 4.8 ‘Antiepileptics’.

‘Guidelines for staff administering and providing training on the use of buccal (or nasal) midazolam in the treatment of prolonged or recurrent seizures in adults with epilepsy’ on Intranet.

SIGN 143 Diagnosis and Management of Epilepsy in Adults, May 2015

Advanced Practice Nurse, Epilepsy, tel: 01463 704000.
GUIDELINE FOR PHENYTOIN DOSE CALCULATIONS

1. Initial loading dose of phenytoin for status epilepticus
If the patient has not already received phenytoin then give:
- **Intravenous phenytoin sodium 18mg/kg** (see Table 1 below). Ensure ECG, blood pressure and respiratory function are monitored throughout the duration of the infusion.

<table>
<thead>
<tr>
<th>Actual body weight (kg)</th>
<th>Intravenous loading dose (mg)</th>
<th>Volume of intravenous phenytoin (mL) (vial = 250mg/5mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>35 to 44</td>
<td>700</td>
<td>14</td>
</tr>
<tr>
<td>45 to 54</td>
<td>900</td>
<td>18</td>
</tr>
<tr>
<td>55 to 64</td>
<td>1100</td>
<td>22</td>
</tr>
<tr>
<td>65 to 74</td>
<td>1250</td>
<td>25</td>
</tr>
<tr>
<td>75 to 84</td>
<td>1450</td>
<td>29</td>
</tr>
<tr>
<td>85 to 94</td>
<td>1600</td>
<td>32</td>
</tr>
<tr>
<td>&gt;94</td>
<td>1800</td>
<td>36</td>
</tr>
</tbody>
</table>

**Intravenous phenytoin administration**
- Give phenytoin over 30 to 40 minutes (rate <50mg/minute). In patients who are elderly, or have pre-existing cardiac disease, give phenytoin over 60 minutes. **NB:** Administration should commence immediately after the mixture has been prepared and completed within 1 hour.
- Ideally, administer undiluted via a syringe pump through a large gauge needle or intravenous catheter into a large forearm vein.
- If dilution is essential, mix with 100 to 250mL sodium chloride 0·9% to a final concentration of <10mg/mL, and administer by infusion pump. Stability of the diluted solution is limited and precipitates may form. Use the solution immediately, ideally with a 0·2 to 0·5micron in-line filter.
- To avoid local venous irritation, inject sterile sodium chloride 0·9% through the vein or catheter before and after each phenytoin infusion.
- **Do not** administer as a continuous infusion.
- Continuous ECG and blood pressure monitoring is essential during infusion.

2. 'Top-up' loading dose of phenytoin for status epilepticus
If phenytoin is already present but the patient is still not controlled, a ‘top-up’ loading dose may be useful.

**Phenytoin sodium 'top-up' dose (mg) = (20 - measured concentration (mg/L)) x 0·7 x wt (kg)**
Table 2 gives the approximate increase in concentration following doses of 250 to 750mg. For example, if the patient weighs 70kg and has a measured concentration of 5mg/L, a single dose of 750mg will increase the concentration to around 20mg/L (5mg/L + 15mg/L).

<table>
<thead>
<tr>
<th>Dose / Weight</th>
<th>50kg</th>
<th>60kg</th>
<th>70kg</th>
<th>80kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>250mg</td>
<td>7mg/L</td>
<td>6mg/L</td>
<td>5mg/L</td>
<td>4-5mg/L</td>
</tr>
<tr>
<td>500mg</td>
<td>14mg/L</td>
<td>12mg/L</td>
<td>10mg/L</td>
<td>9mg/L</td>
</tr>
<tr>
<td>750mg</td>
<td>21mg/L</td>
<td>18mg/L</td>
<td>15mg/L</td>
<td>13-5mg/L</td>
</tr>
</tbody>
</table>

3. Maintenance dose of phenytoin

Phenytoin typical oral doses are 3 to 5mg/kg/day. The first dose should be given 12 to 24 hours after the loading dose.

Oral administration should be used, whenever possible. Administration of phenytoin via enteral feeding tubes is not recommended due to variable absorption of phenytoin. Only use intravenous administration when oral administration is not feasible and where cardiac monitoring is available.
Notes
- There are many drug interactions with phenytoin (consult the BNF Appendix 1 or your clinical pharmacist).
- Phenytoin concentrations increase disproportionately with dose; toxicity may occur if the maintenance dose is increased by more than 25 to 50mg per day. Table 3 below may help with dosage adjustment. Based on the patient's current dose and the measured concentration (columns 1 and 2), column 3 gives a rough guide to interpretation of the result and possible dosage adjustment.
- Different formulations of oral phenytoin preparations may vary in bioavailability. Patients being treated for epilepsy should be maintained on a specific manufacturer's product.

NB: Table 3 below is for maintenance dose adjustment only. For 'top-up' doses in urgent situations see Table 2 above.

Table 3: Phenytoin maintenance dose adjustment (oral)

<table>
<thead>
<tr>
<th>Measured concentration</th>
<th>Current dose</th>
<th>Maximum dose increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5mg/L</td>
<td>&lt;4·5mg/kg/day</td>
<td>100mg</td>
</tr>
<tr>
<td></td>
<td>4·5 to 6mg/kg/day</td>
<td>Check compliance</td>
</tr>
<tr>
<td>5 to 10mg/L</td>
<td>4·5 to 6mg/kg/day</td>
<td>50mg</td>
</tr>
<tr>
<td></td>
<td>&gt;6mg/kg/day</td>
<td>Check compliance</td>
</tr>
<tr>
<td>10 to 20mg/L</td>
<td>-</td>
<td>25mg</td>
</tr>
</tbody>
</table>

4. Therapeutic drug monitoring of phenytoin

Target concentration range: 10 to 20mg/L
Routine monitoring during maintenance therapy
- Trough concentration (ie sample prior to next dose)
- Sample 3 to 5 days after starting a maintenance dose or following a dose change
- Re-analyse 5 to 10 days later as further accumulation may occur.

Monitoring after a loading/top-up dose
- 2 to 4 hours after an intravenous dose or 12 to 24 hours after an oral dose or according to clinical response
- Daily monitoring may be necessary until control is achieved and concentrations stabilise.

Notes
- The interpretation of concentration measurements is altered in:
  - hypoalbuminaemia (especially <32g/L)
  - uraemia
  - pregnancy.

Phenytoin concentrations and low albumin
Phenytoin is highly protein bound but only the unbound concentration is active. In patients with low serum albumin concentrations, a higher proportion of the total (measured) phenytoin concentration is unbound and caution is therefore required when interpreting the result.

The equation below gives an albumin corrected, total phenytoin concentration which can be compared with the target concentration range (10 to 20mg/L).

Corrected phenytoin concentration = \[ \frac{\text{Measured phenytoin concentration}}{(0·9 \times \text{Albumin (g/L) / 42}^*) + 0·1} \]

*Midpoint of reference range for serum albumin

NB: This equation only gives a rough estimate and the patient's clinical condition should be the most important consideration. Seek advice from neurology or pharmacy if you are unsure what to do.
DECISION MAKING ALGORITHM FOR THE ADMINISTRATION OF PHENYTOIN FORMULATIONS

Is the patient in status epilepticus?

YES
Use intravenous phenytoin
(see main guideline for dose details)

NO
Is patient absorbing oral medication?

NO

Is patient conscious with safe swallow?

NO

YES

Use oral phenytoin
(see main guideline for dose details)

YES

Is patient conscious with safe swallow?
**KEY POINTS**

- Refer suspected Parkinson’s disease (PD) patients early, before beginning treatment, to a clinician with relevant expertise, who should be involved in both initiation and ongoing monitoring of drug therapy.
- Therapy for PD should be multi-disciplinary; drug treatment is only one aspect.

Drug treatment of PD aims to alleviate the symptoms whilst seeking to reduce the potential to develop dopaminergic complications; it tends to follow three phases that play out over years and often decades:

**Early:** introduction of medication, often single drug.

**Middle:** increase in medication often requiring balancing several medications and dosing times.

**Late:** typically involves steady reduction of medication to levodopa monotherapy as drug-related side-effects accumulate and efficacy reduces.

Tremor generally responds poorly to most drugs and is not, on its own, a good reason to start treatment.

A clinician with expertise in PD should be involved in drug treatment decisions on the initiation and ongoing monitoring of therapy as the disease progresses. Drugs used in the treatment of PD are detailed in section 4.9.

**COMMON DRUG-RELATED PROBLEMS**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea and vomiting</td>
<td>Domperidone* is now no longer recommended for long-term use however in some patients with PD the benefits may outweigh the risks. Other antiemetics may cause worsening of PD symptoms.</td>
</tr>
<tr>
<td>Dizziness and instability</td>
<td>Balance disturbances are common in PD and unlikely to respond to treatment; consider hypotension, avoid drug treatment, in particular avoid prochlorperazine.</td>
</tr>
<tr>
<td>Depression</td>
<td>For patients on monoamine-oxidase-B inhibitors (eg selegeline) consider mirtazapine as first-line therapy. Monitor as per guidance.</td>
</tr>
<tr>
<td>Correct formulations</td>
<td>Ensure accurate prescribing of all modified-release (m/r) and combination preparations. Doses of m/r and immediate-release preparations are non-transferable.</td>
</tr>
<tr>
<td>Confusion and hallucinations</td>
<td>Patients with Parkinsonian syndromes have a lower threshold for confusion and hallucinations; if these symptoms develop consider drug-related causes, the standard medical causes of delirium and the need for specialist referral. <em>Avoid the use of haloperidol at all times.</em> Dementia is common in PD; see treatment guidance in ‘Shared care guidelines for prescribing cholinesterase inhibitors and memantine for dementia’ on Intranet.</td>
</tr>
<tr>
<td>Anti-cholinergics</td>
<td>There is a particular risk of confusion with anticholinergics such as trihexyphenidyl, which should only be prescribed under specialist advice. Anticholinergics can be used cautiously for urinary symptoms with the understanding that they can lead to confusion.</td>
</tr>
</tbody>
</table>
| Orthostatic hypotension  | Measure postural blood pressures in patients presenting with light-headedness or dizziness. Advise simple measures as first-line treatment:  
- 2 litres fluid daily  
- compression stockings  
- raise head of the bed by 15 degrees.  
Consider reducing antihypertensives; typically antihypertensive doses have to decrease as the PD progresses.  
Increase salt intake; fludrocortisone (or try domperidone*), can be considered under specialist advice [off-label]. |
| Excess salivation         | Avoid anticholinergics. Speech and language therapy can help as there tends to be an associated swallowing problem. Oral application of atropine sulfate drops 1% may be helpful [off-label]. See also Saliva Management guidance in Appendix 7. |

*Domperidone is associated with a small increased risk of serious side-effects and is now contra-indicated in those with underlying cardiac conditions and other risk factors – see [www.gov.uk/drug-safety-update](http://www.gov.uk/drug-safety-update). In patients with PD it is useful as an antiemetic and to treat orthostatic hypotension – please discuss with a specialist before discontinuing treatment and for further information see Association of British Neurologists (ABN) advice.*
ADMINISTRATION OF PARKINSON’S DISEASE MEDICATION IN HOSPITAL
It is vitally important that patients in hospital receive their PD medication at the correct time, even if this is outwith normal drug times; sudden changes in PD medication can lead to sudden, severe deterioration. See www.npsa.nhs.uk.

Symptom control in hospital relies on patients receiving medication at specific times to ensure:
- improvement in the patient’s quality of life
- prevention of deterioration in a patient’s condition which can result in slowness, stiffness, immobility, tremor and rigidity
- prevention of acute withdrawal of medication (which can result in acute adverse reactions)
- prevention of unnecessary extension in a patient’s hospital stay.

When patients with PD are admitted to hospital:
- refer to guidance ‘Inpatient management of Parkinson’s including nil by mouth guidance’.
- the local Parkinson’s team should be informed by telephone
- where possible patients should self-administer their PD medication.

PATIENT JOURNEY
1. GP suspects PD and refers patient to Consultant.
2. Parkinson’s disease clinics held at Caithness General Hospital, Wick, Raigmore Hospital, Inverness and County Hospital, Invergordon and every six weeks in Fort William and in peripheral clinics, eg Skye. The PD service for patients from Argyll & Bute H&SCP is now delivered from GG&C.

   Patients under the age of 65 years with suspicion of PD should be referred to Neurology Outpatients Clinic, Raigmore Hospital.

3. Consultant discusses differential diagnosis, treatment options such as physiotherapy and neuropsychology (ideally from an early stage) and gives information on PD.
4. Consultant refers patient to appropriate members of multidisciplinary team. Consider Occupational Health involvement to maintain employment.
**ALTERNATIVE METHODS OF ADMINISTRATION FOR PARKINSON’S DISEASE MEDICINES**

**Important notes** - please read before using the information in these pages.
- This is general information and may not apply to all patients. If necessary, seek advice from the prescriber, specialists (see contact details in ‘Parkinson’s disease guideline’) or Medicines Information.
- Always clearly prescribe the route of administration, eg ‘crush tablet and give by nasogastric (NG) tube’.
- Crushing or dispersing non-dispersible tablets means that the medicine will be administered outwith the terms of its product licence with liability being assumed by all those involved in the medicines administration process, including prescriber, dispensing pharmacist and nurses administering the medicine.
- Use tablet crushers designed specifically for this purpose, these can be obtained through PECOS system.
- Where tablets are dispersed ensure that the whole tablet content is rinsed from tablet crushers, medicine pots and oral syringes and administered to the patient.
- Poorly soluble crushed tablets may pose an aspiration risk for patients with swallowing difficulties. Aim for a liquid with a uniform consistency.
- Crush or disperse tablets immediately prior to administration.
- It may be necessary to consider switching to a rotigotine patch if there is no route to administer Parkinson’s medicines using the guide below. See guidance in ‘Inpatient management of Parkinson’s including mil by mouth guidance’.
- Covert medicating is the administration of medication in a disguised form without the individual’s knowledge. It is not considered to be good practice. It is not necessarily covert if given by NG, PEG or patch but it may be considered to be if the individual is not told that medication is being given. To avoid this please advise the individual that they are receiving their medication in this way. If they do not have capacity or are unconscious this may need to be discussed with their welfare attorney or guardian. See section 5.7, Policy for the Administration of Medicines by Nurses and Midwives in NHS Highland.

**Administration by enteral feeding tube:**
First flush enteral feeding tube with 15 to 30mL water, crush and/or disperse tablet in 10 to 15mL water (or more if required), immediately administer dose using an oral syringe. Rinse crusher, medicine pot and syringe with 10mL water and administer rinsing fluid. Reflush enteral feeding tube with 15 to 30mL water. Flush tube between each medication and at the end. Use tap water to flush enteral feeding tubes. For administration beyond the stomach sterile water is advised. The time taken to disperse tablets in water can be variable. Suspensions should be used for enteral feeding tubes to avoid blockage. Suspension should be diluted with an equal volume of water for administration via enteral tubes particularly into the jejunum. Suspension contains sorbitol. Use 25mL water per tablet to disperse. Alternatively dilute orange squash can be used but do not use orange juice. Administration after food may delay/reduce absorption of levodopa. See notes below regarding enteral administration of preparations containing levodopa.

**Drug (Section 4.9)** | Alternative methods of administration | Notes |
--- | --- | --- |
Ropinirole tablets (Requip®) | Tablets may be crushed and mixed with water | Tablets can be crushed and mixed with water or soft food for patients with swallowing difficulties. The tablets can be crushed and mixed with water for administration via enteral feeding tubes. Tablets rapidly disintegrate when placed in 20mL water to give a fine dispersion. Administer immediately after preparation. |
Ropinirole modified-release tablets (Requip® XL) | Change to immediate-release ropinirole tablet | For conversion to immediate-release tablets, seek advice. |
Pramipexole tablets (Mirapexin®) | Tablets can be cut into equal halves or Tablets may be crushed and mixed with water | Tablets can be divided into equal halves using a tablet cutter. The tablets are light sensitive and should be administered shortly after crushing. |
Pramipexole modified-release tablets (Mirapexin Prolonged-Release®) | Change to immediate-release pramipexole tablets | For conversion to immediate-release tablets, seek advice. |
Domperidone tablets | Use oral suspension or tablets will disperse in water or can be crushed and mixed with water | Suspensions should be used for enteral feeding tubes to avoid blockage. Suspension should be diluted with an equal volume of water for administration via enteral tubes particularly into the jejunum. Suspension contains sorbitol. The time taken to disperse tablets in water can be variable. |
Co-beneldopa dispersible tablets (Madopar®) | Dispersible tablets can be given via enteral feeding tubes | Use 25mL water per tablet to disperse. Alternatively dilute orange squash can be used but do not use orange juice. Administration after food may delay/reduce absorption of levodopa. See notes below regarding enteral administration of preparations containing levodopa. |
| Co-beneldopa standard capsules (Madopar®) | Use dispersible Madopar® tablets | Madopar® capsules and dispersible tablets are dose equivalent. Onset of action may be quicker for dispersible tablets; monitor the patient for any change in effect due to altered bioavailability. See notes below regarding enteral administration of preparations containing levodopa. |
| Co-beneldopa modified-release capsules (Madopar® CR) | Use dispersible Madopar® tablets | Patients taking Madopar® CR need to have their dosage and administration times tailored when converting to dispersible tablets. Seek advice. See notes below regarding enteral administration of preparations containing levodopa. |
| Co-careldopa tablets (Sinemet®) | Tablets can be dispersed in water or change to dispersible Madopar® | Lower strengths disperse within one minute. 25/250 strength disperses within one to 5 minutes. Give immediately when dispersed as the drug will degrade. The dispersed tablets may settle at the bottom of the container/syringe; ensure that the whole dose is administered. Direct dose conversion between Sinemet® and Madopar® may not be appropriate in all patients. For conversion to Madopar®, withdrawal of therapy and re-titration of dose may be necessary. Seek advice. See notes below regarding enteral administration of preparations containing levodopa. |
| Co-careldopa modified-release tablets | Change to immediate-release Sinemet® tablets and increase dosing frequency or change to dispersible Madopar® | For conversion to immediate-release tablets seek advice. Direct dose conversion between Sinemet® and Madopar® may not be appropriate in all patients. For conversion to Madopar®, withdrawal of therapy and re-titration of dose may be necessary. Seek advice. See notes below regarding enteral administration of preparations containing levodopa. |
| Co-careldopa plus entacapone tablets (Stanek®) | Use the separate components (co-careldopa and entacapone) or change to dispersible Madopar® | The crushed tablets may stain enteral tubes, skin and clothing. A small amount of orange juice, honey or jam may be used to disguise the bitter taste of the tablet contents. If changing to Madopar®, dose adjustments may be necessary, seek advice. See notes below regarding enteral administration of preparations containing levodopa. |
| Selegiline tablets | change to oral lyophilisate tablet (Zelapar®) if the patient has a moist mouth or disperse tablets in water | A dose change is required when converting from tablets to oral lyophilisate. Patients receiving 10mg selegiline hydrochloride tablet can be switched to oral lyophilisate tablet 1.25mg. Oral lyophilisates dissolve on the tongue and is buccally absorbed. Zelapar® oral lyophilisates may not be suitable for patients with reduced buccal flow or who cannot hold the tablet in their mouth, eg after severe stroke, and should not be used for administration via enteral feeding tubes. Patients should not drink, rinse or wash mouth out for 5 minutes after taking the lyophilisate tablet. Selegiline tablets can be dispersed in water and should disperse within one minute. This method is suitable for use with enteral feeding tubes or for patients with swallowing difficulties. |
| Rasagiline | Tablets may be crushed and mixed with water | |
| Entacapone tablets (Comtess®) | Disperse tablets in water | Either place the tablet in a syringe with 10mL water and shake for 5 minutes or place in medicine pot with 10mL water and allow to disperse (takes 1 to 5 minutes). The dispersion is a bright orange colour and will stain enteral tubes, skin and clothing. Entacapone does not fully dissolve in water, so if giving via enteral feeding tube, the tube should be well flushed after administration. Avoid crushing tablets as this produces red dust which will stain. Crushed tablets may be administered with jam, honey or orange juice to cover bitter taste. |
| Amantadine capsules | Capsules may be opened and the contents mixed with water or change to syrup | Amantadine is highly soluble in water. For long-term use consider transferring to syrup. If the syrup is used, monitor total daily intake of sorbitol. |
| Procyclidine tablets | use oral solution or use injection intravenously | The oral solution flushes easily via tube without further dilution. Mixes with water if needed. |

**Notes:** Problems with enteral administration of preparations containing levodopa (Madopar®, Sinemet®, Stanek®)

- Levodopa is absorbed mainly in the jejunum. Administering directly to the site of absorption (J or NJ) may result in unexpected drug levels and side-effects.
- High protein in the gut from enteral feed may alter absorption of levodopa and cause fluctuations in response to the drug. Drug administration should be consistent in relation to feed administration times.
INPATIENT MANAGEMENT OF PARKINSON’S INCLUDING NIL BY MOUTH GUIDANCE

Parkinson’s is a neurological disease affecting mobility, mood and the autonomic nervous system. It can have an impact on movement and function, mental health and other ‘non motor’ aspects in varying amounts between different individuals.

Unfortunately it is associated with an increased risk of complications and an increased length of stay in hospital, which can be averted with good care.

Elective admissions
It is important to consider how to maximize an individual’s health pre-admission. This should take consideration of a general medical review including nutrition, hydration, mobility and function, and cognition. See Comprehensive Geriatric Assessment.

Medication: ensure good concordance pre-admission and maintain this throughout admission.

Elective and unscheduled admissions

- It is important that Parkinson’s medications are given in hospital at the times patients take them at home. The drug Kardex should reflect patients’ usual drug timings rather than the hospital drug round timings.
- Parkinson’s medicines need to be prescribed as the correct preparation and dosage, as well as at the correct timing.
- Sometimes the use of an audible alarm for nursing staff may be an effective way to achieve compliance if medicines are to be administered out with routine hospital drug round timings.

**Note:** If compliance of Parkinsons’ medicines is not achieved this will impact on mobility, swallowing, communication, feeding independently, mood and anxiety, along with general function in ADLs.

Medications which can worsen Parkinson’s or cause delirium

- metoclopramide, prochlorperazine, promethazine, codeine, tramadol, antipsychotics ie haloperidol
- caution with anticholinergics ie oxybutynin, cyclizine, chlorpheniramine (see [Scottish Polypharmacy Guidance 2015](https://www.science.gov.uk/scientific/2015/anticholinergics), Section 3.1 Anticholinergics)
- be aware that hypotension/postural hypotension is common as part of the autonomic dysfunction in Parkinson’s
- antihypertensives may need to be withheld or could be discontinued.

Management of nausea

- use domperidone, after ECG completed
- ondansetron can be used, but is associated with severe constipation and caution with cardiac issues.

General care

In people with Parkinson’s be aware that there is a higher risk of:

- delirium, especially if it has occurred before. If it develops look for common triggers – constipation, urinary retention, infection, pain, medication issues
- urinary difficulties
- constipation
- saliva control, swallowing difficulties
- hypotension.

Acute deterioration of Parkinson’s symptoms suggests acute illness, missed medication or new medication acting as dopamine blockade.

Surgery

Place patients first on operating list where possible, ensure usual morning medication given.
Post-operatively it is important to consider the need for early physiotherapy, hydration and nutrition, along with a healthy bowel habit.

Advanced treatments for Parkinson’s

**DBS advice**
Deep Brain Stimulators are used in people with Parkinson’s and sometimes severe tremors. MRI scan is contraindicated. Monopolar diathermy has been used with caution in patients with a DBS implanted – see manufacturer’s advice. (Heating of electrodes may occur and has resulted in 2 documented cases of severe neurological damage with coma.)

**Apomorphine advice**
Apomorphine is a potent dopamine agonist given by subcutaneous injection. There are small numbers of people where it is prescribed either in bolus form or with a pump. It is not normally used in the short term as a replacement therapy. Seek advice from relevant Parkinson’s team regarding this.

**Duodopa®**
Intrajejunal levodopa infusion – frequent difficulties with equipment failure/tube dislodged. Continue at prescribed rate providing gastric emptying is not delayed and the PEJ tube is patent. If not, discontinue and commence on dopamine agonist (rotigotine) patch. Individual patients should have their own protocols for this.

**Other complications associated with Parkinson’s**
**Falls** relate to many issues including postural instability, freezing, postural hypotension, OA, cognitive deficits. Physiotherapy input is important; walking aids may or may not be relevant.

**Neuroleptic malignant syndrome** may occur on withdrawal of medication, or if medication missed. It can present with delirium, (either hyper or hypo-active) rigidity, fever, and dysautonomia (tachycardia, fever, hypertension or labile BP, sweating) elevated CK; it can be fatal.

**Dyskinesia:** this may be normal for patient, it may indicate that they are receiving higher doses of medication than normal, or absorption of medicines is different.

**For Parkinson’s patients who have impaired oral intake**
Patients who are unwell may be deemed ‘nil by mouth’ if awaiting surgery or investigations, or their swallow may not be effective due to their Parkinson’s, an acute illness or general weakness and frailty.

**Appropriate referrals should be made to the SALT and Dietetics teams**
Every effort should be made to ensure that Parkinson’s medicines are NOT stopped abruptly.

Advice is given below as to:
- how to switch from oral tablets or capsules, to dispersible forms of levodopa to be administered via nasogastric tube.
- how and when to convert to a transdermal dopamine agonist patch.
- which medications are suitable to be given via a nasogastric tube, see ‘Alternative methods of administration for Parkinson’s disease medicines’.

Any patients undergoing a switch away from their normal medication should be referred to the relevant Parkinson’s team for review within one working day of admission – see below for contact details:

Parkinson’s Nurse Specialist ext 6378, Medicine for Elderly ext 5471/5751 or Neurology Secretaries ext 6229/6613.
Impaired oral intake advice for patients with Parkinson's

The conversions below are estimates and clinical review of patients is always necessary to achieve maximal benefit of medication.

**Advice for patients prescribed both dopamine agonists and levodopa therapy**

If switching to rotigotine add calculated doses, maximum equivalent rotigotine is still 16mg/24 hours. The patient’s normal Parkinson’s team should be notified of their admission within 1 working day if following this advice. Review rotigotine patch after 72 hours at the latest, and consider if return to routine medication achievable. Contact either Sharon Sutherland, Parkinson’s Nurse Specialist ext 6378, Medicine for Elderly Secretaries ext 5471/5751; Neurology Secretaries ext 6229/6613.

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**Patient with Parkinson’s and impaired swallow**

- **SALT review**
- **Swallow definitely not safe or absent**
  - Is NG appropriate?
    - **YES**
    - **NO**
      - **Switch to rotigotine patch**

**See Highland Formulary guidance on ‘Alternative methods of administration for Parkinson’s disease medicines’. Consider dietetic referral as part of general care.**

**Swallow impaired, but oral route possible: continue oral intake and oral meds with caution.**

**Co-beneldopa (Madopar®) or co-careldopa (Sinemet®) or Stanek®/Stalevo®**

**Dopamine agonist, ie ropinirole/pramipexole/cabergoline**

**Calculation**

- Calculate total daily levodopa dose (not including carbidopa/benserazide), then divide by 50 to achieve daily rotigotine dose, ie Madopar® 125, 4 times a day = 100 x 4 total daily Levodopa = 400mg then divide by 50 to give rotigotine 8mg/24-hours; max rotigotine 16mg/24 hours †

**Rotigotine patches**

- Round to nearest 2mg (to max of 16mg) and prescribe as 24-hour patch.
- Patches available as 1mg/2mg/3mg/4mg/6mg/8mg strength. More than one patch can be applied. **DO NOT cut patches.**
- If patient on Madopar CR®, Sinemet CR® or Stanek®/Stalevo®, initially calculate switch to rotigotine as above †. These formulations will have slightly different bioavailability and therefore effect: Parkinson’s team will advise further.
- **MAOIs** such as rasagiline and selegiline can be withheld for short periods of time if necessary.
RESTLESS LEG SYNDROME (RLS)

The mean age of onset is the third and fourth decade of life. Typically there is a slow progression over years but onset can be more rapid. There is a higher risk of RLS in those who have first degree relatives who also suffer from it. It has also been linked to iron deficiency anaemia and kidney disease. RLS is common in pregnancy. Medication is not recommended in pregnancy or when breastfeeding and management should follow the behavioural and physical advice below. Sensory symptoms can occur on their own but are often accompanied by periodic repetitive, involuntary leg movements, usually while asleep.

Diagnostic criteria for restless leg syndrome (2012 revised IRLSSG)
(all 5 criteria must be met)
1. An urge to move the legs usually but not always accompanied by or felt to be caused by an uncomfortable and unpleasant sensation in the legs.
2. The urge to move the legs and any accompanying unpleasant sensations begin or worsen during periods of rest or inactivity such as lying down or sitting.
3. The urge to move the legs and accompanying unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues.
4. The urge to move the legs and accompanying unpleasant sensations during rest or inactivity only occur or are worse in the evening or night than during the day.
5. The occurrence of the above features is not solely accounted for by symptoms primary to another medical condition or behavioural condition (eg neuropathy, myalgia, venous stasis, leg oedema, arthritis, leg cramps, positional discomfort or habitual toe tapping).

Investigations
- full blood count
- transferrin
- ferritin - serum ferritin concentrations below 50ng/mL has been associated with RLS
- renal function, liver function, glucose, HbA1c, vitamin B12, folate and calcium levels.

Treatment

Step 1
- Behavioural
  - good sleeping pattern [www.moodjuice.scot.nhs.uk/sleepproblems.asp](http://www.moodjuice.scot.nhs.uk/sleepproblems.asp)
  - avoid alcohol, smoking, caffeine and hot baths in the evening
  - increase daytime activity but not too close to bed time

- Some medication can worsen symptoms – antihistamines, dopamine antagonists, anti-emetics, antidepressants, selective serotonin reuptake inhibitors, mirtazapine, neuroleptics, beta blockers, lithium and some antiepileptics.

- Ensure ferritin concentration is above 50ng/mL and maintained between 50 to 75 ng/mL.

Step 2

Medication to reduce symptoms
Patients should be aware that medication is to reduce the symptoms but that complete eradication is unlikely. Medical treatment should be deferred as long as possible with behavioural measures tried first. Gabapentin and pregabalin can be used in patients with restless legs (advocated by NICE) but is off-label. The choice of drug is also dependent on side-effect profile risk.
Avoid using more than one agent at the same time for restless legs. If one fails titrate off and use another rather than adding on treatment.

**Choices**

**Gabapentin or pregabalin (off-label indication)**

Useful in:
- patients who have sleep disturbance disproportionate to the RLS
- those with co-morbid insomnia, anxiety or pain
- patients in whom a dopamine agonist should be avoided, eg prior history of impulse control disorder.

**Dopamine agonists – ropinirole, pramipexole and rotigotine skin patches**

Patients **must** be made aware that dopamine agonists can cause an impulse control disorder. This means that while taking the drug they are at risk of spending more time/money on things which give them pleasure but which can be harmful, eg gambling, alcohol and drug addiction, excessive shopping, hypersexuality. Avoid dopamine agonists in those with a history of impulse control issues, eg alcohol misuse, substance misuse, gambling.

Impulse control disorders can emerge over time and patients on these medications for a long time should be asked about any emerging problems.

Repeat warnings on impulse control disorders at the time of any dose increases.

Please give the patient this leaflet for further information:

[http://intranetnew/PoliciesLibrary/Documents/Dopamine%20agonist%20medication%20used%20to%20treat%20Parkinson%20or%20Restless%20Legs%20PRINTABLE%20VERSION.pdf](http://intranetnew/PoliciesLibrary/Documents/Dopamine%20agonist%20medication%20used%20to%20treat%20Parkinson%20or%20Restless%20Legs%20PRINTABLE%20VERSION.pdf)

There is a risk of augmentation over time, ie that higher doses are needed to improve symptoms. Long-acting dopamine agonists increase the time to augmentation and should be used in preference to short-acting dopamine agonists. Rotigotine patches may be useful if patient also has daytime symptoms, please note that they can cause application site reactions. Do not exceed the dose stated by the BNF for RLS as this will not improve symptoms and demonstrates augmentation.

**Do not use in pregnancy.**

**Opiates**

Weak opiates (codeines) may be useful in patients with severe augmentation. Refer to BNF and SPCs for prescribing information (see also Highland Formulary section 4.7).

**Step 3**

- Arrange regular follow-up and monitor side-effects
- Reinforce lifestyle changes
- Assess response after 3 months and reconsider need for treatment continuation.
- In prolonged treatment drug doses should be kept to the minimum required to ease symptoms as the higher the dose, the greater the risk of augmentation.

**How can a neurology appointment help?**

- **If there is diagnostic doubt.**
- Restless leg syndrome is more common in those with peripheral neuropathy, myelopathy or myelitis. If you suspect there is another condition which needs to be investigated please refer.
SMOKING CESSATION INTERVENTIONS

FIRST QUIT ATTEMPT: Smoker presents to healthcare professional

Give brief advice on stopping smoking. Offer ‘Aspire’ magazine (http://healthyhighlanders.co.uk/HPAC/Index.jsp) or other suitable leaflet. Record in notes.

Interested in stopping smoking? No

Accept answer non-judgementally, leaving offer of help open. Record in notes. Offer ‘Smoke-free homes’ pack.

Yes

Motivational support is key, refer to:
Specialist Smoking Cessation Advisor, Pharmacy Smoking Cessation Service, Smokeline (tel: 0800 84 84 84), local Practice Nurse or http://smokefreehighland.co.uk/.
If appropriate provide nicotine replacement therapy (NRT) as defined below.

Complete Specialist Smoking Cessation Advisor referral form if required, provisionally indicating suitability for NRT* or varenicline**.

First consultation
NRT (section 4.10) is the usual choice for a first quit attempt – see overleaf for further information.
- Assess motivation, offer behavioural advice and encouragement.
- Discuss strategies including choice of drug/formulation and contra-indications.
- Advise that smoking cessation, with or without pharmacological support, may cause symptoms of depression and affect the metabolism of some medicines. In particular the dose of theophylline, cinacalcet, ropinirole and some antipsychotics (including clozapine, olanzapine, chlorpromazine and haloperidol), may need to be reduced. Monitor for adverse effects.
- People with a high level of nicotine dependence, or who have failed with NRT previously, may benefit from the addition of a second NRT preparation to achieve abstinence, eg combination of a patch and one of the immediate-release preparations.
- Agree a quit date, (7 to 9 days following appointment) prescribe/arrange NRT in patient’s choice of formulation (usually 4 weeks supply, endorsing the prescription ‘Dispense weekly’ to minimise waste) and arrange follow-up, usually within a week. Advise to contact prescriber if adverse effects.
- Advise patient that normal course of NRT is an approximately 12-week period.
- At each visit measure carbon monoxide levels if possible and offer advice on diet and exercise.

Second consultation
Discuss progress and any issues and encourage and reassure. Alter NRT if necessary. If still smoking, offer advice about risks and set new quit date. Studies have shown very poor quit rates if still smoking after first week. Ask again about motivation, suggest alternative smoking cessation strategies and arrange a follow-up appointment.

Third consultation
If not smoking, congratulate and prescribe/arrange 1 month’s NRT supply, stepping down if appropriate. Set new follow-up appointment. Submit the 1 month Client Information Return. If still smoking, offer advice on risks. Only prescribe/arrange further NRT supplies (as per first consultation) if new quit date set.

Fourth consultation
If still not smoking congratulate and prescribe/arrange final month’s supply of NRT (lowest dose) and offer advice on NRT withdrawal and dose tapering.

Fifth consultation (face to face, by telephone or by letter)
If still not smoking, congratulate.

* Accept answer non-judgementally, leaving offer of help open.
** Offer ‘Smoke-free homes’ pack.

Lead reviewer: Smoking Cessation Review Group
Date: August 2015
Version: 7

Approved by: Formulary Subgroup of NHS Highland ADTC
Review date: August 2017
Warning: document uncontrolled when printed
The aim of NRT is to reduce usage over 8 to 12 weeks as per product information. If patients require treatment beyond 12 weeks they should be referred to specialist stop smoking services for further support and advice.

It may be necessary to prescribe NRT for longer than 12 weeks. Patients must meet the following criteria if continuing treatment for more than 12 weeks:

- significant indication that to discontinue treatment would result in relapse due to withdrawal symptoms
- patient is prepared to commit and adhere to reduction plan resulting in discontinuing product within the next six weeks
- patient is completely abstinent.

**SUBSEQUENT QUIT ATTEMPT**

Patient re-presents requesting support to stop smoking.

For further information on the use of NRT in specific patient groups and advice on selection of formulations refer to the [BNF](https://www.gov.uk/government/publications/bnf).  

<table>
<thead>
<tr>
<th>Suitable for NRT?</th>
<th>YES</th>
<th>Prescribe/arrange supply of NRT. Follow first quit attempt pathway.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suitable for varenicline*?</td>
<td>YES</td>
<td>GP, community pharmacist or independent prescriber prescribes as a component of smoking cessation support programme. Set quit date 8 to 14 days after starting.</td>
</tr>
<tr>
<td>suitable for other support to assist quit.</td>
<td>YES</td>
<td>Refer to <a href="http://smokefreehighland.co.uk/">http://smokefreehighland.co.uk/</a> or specialist smoking cessation advisor.</td>
</tr>
</tbody>
</table>

**First choice - Nicotine replacement therapy (NRT)**

There is no evidence that one particular type of NRT is more effective than another. The choice of formulation is down to personal preference.

For full details on doses, adverse effects, cautions and contra-indications of individual products refer to the [BNF](https://www.gov.uk/government/publications/bnf).

### Product

#### Advantages

- easy to use
- discreet
- breaks habits
- supplies nicotine continuously throughout the day.

#### Disadvantages

- with 16-hour patch patient may have early morning craving
- no oral satisfaction
- possible skin reaction — rotate the site of the patch to prevent irritation developing
- 24-hour patch can cause sleep disturbance.

<table>
<thead>
<tr>
<th>Product</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
</table>
| Patch: 12 week course | • easy to use  
• discreet  
• breaks habits  
• supplies nicotine continuously throughout the day. | • with 16-hour patch patient may have early morning craving  
• no oral satisfaction  
• possible skin reaction — rotate the site of the patch to prevent irritation developing  
• 24-hour patch can cause sleep disturbance. |
| 16-hour patch | • use one range of patches and do not interchange  
• apply new patch once daily to a non-hairy area of skin. Take off before bedtime. | |
| 24-hour patch | • new patch once daily, keeping patch on all day and night, changing next morning. | |
| Lozenges | • discreet, flexible and offers good dose control  
• easy to use. | • nicotine destroyed in stomach if product not used properly, leading to heartburn or stomach irritation  
• stinging in mouth, hiccups and localised irritation can occur. |

- [BNF](https://www.gov.uk/government/publications/bnf)

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<table>
<thead>
<tr>
<th>Product</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Microtabs – sublingual: reduce dose after 3 months</strong>&lt;br&gt;the small tablet dissolves under the tongue</td>
<td>• discreet, flexible and offers good dose control&lt;br&gt;• easy to use&lt;br&gt;• side-effects minimal.</td>
<td>• the tablet must not be sucked, chewed or swallowed as this will reduce the amount of nicotine absorbed&lt;br&gt;• stomach upset, stinging mouth, hiccups and localised irritation can occur.</td>
</tr>
<tr>
<td><strong>Inhalator: 12-week course</strong></td>
<td>• good for those who miss the behavioural habit of smoking&lt;br&gt;• easy to use.</td>
<td>• some may feel self-conscious using inhalator.</td>
</tr>
<tr>
<td><strong>Nasal spray: reduce dose after 8 weeks</strong></td>
<td>• fast-acting for heavy smokers&lt;br&gt;• easy control of dose.</td>
<td>• side-effects – nasal irritation, eyes watering, coughing, sneezing etc.&lt;br&gt;• most addictive of the NRT products.</td>
</tr>
<tr>
<td><strong>Gum: reduce dose after 3 months</strong>&lt;br&gt;• use ‘chew/park/chew’ technique&lt;br&gt;• do not use liquorice-flavoured gum in pregnancy.</td>
<td>• easy to use&lt;br&gt;• discreet&lt;br&gt;• side-effects minimal&lt;br&gt;• oral satisfaction&lt;br&gt;• available in a variety of flavours.</td>
<td>• nicotine destroyed in stomach if product not used properly&lt;br&gt;• over-chewing can cause hiccups&lt;br&gt;• can taste slightly peppery at first&lt;br&gt;• can irritate the mouth and throat, increase salivation and aggravate stomach ulcers&lt;br&gt;• not recommended in denture wearers.</td>
</tr>
<tr>
<td><strong>Oral spray</strong></td>
<td>• fast-acting for heavy smokers&lt;br&gt;• immediate effect&lt;br&gt;• easy control of dose.</td>
<td>• hiccups&lt;br&gt;• nausea and dyspepsia&lt;br&gt;• local irritation.</td>
</tr>
<tr>
<td><strong>Oral film (dissolvable)</strong>&lt;br&gt;• DO NOT EAT OR DRINK WHILE NICOTINE FILM IS IN THE MOUTH.</td>
<td>• suitable for smokers who have their first cigarette of the day more than 30 minutes after waking.</td>
<td>• possible sleeplessness&lt;br&gt;• nausea and dyspepsia&lt;br&gt;• hiccups&lt;br&gt;• headache and dizziness.</td>
</tr>
</tbody>
</table>
CHAPTER 5  INFECTIONS

Note: Drugs included in the first part of this chapter are those suitable for the majority of infections seen in primary care and for many cases in secondary care. For information on their use and dosing refer to Management of Infection Guidance and to the ‘Policy for Prescribing Protected Antimicrobials’ on Intranet. The guidance is also available as an app via this link or on iTunes or Google Play. For all other information refer to BNF.

This guidance recommends the following:
1. Avoid prescribing antibiotics for simple coughs and colds.
2. Avoid prescribing antibiotics for viral sore throats.
3. Limit prescribing for uncomplicated urinary-tract infection to 3 days in otherwise fit women.
4. Limit prescribing of intravenous and broad-spectrum antibiotics as far as possible. See guidance on ‘Intravenous to oral switching’.
5. Stop antibiotics, where possible, when Clostridium difficile diarrhoea is suspected or confirmed. This applies particularly to cephalosporins, fluoroquinolones, broad-spectrum penicillins and clindamycin, although any antibiotic may be implicated. Concurrent prescription of a proton pump inhibitor, eg omeprazole/lansoprazole, should also be reviewed as the risk of infection with Clostridium difficile is increased.
6. * denotes Use with caution as high risk of infection with Clostridium difficile; change to an alternative agent where possible, according to Microbiology results.

5.1 ANTIBACTERIAL DRUGS

Refer to guidance on use of antimicrobial drugs following splenectomy in ‘Guidelines for the prevention of sepsis in patients with asplenia or functional hyposplenia’ on Intranet.

Penicillins

**BENZYLPPENICILLIN** injection 600mg, 1.2 grams

**PHENOXYMETHYLPPENICILLIN** (Penicillin V) tablets 250mg; oral solution 125mg/5mL, 250mg/5mL

**FLUCLOXACILLIN** capsules 250mg, 500mg; oral solution 125mg/5mL, 250mg/5mL; injection 250mg, 500mg, 1 gram

**AMOXICILLIN** capsules 250mg, 500mg; oral suspension 125mg/5mL, 250mg/5mL; sachets 3 grams; injection 250mg, 500mg, 1 gram

*CO-AMOXICLAV* tablets 250/125, 500/125 (amoxicillin/clavulanic acid in mg); oral suspension 125/31/5mL, 250/62/5mL, 400/57/5mL; injection 500/100, 1000/200 (in mg)

*PIPERACILLIN WITH TAZOBACTAM* injection 2.25 grams, 4.5 grams

*Cephalosporins

**CEFALEXIN** capsules 250mg, 500mg; oral suspension 125mg/5mL, 250mg/5mL; syrup 500mg/5mL

Cefalexin is only suitable for the treatment of urinary-tract infections.
**CEFIXIME** tablets 200mg
In gonorrhoea, 400mg as a single dose [off-label].

**CEFTRIAXONE** injection 250mg, 1 gram, 2 grams
For patients with an eGFR of less than 10mL/min/1.73m² with hepatic impairment, switch therapy to cefotaxime and dose as per Renal Handbook.

**CEFUXROXIME** tablets 250mg; suspension 125mg/5mL; injection 250mg, 750mg, 1.5 grams

**CEFOTAXIME** injection 500mg, 1 gram
Use as alternative to ceftriaxone for patients with an eGFR of less than 10mL/min/1.73m² with hepatic impairment; dose as per Renal Handbook.

**CEFTAZIDIME** injection 500mg, 1 gram, 2 grams
Reserve for limited indications, contact Microbiology for advice.

Other beta-lactam antibiotics

**AZTREONAM** injection 1 gram, 2 grams

Tetracyclines

**OXYTETRACYCLINE** tablets 250mg

**DOXYCYCLINE** capsules 100mg; dispersible tablets 100mg
For use in the treatment of acne, see section 13.6 and guidance.

Aminoglycosides

**GENTAMICIN** injection 20mg/2mL, 80mg/2mL
**Dose:** Follow local hospital guidelines, monitor drug levels, see:
- gentamicin prescribing, administration and monitoring chart
- gentamicin dose calculator on Intranet
- ‘Policy for use of intravenous gentamicin as part of the management of infective endocarditis in adults’ on Intranet.
For surgical prophylaxis – see dosing table and give as a single dose (no monitoring).

**Macrolides**

<table>
<thead>
<tr>
<th>Note:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythromycin and other macrolide antibiotics inhibit the metabolism of a number of drugs (eg oral anticoagulants, carbamazepine and theophylline) resulting in potentiation of effect.</td>
</tr>
<tr>
<td>In penicillin-allergic patients who fail to respond to, or are unable to tolerate erythromycin, clarithromycin may be an appropriate alternative.</td>
</tr>
<tr>
<td>Use clarithromycin in <em>Helicobacter pylori</em> eradication regimes.</td>
</tr>
</tbody>
</table>

**ERYTHROMYCN** e/c tablets 250mg; oral suspension 125mg/5mL, 250mg/5mL; infusion 1 gram
For use in the treatment of acne, see section 13.6 and guidance.

**CLARITHROMYCN** tablets 250mg, 500mg; oral suspension 125mg/5mL; infusion 500mg
First-line choice in *Helicobacter pylori* eradication. See [eradication therapies](#).

**AZITHROMYCIN** tablets 250mg, tablets 500mg; oral suspension 200mg/5mL

**Clindamycin**

**CLINDAMYCIN** capsules 150mg; injection 600mg/4mL

**Other antibacterials**

**CHLORAMPHENICOL** capsules 250mg; injection 1 gram

**SODIUM FUSIDATE** tablets 250mg; oral suspension (as fusidic acid) 250mg/5mL

Sodium fusidate has a very limited spectrum of activity. **Avoid monotherapy** as it will lead to emergence of resistant strains.

**VANCOMYCIN** capsules 125mg, 250mg; infusion 500mg, 1 gram

*For intravenous use* follow hospital [guidelines](#). Drug levels require monitoring. For the treatment of *Clostridium difficile* diarrhoea refer to [guidance](#) and to the ‘Policy for *Clostridium difficile* infection’ on the [Intranet](#).

Vancomycin is very poorly absorbed and should only be used orally in the treatment of *Clostridium difficile* diarrhoea. For systemic infections where vancomycin is indicated, the intravenous route must be used. Vancomycin and teicoplanin are mainly reserved for treatment of known or suspected MRSA infection.

**TEICOPLANIN** injection 200mg, 400mg

**RIFAMPICIN** capsules 150mg, 300mg; syrup 100mg/5mL; infusion 600mg

Warn patients that rifampicin therapy might colour body secretions orange/red (including soft contact lenses). Be aware of important drug interactions with rifampicin, eg failure of the **oral contraceptive** due to enzyme inducement (refer to **BNF**). **Avoid monotherapy** due to rapid emergence of resistant strains.

**METRONIDAZOLE** tablets 200mg, 400mg; oral suspension 200mg/5mL; suppositories 500mg, 1 gram; infusion 500mg/100mL

Metronidazole is indicated for anaerobic infections. For use in trichomoniasis see [Management of infection guidance](#).

Warn patients of the risk of a disulfiram-like reaction if alcohol is taken whilst on metronidazole.

**Sulfonamides and trimethoprim**

**CO-TRIMOXAZOLE** tablets 480mg; oral suspension 240mg/5mL, 480mg/5mL; infusion 480mg/5mL

For prophylaxis or treatment of *Pneumocystis jirovecii* (*Pneumocystis carinii*) see BNF information.

**TRIMETHOPRIM** tablets 100mg, 200mg; suspension 50mg/5mL

**Quinolones**

**CSM advice**: tendon damage (including rupture) has been reported rarely in patients receiving quinolones. Tendon rupture may occur within 48 hours of starting treatment. The CSM note that:
• quinolones are contra-indicated in patients with a history of tendon disorders related to quinolone use
• older patients are more prone to tendon damage
• the risk of tendon rupture is increased by the concomitant use of corticosteroids
• if tendinitis is suspected, discontinue quinolone immediately.

**CIPROFLOXACIN** tablets 250mg, 500mg; oral suspension 250mg/5mL; infusion 200mg/100mL, 400mg/200mL
Ciprofloxacin has unreliable activity against *Streptococcus pneumoniae* and is unsuitable for the initial treatment of community-acquired pneumonia. Refer to Management of Infection guidance for more appropriate treatment.

**LEVOFLOXACIN** tablets 500mg; infusion 500mg in 100mL
Levofloxacin has increased activity against *Streptococcus pneumoniae* therefore is a suitable alternative in the management of respiratory infections in patients with an allergy to penicillin. It is the drug of choice in the treatment of known or suspected *Legionella* infection.

**OFLOXACIN** tablets 200mg, 400mg; infusion 200mg/100mL

Urinary-tract infections

**NITROFURANTOIN** tablets 50mg, 100mg; m/r capsules 100mg; oral suspension 25mg/5mL
Nitrofurantoin may be used for urinary-tract infections in the first and second trimesters in pregnancy. The m/r preparation has improved patient tolerability and may reduce the need for second-line antibiotics.

5.2 ANTIFUNGAL DRUGS

**FLUCONAZOLE** capsules 50mg, 150mg<sup>OTC</sup>, 200mg; oral suspension 50mg/5mL; infusion 200mg/100mL

**ITRACONAZOLE** capsules 100mg; oral liquid 50mg/5mL
For haematology patients who are, or are likely to become, neutropenic, use the oral liquid in a dose of 200mg twice daily.

**TERBINAFINE** tablets 250mg
Oral terbinafine is reserved for proven dermatophyte infections. Take nail clippings: start therapy only if infection is confirmed by laboratory. Idiosyncratic liver reactions occur rarely with terbinafine; see BNF monitoring requirements. Advise patients to report immediately any signs or symptoms suggestive of liver dysfunction. For children seek advice from Dermatology.

Preparations for the treatment of vaginal candidiasis are included in section 7.2, for oropharyngeal infections in section 12.3 and for dermatological infections in section 13.10.

5.3 ANTIVIRAL DRUGS

**ACICLOVIR** tablets 200mg, 400mg, 800mg; suspension 200mg/5mL; infusion 250mg

**FAMCICLOVIR** tablets 250mg
5.4 ANTIMALARIAL DRUGS

Up-to-date information on malaria prophylaxis is available from www.travax.scot.nhs.uk or from Medicines Information. For guidance on prescribing medicines for travel refer to ‘Guidance on prescribing vaccines and medicines for travel’.

5.5 DRUGS FOR THREADWORMS

Anthelmintics

For guidance on threadworm infestations see Management of infection guidance.

MEBENDAZOLE chewable tablets 100mg OTC; suspension 100mg/5mL

Only licensed for children of 2 years and older; refer to BNF for Children. It is given as a single dose. If re-infection occurs a second dose may be needed after 2 weeks, if one person is infected then treat the whole family.
ANTIMICROBIALS FOR SPECIALIST USE WITHIN HIGHLAND

Use only in accordance with protocols or on advice of Microbiology, Infectious Diseases or appropriate Consultant Specialist.

Penicillins

TEMOCILLIN injection 1 gram

PIVMECILLINAM tablets 200mg

FLUCLOXACILLIN continuous infusion prefilled device 8g/240mL, 12g/240mL [off-label]

Other beta-lactam antibiotics

ERTAPENEM infusion 1 gram

MEROPENEM injection 500mg, 1 gram

Tetracyclines

DEMECLOCYCLINE capsules 150mg

Aminoglycosides

AMIKACIN injection 500mg/2mL

TOBRAMYCIN injection 40mg/1mL, 80mg/2mL; nebuliser solution 300mg/4mL; dry powder for inhalation 28mg/capsule (Tobi® Podhaler)

NEOMYCIN tablets 500mg

Other antibacterials

COLISTIMETHATE SODIUM injection 1 million units; powder for nebuliser solution 1 million units; dry powder for inhalation 1.66 million units/capsule (Colobreathe®)

DALBAVANCIN powder for concentrate for solution for infusion 500mg

DAPTO Mycin infusion 350mg, 500mg

FIDAXOMICIN tablets 200mg

See Clostridium difficile policy on Intranet.

FOSFOMYCIN oral sachets 3 grams; powder for solution for intravenous infusion 2 grams, 4 grams

LINEZOLID tablets 600mg; oral suspension 100mg/5mL; infusion 600mg/300mL

RIFAXIMIN tablets 550mg

TIGECYCLINE powder for solution for infusion 50mg

Antituberculous drugs

To support monitoring and safe use see: http://www.tbdrugmonographs.co.uk.

ETHAMBUTOL tablets 100mg, 400mg

ISONIAZID tablets 100mg; injection 50mg/2mL

RIFINAH® 150/100 (rifampicin 150mg, isoniazid 100mg) tablets

RIFINAH® 300/150 (rifampicin 300mg, isoniazid 150mg) tablets

RIFATER® (rifampicin 120mg, isoniazid 50mg, pyrazinamide 300mg) tablets

Antileprotic drugs

DAPSONE tablets 50mg

Antifungal drugs

POSACONAZOLE tablets 100mg; oral suspension 200mg/5mL

Use tablets in preference to the oral suspension. Due to differences in the dosing of each formulation the tablets and oral suspension are not interchangeable.

VORICONAZOLE tablets 50mg, 200mg; oral suspension 200mg/5mL; intravenous infusion 200mg

AMPHOTERICIN (Fungizone®) infusion 50mg

AMPHOTERICIN (AmBisome®) liposomal infusion 50mg

ANIDULAFUNGIN infusion 100mg

CASPOFUNGIN infusion 50mg, 70mg
**FLUCYTOSINE** infusion 2.5 grams/250mL

**Antiviral drugs for HIV**

**Nucleoside reverse transcriptase inhibitors**

**ABACAVIR** tablets 300mg; oral solution 100mg/5mL

**TRIUMEQ**® (dolutegravir 50mg, abacavir 600mg, lamivudine 300mg) tablets

**KIVEXA**® (abacavir 600mg, lamivudine 300mg) tablets

**TRIZIVIR**® (abacavir 300mg, lamivudine 150mg, zidovudine 300mg) tablets

**LAMIVUDINE** tablets 100mg (Zeffix®), 150mg (Epivir®); oral solution (Epivir®) 50mg/5mL

**TENOFOVIR** disoproxil (as fumarate) tablets 245mg

**GENVOYA**® (elvitegravir 150mg, cobicistat 150mg, emtricitabine 200mg, tenofovir alafenamide 10mg tablets

**STRIBILD**® (elvitegravir 150mg, cobicistat 150mg, emtricitabine 200mg, tenofovir disoproxil (as fumarate) 245mg) tablets

**TRUVADA**® (tenofovir disoproxil (as fumarate) 245mg, emtricitabine 200mg) tablets

See SMC 237/06, 1225/17.

**ATRIPLA**® (efavirenz 600mg, emtricitabine 200mg, tenofovir disoproxil (as fumarate) 245mg) tablets

**EVIPLERA**® (emtricitabine 200mg, rilpivirine 25mg, tenofovir disoproxil as fumarate) 245mg) tablets

**ZIDOVUDINE** capsules 250mg; oral solution 50mg/5mL; infusion 200mg/20mL (requires dilution)

**COMBIVIR**® (zidovudine 300mg, lamivudine 150mg) tablets

**Protease inhibitors**

**ATAZANAVIR** capsules 150mg, 200mg, 300mg

**DARUNAVIR** tablets 600mg, 800mg; oral suspension 500mg/5mL

**KALETRA**® (lopinavir 200mg, ritonavir 50mg) tablets; (lopinavir 400mg, ritonavir 100mg/5mL) oral solution

**RITONAVIR** tablet 100mg

**Non-nucleoside reverse transcriptase inhibitors**

**EFAVIRENZ** tablets 600mg; capsules 50mg, 100mg, 200mg

**ETRAVIRINE** tablets 100mg

**NEVIRAPINE** tablets 200mg, m/r tablets 400mg

**Other antiretrovirals**

**RALTEGRAVIR** tablets 400mg, 600mg

**DOLUTEGRAVIR**® tablets 10mg, 25mg, 50mg

**Antiviral drugs for cytomegalovirus**

**GANCICLOVIR** infusion 500mg

**VALGANCICLOVIR** tablets 450mg; oral solution 250mg/5mL

**Antiviral drugs for influenza**

**OSELTAMIVIR** capsules 30mg, 45mg, 75mg; oral suspension 30mg/5mL

**ZANAMIVIR** dry powder for inhalation, 5mg/dose

**Respiratory syncytial virus**

**PALIVIZUMAB** injection 50mg/0.5mL, 100mg/1mL
For use in paediatrics only.
Viral hepatitis

**DACLATASVIR** tablets 30mg, 60mg

**DASABUVIR** tablets 250mg

**LEDIPASVIR/SOFOSBUVIR** tablets 90mg/400mg (Harvoni®)

**OMBITASVIR/PARITAPREVR/ RITONAVIR** tablets 12.5mg/75mg/50mg (Viekirax®)

**RIBAVIRIN** capsules 200mg

**SIMEPREVIR** capsules 150mg

**SOFOSBUVIR** tablets 400mg

**TENOFOVIR** tablets 245mg

**ELBASVIR/GRAZOPREVIR** tablets 50mg/100mg (Zepatier®)

**SOFOSBUVIR/VELPATASVIR** tablets 400mg/100mg (Epclusa®)

**Antimalarials**

**CHLOROQUINE** tablets OTC 250mg

**ARIESUNATE** injection 60mg [unlicensed]. Preferred choice in severe malaria; for further information see UK malaria treatment guidelines 2016.

**ARTEMETHER WITH LUMEFANTRINE** tablets (artemether 20mg, lumefantrine 120mg) (Riamet®)

**Drugs for Pneumocystis jiroveci** (formerly carinii)

See also co-trimoxazole and BNF.

**ATOVAQUONE** suspension 750mg/5mL

**PENTAMIDINE** injection 300mg; nebuliser solution 300mg
ANTIMICROBIAL MANAGEMENT OF NEUTROPENIC SEPSIS/FEBRILE NEUTROPNIA IN ADULT PATIENTS

NEUTROPENIC SEPSIS (NS) SUSPECTED - Requires URGENT SENIOR medical assessment.

See intranet for full management: Guidelines for the Treatment of Neutropenic Sepsis in Adult Patients

Definition of Neutropenic Sepsis - Neutrophil count < 0·5 x 10⁹/L with other features of possible sepsis i.e. SIRS or high index of clinical suspicion. Patients on chemotherapy or with neutropenia with or without fever are at risk of serious complications. These patients are at risk of serious, potentially fatal infections.

First Line Investigations
- FBC, Coag, U&E, LFT, Glucose,
- Ca2+, PO4-, Mg2+, Lactate, CRP
- Blood Cultures x 2 - peripheral plus CVC (all lumens). If no CVC then 2 sets (separate venepuncture).

Other Investigations
- MSU
- CXR
- Throat & Nasal Swabs
- Swabs CVC exit/skin lesions
- Stool Culture/C. diff (if appropriate).

First Hour Management – INITIATE HIGHLAND SEPSIS RECORD Initial Bundle
- If positive culture results are available, commence antibiotic regimen to cover known pathogens.
- Assess risk. High risk patients are those with septic shock or NEWS of 7 or above plus all patients with acute leukaemia or allogeneic transplant.

For Haematology/Oncology patients, as soon as treatment is initiated, contact patient’s Consultant at Raigmore Hospital if during working hours. If admitted out of hours and the patient is clinically stable this can be done the following morning. On-call Consultant Haematologist or Oncologist can be contacted through Raigmore switchboard if necessary. Contact should be clearly documented in the medical notes.

EMPIRIC ANTIMICROBIAL TREATMENT GUIDELINES (all doses by intravenous route only)

Antibiotics should be administered within one hour of presentation

**If patient has received or is receiving cisplatin, discuss with Oncology/Haematology/Microbiology Consultant for alternative to gentamicin or vancomycin (risk of nephrotoxicity). Please note treatment with gentamicin should be limited to minimise toxicity.

All prescriptions should be reviewed after 72 hours in conjunction with microbiology results and treatment continued only on the advice of a Microbiologist or Infectious Diseases Consultant.

<table>
<thead>
<tr>
<th>Piperacillin/tazobactam 4·5 gram FOUR times daily</th>
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</thead>
<tbody>
<tr>
<td>If allergy/intolerance/interaction with piperacillin/tazobactam: Aztreonam 2 gram FOUR times daily PLUS vancomycin**</td>
</tr>
<tr>
<td>**If high risk: ADD ** Gentamicin (use Adult Parenteral Gentamicin Prescription Chart)</td>
</tr>
</tbody>
</table>

Review at 2 to 3 days
- If patient not improving or is deteriorating and no positive culture: Seek Consultant approval for SWITCH to Meropenem 1 gram THREE times daily

Review at 4 to 7 days
- If patient not improving or is deteriorating no positive culture despite broad antibiotic cover, consider adding Caspofungin* 70mg ONCE daily

* Caspofungin
If patient weighs less than 80kg, reduce maintenance dose to 50mg

ADD antimicrobial cover for specific infection risks:
- **If high risk: ADD ** Gentamicin (use Adult Parenteral Gentamicin Prescription Chart)
- IV teicoplanin / vancomycin** (follow local guidelines) if MRSA colonised (current or previous, or suspected central line infection.
- IV clarithromycin 500mg 12-hourly if Community-Acquired Pneumonia suspected and atypical cover required (check drug interactions)
- IV metronidazole 500mg 8-hourly for mucositis in penicillin allergy only
- Previous ESBL infection or known ESBL carrier use a carbapenem in place of piperacillin/ tazobactam. Check previous microbiology results for resistance information.

If fungal infection strongly suspected and patient not improving or is deteriorating after 72 hours of caspofungin, review with Micro/ID specialist and SWITCH to Ambisome® 3mg/kg ONCE daily

All therapy should be reviewed regularly and de-escalated according to confirmed site/source of infection or positive culture and sensitivity information.

If patient has received or is receiving cisplatin, discuss with Oncology/Haematology/Microbiology Consultant for alternative to gentamicin or vancomycin (risk of nephrotoxicity). Please note treatment with gentamicin should be limited to minimise toxicity.

All prescriptions should be reviewed after 72 hours in conjunction with microbiology results and treatment continued only on the advice of a Microbiologist or Infectious Diseases Consultant.
Notes:

1. If *aspergillus spp.* microbiologically proven or clinically suspected, eg symptoms, chest x-ray, CT scan, switch caspofungin/Ambisome® to voriconazole. If fungal disease is suspected or proven in the CNS then switch caspofungin/Ambisome® to voriconazole.

   **Avoid voriconazole if**
   - infection occurred in presence of azole prophylaxis
   - a vinca alkaloid has been given or will be given within 48 hours (↑ risk of neurotoxicity).

2. In the presence of CXR changes assess risk of pneumocystis pneumonia (Pneumocystis jiroveci pneumonia (PJP)).

3. G-CSF therapy may be indicated in patients with deep neutropenia +/- sepsis who have not had pegfilgrastim therapy immediately following their latest chemotherapy cycle and whose marrow function is expected to be able to recover within several days. Discuss with the patient’s Haematology or Oncology Consultant.

4. For all patients empirical therapy should only be changed within the first 48 to 72 hours if:
   a. there is microbiologically documented infection resistant to empirical therapy, and appropriate sensitivities are available.
   b. there is a significant deterioration in clinical state despite empirical therapy including development of shock, acute respiratory distress syndrome, disseminated intravascular coagulation, multiple organ failure, clinical progression in primary focus of infection, eg lung or skin. In these situations therapy should be decided in consultation with senior haematological and microbiological staff.
MANAGEMENT OF INFECTION GUIDANCE

Aims
- To provide a simple, evidence-based approach to the empirical treatment of common infections - if a severe infection is not covered in this document, seek microbiological advice. Contact Microbiology at Raigmore Hospital, tel: 01463 704000 (switchboard).
- To promote the safe, effective and economic use of antibiotics.
- To minimise the emergence of bacterial resistance.

Principles of treatment
1. This guidance is based on the best available evidence however its application must be modified by professional judgement. Further information regarding dosages should be sought. The guideline should be available in all healthcare settings at the point of prescribing.

2. Guidance to support diagnosis of infection should be available, eg UTI decision aid, CURB/CRB-65 score information, sepsis recognition and severity assessment, management of *C. difficile* infection (CDI), recommended samples for microbiology investigations.

3. Prescribe an antibiotic **only** when there is likely to be a clear clinical benefit. Consider the anticipated clinical benefit of treatment, the nature and severity of the infection, co-morbidities, **polypharmacy** and other concomitant health issues. Bacteriuria should only be treated if signs of systemic infection are present.

4. Avoid telephone consultation and prescription of antimicrobials in primary care as this does not permit adequate evaluation of these issues.

5. **Do not prescribe** an antibiotic for viral sore throat, simple coughs and colds.

6. Consider a no, or delayed, antibiotic strategy for acute self-limiting upper respiratory-tract infections.

7. Use narrow-spectrum, generic antibiotics whenever possible.

8. Be alert to the potential for infections due to resistant organisms. Treatment should be informed by any infections during the preceding 12 weeks and how they have responded to previous therapy. **Avoid** use of topical antibiotics to prevent increasing the risk of resistance, particularly for those agents that are also available systemically.

9. Check potential drug interactions in the current BNF, Appendix 1. The risk of adverse events caused by altered pharmacokinetic parameters of medicines is increased in older people due to low body weight, impaired absorption and reduced clearance. Check for chronic kidney disease and adjust dosage accordingly to avoid adverse effects (see BNF). Elderly patients often become dehydrated, especially when unwell; consider this when interpreting eGFR or serum creatinine results.

10. To reduce the risk of infection with *C. difficile*, avoid the following high-risk antibiotics known as the 4Cs (cephalosporins, clindamycin, co-amoxiclav and quinolones, eg ciprofloxacin), especially if currently prescribed a proton pump inhibitor (PPI). For review of PPI use see section 1.3.

11. All patients commenced on intravenous antibiotics should be reviewed frequently, at least after 48 to 72 hours **by the medical team responsible for the patient**, to determine whether the patient can be switched to an antibiotic that can be administered orally, and/or is narrow-spectrum (based on Microbiology results).
12. Assess the resolution of symptoms regularly (daily in hospital), e.g. normal temperature, increased energy, alertness, mobility and appetite, and also identify adverse effects such as nausea and vomiting, diarrhoea, skin rash. Lack of response after 48 hours of treatment and any adverse effects should be highlighted to medical staff.

13. Review microbiology results when available to ensure that empirical therapy is suitable: de-escalate broad-spectrum therapy to narrow-spectrum agents if appropriate.

14. In pregnancy AVOID tetracyclines, aminoglycosides, quinolones, and *high-dose* metronidazole. Use trimethoprim (theoretical risk in first trimester in patients with poor diet, as folate antagonist) and nitrofurantoin (at term, theoretical risk of neonatal haemolysis) with caution.

15. When ‘end of life’ care has been initiated or an anticipatory/advanced care plan is in place, consider the relative benefits and risks of treatment carefully, in particular, inappropriate escalation of antimicrobial therapy. Treatment of symptomatic infections may still be appropriate even in the last few days of life. Seek local palliative care advice if required.

In cases of severe sepsis, consider immunocompromised states such as HIV.

**Click on the following links to go straight to specific sections:**
- Meningitis
- Systemic and other infections
- Dental infections
- Respiratory-tract infections
- Urinary-tract infections
- Skin/soft-tissue infections
- Bone and joint infections
- Viral infections
- Gastro-intestinal tract infections
- Intra-abdominal infections
- Parasitic infestations
- Genital-tract infections
- Diabetic foot infections
- Lyme disease

*Note: Doses are oral and for adults unless otherwise stated. Refer to BNF for further information.*
# MENINGITIS (Updated April 2017)

<table>
<thead>
<tr>
<th>Illness</th>
<th>Comments</th>
<th>Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfer all patients to hospital immediately</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Suspected bacterial meningitis prior to admission into secondary care</td>
<td>Administer antibiotics if hospital admission delayed by more than one hour. Ideally intravenous but intramuscular if a vein cannot be found.</td>
<td>Benzylpenicillin (intravenous or intramuscular)</td>
<td>Adults and children 10 years and over 1-2 grams</td>
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<td></td>
<td></td>
<td></td>
<td>Children 1 to 9 years 600mg</td>
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<td></td>
<td></td>
<td>Children under 1 year 300mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In penicillin allergy</td>
<td>Ceftriaxone (intravenous or intramuscular)</td>
<td>Adults and children 50kg and over 2 gram</td>
<td></td>
<td></td>
<td>As a single dose</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Children under 50kg 80mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR</td>
<td>Cefotaxime (intravenous or intramuscular)</td>
<td>Adults 2 gram</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Children 11 to 17 years 1 gram</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Children 1 month to 11 years 50mg/kg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Penicillin/cephalosporin anaphylaxis</td>
<td>Await admission to hospital before administering antibiotics – contact infection specialist</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>'Blind' treatment of bacterial meningitis following admission to secondary care</td>
<td>Rationalise treatment on making diagnosis.</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>If recent foreign travel contact infection specialist as vancomycin may be indicated (aim for trough of 15 to 20mg/L).</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>Penicillin-resistant pneumococci uncommon in Highlands.</td>
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<tr>
<td></td>
<td>For patients with severe renal impairment, give the first dose then seek advice.</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>With (or just before) the first dose of antibiotics or up to 12 hours after</td>
<td>Dexamethasone (intravenous)</td>
<td>Adults 10mg</td>
<td>Every 6 hours</td>
<td>4 days if S. pneumoniae confirmed or probable pathogen</td>
<td></td>
</tr>
<tr>
<td>Adults under 60 years of age</td>
<td></td>
<td>Children 0-15mg/kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If clear history of anaphylaxis to penicillins or cephalosporins</td>
<td>*Ceftriaxone (intravenous)</td>
<td>2 grams</td>
<td>Every 12 hours</td>
<td>N. meningitidis confirmed: adult 5 days, child 7 days; duration depends on recovery</td>
<td></td>
</tr>
<tr>
<td>Adults 60 years and over OR immunocompromised (including alcohol dependency and diabetes)</td>
<td>Chloramphenicol (intravenous)</td>
<td>25mg/kg</td>
<td>Every 6 hours</td>
<td>H. influenza 10 days</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ceftriaxone (intravenous) PLUS Amoxicillin (intravenous)</td>
<td>2 grams</td>
<td>Every 12 hours</td>
<td>S. pneumoniae 10 to 14 days depending on recovery</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Chloramphenicol (intravenous) PLUS Co-trimoxazole (intravenous)</td>
<td>25mg/kg</td>
<td>Every 6 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>See BNF for Children for dosing</td>
<td>30mg/kg</td>
<td>Every 6 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Children under 3 months, cover Listeria</td>
<td>Ceftriaxone (intravenous) PLUS Amoxicillin (intravenous)</td>
<td>80mg/kg</td>
<td>Once daily</td>
<td>Listeria (confirmed cases) 21 days</td>
<td></td>
</tr>
<tr>
<td>Children 3 months and over</td>
<td>*Ceftriaxone (intravenous)</td>
<td>80mg/kg</td>
<td>Once daily</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note:** Doses are oral and for adults unless otherwise stated. Refer to BNF for further information.
<table>
<thead>
<tr>
<th>If viral encephalitis suspected (reduce dose in renal impairment) <strong>If obese, calculate the dose using ideal bodyweight.</strong></th>
<th><strong>ADD</strong></th>
<th><strong>Adults and children over 12 years</strong></th>
<th><strong>If unconfirmed but clinically suspected cases</strong></th>
<th><strong>Ceftriaxone</strong></th>
<th><strong>Adults</strong></th>
<th><strong>Children</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Aciclovir (intravenous)</td>
<td>Every 8 hours</td>
<td>10mg/kg</td>
<td>Every 8 hours</td>
<td>1000mg</td>
<td>Twice daily</td>
<td>Twice daily</td>
</tr>
<tr>
<td>Children 3 months to 12 years 500mg/m²</td>
<td></td>
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</tr>
</tbody>
</table>

**ADD**

- **Aciclovir** (intravenous)

**Adults and children over 12 years**

- Every 8 hours

**Children 3 months to 12 years**

- 500mg/m²

**Unconfirmed but clinically suspected cases**

- Ceftriaxone

**Adults**

- 2 grams

**Child**

- As per BNF for Children

**Prevention of secondary case of meningitis**

- Seek immediate advice from Public Health Department (tel: 01463 704886 during normal working hours, 01463 704000 for out of hours). Patient information leaflets on ‘Ciprofloxacin’ and ‘Meningococcal disease’ are available on [intranet](#).

- Patients treated solely with benzylpenicillin or cefotaxime require a single dose of oral ciprofloxacin to eradicate nasal carriage.

*In children, avoid simultaneous administration of ceftriaxone and calcium containing intravenous fluids (including parenteral nutrition). Infusions can be given sequentially or ceftriaxone replaced by cefotaxime in doses listed in the current edition of BNF for Children.*

See BNFS for more information.
<table>
<thead>
<tr>
<th>Illness</th>
<th>Comments</th>
<th>Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis unclear. Infection source likely respiratory or urinary-tract. (? UTI/?Chest)</td>
<td>Review within 24 hours to confirm diagnosis then follow appropriate infection specific recommendations.</td>
<td>Mild to moderate infection</td>
<td>See UTI and acute bronchitis/community-acquired pneumonia sections of the guidance, choosing the first-line options for each infection. This will result in a combination of two or more antibiotics being prescribed.</td>
<td></td>
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</tr>
<tr>
<td>Severe infection</td>
<td>Refer to guidance for hospital-acquired pneumonia as this combination will provide the same cover.</td>
<td></td>
<td></td>
<td>7 to 14 days</td>
<td></td>
</tr>
<tr>
<td>Neutropenic Sepsis</td>
<td>See ‘Antimicrobial Management of Neutropenic Sepsis in Adult/Haematology/Oncology Patients’</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Sepsis with unknown focus</td>
<td>If sepsis has a cutaneous component or is arising from the skin, REFER TO SECTION ON NECROTISING FASCIITIS</td>
<td>Community-acquired infection</td>
<td>Amoxicillin (intravenous) PLUS Gentamicin (intravenous) PLUS Metronidazole (intravenous)</td>
<td>1 gram</td>
<td>Every 8 hours</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Refer to NHS Highland gentamicin dosing guidelines</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>500mg</td>
<td>Every 8 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td>If Staphylococcus aureus infection suspected</td>
<td>ADD Flucloxacillin (intravenous)</td>
<td>2 grams</td>
<td>Every 6 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• In penicillin allergy</td>
<td>Aztreonam (intravenous) PLUS Vancomycin (intravenous) PLUS Metronidazole (intravenous)</td>
<td>2 grams</td>
<td>Every 6 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• severe renal impairment</td>
<td></td>
<td>Refer to NHS Highland vancomycin dosing guidelines</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• acute kidney injury</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• hospital-acquired infection</td>
<td></td>
<td>500mg</td>
<td>Every 8 hours</td>
<td></td>
</tr>
</tbody>
</table>
**DENTAL INFECTIONS (Updated November 2016)**

This guidance is not designed to be a definitive guide to oral conditions. It is for GPs for the management of acute oral conditions pending being seen by a dentist or dental specialist. GPs should not routinely be involved in dental treatment and, if possible, advice should be sought from the patient’s dentist. When the patient is not registered with a general dental practitioner (GDP), advise to seek local registration or contact the dental helpline, tel: 0845 644 2271. For out of hours contact NHS 24 on 111. Refer to the GDP/dental helpline for follow-up.

**NB:** Antibacterial prophylaxis and chlorhexidine mouthwash are **NOT** recommended for the prevention of endocarditis in patients undergoing dental procedures. Refer to BNF for further information.

<table>
<thead>
<tr>
<th>Illness</th>
<th>Comments</th>
<th>Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mucosal ulceration and inflammation</strong></td>
<td>The primary cause for mucosal ulceration or inflammation (aphthous ulcers, oral lichen planus, herpes simplex infection, oral cancer) needs to be evaluated and treated.</td>
<td><strong>Temporary pain and swelling relief can be attained with saline mouthwash. Use antiseptic mouthwash if more severe and pain limits oral hygiene to treat or prevent secondary infection.</strong></td>
<td><strong>Simple saline mouthwash</strong>&lt;br&gt;Chlorhexidine 0.12-0.2% (do not use within 30 mins of toothpaste)&lt;br&gt;Hydrogen peroxide 6% (spit out after use)</td>
<td>½ tsp salt dissolved in glass warm water&lt;br&gt;10mL&lt;br&gt;Can be diluted with 10mL water.&lt;br&gt;15mL diluted in ½ glass warm water</td>
<td>As required for pain relief&lt;br&gt;Rinse mouth for 1 minute twice daily&lt;br&gt;Rinse mouth for 2 mins 3 times daily</td>
</tr>
<tr>
<td><strong>Acute necrotising ulcerative gingivitis</strong></td>
<td>If the patient is immunocompromised, they should advise the dental helpline operator who in turn will prioritise their call directly to the Clinical Dental Manager.</td>
<td><strong>Commence therapy and refer to dentist for scaling and oral hygiene advice. Use in combination with antiseptic mouthwash if pain limits oral hygiene.</strong>&lt;br&gt;Metronidazole&lt;br&gt;Chlorhexidine or hydrogen peroxide</td>
<td>400mg&lt;br&gt;400mg&lt;br&gt;500mg</td>
<td>3 times daily&lt;br&gt;3 times daily&lt;br&gt;3 times daily</td>
<td>3 days&lt;br&gt;3 days&lt;br&gt;3 days</td>
</tr>
<tr>
<td><strong>Pericoronitis</strong></td>
<td>Refer to dentist for irrigation and debridement. If persistent swelling or systemic symptoms use metronidazole. Use antiseptic mouthwash if pain and trismus limit oral hygiene.</td>
<td><strong>Metronidazole</strong>&lt;br&gt;<strong>OR</strong>&lt;br&gt;Amoxicillin&lt;br&gt;Chlorhexidine or hydrogen peroxide</td>
<td>400mg&lt;br&gt;500mg</td>
<td>3 times daily&lt;br&gt;3 times daily</td>
<td>3 days&lt;br&gt;3 days</td>
</tr>
</tbody>
</table>

*Note: Doses are oral and for adults unless otherwise stated. Refer to BNF for further information.*
Dental abscess

- Regular analgesia should be first option until a dentist can be seen for urgent drainage, as repeated courses of antibiotics for abscess are not appropriate; repeated antibiotics alone, without drainage are ineffective in preventing spread of infection.
- Antibiotics are recommended if there are signs of severe infection, systemic symptoms or high risk of complications.
- Severe odontogenic infections; defined as cellulitis plus signs of sepsis, difficulty in swallowing, impending airway obstruction, Ludwigs angina. Refer urgently for admission to protect airway, achieve surgical drainage and IV antibiotics.
- The empirical use of cephalosporins, co-amoxiclav, clarithromycin, and clindamycin do not offer any advantage for most dental patients and should only be used if no response to first-line drugs when referral is the preferred option.

<table>
<thead>
<tr>
<th>If pus drain by incision, tooth extraction or via root canal. Send pus for microbiology.</th>
<th>Amoxicillin OR Phenoxymethyl penicillin</th>
<th>500mg 500mg to 1gram</th>
<th>3 times daily 4 times daily</th>
<th>Up to 5 days with review at 3 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>In penicillin allergy</td>
<td>Metronidazole</td>
<td>400mg</td>
<td>3 times daily</td>
<td></td>
</tr>
<tr>
<td>If spreading infection (lymph node involvement, or systemic signs, ie fever or malaise)</td>
<td>ADD Metronidazole</td>
<td>400 mg</td>
<td>3 times daily</td>
<td>5 days</td>
</tr>
<tr>
<td>In penicillin allergy (spreading infection) OR unresponsive to first-line antibiotics</td>
<td>Clindamycin</td>
<td>300mg</td>
<td>4 times daily</td>
<td>5 days</td>
</tr>
</tbody>
</table>

**Dosage of antimicrobials recommended in this guidance:**

The Scottish Dental Clinical Effectiveness Programme 2016 recommends a dose of 200mg metronidazole when antimicrobials are appropriate. The BNF recommends a higher dose of 400mg metronidazole. The rationale for this is when antimicrobials are considered appropriate, it is important to have sufficient concentrations at the site of infection. For metronidazole, the killing effect is dose-dependent and the greater the concentrations above the MIC the better. AUC/MIC >70 is only attainable against *Bacteroides fragilis* with a 400mg dose.
RESPIRATORY-TRACT INFECTIONS

The following severity assessment should be employed for respiratory-tract infections:

- CENTOR criteria for sore throat
- CURB65 or CRB 65 for community-acquired pneumonia
- SIRS for non-pneumonic chest infection, aspiration pneumonia or hospital-acquired pneumonia.

SEE INDIVIDUAL INFECTIONS FOR OTHER ADVICE

RESPIRATORY-TRACT INFECTIONS – SELF-LIMITING CONDITIONS (Updated October 2017)

Many respiratory-tract infections are self-limiting and/or viral and do not routinely require antibiotic therapy. Consider a 'delayed antibiotic prescription' strategy. Advise symptomatic relief, e.g. paracetamol or low-dose ibuprofen, where appropriate. The relevant conditions include (with timescale for illness):

- acute otitis media (4 days)
- acute sore throat/pharyngitis/tonsillitis (1 week)
- common cold (1 week)
- acute rhinosinusitis (2½ weeks)
- acute bronchitis (3 weeks)

For the above conditions, consider using antibiotics in the following situations (Number Needed to Treat for benefit):

- children under 2 years with bilateral otitis media (NNT = 4)
- acute otitis media in children with otorrhoea (NNT = 3)
- acute sore throat with FeverPAIN score of 4 or more (replaces CENTOR criteria)
  - Fever in last 24 hours
  - Purulence
  - Attend rapidly in under 3 days
  - Inflamed tonsils (severe)
  - No cough or coryza
- systemically very unwell
- pre-existing co-morbidity
- patients over 65 with at least two of the following, or over 80 and at least one of the following: admission to hospital in past 12 months; diabetes; LVF; glucocorticoids.

UPPER RESPIRATORY-TRACT INFECTIONS (Updated October 2017)

<table>
<thead>
<tr>
<th>Illness</th>
<th>Comments</th>
<th>Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza treatment and prophylaxis</td>
<td>Annual vaccination is essential for all those at risk of influenza. See Health Protection Scotland recommendations for Treatment and Prophylaxis of Influenza. For otherwise healthy adults, antivirals are not recommended. <strong>Treat 'at risk' patients</strong>, when influenza is circulating in the community and ideally within 48 hours of onset (do not wait for lab report) or in a care home where influenza is likely. <strong>At risk</strong>: pregnant (including up to 2 weeks post partum), 65 years or over, chronic respiratory disease (including COPD and asthma), significant cardiovascular disease (not hypertension), immunocompromised, diabetes mellitus, chronic neurological, renal or liver disease, morbid obesity (BMI ≥40). Seek advice for patients under 13 years or in severe immunosuppression. Patients admitted to hospital with influenza should be treated with antivirals.</td>
<td>Oseltamivir</td>
<td>75mg</td>
<td>Twice daily</td>
<td>5 days</td>
</tr>
<tr>
<td></td>
<td>If resistance to oseltamivir or severe immunosuppression</td>
<td>Zanamivir (inhaled)</td>
<td>10mg</td>
<td>Twice daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prophylaxis of influenza</td>
<td>Oseltamivir</td>
<td>75mg</td>
<td>Once daily</td>
<td>10 days</td>
</tr>
<tr>
<td></td>
<td>If resistance to oseltamivir</td>
<td>Zanamivir (inhaled)</td>
<td>10mg</td>
<td>Once daily</td>
<td></td>
</tr>
<tr>
<td>Acute sore throat</td>
<td>Generally avoid antibiotics as 90% resolve in 7 days without, and pain only reduced by 16 hours. <strong>Use FeverPAIN score as above</strong>. Always share self-care advice and safety-net. Amoxicillin and other broad-spectrum penicillins should not be used for the blind treatment of sore throat. Maculopapular rashes occur commonly with ampicillin and amoxicillin but are not usually related to true penicillin allergy. They almost always occur in people with infectious mononucleosis. Complications are rare: antibiotics to prevent quinsy, NNT &gt;4000;to prevent otitis media, NNT 200</td>
<td></td>
<td></td>
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</tbody>
</table>

Note: Doses are oral and for adults unless otherwise stated. Refer to BNF for further information.
<table>
<thead>
<tr>
<th>Score 0-1; 13-18% streptococci, use NO antibiotics strategy;  Score 2-3; 34-40% streptococci, use 3 day delayed prescription;  Score 4-5; 62-65% streptococci, use immediate antibiotic if severe, or 48 hour back-up prescription.</th>
<th>Phenoxymethyl-penicillin</th>
<th>500mg</th>
<th>4 times daily</th>
<th>10 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>In penicillin allergy  Clarithromycin</td>
<td>500mg</td>
<td>Twice daily</td>
<td>5 days</td>
<td></td>
</tr>
<tr>
<td>In penicillin allergy and pregnant  Erythromycin</td>
<td>500mg</td>
<td>4 times daily</td>
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</tbody>
</table>

| Scarlet fever (GAS)  Prompt treatment with appropriate antibiotics significantly reduces the risk of complications. Observe immune-compromised individuals (diabetes; women in the puerperal period; chickenpox) as they are at increased risk of developing invasive infection. | First-line (mild): analgesia  Phenoxymethylpenicillin | 500mg | 4 times daily | 10 days |
| Penicillin allergy: clarithromycin | 250mg to 500mg | Twice daily | 5 days |

| Acute otitis media (in children)  (Average duration of illness 4 days) | Haemophilus is an extracellular pathogen, thus macrolides, which concentrate intracellularly, are less effective treatment.  Optimise analgesia and target antibiotics  AOM resolves in 60% in 24hrs without antibiotics, which only reduce pain at 2 days (NNT15) and does not prevent deafness.  Consider 2 or 3-day delayed or immediate antibiotics for pain relief if: <2 years AND bilateral AOM (NNT4) or bulging membrane or symptom score above 8 for: fever, tugging ears, crying, irritability, difficulty sleeping, less playful, eating less (0 = no symptoms, 1 = a little, 2 = a lot). All ages with otorrhoea NNT3. Antibiotics to prevent mastoiditis NNT > 4000 | Amoxicillin | For dosing information, see BNF for Children |
| Anaphylaxis to beta-lactams | Clarithromycin | For dosing information, see BNF for Children |
| In penicillin intolerance | Cefuroxime | For dosing information, see BNF for Children |

| Acute otitis externa  See Section 12.1 |

| Acute rhinosinusitis  (Average duration of illness 2½ weeks) | Avoid antibiotics as 80% resolve in 14 days without; they offer marginal benefit after 7 days NNT 15. Use adequate analgesia. Consider a 7-day delayed antibiotic prescription when purulent nasal discharge (NNT = 8). In persistent infection, use an agent with anti-anaerobic activity, eg co-amoxiclav. | Phenoxyxmethyl-penicillin OR Amoxicillin | 500mg | 4 times daily | 5 days |
| Phenoxymethyl-penicillin OR Amoxicillin | 500mg OR 1 gram if severe | 3 times daily |
| In penicillin allergy  Doxycycline | 200mg stat then 100mg | Once daily | 7 days |
| Very unwell or worsening | Co-amoxiclav | 625mg | 3 times daily | 7 days |
**LOWER RESPIRATORY-TRACT INFECTIONS** (Updated October 2017)

<table>
<thead>
<tr>
<th>Illness</th>
<th>Comments</th>
<th>Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute cough, bronchitis</td>
<td>Systematic reviews indicate benefits of antibiotics are marginal in otherwise healthy adults. Consider treatment in older patients and those with co-morbidity. Consider immediate antibiotics if over 80 years AND one of: hospitalisation in last year, oral steroids, insulin-dependent diabetic, congestive heart failure, serious neurological disorder/stroke OR if over 65 years and 2 of above.</td>
<td>First-line Consider 7 to 14 day delayed antibiotic with symptomatic advice or leaflet.</td>
<td>Amoxicillin OR Doxycycline</td>
<td>500mg 200mg stat then 100mg</td>
<td>3 times daily Once daily</td>
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<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute exacerbation of chronic obstructive pulmonary disease (COPD)</td>
<td>Treat with antibiotics if purulent sputum and increased shortness of breath and/or increased sputum volume. Refer to <a href="#">Shared Clinical Guidelines (Respiratory) for COPD Education and Self-Management</a> for use of rescue medication.</td>
<td>Doxycycline OR Amoxicillin (if sensitive) OR Clarithromycin</td>
<td>200mg stat then 100mg 500mg 500mg</td>
<td>Once daily 3 times daily Twice daily</td>
<td>5 days</td>
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<td></td>
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<td></td>
<td>If resistance likely (co-morbid disease, severe COPD, frequent exacerbations, antibiotics in last 3 months). *IV therapy only required if nil by mouth</td>
<td>Co-amoxiclav OR Doxycycline</td>
<td>625mg (oral) OR 1-2 gram (intravenous) 200mg stat then 100mg</td>
<td>3 times daily</td>
<td>5 to 7 days</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>For hospital in-patients with penicillin allergy</td>
<td>Levofloxacin (oral or * intravenous)</td>
<td>500mg</td>
<td>Once daily</td>
<td></td>
</tr>
</tbody>
</table>

**Notes:** Avoid tetracyclines in pregnancy. Low doses of penicillins are more likely to select out resistance. Do not use ciprofloxacin or ofloxacin first-line due to poor pneumococcal activity. Reserve all quinolones for proven resistant organisms or in penicillin allergy according to guidelines. Local resistance information for NHS Highland indicates low levels of penicillin and tetracycline resistance to *Streptococcus pneumoniae*, the major pathogen in community acquired pneumonia. Tetracycline resistance is also low in *Haemophilus influenzae*, a common respiratory pathogen in COPD exacerbations.

*IV therapy only required if nil by mouth*
Community-acquired pneumonia (CAP)

Antibiotic therapy in CAP is not dependant on CRP level

**START ANTIBIOTICS IMMEDIATELY ONCE THE DIAGNOSIS HAS BEEN MADE.**

Assess severity using CURB65 score and markers of sepsis:

- **CURB65** score is defined by 1 point being scored for each of the following:
  - Confusion (mental test score 8 or less, new disorientation in person, time or place);
  - Urea >7mmol/L;
  - Respiratory rate ≥30/min;
  - Blood pressure (SBP <90mmHg, diastolic ≤ 60mmHg);
  - Age ≥ 65 years. GPs without access to a recent blood urea level should use CRB65 score.

The CURB65 or CRB65 should be recorded in the patient’s medical notes.

CURB65 or CRB65 score identifies those patients that may safely be treated out of hospital. Social support and treatment compliance issues should be considered in addition to CURB635 score. The use of CURB65 can over-estimate the severity of illness in the frail patient. It is not appropriate to use CURB65 score to assess severity in a post-operative patient as these parameters may already be raised in the immediate post-operative period. There are a number of significant drug interactions with clarithromycin and levofloxacin, eg warfarin, theophylline; see BNF for a comprehensive list. Clarithromycin is contra-indicated in patients taking simvastatin. If treatment with clarithromycin is necessary simvastatin should be temporarily discontinued and replaced with atorvastatin, up to a maximum of 20mg daily, for the duration of clarithromycin therapy. Levofloxacin can lower the seizure threshold and can cause tendon damage (including rupture) occurring within 48 hours of starting treatment or several months after stopping; avoid if there is a history of quinolone-associated tendon damage. The risk of tendon damage increases in patients over 60 years of age and in those taking concomitant steroids. Use with caution in patients with a prolonged QT interval or on other drugs known to have this effect. See BNF for more detailed information.

Consider early intravenous to oral switch with clinical improvement. Duration of therapy includes intravenous and oral treatment.

**Remember the risk of tuberculosis, particularly in immunocompromised patients and in travellers or recent settlers from abroad.**

### For CAP with features of SEPSIS, treat as CURB65 score 3 to 5

<table>
<thead>
<tr>
<th>Illness</th>
<th>Comments</th>
<th>Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAP with history of recent foreign travel</td>
<td>Discuss with consultant microbiologist or infectious diseases, including options for penicillin allergy</td>
<td>Clarithromycin (oral or intravenous) <strong>PLUS</strong> Amoxicillin (oral or intravenous)</td>
<td>500mg</td>
<td>Twice daily</td>
<td>7 days</td>
</tr>
<tr>
<td>CAP (Mild to moderate, home or hospital-treated, CURB65 or CRB65 = 0 to 1)</td>
<td>If no response in 48 hours add doxycycline to amoxicillin for atypical cover and consider admission</td>
<td>Amoxicillin</td>
<td>500mg</td>
<td>3 times daily</td>
<td>CRB65 = 0: 5 days. Review at 3 days and extend to 7-10 days if poor response. CURB65 = 1 7-10 days</td>
</tr>
<tr>
<td>CAP (hospital-treated, moderate severity, CURB65 = 2)</td>
<td>If nil by mouth, give penicillin allergy alternative</td>
<td>Amoxicillin <strong>PLUS</strong> Doxycycline</td>
<td>500mg</td>
<td>3 times daily</td>
<td>7 days</td>
</tr>
<tr>
<td></td>
<td>In penicillin allergy (rare need for intravenous therapy due to excellent oral bioavailability)</td>
<td>Levofloxacin (oral or intravenous)</td>
<td>500mg</td>
<td>Twice daily</td>
<td>7 days</td>
</tr>
</tbody>
</table>

**Note:** Doses are oral and for adults unless otherwise stated. Refer to BNF for further information.
<table>
<thead>
<tr>
<th>CAP (severe, CURB65 = 3 to 5) Or CAP with sepsis features</th>
<th>If no prior antibiotic treatment in community</th>
<th>Amoxicillin (intravenous) PLUS Doxycycline</th>
<th>1 gram</th>
<th>3 times daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>If unable to take oral medication</td>
<td>Levofloxacin (intravenous)</td>
<td>500mg</td>
<td>Twice daily</td>
<td></td>
</tr>
<tr>
<td>If antibiotics given in community before admission or in penicillin allergy or proven or suspected Legionella infection</td>
<td>Levofloxacin (oral or intravenous)</td>
<td>500mg</td>
<td>Twice daily</td>
<td></td>
</tr>
<tr>
<td>If risk factors for Staph. aureus including post influenza or chicken pox infection or haemorrhagic infection, discuss with infection specialist</td>
<td>Amoxicillin (intravenous) PLUS Flucloxacillin (intravenous) PLUS Clarithromycin (intravenous)</td>
<td>1 gram</td>
<td>3 times daily</td>
<td></td>
</tr>
<tr>
<td>If risk factors for Staph. aureus including post influenza or chicken pox infection or haemorrhagic infection, discuss with infection specialist</td>
<td>Amoxicillin (intravenous) PLUS Flucloxacillin (intravenous) PLUS Clarithromycin (intravenous)</td>
<td>2 grams</td>
<td>4 times daily</td>
<td></td>
</tr>
<tr>
<td>If bilateral/ cavitory changes or known/suspected MRSA</td>
<td>ADD Vancomycin (intravenous)</td>
<td>Refer to NHS Highland vancomycin dosing guidelines</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**ASPIRATION PNEUMONITIS DOES NOT REQUIRE ANTIMICROBIAL THERAPY.**

<table>
<thead>
<tr>
<th>Aspiration pneumonia</th>
<th>Consider aspiration pneumonia if:</th>
</tr>
</thead>
<tbody>
<tr>
<td>(mild to moderate)</td>
<td>- history of impaired swallowing or</td>
</tr>
<tr>
<td></td>
<td>- vomiting with possible aspiration 48 hours before.</td>
</tr>
<tr>
<td></td>
<td><strong>Infection is indicated by change in sputum quality to purulent or mucopurulent or fever AND new chest x-ray changes.</strong></td>
</tr>
<tr>
<td>If nil by mouth, give same doses intravenously</td>
<td>Metronidazole PLUS Amoxicillin OR Clarithromycin (in penicillin allergy)</td>
</tr>
<tr>
<td></td>
<td>400mg</td>
</tr>
<tr>
<td></td>
<td>500mg</td>
</tr>
<tr>
<td></td>
<td>500mg</td>
</tr>
<tr>
<td>Severe pneumonia ? aspiration</td>
<td>Pseudomonas, Gram-negative bacilli and MRSA are possibilities. Seek advice. Assess severity using SEPSIS criteria</td>
</tr>
<tr>
<td>In penicillin allergy</td>
<td>Metronidazole (intravenous) PLUS Amoxicillin (intravenous) PLUS Gentamicin (intravenous)</td>
</tr>
<tr>
<td></td>
<td>500mg</td>
</tr>
<tr>
<td></td>
<td>1 gram</td>
</tr>
<tr>
<td></td>
<td>Refer to NHS Highland gentamicin guidelines (Stop after 3 days if no evidence of gram negative infection)</td>
</tr>
<tr>
<td></td>
<td>7 to 14 days</td>
</tr>
<tr>
<td>If MRSA likely or over 65 years follow penicillin allergy option and</td>
<td>Levofoxacin (intravenous or oral) PLUS Metronidazole (intravenous)</td>
</tr>
<tr>
<td></td>
<td>500mg</td>
</tr>
<tr>
<td></td>
<td>500mg</td>
</tr>
</tbody>
</table>

**Note:** Doses are oral and for adults unless otherwise stated. Refer to BNF for further information.
**Hospital-acquired pneumonia**
For pneumonia presenting more than 3 days into hospital admission, it is important to give broad-spectrum antibiotics which are active against Gram-negative organisms in the first instance. In more severe infection, consider cover for Legionella, *Staph aureus*, both MSSA and MRSA. Use SIRS criteria for severity assessment.

<table>
<thead>
<tr>
<th>Hospital-acquired pneumonia (not severe)</th>
<th>Co-trimoxazole OR Doxycycline</th>
<th>960mg</th>
<th>Twice daily</th>
<th>Up to 8 days for clinical responders</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital-acquired pneumonia (severe)</td>
<td>Infection with an atypical pathogen is uncommon, if suspected, discuss with Microbiology</td>
<td>Aztreonam (intravenous) PLUS Vancomycin (intravenous)</td>
<td>2 gram</td>
<td>3 times daily</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>Before starting antibiotics, a sputum sample should be sent for culture, when possible. Previous sputum microbiology should be used to guide therapy, particularly if <em>Pseudomonas aeruginosa</em> isolated. Seek advice from Microbiology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tuberculosis (TB)</td>
<td>See NICE guideline (<a href="http://www.nice.org.uk">www.nice.org.uk</a>). Advice must be sought from a Chest Physician (Raigmore Hospital, tel: 01463 704363 or 704364. Test for HIV in all newly diagnosed cases of TB. Report all cases to the Health Protection Team (tel: 01463 704886 during normal working hours, 704000 for out of hours).</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Note: Doses are oral and for adults unless otherwise stated. Refer to BNF for further information.*
**URINARY-TRACT INFECTIONS (UTI) (Updated December 2017)**

For advice on the diagnosis of UTI, see Urology Shared Clinical Guidelines. Only patients with signs and symptoms of urinary-tract infection require treatment with antibiotics (except in pregnancy).

**Note:** Asymptomatic bacteriuria (presence of bacteria in the urine without signs or symptoms of infection) occurs in 25% of women and 10% of men aged 65 years and over and is not associated with increased morbidity. In the presence of a catheter, antibiotics will not eradicate bacteria. Bacteriuria alone is rarely an indication for antibiotics.

**Narrow-spectrum antibiotics for UTI** include trimethoprim, nitrofurantoin and amoxicillin. As a first generation cephalosporin, cefalexin has a reduced risk of infection with *Clostridium difficile* but has broader cover. Avoid empiric use of quinolones except where indicated. Review therapy once microbiological sensitivities are known and change to narrow spectrum agent where possible. A **decision aid** for the diagnosis and management of suspected UTI in older people has been developed by the Scottish Antimicrobial Prescribing Group.

In pregnancy, short-term use of nitrofurantoin is unlikely to cause problems to the foetus (at term, theoretical risk of neonatal haemolysis). Trimethoprim, as a folate antagonist, has a theoretical risk in first trimester in patients with poor diet or on another folate antagonist.

In catheterised patients, only send urine samples for laboratory culture if the patient has clinical signs and symptoms of urinary-tract origin, not because the appearance or smell of the urine suggests that bacteriuria is present. The Scottish Antimicrobial Prescribing Group has developed a **flowchart** to assist nursing and care staff and prescribers to manage catheterised patients or residents with urinary tract infection. Discuss management of post-joint replacement patients with Microbiology.

**Nitrofurantoin should not be used in severe renal impairment** (eGFR less than 30mL/min) as it can result in toxic plasma levels and an effective drug concentration in the urine cannot be achieved. Use with caution at eGFR levels between 30 and 45 mL/min in individual patients with resistant pathogens and limited treatment options where the benefit outweighs the risk. Review regularly for clinical effectiveness. It is unsuitable for treating upper urinary-tract infection. Alkalinising agents (such as potassium citrate) greatly reduce the efficacy of nitrofurantoin and should not be taken at the same time.

**Trimethoprim** resistance increases following the use of other systemic antibiotics as the resistance is often linked. Monitor for clinical improvement if trimethoprim is used empirically after other antibiotics. Use with caution in renal impairment and with drugs that promote hyperkalaemia and monitor serum potassium levels if used for longer than 3 days.

Due to competition for renal secretion, serum creatinine may rise – use with caution in renal transplant patients as the rise can be difficult to interpret.

**Discuss with Microbiology** if there is high risk of, or previously infection/ colonisation with a VRE, ESBL producer, or other multi-resistant organism. Due to the risk of infection following joint replacement, discuss the need for antimicrobial therapy with Microbiology.

### ACUTE LOWER URINARY-TRACT INFECTION

<table>
<thead>
<tr>
<th>Illness</th>
<th>Comments</th>
<th>Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence of bacteria in urine (culture or positive dipstick test) but NO signs or symptoms of infection</td>
<td>Antibiotic therapy is not required except in pregnancy*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women with symptoms or signs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• For women with less severe or limited symptoms, a delayed prescription for antibiotics may be a suitable management option in some patients.</td>
<td>Trimethoprim</td>
<td>200mg</td>
<td>Twice daily</td>
<td>3 days</td>
<td></td>
</tr>
<tr>
<td>• Symptom relief with ibuprofen along with general advice about maintaining fluid intake may provide resolution of symptoms without need for antibiotics.</td>
<td>Nitrofurantoin</td>
<td>100mg m/r</td>
<td>Twice daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR</td>
<td>Cefalexin</td>
<td>500mg</td>
<td>3 times daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If no response in 3 days, send mid-stream sample (MSU), continue on the same antibiotic and await sensitivity of organism isolated. Use narrow-spectrum where possible. When treating symptomatic UTI in pregnancy only, perform a culture 7 days after completion of antibiotics as a test of cure.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men with symptoms or signs</td>
<td>Send urine sample for culture before starting empiric treatment and rationalise once sensitivity information available. If fever present, treat as prostatitis. If uncomplicated lower UTI suspected, treat as for women with signs and symptoms for 7 days.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>*Asymptomatic bacteriuria in pregnancy</td>
<td>Confirm bacteriuria with second MSU sample and treat according to sensitivity. Repeat urine culture at each antenatal visit until delivery.</td>
<td></td>
<td></td>
<td></td>
<td>7 days</td>
</tr>
</tbody>
</table>

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**Note:** Doses are oral and for adults unless otherwise stated. Refer to BNF for further information.
Recurrent UTI – Refer to Urology Shared clinical guideline on Recurrent UTIs, consider discussing treatment of recurrent UTI in women and catheterised patients with Microbiology. Consider alternatives to antimicrobial management due to high risk of resistance developing.

If a patient has 2 or more episodes of symptomatic UTI in a 6 month period, continuous low-dose antibiotic prophylaxis or single dose post-coital prophylaxis can be considered. After counselling, and when behavioural modifications and non-antimicrobial measures have been unsuccessful, a 3 month course of low-dose nitrofurantoin 50mg daily may be appropriate. This can be extended to 6 months in total but must be reviewed thereafter. After 6 months of continuous therapy with nitrofurantoin there is a significant risk of developing hepatitis or chronic pulmonary reactions such as pulmonary fibrosis and diffuse interstitial pneumonitis.

For advice in pregnancy or where nitrofurantoin is unsuitable (see above) please discuss with Microbiology. The decision to initiate low dose prophylaxis must be clearly documented to ensure all staff caring for the patient are clear of the date for review and expected duration of therapy.

Acute lower urinary-tract infection

<table>
<thead>
<tr>
<th>Illness</th>
<th>Comments</th>
<th>Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper urinary-tract infection (pyelonephritis) in men, women</td>
<td>Symptomatic infection in catheterised patients (both sexes)</td>
<td>In catheterised patients, treat infection based on clinical signs and symptoms of urinary-tract origin. Send urine for culture only if infection strongly suspected and include symptom details (not dipstick results) on the Microbiology request form. Long-term catheters should be changed after starting antibiotic treatment. See NHS Highland Control of Infection policy for ‘Preventing Infections Associated with the Insertion and Maintenance of Indwelling Urethral Catheters’. <strong>Send urine sample to bacteriology before treatment commences. If no response in 24 hours consider hospital admission.</strong> For management of kidney transplant patients, immunocompromised patients and known or suspected infections with multi-drug resistant pathogens including ESBLs, contact Microbiology for discussion of treatment options. Discuss antimicrobial cover for urinary catheter exchange in a patient with a recent joint replacement with Microbiology.</td>
<td>Co-amoxiclav OR Ciprofloxacin</td>
<td>625mg</td>
<td>3 times daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ciprofloxacin 500mg</td>
<td>500mg</td>
<td>Twice daily</td>
<td>7 days</td>
</tr>
</tbody>
</table>
| For severe infection (hospital treated) mandatory review of gentamicin following culture and sensitivity information. |                                                                           | Amoxicillin PLUS $\ \begin{array}{l} \text{intravenous} \\
\text{intravenous} \end{array}$ | 1 gram    | 3 times daily | 7 to 14 days |
| *In penicillin allergy* OR *In severe renal impairment (CrCl less than 10mL/min) or renal replacement therapy or where gentamicin unsuitable.* |                                                                           | Aztreonam PLUS $\ \begin{array}{l} \text{intravenous} \\
\text{intravenous} \end{array}$ | 1 gram 1 gram stat then 250mg | 3 times daily | 7 to 14 days |

*For infections arising within 24 hours of surgery where gentamicin has been given as part of surgical prophylaxis, substitute intravenous aztreonam. 1 gram three times daily for gentamicin.*

**PROSTATITIS AND EPIDIDYMITIS**

<table>
<thead>
<tr>
<th>Illness</th>
<th>Comments</th>
<th>Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacterial prostatitis</strong></td>
<td>Send initial voided urine sample (first 5 to 10mL) to virology for chlamydial DNA strand amplification and MSU to bacteriology. Consider semen culture. 4 weeks treatment may prevent chronic infection.</td>
<td>Trimethoprim OR Ciprofloxacin</td>
<td>200mg</td>
<td>Twice daily</td>
<td>14 days</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ciprofloxacin 500mg</td>
<td>500mg</td>
<td>Twice daily</td>
<td>14 days</td>
</tr>
<tr>
<td><strong>Epiddymitis</strong></td>
<td>Age 35 years and under, likely to be sexually transmitted. Send urine samples to Virology and Microbiology as for bacterial prostatitis. If chlamydia isolated treat partner (see section on genital-tract infections). Age over 35 years, common uropathogens responsible. Send MSU to bacteriology and treat according to sensitivities. Suitable agents with good tissue penetration include ciprofloxacin, trimethoprim and cefalexin. If recurrent, refer to Urology Outpatients.</td>
<td>Cefalexin OR Trimethoprim OR Ciprofloxacin</td>
<td>500mg</td>
<td>3 times daily</td>
<td>14 days</td>
</tr>
<tr>
<td></td>
<td>Age 35 years and under</td>
<td>Doxycycline 100mg</td>
<td>100mg</td>
<td>Twice daily</td>
<td>14 days</td>
</tr>
<tr>
<td></td>
<td>Age over 35 years</td>
<td>Cefalexin OR Trimethoprim OR Ciprofloxacin</td>
<td>500mg</td>
<td>Twice daily</td>
<td>14 days</td>
</tr>
</tbody>
</table>

**Note:** Doses are oral and for adults unless otherwise stated. Refer to BNF for further information.
For skin and soft tissue infections requiring intravenous therapy, consider referral to the Out-patient Parenteral Antibiotic Therapy Service (OPAT). Refer to the OPAT website for the SSTI pathway and referral form.

As resistance is increasing reserve topical antibiotics for very localised lesions. For minor infections and impetigo only and where Emulsiderm® will not suffice, topical sodium fusidate 2% cream can be used for a maximum of 10 days treatment. For extensive, severe or bullous impetigo, use oral antibiotics. For paediatric patients, please refer to the current edition of BNF for Children for drug doses.

For the management of cellulitis in a lymphodema patient, refer to the Shared Clinical Guidelines Pathway documents on the Intranet. For leg ulcers, microbiological investigations should only be undertaken when there are clinical signs of infection. Cleanse wound with tap water or saline to remove surface contaminants. Remove slough and necrotic tissue. Swab viable tissue displaying signs of infection. Treat according to sensitivity results.

* Gentamicin therapy must be reviewed at 48 to 72 hours and continued on specialist advice only.

### BITE WOUNDS SHOULD NOT BE SUTURED

<table>
<thead>
<tr>
<th>Illness</th>
<th>Comments</th>
<th>Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor furunculosis, folliculitis and small abscesses WITHOUT cellulitis</td>
<td>NO antibiotics, perform incision and drainage if necessary</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minor/moderate cellulitis including facial cellulitis or wound infection. Seek advice from Infection Specialist early if peri-orbital cellulitis suspected.</td>
<td>Minor infection</td>
<td>Flucloxacillin</td>
<td>500mg</td>
<td>4 times daily</td>
<td>7 days. If slow response, continue for further 7 days.</td>
</tr>
<tr>
<td>Moderate infection</td>
<td>Flucloxacillin</td>
<td>1 gram</td>
<td>4 times daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In penicillin allergy or if MRSA suspected</td>
<td>Doxycycline</td>
<td>100mg</td>
<td>Twice daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If dirty or penetrating wound ensure surgical washout and assess tetanus immunisation status</td>
<td>ADD Metronidazole</td>
<td>400mg</td>
<td>3 times daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major cellulitis or wound infection with gross contamination or in IV drug user</td>
<td>Flucloxacillin (intravenous)</td>
<td>1 to 2 grams</td>
<td>4 times daily</td>
<td>Up to 14 days – rationalise to oral route when responding</td>
<td></td>
</tr>
<tr>
<td>In penicillin allergy or if MRSA suspected</td>
<td>Vancomycin (intravenous)</td>
<td>Refer to NHS Highland vancomycin dosing guidelines</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If dirty or penetrating wound</td>
<td>ADD Gentamicin* (intravenous) PLUS Metronidazole (intravenous)</td>
<td>Refer to NHS Highland gentamicin dosing guidelines</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orbital cellulitis</td>
<td>Seek advice and refer to Ophthalmologist</td>
<td>Ceftriaxone (intravenous)</td>
<td>2 grams</td>
<td>Once daily</td>
<td>7 days</td>
</tr>
<tr>
<td>Necrotising fasciitis**</td>
<td>SEEK URGENT SURGICAL OPINION AND CONSULT MICRO-BILOGIST</td>
<td>Meropenem (intravenous) PLUS Clindamycin (intravenous)</td>
<td>2 grams</td>
<td>3 times daily</td>
<td>Review at 12 hour intervals and reconsult as necessary</td>
</tr>
</tbody>
</table>

** Notifiable disease – contact local Health Protection Team

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Note: Doses are oral and for adults unless otherwise stated. Refer to BNF for further information.
<table>
<thead>
<tr>
<th>Bite wound</th>
<th>BITE WOUNDS SHOULD NOT BE SUTURED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic prophylaxis is advised if &gt; 50 years, cat bite/puncture wound, bite to hand, foot, face, joint, tendon, ligament; immunocompromised/diabetic/asplenic/cirrhotic/ presence of prosthetic valve or prosthetic joint. Assess rabies risk (animal bite); assess risk of blood-borne virus transmission (human or primate bite). Consider hepatitis B vaccination.</td>
<td></td>
</tr>
<tr>
<td>Co-amoxiclav</td>
<td>625mg</td>
</tr>
<tr>
<td>In penicillin allergy</td>
<td>Doxycycline PLUS Metronidazole</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Conjunctivitis</th>
<th>Most bacterial conjunctivitis is self-limiting. 65% resolve on placebo by day five.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red eye with mucopurulent, not watery discharge. Usually unilateral but may spread.</td>
<td>Chloramphenicol 0-5% eye drops PLUS Chloramphenicol 1% eye ointment OR Fusidic acid eye drops 1% (m/r, in gel basis)</td>
</tr>
<tr>
<td>Fusidic acid has less Gram-negative activity</td>
<td>Apply</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dermatophyte infection of the skin</th>
<th>Terbinafine is fungicidal; 1 week of terbinafine is as effective as 4 weeks azole. If intractable, send skin scrapings and consider oral itraconazole (see section on nail infections).</th>
<th>Clotrimazole cream 1% (topical) OR Terbinafine 1% cream (topical)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Apply</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dermatophyte infection of the proximal fingernail or toenail (adults)</th>
<th>Information on the diagnosis and laboratory investigation of fungal nail infections can be found on the Public Health England website. Clinical evidence for effectiveness of amorolfine is limited, relies on stringent compliance with therapy for recommended duration and is suitable for superficial infections only.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Take nail clippings: start therapy only if infection is confirmed by laboratory. Oral terbinafine is more effective than oral azole. Liver reactions are rare with oral antifungals. If candida or non-dermatophyte infection confirmed, use itraconazole. For children seek advice from Dermatology.</td>
<td>Terbinafine OR Itraconazole OR Amorolfine paint (topical)</td>
</tr>
<tr>
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</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: Doses are oral and for adults unless otherwise stated. Refer to BNF for further information.
The following advice applies to acute osteomyelitis and septic arthritis caused by haematogenous spread. **It does not apply to infection by contiguous spread (eg related to chronic ulcers or trauma), to chronic infections, or where prosthetic material is present.**

The following advice is for empiric therapy. Definitive therapy should be discussed with infection specialist or paediatrician. It should usually be guided by joint aspirate or bone biopsy **which should be taken before antibiotics are instituted where possible.** For osteomyelitis and septic arthritis consider referral to Outpatient Parenteral Antimicrobial Therapy (OPAT) service. Sodium fusidate must be avoided if the patient has been prescribed a statin due to the increased risk of rhabdomyolysis.

<table>
<thead>
<tr>
<th>Illness</th>
<th>Comments</th>
<th>Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Osteomyelitis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staph aureus</td>
<td>is commonest pathogen in children and adults</td>
<td>Flucloxacillin (intravenous)</td>
<td>2 grams</td>
<td>4 times daily</td>
<td>4 to 6 weeks minimum with regular review. (For childhood osteomyelitis, consider early oral switch. Choice of oral antibiotic should be individualised.)</td>
</tr>
<tr>
<td>H. influenzae and Kingella sp. are possible in children</td>
<td>Ceftriaxone (intravenous)</td>
<td>See BNF for Children for dosing advice</td>
<td>Once daily</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In penicillin allergy</td>
<td></td>
<td>Vancomycin (intravenous)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In penicillin allergy or if MRSA is known or suspected</td>
<td>Refer to NHS Highland vancomycin dosing guidelines</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Septic arthritis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staph aureus and beta-haemolytic streptococci are the commonest pathogens. Seek Microbiology advice if at risk of sexually transmitted disease.</td>
<td>Flucloxacillin (intravenous)</td>
<td>2 grams</td>
<td>4 times daily</td>
<td>4 weeks. Consider possible IV to oral switch after 2 weeks.</td>
<td></td>
</tr>
<tr>
<td>In penicillin allergy or if MRSA is known or suspected</td>
<td>Vancomycin (intravenous)</td>
<td>Refer to NHS Highland vancomycin dosing guidelines</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H. influenzae and Kingella sp. are possible in children</td>
<td>See above for osteomyelitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note:** Doses are oral and for adults unless otherwise stated. Refer to BNF for further information.
### VIRAL INFECTIONS (Updated October 2017)

<table>
<thead>
<tr>
<th>Illness</th>
<th>Comments</th>
<th>Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varicella zoster/chicken pox</td>
<td>Pregnant/immunocompromised/neonate: seek urgent specialist advice.</td>
<td>Aciclovir</td>
<td>800mg</td>
<td>5 times daily</td>
<td>7 days</td>
</tr>
<tr>
<td>Herpes zoster/shingles</td>
<td><strong>Chicken pox:</strong> consider aciclovir if onset of rash &lt;24hrs and one of the following: &gt;14 years; severe pain; dense/oral rash; taking steroids; smoker. <strong>Shingles:</strong> treat if &gt;50 years (PHN rare if &lt;50 years) and within 72 hrs of rash or if one of the following: active ophthalmic; Ramsey Hunt; eczema; non-truncal involvement; moderate or severe pain; moderate or severe rash. If treatment not within 72 hours: consider starting antiviral drug up to one week after rash onset, if high risk of severe shingles or complications (continued vesicle formation; older age; immunocompromised; severe pain).</td>
<td>Famciclovir</td>
<td>250mg to 500mg OR 750mg</td>
<td>3 times daily</td>
<td>Twice daily</td>
</tr>
<tr>
<td></td>
<td><strong>Second-line for shingles if poor compliance</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cold sores</td>
<td>Most resolve after 5 days without treatment. Topical antivirals applied prodromally can reduce duration by 12 to 18 hours. If frequent, severe and predictable triggers, consider oral prophylaxis: aciclovir 400mg twice daily for 5 to 7 days.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### GASTRO-INTESTINAL TRACT INFECTIONS (Updated June 2016)

<table>
<thead>
<tr>
<th>Illness</th>
<th>Comments</th>
<th>Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eradication of Helicobacter pylori</td>
<td>Triple treatment attains &gt;85% eradication. As resistance is increasing, avoid clarithromycin or metronidazole if used in past year for any infection. <strong>In penicillin allergy or if had clarithromycin in past year</strong></td>
<td>Lansoprazole PLUS Amoxicillin PLUS Clarithromycin Substitute Metronidazole</td>
<td>30mg 1 gram 500mg</td>
<td>Twice daily Twice daily Twice daily</td>
<td>For 7 days For 7 days For 7 days</td>
</tr>
<tr>
<td></td>
<td>If unable to tolerate lansoprazole</td>
<td>Omeprazole</td>
<td>20mg</td>
<td>Twice daily</td>
<td>For 7 days</td>
</tr>
<tr>
<td></td>
<td>In treatment failure, contact infection specialist or gastroenterologist for advice.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clostridium difficile diarrhoea</td>
<td><strong>Review antibiotic therapy and stop where possible.</strong> Cephalosporins, clindamycin, broad-spectrum penicillins and quinolones are high-risk. <strong>Stop proton pump inhibitors (see algorithm) and anti-motility agents whilst symptomatic, if possible.</strong> Assess severity of disease according to treatment algorithm appended to the NHS Highland Infection Control Policy.</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>(See NHS Highland Infection Control Policy)</td>
<td>Mild disease with no severity markers</td>
<td>Metronidazole</td>
<td>400mg</td>
<td>3 times daily</td>
<td>10 to 14 days</td>
</tr>
<tr>
<td></td>
<td>One or more severity markers or second-line</td>
<td>Vancomycin (ORAL ONLY)</td>
<td>125mg to 500mg</td>
<td>4 times daily</td>
<td>10 to 14 days</td>
</tr>
<tr>
<td></td>
<td>First recurrent episode on advice from Microbiologist</td>
<td>Fidaxomicin</td>
<td>200mg</td>
<td>Twice daily</td>
<td>10 days</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>Fluid replacement essential. <strong>Antibiotic therapy is not usually indicated as it only reduces diarrhea by 1 to 2 days</strong> and can cause resistance. Initiate treatment, on advice of Microbiologist, if the patient is systemically unwell. Antibiotics can worsen E. coli 0157 and should be avoided. Please notify Health Protection Team Doctor regarding suspected cases of food poisoning and seek advice on exclusion of patients. Send stool samples in these cases.</td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note:** Doses are oral and for adults unless otherwise stated. Refer to BNF for further information.
<table>
<thead>
<tr>
<th>Illness</th>
<th>Comments</th>
<th>Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra-abdominal sepsis including hepato-biliary</td>
<td>As timely administration in sepsis is vital, ensure agents covering gram-negative pathogens (gentamicin or ciprofloxacin) are given first.</td>
<td>#Gentamicin (intravenous) <strong>PLUS</strong> Amoxicillin (intravenous) <strong>PLUS</strong> Metronidazole (intravenous)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Doses and monitoring as per Highland Formulary Guidelines</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>1 gram 3 times daily</td>
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<tr>
<td></td>
<td></td>
<td>500mg 3 times daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In penicillin allergy</td>
<td></td>
<td>Ciprofloxacin (intravenous) <strong>PLUS</strong> * Vancomycin (intravenous) <strong>PLUS</strong> Metronidazole (intravenous)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Doses and monitoring as per Highland Formulary Guidelines</td>
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<tr>
<td></td>
<td></td>
<td>400mg Twice daily</td>
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<tr>
<td></td>
<td></td>
<td>500mg 3 times daily</td>
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<tr>
<td>* Where vancomycin cannot be used, substitute with teicoplanin using BNF dosing for streptococcal endocarditis, ie 10mg per kg per day with the first three doses given every 12 hours. # For infections arising within 24 hours of surgery where gentamicin has been given as part of surgical prophylaxis, substitute intravenous aztreonam 1 gram 3 times daily for gentamicin.</td>
<td></td>
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</tr>
<tr>
<td>In severe illness, unresponsive to first-line therapy, contact Microbiology for advice.</td>
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</tr>
<tr>
<td>For oral switch when no positive microbiology results are available</td>
<td></td>
<td>*Co-trimoxazole <strong>PLUS</strong> Metronidazole</td>
<td>960mg</td>
<td>Twice daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>400mg 3 times daily</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In renal impairment (CrCl 30mL/min or less)</td>
<td></td>
<td>*Co-trimoxazole <strong>PLUS</strong> Metronidazole</td>
<td>480mg</td>
<td>Twice daily</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>400mg 3 times daily</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>* Use co-trimoxazole with caution in renal impairment or in combination with other drugs which promote hyperkalaemia, monitor potassium levels if used for longer than 3 days.</td>
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</tr>
<tr>
<td>Spontaneous bacterial peritonitis (SBP)</td>
<td>Ascitic fluid neutrophil count &gt; 250 cells/mm$^3$ or &gt;0.25 x 10$^9$/L. Inform gastroenterologist of admission.</td>
<td>Co-amoxiclav (intravenous)</td>
<td>1.2 grams</td>
<td>3 times daily</td>
<td>7 days</td>
</tr>
<tr>
<td>In penicillin allergy</td>
<td></td>
<td>Ceftriaxone (intravenous)</td>
<td>2 grams</td>
<td>Once daily</td>
<td>7 days</td>
</tr>
<tr>
<td>Secondary prophylaxis after episode of SBP</td>
<td></td>
<td>Ciprofloxacin</td>
<td>500mg</td>
<td>Once daily</td>
<td>Lifelong</td>
</tr>
<tr>
<td>Primary prophylaxis following upper GI bleed in presence of cirrhosis</td>
<td></td>
<td>Ciprofloxacin</td>
<td>500mg</td>
<td>Twice daily</td>
<td>5 days</td>
</tr>
<tr>
<td>CAPD/APD Peritonitis</td>
<td>See separate policy ‘Initial management of Suspected Peritonitis in Adults’ on Intranet.</td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>
### PARASITIC INFESTATIONS (Updated June 2016)

<table>
<thead>
<tr>
<th>Illness</th>
<th>Comments</th>
<th>Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treat all household contacts at the same time PLUS advise hygiene measures for 2 weeks (hand hygiene, wear pants at night, morning shower (include perianal area) PLUS wash sleepwear, bed linen, and dust, vacuum on day one. Children under 6 months, add perianal wet wiping or washes 3-hourly during day.</td>
<td>Note: mebendazole is unlicensed in children under 2 years of age.</td>
<td>Adults and children aged 6 months and over</td>
<td>Mebendazole</td>
<td>100mg</td>
<td>As a single dose</td>
</tr>
</tbody>
</table>

| Children aged under 6 months | Use hygiene measures alone for 6 weeks                                    |

### GENITAL-TRACT INFECTIONS – UK NATIONAL GUIDELINES (Updated June 2016)

<table>
<thead>
<tr>
<th>Illness</th>
<th>Comments</th>
<th>Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treat partners simultaneously. Avoid 2 gram oral dose in pregnancy and breast-feeding.</td>
<td>For treatment of complicated or symptomatic infection with chlamydia, see <a href="#">Shared Care Guideline</a> on Intranet.</td>
<td>Metronidazole OR Metronidazole 0.75% vaginal gel OR Clindamycin 2% vaginal cream</td>
<td>400mg</td>
<td>Twice daily</td>
<td>5 to 7 days</td>
</tr>
</tbody>
</table>

| OR Clindamycin 2% vaginal cream | 5 grams | Applicator full at night | 7 days |

| Chlamydia trachomatis – uncomplicated (asymptomatic) | For treatment in pregnancy or infection of upper genital tract seek advice. Treat partners. Refer contacts to Sexual Health* | Azithromycin OR Doxycycline | 1 gram OR 100mg | As a single dose OR Twice daily | 1 hour before or 2 hours after food OR 7 days |

| For rectal infections | Doxycycline | 100mg | Twice daily | 7 days |

| In pregnancy | Azithromycin | 1 gram | As a single dose | 1 hour before or 2 hours after food |

<p>| For symptomatic relief in pregnancy. Treat postnatally. | Clotrimazole pessary | 100mg | Once daily at night | 6 days |</p>
<table>
<thead>
<tr>
<th>Pelvic inflammatory disease (PID) (excluding elderly and post-operative patients)</th>
<th>Test for <em>Chlamydia</em> and <em>N. gonorrhoea</em>. Test to ensure successful eradication. Refer contacts to Sexual Health*.</th>
<th>Metronidazole PLUS Doxycycline OR Ofloxacin OR Levofloxacin</th>
<th>400mg 100mg</th>
<th>Twice daily Twice daily Twice daily</th>
<th>14 days 14 days 14 days</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>In a sexually active patient at risk of gonococcal PID. Avoid quinolones due to high levels of resistance.</td>
<td><strong>ADD</strong> <em>Ceftriaxone</em> (intramuscular)</td>
<td>500mg</td>
<td>As a single dose</td>
<td></td>
</tr>
<tr>
<td>Gonorrhoea ( uncomplicated)</td>
<td>Refer contacts to Sexual Health*. Test to ensure successful eradication. Combination therapy is required to reduce cephalosporin resistance in <em>N. Gonorrhoea</em>. Co-infection with <em>Chlamydia</em> is common.</td>
<td><em>Ceftriaxone</em> (intramuscular) PLUS <em>Azithromycin</em></td>
<td>500mg 1gram</td>
<td>As a single dose As a single dose</td>
<td></td>
</tr>
<tr>
<td></td>
<td>If treating rectal infection of <em>Chlamydia trachomatis</em></td>
<td><strong>ADD</strong> <em>Doxycycline</em></td>
<td>100mg</td>
<td>Twice daily</td>
<td>7 days</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Very rare, refer to Sexual Health*.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note:** Refer patients with sexually transmitted diseases, including trichomoniasis, for contact tracing. *Contact Highland Sexual Health, tel: 01463 704000 (switchboard) or for Argyll & Bute contact the Sandyford Initiative, tel: 0141 2118130.*
**DIABETIC FOOT INFECTIONS** (Updated August 2016)

- only use antibiotics if clinical signs of infection.
- send microbiological samples early in infection – tissue, aspirates are preferable to wound swabs.
- continue therapy until the infection has resolved, not until the wound has healed.
- treatment plan should include wound care and pressure relief – see [Wound Formulary](#).

**osteomyelitis**
- suspect if able to touch bone through the wound with a sterile probe
- suspect in a non-healing diabetic ulcer with adequate blood supply
- refer to Combined Diabetic Foot Clinic
- deep swab or tissue samples are essential for diagnosis. Delay therapy pending microbiology results in chronic cases.
- treat for 6 weeks minimum.

**typical pathogens** (antibiotic-naïve = no antimicrobials in last 3 months)
- antibiotic-naïve: *Staph aureus* and β-haemolytic streptococci.
- not antibiotic-naïve or chronic: as above plus Gram-negative bacilli, enterococci, anaerobes.

**all doses are for adults with normal renal function or mild renal impairment.**


**Clinical classification of a diabetic foot infection** *(from reference above)*

<table>
<thead>
<tr>
<th>Clinical manifestations of infection</th>
<th>Infection severity</th>
<th>PEDIS grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound lacking purulence or any manifestations of inflammation</td>
<td>Uninfected</td>
<td>1</td>
</tr>
</tbody>
</table>

Presence of ≥ 2 manifestations of inflammation (purulence, or erythema, pain, tenderness, warmth, or induration), but any cellulitis/erythema extends ≤2 cm around the ulcer, and infection is limited to the skin or superficial subcutaneous tissues; no other local complications or systemic illness.

Infection (as above) in a patient who is systemically well and metabolically stable but which has 1 of the following characteristics: cellulitis extending 12 cm, lymphangitic streaking, spread beneath the superficial fascia, deep-tissue abscess, gangrene, and involvement of muscle, tendon, joint or bone.

Infection in a patient with systemic toxicity or metabolic instability (eg, fever, chills, tachycardia, hypotension, confusion, vomiting, leukocytosis, acidosis, severe hyperglycaemia, or azotaemia).

**Note:** Definitions of terms can be found in footnotes to Table 4.

Foot ischaemia may increase the severity of any infection, and the presence of critical ischaemia often makes the infection severe. PEDIS: perfusion, extent/size, depth/tissue loss, infection, and sensation.

<table>
<thead>
<tr>
<th>Illness</th>
<th>Comments</th>
<th>Drug</th>
<th>Dose</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infected diabetic foot ulcer: IDSA – mild</td>
<td><strong>Antibiotic-naïve</strong></td>
<td>Flucloxacillin (intravenous or oral)</td>
<td>1 gram</td>
<td>4 times daily</td>
<td>5 to 7 days then review according to clinical response and with culture and sensitivity results.</td>
</tr>
<tr>
<td></td>
<td><strong>Not antibiotic-naïve or in penicillin allergy</strong></td>
<td>Doxycycline (oral)</td>
<td>100mg</td>
<td>Twice daily</td>
<td></td>
</tr>
<tr>
<td>Infected diabetic foot ulcer: IDSA – moderate</td>
<td><strong>Antibiotic-naïve</strong> Consider admission and bed rest. If patient remains outpatient, ensure early clinic review.</td>
<td>Flucloxacillin (intravenous or oral) PLUS Metronidazole (intravenous or oral)</td>
<td>1 gram 500mg (intravenous) 400mg (oral)</td>
<td>4 times daily 3 times daily</td>
<td></td>
</tr>
</tbody>
</table>

**Note:** Doses are oral and for adults unless otherwise stated. Refer to BNF for further information.
<table>
<thead>
<tr>
<th>In penicillin allergy</th>
<th>Clindamycin (oral)</th>
<th>450mg</th>
<th>4 times daily</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Not antibiotic-naïve</strong>&lt;br&gt;MRSA is common in these patients. Review once culture results known.</td>
<td><strong>Piperacillin/tazobactam</strong> (intravenous) <strong>PLUS</strong> Vancomycin (intravenous)</td>
<td>4.5 grams</td>
<td>3 times daily</td>
</tr>
<tr>
<td>If MRSA osteomyelitis suspected</td>
<td><strong>ADD</strong>&lt;br&gt;Rifampicin (oral) <strong>OR</strong> Sodium fusidate (oral)</td>
<td>600mg</td>
<td>Twice daily</td>
</tr>
<tr>
<td>In penicillin allergy</td>
<td>Vancomycin (intravenous) <strong>PLUS</strong>&lt;br&gt;★Aztreonam (intravenous) <strong>PLUS</strong> ★Metronidazole (intravenous)</td>
<td>2 grams</td>
<td>Twice daily</td>
</tr>
<tr>
<td><strong>Infected diabetic foot ulcer:</strong>&lt;br&gt;IDSA – severe</td>
<td><strong>Antibiotic-naïve</strong>&lt;br&gt;Likely pathogens include <em>Staph. aureus</em> or beta-haemolytic streptococci. Anaerobes, enterobacteriaceae and <em>Pseudomonas aeruginosa</em> may also require treatment. Admission essential with urgent surgical review.</td>
<td><strong>Piperacillin/tazobactam</strong> (intravenous) <strong>PLUS</strong> ★Gentamicin (intravenous)</td>
<td>4.5 grams</td>
</tr>
<tr>
<td>In penicillin allergy or if MRSA suspected</td>
<td>Vancomycin (intravenous) <strong>PLUS</strong> ★Ciprofloxacin (intravenous) <strong>PLUS</strong> ★Metronidazole (intravenous)</td>
<td>Refer to NHS Highland vancomycin dosing guidelines</td>
<td>Aim for trough 15 to 20mg/L&lt;br&gt;Aim for trough 15 to 20mg/L</td>
</tr>
<tr>
<td><strong>Not antibiotic-naïve</strong></td>
<td>★Meropenem (intravenous)</td>
<td>500mg</td>
<td>3 times daily</td>
</tr>
<tr>
<td>If MRSA suspected</td>
<td><strong>ADD</strong> Vancomycin (intravenous)</td>
<td>Refer to NHS Highland vancomycin dosing guidelines. Aim for trough 15 to 20mg/L.</td>
<td></td>
</tr>
</tbody>
</table>

★Dose to be adjusted in moderate or severe renal impairment or in renal replacement therapy.

---

**Note:** Doses are oral and for adults unless otherwise stated. Refer to BNF for further information.
## LYME DISEASE (May 2016)

British Infection Association published a [UK position statement on Lyme borreliosis](#) in 2011. NHS Highland Laboratory Handbook contains a [Lyme borreliosis user guide](#). If diagnostic or management uncertainty please discuss with Raigmore microbiology, infectious diseases (ID) or paediatric consultants. Erythromycin should not be used to treat Lyme disease. In children, consult the [BNF for Children](#) for antibiotic dosing information and prescribe the highest recommended dose under Lyme disease where applicable. For ceftriaxone, use the highest recommended dose under ‘meningitis’.

### Table 1

<table>
<thead>
<tr>
<th>Illness</th>
<th>Comment</th>
<th>Drug</th>
<th>Dose / route</th>
<th>Frequency</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prophylaxis following tick bite</strong></td>
<td>NOT ROUTINELY RECOMMENDED</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early Lyme disease (without cardiac or neurological signs)</td>
<td>Includes:</td>
<td>1st line</td>
<td>Doxycycline (^b) OR Amoxicillin</td>
<td>100mg 500mg</td>
<td>Twice daily 3 times daily</td>
</tr>
<tr>
<td>erythema migrans or atypical rash(^a)</td>
<td></td>
<td>2nd line</td>
<td>Cefuroxime (^c)</td>
<td>500mg</td>
<td>Twice daily</td>
</tr>
<tr>
<td>flu-like syndrome</td>
<td></td>
<td>3rd line</td>
<td>Azithromycin (^d)</td>
<td>500mg</td>
<td>Once daily</td>
</tr>
<tr>
<td>Borrelia lymphocytoma.</td>
<td>Lyme carditis</td>
<td>Requires hospital admission due to risk of worsening heart block</td>
<td>Ceftriaxone (intravenous)</td>
<td>2 gram</td>
<td>Once daily</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lyme arthritis (^i)</td>
<td>1st line</td>
<td>Doxycycline (^c)</td>
<td>100mg</td>
<td>Twice daily</td>
<td>28 days</td>
</tr>
<tr>
<td></td>
<td>2nd line</td>
<td>Amoxicillin</td>
<td>500mg</td>
<td>3 times daily</td>
<td></td>
</tr>
<tr>
<td>Isolated facial nerve palsy (^g)</td>
<td>1st line</td>
<td>Doxycycline (^b)</td>
<td>100mg</td>
<td>Twice daily</td>
<td>14 days (^e)</td>
</tr>
<tr>
<td></td>
<td>2nd line</td>
<td>Amoxicillin</td>
<td>500mg</td>
<td>3 times daily</td>
<td></td>
</tr>
<tr>
<td>Radiculitis or meningitis (^h)</td>
<td>1st line</td>
<td>Doxycycline (^b) OR Ceftriaxone (intravenous)</td>
<td>100mg 2 gram</td>
<td>Twice daily Once daily</td>
<td>14 days (^e)</td>
</tr>
<tr>
<td>Neuroborreliosis with vasculitis, encephalitis or myelitis</td>
<td>Refer to ID consultant</td>
<td>Ceftriaxone (intravenous)</td>
<td>2 gram</td>
<td>Once daily</td>
<td>14 to 28 days</td>
</tr>
<tr>
<td>Acrodermitis chronicum atrophicans (ACA)</td>
<td>Refer to dermatologist for diagnosis</td>
<td>1st line</td>
<td>Doxycycline (^c) OR Amoxicillin</td>
<td>100mg 500mg</td>
<td>Twice daily 3 times daily</td>
</tr>
<tr>
<td></td>
<td>2nd line</td>
<td>Cefuroxime (^c)</td>
<td>500mg</td>
<td>Twice daily</td>
<td></td>
</tr>
</tbody>
</table>

\(a\) The rash of Lyme disease is an expanding erythematous rash usually at site of tick bite, appearing 3 to 30 days after tick attachment and reaching 5cm in diameter. A lesion appearing within 24 hours of tick attachment and resolving in 48 hours is likely to be a hypersensitivity reaction.

\(b\) Doxycycline is preferred over amoxicillin if no contraindication. Avoid doxycycline in children under 12 years, pregnancy and breastfeeding.

\(c\) Cefuroxime is as active as amoxicillin but is more expensive and has a higher risk of *Clostridium difficile* infection.

\(d\) Treatment failure recognised with azithromycin, monitor for unresolved infection.

\(e\) A range of 14 to 21 days is given in many texts, but there is no evidence that longer regimens have a better outcome. If more than 14 days considered suggest discuss with Microbiologist.

\(f\) Refer to consultant rheumatologist for diagnosis and initial management of suspected Lyme arthritis. NSAIDs can be used during initial treatment. Retreatment is indicated if non-response or relapse, discuss with Microbiologist.

\(g\) For other cranial nerve palsies discuss with Microbiology, oral doxycycline or IV ceftriaxone have been used successfully.

\(h\) Refer for lumbar puncture to exclude other causes if clinical meningitis, and refer to ID consultant or paediatrician.

---

**Note:** Doses are oral and for adults unless otherwise stated. Refer to BNF for further information.
NHS HIGHLAND POLICY FOR TREATMENT OF INFECTIVE ENDOCARDITIS  
(Updated August 2016)

Principles

- Endocarditis is a clinical diagnosis confirmed by appropriate microbiology. Early involvement of Microbiology, Cardiology and a clinician with expertise in infection is essential.
- If the patient's clinical condition is already severe or deteriorating, start antibiotic therapy immediately after a minimum of 3 sets of blood cultures. **DISCUSS ANTIBIOTIC CHOICE WITH INFECTION SPECIALIST.** If gentamicin is recommended, follow hospital **gentamicin endocarditis guidelines.**

Cardiology opinion and referral is required for ALL patients with endocarditis

- Take 6 sets if the patient has had antibiotic treatment in the past 2 weeks.
- Note a positive blood culture for *Staphylococcus aureus* requires a transthoracic echocardiogram and potential further discussion with a consultant cardiologist even in the absence of a murmur. **National guidance** on the management of *Staphylococcus aureus* bacteraemia in adults (SAB) is available.
- Murmur and fever - suspect endocarditis.
- 'Normal' echo (transthoracic (TTE) or transoesophageal (TOE)) does **not** exclude endocarditis.
- TOE may help if TTE is 'normal' or if images are poor (eg lung disease, obesity).
- TOE is unnecessary if TTE shows vegetations unless aortic valve endocarditis suspected.
- If aortic valve endocarditis is suspected TOE should be considered routinely to look for abscess formation.
- Deteriorating heart failure or rhythm instability despite antibiotic therapy should prompt an urgent cardiac/surgical assessment.
- Delay in valve replacement can prove fatal.

General

- Insert an intravenous cannula using aseptic technique and dress with topical povidone-iodine.
- Always give antibiotic therapy intravenously.
- Change the intravenous cannula every 48 hours.
- For long-term IV antibiotic administration (>2 weeks) consider insertion of a PICC line or Hickman line using full surgical technique in the operating theatre.
- Consider referral to Outpatient Parenteral Antimicrobial Therapy (OPAT) service.

Modified Duke Criteria for the Diagnosis of Infective Endocarditis (IE)

<table>
<thead>
<tr>
<th>MAJOR CRITERIA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood culture positive for IE:</strong></td>
</tr>
<tr>
<td>Typical microorganisms consistent with IE from 2 separate blood cultures:</td>
</tr>
<tr>
<td>Vinidans streptococci, <em>Streptococcus bovis</em>, HACEK group, <em>Staphylococcus aureus</em>; or</td>
</tr>
<tr>
<td>Community-acquired enterococci, in the absence of a primary focus; or</td>
</tr>
<tr>
<td>Microorganisms consistent with IE from persistently positive blood cultures, defined as follows:</td>
</tr>
<tr>
<td>At least 2 positive cultures of blood samples drawn &gt;12h apart; or</td>
</tr>
<tr>
<td>All of 3 or a majority of &gt;4 separate cultures of blood (with first and last sample drawn at least 1h apart)</td>
</tr>
<tr>
<td>Single positive blood culture for <em>Coxiella burnetii</em> or phase I IgG antibody titre &gt;1 : 800</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Evidence of endocardial involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echocardiogram positive for IE</td>
</tr>
<tr>
<td>Vegetation – Abscess - New partial dehiscence of prosthetic valve</td>
</tr>
<tr>
<td>New valvular regurgitation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MINOR CRITERIA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Predisposition:</strong> predisposing heart condition, injection drug use</td>
</tr>
<tr>
<td><strong>Fever:</strong> temperature &gt;38°C</td>
</tr>
<tr>
<td>Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and Janeway lesions</td>
</tr>
<tr>
<td>Immunologic phenomena: glomerulonephritis, Osler’s nodes, Roth’s spots, rheumatoid factor</td>
</tr>
<tr>
<td>Microbiological evidence: positive blood culture but does not meet a major criterion or serological evidence of active infection with organism consistent with IE</td>
</tr>
</tbody>
</table>

Diagnosis of IE is definitive in the presence of

- 2 major criteria, or
- 1 major and 3 minor criteria, or
- 5 minor criteria

Diagnosis of IE is possible in the presence of

- 1 major and 1 minor criteria, or
- 3 minor criteria

**ANTIBIOTIC PROPHYLAXIS IN SURGERY – GENERAL PRINCIPLES**  
(Updated October 2017)

- Prophylaxis should be started pre-operatively, ideally within 30 to 60 minutes before skin incision.
- The antibiotics selected for prophylaxis must cover the common or suspected pathogens, e.g., adding teicoplanin (800mg) if MRSA suspected or known MRSA carrier. *For patients weighing 65kg or less, reduce teicoplanin dose to 400mg. Note: many MRSA isolates in NHS Highland are sensitive to gentamicin.*
- Gentamicin doses are based on 3mg/kg ideal body weight (derived from height). A dosage table based on height is appended. AVOID gentamicin if eGFR < 10mL/min or on dialysis: seek advice from Microbiology.
- Patients with a history of anaphylaxis or urticaria or rash occurring immediately after penicillin therapy are at increased risk of immediate hypersensitivity to penicillins and should not receive prophylaxis with a beta-lactam antibiotic.
- An additional dose of prophylactic agent is not indicated in adults, unless there is blood loss of greater than 1500mL during surgery or surgery is prolonged. See table below for advice for specific drugs.
- Always record prophylaxis in the “once only” section of the drug chart.

<table>
<thead>
<tr>
<th>Category of surgery</th>
<th>Procedure(s)</th>
<th>Antibiotics (single intravenous dose unless stated)</th>
<th>Comment and alternatives for beta-lactam hypersensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiothoracic</td>
<td>Cardiac pacemaker insertion</td>
<td>Teicoplanin 800mg *</td>
<td>N/A</td>
</tr>
<tr>
<td>ENT surgery</td>
<td>Head and neck surgery – contaminated/clean contaminate only</td>
<td>Flucloxacillin 1 gram PLUS Metronidazole 500mg</td>
<td>Teicoplanin* (dose as table) PLUS Metronidazole 500mg</td>
</tr>
<tr>
<td></td>
<td>Grommet insertion</td>
<td>Topical Sofradex: 3 drop into each ear post-procedure</td>
<td></td>
</tr>
<tr>
<td>Orthopaedic surgery</td>
<td>Major procedures involving prosthetic implants Closed fracture fixation Hip fracture repair Spinal surgery</td>
<td>Teicoplanin* (dose as table)</td>
<td></td>
</tr>
<tr>
<td>General surgery</td>
<td>Appendicectomy Small bowel surgery Open biliary surgery Gastroduodenal surgery Oesophageal surgery Liver surgery</td>
<td>Gentamicin** (dose as table) PLUS Metronidazole 500mg</td>
<td>Gentamicin** (dose as table) PLUS Metronidazole 500mg</td>
</tr>
<tr>
<td>Colorectal surgery</td>
<td>PLUS Amoxicillin 1 gram PLUS Teicoplanin* (dose as table)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast surgery</td>
<td>Co-amoxiclav 1-2 grams</td>
<td>Clarithromycin 500mg</td>
<td></td>
</tr>
<tr>
<td>Endoscopic gastrostomy</td>
<td>Co-amoxiclav 1-2 grams</td>
<td>Teicoplanin* (dose as table)</td>
<td></td>
</tr>
<tr>
<td>Obstetrics and gynaecology</td>
<td>Caesarean section (dose at induction of anaesthesia)</td>
<td>Co-amoxiclav 1-2 grams</td>
<td>Clindamycin 600mg</td>
</tr>
<tr>
<td></td>
<td>Manual removal of placenta Hysterectomy Repair of obstetric anal sphincter injury (3rd/4th degree tear)</td>
<td>Co-amoxiclav 1-2 grams</td>
<td>Gentamicin** (dose as table) PLUS Metronidazole 500mg</td>
</tr>
<tr>
<td></td>
<td>Surgical termination of pregnancy (For women who screen positive for chlamydia or no result)</td>
<td>Oral metronidazole 400mg PLUS Oral azithromycin 1 gram</td>
<td>Refer to departmental guidelines</td>
</tr>
<tr>
<td>Urology</td>
<td>Elective admission screened and MRSA negative</td>
<td>Flucloxacillin 1 gram PLUS Gentamicin (dose as table)</td>
<td>Teicoplanin* (dose as table) PLUS Gentamicin (dose as table)</td>
</tr>
<tr>
<td>Vascular surgery</td>
<td>Emergency admissions, MRSA positive or penicillin allergy</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prevention of gas gangrene in major amputations or following major trauma</td>
<td>Metronidazole 500mg intravenously every 8 hours for 5 days</td>
<td></td>
</tr>
</tbody>
</table>

** Where the use of gentamicin is unsuitable or not recommended.
GENTAMICIN DOSING TABLE FOR SURGICAL PROPHYLAXIS

<table>
<thead>
<tr>
<th>Height range</th>
<th>Gentamicin dose for prophylaxis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Feet &amp; inches</strong></td>
<td><strong>Metres</strong></td>
</tr>
<tr>
<td>4’8” to 4’10”</td>
<td>1.42m to 1.47m</td>
</tr>
<tr>
<td>4’11” to 5’3”</td>
<td>1.48m to 1.60m</td>
</tr>
<tr>
<td>5’4” to 5’10”</td>
<td>1.61m to 1.78m</td>
</tr>
<tr>
<td>5’11” and taller</td>
<td>1.79m and taller</td>
</tr>
</tbody>
</table>

AVOID gentamicin if eGFR <10mL/min or on dialysis: seek advice from Microbiology
- Doses of up to 300mg can be given as a bolus injection over 3 to 5 minutes but it is recommended that higher doses are administered as a short infusion.
- A single dose of gentamicin will provide cover for 8 hours in patients with normal renal function and will not result in toxicity even in patients with impaired renal function.

TEICOPLANIN DOSING TABLE FOR SURGICAL PROPHYLAXIS

<table>
<thead>
<tr>
<th>Actual Bodyweight</th>
<th>Teicoplanin Dose (based on 6mg/kg and rounded to nearest 200mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>35kg to 65kg</td>
<td>400mg</td>
</tr>
<tr>
<td>66kg to 99kg</td>
<td>600mg</td>
</tr>
<tr>
<td>100kg to 130kg</td>
<td>800mg</td>
</tr>
<tr>
<td>131kg to 166kg</td>
<td>1000mg</td>
</tr>
<tr>
<td>167kg to 200kg</td>
<td>1200mg</td>
</tr>
</tbody>
</table>

- Seek advice if patient weighs more than 200kg or is on renal dialysis
- No dose adjustment is necessary in renal impairment for a single dose of teicoplanin.
- All doses should be given as a bolus injection over 3 to 5 minutes.

Dosing advice for long procedures or extensive blood loss (above 1500mL)

<table>
<thead>
<tr>
<th>Drug &amp; dose</th>
<th>Notes</th>
<th>Time since first antibiotic dose</th>
<th>Blood loss above 1500mL (Give after fluid replacement)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamicin 3mg/kg</td>
<td>-</td>
<td>4 hours</td>
<td>Repeat dose</td>
</tr>
<tr>
<td>Metronidazole 500mg</td>
<td>-</td>
<td>4 hours</td>
<td>Repeat dose</td>
</tr>
<tr>
<td>Teicoplanin 6mg/kg</td>
<td>-</td>
<td>4 hours</td>
<td>Repeat dose</td>
</tr>
<tr>
<td>Amoxicillin 1gram</td>
<td>Repeat dose</td>
<td>8 hours</td>
<td>Repeat dose</td>
</tr>
<tr>
<td>Co-amoxiclav 1.2gram</td>
<td>Repeat dose</td>
<td>8 hours</td>
<td>Repeat dose</td>
</tr>
<tr>
<td>Fluocxacillin 1gram</td>
<td>Repeat dose</td>
<td>8 hours</td>
<td>Repeat dose</td>
</tr>
<tr>
<td>Clindamycin 600mg</td>
<td>Repeat dose</td>
<td>8 hours</td>
<td>Repeat dose</td>
</tr>
</tbody>
</table>
ADULT PARENTERAL GENTAMICIN (GGC): PRESCRIBING, ADMINISTRATION & MONITORING CHART April 2017

Use for all non-cystic fibrosis patients prescribed intravenous gentamicin unless prophylactic indication, renal replacement therapy or synergistic doses (usually in endocarditis) are being used

AVOID AMINOGLOSIDES IN ADVANCED LIVER DISEASE

**PROMPT ADMINISTRATION within 1 hour of recognition of sepsis reduces mortality**

**RENAH**: ↑ creatinine (plus risk of accumulation if ↓ urine output/oliguria). **MANDATORY DAILY MONITORING**

**OTOTOXICITY**: New tinnitus, dizziness, poor balance, hearing loss, oscilating vision.

Toxicity is associated with prolonged aminoglycoside use due to accumulation in the inner ear (usually > 10 days but may be > 72 hours). If suspected, refer to ENT and discuss alternative drug with infection specialist.

---

**Initial Gentamicin Dose**: *this is not a prescription and may change. Doses must be prescribed individually below.*

**Predicted Frequency**: 

---

**Source of first dose**: Online calculator [preferred option] ❑ Manual calculation ❑ Weight based, creatinine not known ❑

---

**TOXICITY Before prescribing each dose check and record:**

**Gentamicin Prescription Record**

Complete each time a dose is to be given (ensuring gentamicin is prescribed ‘as per chart’ on the kardex)

<table>
<thead>
<tr>
<th>Ototestibular</th>
<th>Renal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Date to be given</td>
</tr>
<tr>
<td>Creatinine = micromol/L</td>
<td></td>
</tr>
<tr>
<td>Creatinine = micromol/L</td>
<td></td>
</tr>
<tr>
<td>Creatinine = micromol/L</td>
<td></td>
</tr>
</tbody>
</table>

**Administration Record**

Complete each time gentamicin is administered (plus on the kardex)

<table>
<thead>
<tr>
<th>Time given</th>
<th>Time started 24 h clock</th>
<th>Infuse over 30 mins*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Monitoring Record**

Record ALL sample dates/times accurately below. See overleaf for monitoring advice.

<table>
<thead>
<tr>
<th>Date of sample</th>
<th>Sample time 24 h clock</th>
<th>Gent level (mg/L)</th>
<th>Action/Comments (please initial action to be taken)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>24 hourly ❑ 48 hourly ❑ Withhold ❑ Stop ❑ Details/other:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>24 hourly ❑ 48 hourly ❑ Withhold ❑ Stop ❑ Details/other:</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>24 hourly ❑ 48 hourly ❑ Withhold ❑ Stop ❑ Details/other:</td>
</tr>
</tbody>
</table>

---

The risks of prolonged treatment beyond 72 hours must be considered and treatment options discussed with Microbiology or infection specialist. Document authorisation code here before continuing therapy on next sheet

**AUTHORISATION CODE:**
ADULT PARENTERAL GENTAMICIN (GGC): PRESCRIBING, ADMINISTRATION & MONITORING CHART

Calculating the first dose of gentamicin
- If creatinine is known - use the online gentamicin dose calculator.
- If creatinine is not known - give 5 mg/kg gentamicin (maximum 400 mg) or, if CKD 4 or 5, give 2.5 mg/kg (maximum 180 mg) on advice of senior medical staff.
- Calculate the dosage regimen once creatinine is available.
- If the online calculator is not available, manually calculate the dose referring to the gentamicin policy.
- Dilute in 100mls of sodium chloride 0.9% or glucose 5% and administer over 30 minutes.

Checking the patient’s gentamicin concentration
- Take a blood sample 6-14 hours after the start of the first gentamicin infusion (or after 24 hours if CrCl <21 ml/min).
- Thereafter, sample at least every 2 days.
- Record the exact time of all gentamicin samples overleaf AND on the sample request form.

Interpreting gentamicin results and re-prescribing
- Record the measured concentration overleaf.
- If creatinine clearance is ≥221 ml/min and therapy is to continue, plot the gentamicin concentration on the graph opposite & reassess the dose/dosing interval as indicated.
- If creatinine clearance is <21 ml/min and therapy is to continue, give a further dose once the measured concentration is <1 mg/L.
- Document the action taken in the medical notes and overleaf. Prescribe the next dose overleaf as appropriate.
- Contact pharmacy for further advice as necessary (e.g. if renal function is changing, the gentamicin concentration is unexpectedly high or low or the concentration is on the line between dosage intervals).
- Consider narrow spectrum oral alternatives and refer to IV to Oral switch policy.

If the measured concentration is unexpectedly HIGH or LOW
- Were dose and sample times recorded accurately?
- Was the correct dose administered?
- Was the sample taken from the line used to administer the drug?
- Was the sample taken during drug administration?
- Has renal function declined or improved?
- Does the patient have oedema or ascites?

If in doubt, take another sample before re-prescribing and/or contact pharmacy for advice.

Prepared by: Alison MacDonald Lead Reviewer: Antimicrobial Management Team Authorised by: Formulary Subgroup of NHS Highland ADTC Date of Issue: June 2017 Date of Review: June 2019 Version 6
A loading dose should be administered based on patient’s actual body weight.

<table>
<thead>
<tr>
<th>Actual body weight</th>
<th>Dose</th>
<th>Volume of sodium chloride 0.9%</th>
<th>Duration of infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40kg</td>
<td>750mg</td>
<td>250mL</td>
<td>90 minutes</td>
</tr>
<tr>
<td>40-59kg</td>
<td>1000mg</td>
<td>250mL</td>
<td>2 hours</td>
</tr>
<tr>
<td>60-90kg</td>
<td>1500mg</td>
<td>500mL</td>
<td>3 hours</td>
</tr>
<tr>
<td>&gt;90kg</td>
<td>2000mg</td>
<td>500mL</td>
<td>4 hours</td>
</tr>
</tbody>
</table>

Calculate patient’s ideal body weight (IBW):
Males: 50 kg + 2.3 kg for every inch above 5 feet (or 2.5 cm above 152 cm)
Females: 45.5 kg + 2.3 kg for every inch above 5 feet (or 2.5 cm above 152 cm)

Is patient obese (obese = actual body weight >20% over ideal body weight)?

YES
Calculate creatinine clearance using IBW

Creatinine clearance (mL/min):
(140 – age (years) x weight (kg))
Creatinine (micromoles/L)

Multiply figure obtained by:
1.23 for males
or 1.04 for females

NO
Calculate creatinine clearance using actual body weight

Note: In patients with low creatinine less than 60mmol/L, use 60mmol/L.
Use of estimated GFR (eGFR) is not recommended.

Prescribe the first maintenance infusion 12, 24 or 48 hours after the loading infusion according to the table.

**VANCOMYCIN PULSED INFUSION – INITIAL MAINTENANCE DOSAGE GUIDELINES**

<table>
<thead>
<tr>
<th>CrCl (mL/min)</th>
<th>Dose amount</th>
<th>Volume of sodium chloride 0.9%</th>
<th>Dose interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>500mg over 1 hour</td>
<td>250mL</td>
<td>48 hours</td>
</tr>
<tr>
<td>20-29</td>
<td>500mg over 1 hour</td>
<td>250mL</td>
<td>24 hours</td>
</tr>
<tr>
<td>30-39</td>
<td>750mg over 1-5 hours</td>
<td>250mL</td>
<td>24 hours</td>
</tr>
<tr>
<td>40-54</td>
<td>500mg over 1 hour</td>
<td>250mL</td>
<td>12 hours</td>
</tr>
<tr>
<td>55-74</td>
<td>750mg over 1-5 hours</td>
<td>250mL</td>
<td>12 hours</td>
</tr>
<tr>
<td>75-89</td>
<td>1000mg over 2 hours</td>
<td>250mL</td>
<td>12 hours</td>
</tr>
<tr>
<td>90-110</td>
<td>1250mg over 2-5 hours</td>
<td>250mL</td>
<td>12 hours</td>
</tr>
<tr>
<td>&gt;110</td>
<td>1500mg over 3 hours</td>
<td>500mL</td>
<td>12 hours</td>
</tr>
</tbody>
</table>

Take a trough sample (pre-dose) within 48 hours of starting therapy then every 2 to 3 days if patient is stable or daily if patient has unstable renal function. Monitor creatinine daily. **Record the time of the last dose and the blood sampling time on the request form and the vancomycin prescribing chart.** If renal function is stable, give the next dose before the trough result is available. **Contact pharmacy or microbiology if you require any further advice.**

**Vancomycin concentration**

<table>
<thead>
<tr>
<th>Suggested dose change</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10mg/L</td>
</tr>
<tr>
<td>Increase dose by 50% and consider reducing the dosing interval (eg from 1 gram every 12 hours to 1 gram every 8 hours) or seek advice.</td>
</tr>
<tr>
<td>10 – 15mg/L</td>
</tr>
<tr>
<td>If the patient is responding, maintain the present dose regimen. If the patient is seriously ill, consider increasing the dose or reducing the dosing interval to achieve a trough level of 15 to 20mg/L.</td>
</tr>
<tr>
<td>15 – 20mg/L</td>
</tr>
<tr>
<td>Maintain the present dose regimen.</td>
</tr>
<tr>
<td>&gt;20mg/L</td>
</tr>
<tr>
<td>Stop until &lt;20mg/L then seek advice.</td>
</tr>
</tbody>
</table>
ANTIBIOTICS: INTRAVENOUS TO ORAL POLICY

The Management of Infection Guidance provides advice on when the intravenous route is appropriate.

A. FREQUENT REVIEW

All patients commenced on intravenous antibiotics MUST be reviewed DAILY by the medical team responsible for the patient. Questions to be answered:

- is the patient responding?
- what is the causative organism and site of infection?
- can therapy be rationalised from broad-spectrum to narrow-spectrum?
- can the patient be switched from intravenous to oral antibiotics?

Expert advice is available from Medical Microbiology and Pharmacy, if required.

NB: For advice on drug administration via enteral tubes consult the ward pharmacist or Medicines Information.

B. EXCLUSIONS FROM INTRAVENOUS TO ORAL SWITCH:

(high tissue concentrations required)

- infective endocarditis
- meningitis
- bone or joint infection (osteomyelitis, septic arthritis)
- deep seated infection or abscess
- infected implant or prosthesis
- severe, necrotising skin and soft-tissue infection
- Staphylococcus aureus bacteraemia
- cavitating pneumonia
- immunosuppression.

C. SUGGESTED CRITERIA TO BE MET BEFORE INTRAVENOUS TO ORAL SWITCH:

- evidence of clinical improvement from infection
- no signs of systemic inflammation (SSI) (i.e. temp>38 or <36°C, heart rate > 90 bpm, respiratory rate > 20/minute, WCC > 12 or < 4, acutely altered mental state, blood glucose above the normal range without diabetes)
- no absorption problems
- oral fluid and food tolerated
- suitable oral alternative available.

D. ADVANTAGES OF INTRAVENOUS TO ORAL SWITCH:

- reduction in infusion-associated complications, e.g. peripheral venous catheter phlebitis, healthcare-acquired infection
- saves both medical and nursing staff time
- improved patient comfort and mobility
- possibility of earlier discharge
- potential reduction in risk of adverse events; errors in preparation are significantly higher with parenteral drugs, compared with oral formulations
- potential to significantly reduce treatment costs.
CHAPTER 6   ENDOCRINE SYSTEM

6.1   DRUGS USED IN DIABETES

For information on the management of diabetes refer to SIGN guidelines 116 and 154. An HbA1c of ≤53mmol/mol has been shown to reduce the risk of vascular complication of diabetes. A target of ≤48mmol/mol may be appropriate at diagnosis in individuals controlled with diet and/or metformin. However, a higher HbA1c target eg ≤58mmol/mol should be considered in those at risk of hypoglycaemia, eg the elderly, patients treated with insulin or sulfonylureas, and in individuals with pre-existing cardiovascular disease.

Insulins

Insulin preparations should be initiated by appropriately trained individuals in accordance with the 'NHS Highland patient pathways for introduction and management of insulin therapy for people with diabetes' on Intranet. Thereafter, tailor therapy to the patient's needs.

• **Type 2 patients who are newly prescribed insulin should usually be started on once-daily Insuman® Basal given at bedtime.** Long-acting recombinant human insulin analogues (eg Levenir®, Abasaglar®, Lantus®, Toujeo®) are much more expensive and are not required for the majority of patients with type 2 diabetes, however they may be useful for patients requiring help administering insulin or if there are concerns regarding hypoglycaemia.

• Choose devices and insulin on the basis of patient suitability and review regularly; refer to the **insulins table** for prescribing guidance.

• Changes should, where possible, be implemented when current patient supplies have been used up. Patients whose diabetes is stable should remain on their current insulin regimen unless a change is clinically indicated.

The following insulins are available (see summary).

**Short-acting: soluble insulin – human sequence**

<table>
<thead>
<tr>
<th>FIRST CHOICE: INSUMAN RAPID (for patients with Type 2 diabetes)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INSUMAN® RAPID</strong> injection 100 units/mL; 3mL cartridge (for ClikSTAR®, Autopen®)</td>
</tr>
<tr>
<td><strong>ACTRAPID®</strong> injection 100 units/mL; 10mL vial</td>
</tr>
<tr>
<td><strong>HUMULIN S®</strong> injection 100 units/mL; 3mL cartridge (for Autopen®, HumaPen® Savvio)</td>
</tr>
</tbody>
</table>

**Rapid-acting: recombinant human insulin analogues**

• Insulin aspart

  | NOVORAPID® injection 100 units/mL; 10mL vial; 3mL cartridge (for NovoPen® 4); 3mL pre-filled disposable injection device (FlexPen®, FlexTouch®) |

• Insulin glulisine

  | APIDRA® injection 100 units/mL; 10mL vial; 3mL cartridge (for ClikSTAR®, Autopen® 24); 3mL pre-filled disposable injection device (SoloStar®) |

• Insulin lispro
HUMALOG® injection 100 units/mL, 10mL vial; 3mL cartridge (for Autopen®, HumaPen® Savvio); 3mL pre-filled disposable injection device (KwikPen®)

**Ultrafast rapid-acting: recombinant human insulin analogues**

- **Insulin aspart**
- **FIASP®▼** injection 100 units/mL, 10mL vial; 100 units/mL, 3mL pre-filled pen (Flextouch®); 100 units/mL, 3mL cartridge (Penfill®)

**Long-acting: recombinant human insulin analogues**

- **Insulin detemir**
- **S LEVEMIR®** injection 100 units/mL; 3mL cartridge (for NovoPen® 4); 3mL pre-filled disposable injection device (FlexPen®, InnoLet®)
- **Insulin glargine**
- **LANTUS®** injection 100 units/mL; 10mL vial; 3mL cartridge (for ClikSTAR®, Autopen®24); 3mL pre-filled disposable injection device (SoloStar®)
- **ABASAGLAR®▼** injection 100 units/mL; 3mL cartridge (for Autopen®, HumaPen®); 3mL pre-filled disposable injection device (KwikPen®)

**Higher concentration long-acting recombinant human insulin analogues**

- **STOUJE®** injection 300 units/mL; 1.5mL pre-filled disposable injection device (SoloStar®)

Insulin glargine 300 units/mL (Toujeo®) has similar efficacy but is not bioequivalent to insulin glargine 100 units/mL (Abasaglar®, Lantus®) and is therefore not interchangeable without dose adjustment. When changing to Toujeo®, patients should start with the same insulin glargine dose then a small dose titration may be needed.

**Intermediate-acting: isophane insulin**

- **Human sequence**

**FIRST CHOICE:** INSUMAN BASAL (for patients with Type 2 diabetes)

- **INSUMAN® BASAL** injection 100 units/mL; 5mL vial; 3mL cartridge (for ClikSTAR®, Autopen®); 3mL pre-filled disposable injection device (SoloStar®)
- **HUMULIN I®** injection 100 units/mL; 10mL vial; 3mL cartridge (for Autopen®, HumaPen® Savvio); 3mL pre-filled disposable injection device (KwikPen®)
- **INSULATARD®** injection 100 units/mL; 10mL vial; 3mL cartridge (for NovoPen® 4); 3mL pre-filled disposable injection device (InnoLet®)

**Biphasic recombinant human insulin analogue**

- **Biphasic insulin aspart**
- **NOVOMIX® 30** injection 30% insulin aspart, 70% insulin aspart protamine 100 units/mL; 3mL cartridge (for NovoPen® 4); 3mL pre-filled disposable injection device (FlexPen®)
• Biphasic insulin lispro

**HUMALOG® MIX25** injection 25% insulin lispro, 75% insulin lispro protamine 100 units/mL; 10mL vial; 3mL cartridge (for Autopen® and HumaPen® Savvio); 3mL pre-filled disposable injection device (KwikPen®)

**HUMALOG® MIX50** injection 50% insulin lispro, 50% insulin lispro protamine 100 units/mL; 3mL cartridge (for Autopen® and HumaPen® Savvio); 3mL pre-filled disposable injection device (KwikPen®)

Biphasic isophane insulins

• Human sequence

**FIRST CHOICE:** **INSUMAN COMB** (for patients with Type 2 diabetes)

**INSUMAN® COMB 25** injection 25% soluble, 75% isophane 100 units/mL; 5mL vial; 3mL cartridge (for ClikSTAR®, Autopen®); 3mL pre-filled disposable injection device (SoloStar®)

**INSUMAN® COMB 50** injection 50% soluble, 50% isophane 100 units/mL; 3mL cartridge (for ClikSTAR®, Autopen®)

**HUMULIN M3®** injection 30% soluble, 70% isophane 100 units/mL; 10mL vial; 3mL cartridge (for Autopen®, HumaPen® Savvio); 3mL pre-filled disposable injection device (KwikPen®)

Hypodermic equipment

A needle clipping (chopping) device consisting of a clipper to remove a needle from its hub and a container from which cut-off needles cannot be retrieved, can be prescribed for patients to use in the community. It is designed to hold 1500 needles; it is unsuitable for use with lancets. In hospitals, needle clipping devices can be ordered from Supplies for patients at discharge. Containers for sharps are available on prescription in primary care, however arrangements for their disposal must be agreed with the prescriber. If insulin administration is being carried out to a patient by a healthcare professional then a safety engineered device must be used.

**Oral antidiabetic drugs**

For use in type 2 diabetes, refer to guidance.

Biguanides

**FIRST CHOICE:** **METFORMIN TABLETS**

**SECOND CHOICE:** **METFORMIN M/R TABLETS**

**METFORMIN** tablets 500mg, 850mg, m/r tablets 500mg, 750mg, 1gram

**Dose:** Tablets (immediate-release), initially 500mg with breakfast for 1 week then 500mg with breakfast and evening meal for 1 week then titrated as required; maximum 2 grams daily in divided doses. Tablets (m/r), patients who have been taking the immediate-release metformin may start with the same daily dose of metformin m/r tablets and titrate up to a maximum of 2 grams daily.
Note: Metformin:
- Advise patients to stop metformin during vomiting or diarrhoeal illnesses
- The m/r tablets are restricted to use in patients intolerant of immediate-release metformin and in whom the m/r tablet allows the use of a dose of metformin not previously tolerated or in patients for whom a once-daily preparation offers a clinically significant benefit.

Use of metformin in surgery, investigations with contrast media and conditions predisposing to tissue hypoxia

<table>
<thead>
<tr>
<th>Surgical procedures</th>
<th>Stop 24 hours beforehand. Withhold for at least 48 hours.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investigations with contrast media</td>
<td>Discontinue on day of examination. Restart 48 hours later. If eGFR less than 60 mL/min/m² then check renal function before restarting.</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>Withhold at time of infarct. Consider restarting 5 days post-infarct.</td>
</tr>
<tr>
<td>Acute coronary syndrome</td>
<td>Withhold during ischaemic pain. Restart when pain free for 48 hours.</td>
</tr>
<tr>
<td>Acute limb ischaemia</td>
<td>Withhold until acute event resolved.</td>
</tr>
<tr>
<td>Sepsis</td>
<td>Withhold until acute event resolved.</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>Withhold until acute event resolved.</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>Only restart metformin when the eGFR is greater than 30mL/min and back to patient’s normal baseline.</td>
</tr>
</tbody>
</table>

Sulfonylureas

**FIRST CHOICE: GLICLAZIDE**

**GLICLAZIDE** tablets 80mg

**Dose:** Initially 40 to 80mg daily, adjusted according to response; up to 160mg as a single dose, before breakfast; take higher doses twice daily (before breakfast and main meal); maximum 320mg daily.

**GLIPIZIDE** tablets 5mg

**Dose:** Initially 2.5 to 5mg daily before breakfast adjusted according to response, maximum 20mg daily; up to 15mg may be given as a single dose, higher doses divided.

Thiazolidinediones

**PIOGLITAZONE** tablets 15mg, 30mg, 45mg

**Dose:** Refer to [pioglitazone prescribing algorithm](#).

Dipeptidylpeptidase-4 (DPP-4) inhibitors

**FIRST CHOICE: SITAGLIPTIN**

**SITAGLIPTIN** tablets 25mg, 50mg, 100mg

**Dose:** Refer to [guidance](#).

**LINAGLIPTIN** tablets 5mg

**Dose:** Refer to [guidance](#).

First-line DPP-4 inhibitor of choice in any degree of renal impairment.
CHAPTER 6  ENDOCRINE SYSTEM

Sodium-glucose co-transporter 2 (SGLT2) inhibitors

**Note:** There have been reports of atypical diabetic ketoacidosis (DKA) with the use of SGLT2 inhibitors. Although extremely rare, atypical DKA has been reported in patients with type 1 and type 2 diabetes at blood sugar levels not normally associated with DKA, i.e. 14mmol/L. There is no need to withdraw the SGLT2 inhibitor but specialist advice is as follows:

- test for raised ketones in patients with symptoms of diabetic ketoacidosis (DKA); omitting this test could delay diagnosis of DKA (includes patients with type 2 diabetes at any blood glucose level).
- if DKA is suspected, stop SGLT2 inhibitor treatment.
- if DKA is confirmed, take appropriate measures to correct the DKA and to monitor glucose levels.
- inform patients of the symptoms and signs of DKA (see below); advise them to get immediate medical help if these occur.
- be aware that SGLT2 inhibitors are not approved for treatment of type 1 diabetes.
- avoid dehydration and ask patients to follow sick day rules (avoid taking for 24 to 48 hours if symptoms of diarrhoea or vomiting).
- please continue to report suspected side-effects to SGLT2 inhibitors or any other medicines on a **Yellow Card**.
- this is a class effect associated with licensed SGLT2 inhibitors.

DAPAGLIFLOZIN tablets 5mg, 10mg
**Dose:** Refer to [guidance](#).

EMPAGLIFLOZIN tablets 10mg, 25mg
**Dose:** Refer to [guidance](#).

Injectable therapy for type 2 diabetes

Glucagon-like peptide-1 (GLP-1) receptor agonists

**FIRST CHOICE:** LIRAGLUTIDE

S **LIRAGLUTIDE** injection 18mg/3mL pre-filled pen
**Dose:** Refer to [protocol for use of GLP-1 analogues](#).

S **EXENATIDE** injection, pre-filled pen 5 micrograms/dose, 10 micrograms/dose; m/r powder for reconstitution 2mg/pre-filled pen
**Dose:** Refer to [protocol for use of GLP-1 analogues](#).

S **DULAGLUTIDE** injection, pre-filled pen 750 micrograms/0.5mL, 1.5mg/0.5mL
**Dose:** Refer to [protocol for use of GLP-1 analogues](#).

Treatment of hypoglycaemia

For guidance on the treatment of hypoglycaemia refer to: [http://www.nhshighland.scot.nhs.uk/YourHealth/Diabetes/Documents/Management%20of%20hypoglycaemia.pdf](http://www.nhshighland.scot.nhs.uk/YourHealth/Diabetes/Documents/Management%20of%20hypoglycaemia.pdf). Glucose gel is a convenient form of oral glucose, however for unconscious patients glucagon can be given by subcutaneous, intramuscular or intravenous injection. If ineffective within 10 minutes, then give intravenous glucose as per above guidance.

**GLUCOSE** oral gel 40%

**GLUCOSE** intravenous injection 20%
CHAPTER 6  ENDOCRINE SYSTEM

GLUCAGON (GlukaGen® Hypokit) injection 1mg

Diagnostic and monitoring agents for diabetes mellitus

Oral glucose tolerance test (OGTT)

The OGTT is used in the diagnosis of gestational diabetes: see ‘Screening and Diagnosis of Diabetes’. Polycal® liquid is considerably cheaper than Rapilose® but must be measured accurately. Both are licensed as medical devices and available through hospital medical supplies or on prescription in primary care.

POLYCAL® liquid
Polycal® liquid is a feed supplement. Mix 113mL with water and make up to a volume of 200 to 300mL.

RAPILOSE® OGTT solution
A ready to drink product, marketed specifically for this test.

Blood monitoring test strips
Refer to ‘Guideline for blood glucose monitoring’.

Urinalysis

KETOSTIX® OTC test strips for detection of ketones in urine

6.2  THYROID AND ANTITHYROID DRUGS

LEVOTHYROXINE tablets 25 micrograms, 50 micrograms, 75 micrograms, 100 micrograms; oral solution 100 micrograms/5mL

Dose: Initially 50 to 100 micrograms daily, adjusted in steps of 25 to 50 micrograms every 6 to 8 weeks until normal metabolism maintained (usually 100 to 200 micrograms daily). Older people or cardiac disease, initially, 25 to 50 micrograms daily.

If a liquid levothyroxine preparation is required for patients with swallowing difficulties, crush tablets in 10 to 15mL water to make a suspension and take immediately washed down with some more liquid. The generic tablets from Concordia International and Actavis UK Ltd include this advice within their marketing authorisation (SPC). For specific advice for administration via an enteral feeding tube, refer to your pharmacist.

After changes in dose of levothyroxine, thyroid function tests (request TSH and FT4 and state patient is on levothyroxine) should normally be repeated after 8 weeks to allow steady state to be achieved. Once stable, check thyroid stimulating hormone (TSH) every 12 months and adjust the dose to normalise the TSH. The total daily dose can usually be administered as a single dose taken at least one hour apart from food and other medicines. For further guidance refer to www.british-thyroid-association.org.

LIOTHYRONINE tablets 20 micrograms; injection 20 micrograms

Dose: By mouth, short-term use only in thyroid cancer patients post-thyroidectomy/pre-radioiodine therapy or iodine uptake scan, 20 micrograms three times daily; by slow intravenous injection, hypothyroid coma, 5 to 20 micrograms repeated every 12 hours or as often as every 4 hours if necessary; alternatively 50 micrograms initially then 25 micrograms every 8 hours reducing to 25 micrograms twice daily.
Antithyroid drugs

**FIRST CHOICE:** CARBIMAZOLE  
**SECOND CHOICE:** PROPYLTHIOURACIL

During either carbimazole or propylthiouracil treatment, advise patients to report signs and symptoms of infection, especially sore throat, which may indicate bone marrow suppression, and to discontinue medication pending further investigation. The drug should only be recommenced once neutropenia has been excluded following a blood count. Routine monitoring of white blood cell count is unnecessary. If sensitivity (eg rash) occurs with carbimazole then propylthiouracil is an alternative. Propylthiouracil is the drug of choice in pregnant women. For information on the treatment of thyrotoxic crisis, refer to BNF section 6.2.2.

**S CARBIMAZOLE** tablets 5mg, 20mg  
**Dose:** Initially 20 to 40mg once daily. Repeat TFTs after 4 to 6 weeks and adjust the dose following specialist advice.

**S PROPYLTHIOURACIL** tablets 50mg  
**Dose:** Initially 200mg daily in divided doses. Repeat TFTs after 4 to 6 weeks and adjust the dose following specialist advice.

**PROPRANOLOL** m/r capsules 80mg, 160mg  
**Dose:** *By mouth*, for the relief of thyrotoxic symptoms m/r capsules 80 to 160mg daily.

**S AQUEOUS IODINE ORAL SOLUTION** (Lugol’s Solution) total iodine 130mg/mL  
**Dose:** 0·1 to 0·3mL 3 times daily, well diluted with milk or water. Requires extemporaneous preparation [unlicensed].

6.3 CORTICOSTEROIDS

Mineralocorticoid therapy

**FLUDROCORTISONE** tablets 100 micrograms  
**Dose:** 50 to 200 micrograms daily. Patients with Addison’s disease (primary adrenocortical insufficiency) require mineralocorticoid replacement with fludrocortisone normally in a dose of 50 to 200 micrograms daily. The adequacy of replacement can be assessed by measurement of plasma renin activity and clinically through postural blood pressure measurement and assessment of oedema. The tablets should be stored in the refrigerator between 2 to 8°C. For use in orthostatic hypotension [off-label] refer to Parkinsons Disease guideline.

Glucocorticoid therapy

Prednisolone has predominantly glucocorticoid activity (anti-inflammatory) and is the most commonly used corticosteroid for long-term administration (see also section 3.2 for use in asthma/COPD and section 10.1 for use in rheumatic diseases). There is no evidence that the use of enteric-coated tablets prevents peptic ulceration. Dexamethasone is mainly used where mineralocorticoid activity is undesirable (eg in cerebral oedema) and for the prevention or treatment of nausea and vomiting induced by chemotherapy or opiates (see section 4.6). Hydrocortisone is used for replacement therapy in adrenal insufficiency.

**Note:** Issue steroid cards with long-term therapy.

**PREDNISOLONE** tablets 1mg, 5mg, 25mg; soluble tablets 5mg  
**Dose:** Dose varies according to condition. Refer to BNF.  
If possible, avoid use of the high-cost prednisolone tablets 25mg and soluble tablets 5mg.
HYDROCORTISONE tablets 10mg, 20mg; injection (as sodium succinate) 100mg; injection (as sodium phosphate) 100mg/1mL, 500mg/5mL
Dose: By mouth, replacement therapy, 15 to 25mg daily in 2 to 3 divided doses. Take the first dose on waking in the morning and the last dose early in the evening. For use of hydrocortisone oromucosal tablets in oral ulceration or inflammation, refer to section 12.3.

DEXAMETHASONE tablets 500 micrograms, 2mg, 4mg; soluble tablets 2mg, 4mg, 8mg; oral solution (as sodium phosphate) 2mg/5mL; injection (as sodium phosphate) 3.3mg/1mL, 6.6mg/2mL
Dose: Dose varies according to condition. Refer to BNF. Most patients can either take the tablets as they are or dispersed in a little water prior to use [off-label].

BETAMETHASONE soluble tablets 500 micrograms; injection 4mg/1mL
Dose: For use of betamethasone soluble tablets in oral ulceration or inflammation refer to section 12.3 [off-label].

METHYLPREDNISOLONE tablets 100mg; injection (as sodium succinate) 40mg, 1 gram
Dose: Dose varies according to condition. Refer to BNF.

6.4 SEX HORMONES

Oestrogens and hormone replacement therapy (HRT)

Refer to HRT guidance for further information, also note NICE guidance NG23 ‘Menopause: diagnosis and management’. Oral preparations are usually first-line unless not tolerated. Where patients have persistent oestrogenic side-effects, reduce dose and change preparation or move to a transdermal preparation. For patients with risk factors for venous thromboembolism or stroke consider transdermal preparations.

For women with an intact uterus

Women with a uterus require progestogen in addition to oestrogen to protect the endometrium.

Oestrogen with cyclical progestogen

Oral

**FIRST CHOICE:** ELLESTE-DUET®

**SECOND CHOICE:** FEMOSTON®

**ELLESTE-DUET®** estradiol 1mg tablets and estradiol 1mg/norethisterone 1mg tablets; estradiol 2mg tablets and estradiol 2mg/norethisterone 1mg tablets
Dose: 1 estradiol-only tablet daily for 16 days, starting on day 1 of menstruation (or at any time if cycles have ceased or are infrequent) then 1 estradiol/norethisterone tablet daily for 12 days; subsequent courses are repeated without interval.

**FEMOSTON®** estradiol 1mg tablets and estradiol 1mg/dydrogesterone 10mg tablets; estradiol 2mg tablets and estradiol 2mg/dydrogesterone 10mg tablets
Dose: 1 estradiol-only tablet daily for 14 days, starting within 5 days of onset of menstruation (or any time if cycles have ceased or are infrequent), then 1 estradiol/dydrogesterone tablet for 14 days; subsequent courses are repeated without interval.

CYCLO-PROGYNова® estradiol 2mg tablets and estradiol 2mg/norgestrel 500 micrograms tablets  
Dose: Starting on 5th day of cycle or at any time if not menstruating regularly, 1 estradiol-only tablet daily for 11 days then 1 estradiol/norgestrel tablet daily for 10 days followed by 7 tablet-free days.

Transdermal  

FIRST CHOICE: EVOREL® SEQUI

EVOREL® SEQUI estradiol 50 micrograms/24 hours patches and estradiol 50 micrograms/24 hours; norethisterone 170 micrograms/24 hours patches  
Dose: 1 estradiol-only patch to be applied twice weekly for 2 weeks followed by 1 estradiol/norethisterone patch twice weekly for 2 weeks; subsequent courses are repeated without interval.

FEMSEVEN® SEQUI estradiol 50 micrograms/24 hours patches and estradiol 50 micrograms/24 hours; levonorgestrel 10 micrograms/24 hours patches  
Dose: 1 estradiol-only patch to be applied once weekly for 2 weeks followed by 1 estradiol/levonorgestrel patch once weekly for 2 weeks; subsequent courses are repeated without interval.

Oestrogen with continuous progestogen

Oral

PREMIQUE® LOW DOSE (conjugated oestrogen (equine) 300 micrograms, medroxyprogesterone acetate 1·5mg) m/r tablets  
Dose: 1 tablet daily, continuously. Start at end of scheduled bleed if changing from cyclical HRT.

KLIOFEM® estradiol 2mg, norethisterone acetate 1mg tablets  
Dose: 1 tablet daily, continuously. Start at end of scheduled bleed if changing from cyclical HRT.

Transdermal

FIRST CHOICE: EVOREL® CONTI

EVOREL® CONTI (estradiol 50 micrograms/24 hours-norethisterone 170 micrograms/24 hours) patches  
Dose: 1 patch to be applied twice weekly continuously.

FEMSEVEN® CONTI (estradiol 50 micrograms/24 hours-levonorgestrel 7 micrograms/24 hours) patches  
Dose: 1 patch to be applied once weekly continuously.

For women without a uterus

Oral

FIRST CHOICE: ELLESTE-SOLO®  
SECOND CHOICE: PREMARIN®
CHAPTER 6  ENDOCRINE SYSTEM

ELLESTE-SOLO® estradiol tablets 1mg, 2mg
Dose: 1 to 2mg daily.

PREMARIN® conjugated oestrogens (equine) tablets 300 micrograms, 625 micrograms, 1·25mg
Dose: 300 micrograms to 1·25mg daily.

Transdermal

**FIRST CHOICE: EVOREL®**

EVOREL® estradiol patches 25, 50, 75, 100 micrograms/24 hours
Dose: 1 patch to be applied twice weekly continuously. Initiate therapy with 50 microgram patch for first month, subsequently adjusted to lowest effective dose.

ESTRADERM MX® estradiol patches 25, 50, 75, 100 micrograms/24 hours
Dose: 1 patch to be applied twice weekly continuously. Initiate therapy with the 25 microgram patch for first 3 months, subsequently adjusted to lowest effective dose.

$ESTRADOT® estradiol patches 25, 37·5, 50, 75, 100 micrograms/24 hours
Dose: for patients undergoing gender reassignment [off-label], 1 patch to be applied twice weekly continuously.

Tibolone

MHRA: Take into account the risk of stroke in older women when considering the benefits and risks of prescribing tibolone; refer to www.gov.uk/drug-safety-update.

TIBOLONE tablets 2·5mg
Dose: for the short-term treatment of symptoms of oestrogen deficiency (including women being treated with gonadotrophin releasing hormone analogues (section 6.7)), 2·5mg daily.

Progestogens for HRT

MIRENA® (releasing levonorgestrel 20 micrograms/24 hours) intra-uterine system (IUS)
Used for the prevention of endometrial hyperplasia during oestrogen replacement therapy. In line with guidelines from the Faculty of Sexual Health and Reproductive Medicine the Mirena® IUS should be changed no later than 5 years after insertion [off-label the licence states 4 years] irrespective of age at insertion; refer to https://www.fsrh.org/standards-and-guidance/documents/fsrh-guidance-contraception-for-women-aged-over-40-years-2017/.

Menorrhagia and dysmenorrhea

For the relief of pain in dysmenorrhea NSAIDS are suitable; naproxen is a lower-cost alternative to mefenamic acid.

For the treatment of menorrhagia, the Mirena® IUS is first choice and may be particularly useful in women with menorrhagia who also need contraception; for this indication Mirena® is effective for 5 years. If the Mirena® IUS is unsuitable, tranexamic acid, NSAIDs or combined oral contraceptives (section 7.3) should be considered as second choice treatment. If a NSAID is to be used, naproxen [off-label], mefenamic acid or ibuprofen [off-label] (section 10.1) should be prescribed.

Refer also to local guidelines on the management of menorrhagia on Intranet and to NICE guideline CG44.

MIRENA® (releasing levonorgestrel 20 micrograms/24 hours) intra-uterine system.
TRANEXAMIC ACID tablets 500mg; injection 500mg/5mL
Dose: *By mouth*, menorrhagia (initiated when menstruation has started), 1 gram 3 times daily for up to 4 days; maximum 4 grams daily.

NAPROXEN tablets 250mg
Dose: *By mouth*, for dysmenorrhoea 250mg 3 times daily; for menorrhagia, 250mg to 500mg 3 times daily for 5 days starting at the onset of bleeding [off-label]. Refer to ‘Non-steroidal anti-inflammatory drugs’ guidance for cautions and contra-indications.

MEFENAMIC ACID tablets 500mg
Dose: *By mouth*, for dysmenorrhoea 500mg 3 times daily; for menorrhagia, 500mg 3 times daily for 5 days starting at the onset of bleeding. Refer to ‘Non-steroidal anti-inflammatory drugs’ guidance for cautions and contra-indications.

NORETHISTERONE tablets 5mg
Dose: To arrest prolonged bleeding or delay menstruation this may be given, 5mg 3 times daily, for up to 3 weeks. For routine maintenance of menorrhagia, further guidance is available in the ‘Menorrhagia’ referral guideline on Intranet.

MEDROXYPROGESTERONE tablets 5mg
Dose: Mild to moderate endometriosis, 10mg 3 times daily for 90 consecutive days, beginning on day 1 of cycle. Refer to BNF for all other indications.

Gonadorelin analogues (section 6.7) may also be used in menorrhagia.

**Progesterone receptor modulators**

S ULIPRISTAL tablets 5mg (Esmya®)
Dose: Pre-operative treatment of moderate to severe symptoms of uterine fibroids, 5mg daily for up to 3 months, starting during the first week of menstruation.

**Male sex hormones and antagonists**

**Testosterone and esters**

S TESTOSTERONE gel 10mg-metered application (Tostran®), injection 1 gram/4mL (Nebido®)
Dose: Androgen deficiency, gel initially 60mg testosterone (3 grams gel) applied once daily then adjusted to lowest effective dose; *intramuscular injection*, for long-term maintenance 1 gram every 10 to 14 weeks.

**Anti-androgens**

Refer to ‘Male lower urinary-tract symptoms’ guidance on Intranet.

FINASTERIDE tablets 5mg
Dose: Benign prostatic hyperplasia, 5mg daily (may require several months treatment before benefit is obtained).

**6.5 HYPOTHALAMIC AND PITUITARY HORMONES AND ANTI-OESTROGENS**

**Anti-oestrogens**

S CLOMIFENE tablets 50mg
Dose: 50mg daily for 5 days, starting within 5 days of onset of menstruation (preferably on 2nd day). Dose may be increased following specialist advice. Clomifene should always be initiated and monitored at a Specialist Infertility Clinic.

Anterior pituitary hormones

**Tetracosactide** injection 250 micrograms/1mL

*Dose:* For assessment of adrenal response in the short synacthen test, *by intravenous or intramuscular injection*, 250 micrograms given at zero minutes. Samples are taken for serum cortisol at zero and 30 minutes.

**Somatropin** powder and solvent for solution for injection cartridges 5-3mg, 12mg (Genotropin®); powder and solvent for solution for injection pre-filled disposable devices, 200 micrograms, 400 micrograms, 600 micrograms, 800 micrograms, 1mg, 1.2mg, 1.4mg, 1.6mg, 1.8mg, 2mg (Genotropin MiniQuick®); solution for injection cartridges 5mg/1.5mL, 10mg/1.5mL, 15mg/1.5mL (Norditropin Simplexx®); solution for injection in cartridge for use with Omnitrope® Pen 5mg/1.5mL, 10mg/1.5mL (Omnitrope®); solution for injection cartridges 5mg/1.5mL, 10mg/1.5mL, 15mg/1.5mL (Omnitrope Surepal®); solution for injection cartridges 6mg/1.03mL, 12mg/1.5mL, 20mg/2.5mL (Saizen®)

Somatropin should be prescribed by brand name.

Hypothalamic hormones

**Gonadorelin** injection 100 micrograms (hospital use only)

*Dose:* For assessment of pituitary function in the luteinizing hormone-releasing hormone (LH-RH) test, *by intravenous injection*, 100 micrograms.

Posterior pituitary hormones and antagonists

**Desmopressin** tablets 200 micrograms; intranasal solution 250 micrograms/2.5mL; injection 4 micrograms/1mL; nasal spray 150 micrograms/metered spray (Octim®)

*Dose:* For use in nocturnal enuresis, see section 7.4; other indications, refer to BNF.

** Vasopressin** injection 20 units/1mL

**Tolvaptan** (Jinarc®) tablets 15mg, 30mg, 45mg, 60mg, 90mg

*Dose:* To slow the progression of polycystic kidney disease, refer to SPC.

Terlipressin is used for bleeding from oesophageal varices, see section 1.10.

### 6.6 DRUGS AFFECTING BONE METABOLISM

#### Osteoporosis

Identification of patients at risk of osteoporosis should be guided by national guidance (refer to links below) and, in special situations where knowledge of bone density will change medical management, eg hyperparathyroidism. Advice is summarised in the current DXA referral form and the Management of Osteoporosis advice leaflet available on the Rheumatology webpage on NHS Highland Intranet.

As a general principle, all patients being considered for treatment should have undergone a DXA scan. The exceptions to this would be patients over 65 years on maintenance steroids or low trauma fracture patients considered too frail to attend for DXA.
Useful links:
- Osteoporosis – Secondary Prevention (www.nice.org.uk)
- WHO Fracture Risk Assessment tool (http://www.shef.ac.uk/FRAX/tool.jsp)

Calcium and vitamin D

Those at risk of osteoporosis should maintain an adequate dietary intake of calcium and vitamin D: calcium and vitamin D must be prescribed with all oral and intravenous bone active therapies unless a patient is hypercalcaemic or has a risk of hypercalcaemia, eg sarcoidosis, has had renal stones in the past year or where renal impairment dictates that alfalcacidol should be an alternative.

- Where patients on bone-active therapy for osteoporosis are intolerant of Adcal D₃®/Calcī-D®, consider colecalciferol capsules/tablets 800 units daily. For further information on the use of vitamin D outwith this patient group refer to section 9.6.
- The dose should be to the equivalent of 1000mg of calcium per day and 20 micrograms (800 units) of vitamin D.
- To avoid any potential interaction when taken within 4 hours of a bisphosphonate, consider prescribing calcium and vitamin D supplements to be taken at bedtime, when the stomach is more likely to be empty, to minimise calcium loss.
- For patients with peanut/soya allergy prescribe Adcal D₃® caplets, Calcī-D® tablets or colecalciferol tablets.
- Calcium and vitamin D as monotherapy has only been shown to be effective in osteoporosis in ambulant nursing home residents however this should not be used in place of a proper fracture assessment in these individuals.
- For further information refer to ‘Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management’ (https://nos.org.uk/resource-centre/#).

FIRST CHOICE: ADCAL-D₃®
CALCI-D®

**ADCAL-D₃®** (calcium 600mg or 15mmol, vitamin D 10 micrograms or 400 units/tablet) chewable tablets (lemon or tutti-fruitti flavour), effervescent tablets (contain 52mg sodium per tablet); (calcium 300mg or 7.5mmol, vitamin D 5 micrograms or 200 units/caplet) caplets  
**Dose:** Tablets, 2 tablets at bedtime or one tablet twice daily; caplets, 2 caplets twice daily. Advise patients to avoid taking within 4 hours of a bisphosphonate.

**CALCI-D®** (calcium 1000mg or 25mmol, vitamin D 25 micrograms or 1000 units/tablet) chewable tablets  
**Dose:** 1 tablet in the evening. Advise patients to avoid taking within 4 hours of a bisphosphonate.

**COLECALCIFEROL** (vitamin D) capsules 20 micrograms (800 units), 500 micrograms (20 000 units); tablets 20 micrograms (800 units)  
**Dose:** By mouth, patients on bone-active therapy for osteoporosis who are intolerant of Adcal-D₃®, 800 units daily; prior to zoledronic acid or denosumab where there is a concern about vitamin D deficiency prior to treatment, 40 000 units weekly for 7 weeks. Patients with peanut allergy should avoid the capsules which may contain arachis (peanut) oil. The tablets do not contain arachis (peanut) oil and are suitable for those with peanut allergy.
Bisphosphonates used in osteoporosis

- Counsel patients to swallow bisphosphonate tablets whole with a full glass of water on an empty stomach and to stand or sit upright for at least 30 minutes afterwards. After swallowing the tablet they should wait at least 30 minutes before eating breakfast.
- Avoid in patients with oesophageal abnormalities and other factors which delay transit or emptying (e.g. stricture or achalasia).
- Correct disturbances of calcium and mineral metabolism (e.g. vitamin D deficiency, hypocalcaemia) before starting.
- For information on the duration of bisphosphonate therapy and ‘bisphosphonate holidays’ refer to guidance on the Intranet.

Note: Bisphosphonates and denosumab

Osteonecrosis of the jaw (ONJ):
All bisphosphonates and denosumab are associated with ONJ:
- alendronic acid and risedronate are associated with a very small risk of ONJ (less than 1 case per 10,000). Advise patients to minimise the risk by maintaining good oral hygiene, attending routine dental check-ups and immediately reporting any oral symptoms such as dental mobility, pain or swelling to a doctor and dentist.
- denosumab and intravenous bisphosphonates; give patients the patient reminder card for their medicine, explain the risk of ONJ and advise on precautions to take, see www.gov.uk/drug-safety-update.

Osteonecrosis of the external auditory canal: Denosumab has been reported to be associated with osteonecrosis of the external auditory canal. Consider the possibility of osteonecrosis of the external auditory canal in patients receiving denosumab who present with ear symptoms including chronic ear infections or in those with suspected cholesteroloma. Advise patients to report any ear pain, discharge from the ear, or an ear infection during denosumab treatment. For further information see www.gov.uk.

Atypical fracture:
Long-term treatment with bisphosphonates and denosumab is associated with a very small risk of atypical femoral fractures. The risk of fracture increases with duration of therapy and has been shown to decrease rapidly following drug cessation. Treatment may need to be discontinued while patients are being evaluated for suspected stress fracture. Stress fractures may often be bilateral and therefore the contralateral side should also be investigated. Advise patients to report new hip or thigh pain while on treatment (www.gov.uk/drug-safety-update).

Note: Inability to tolerate medication, lack of persistence or treatment failure
- Bisphosphonate treatment is only recommended in high-risk patients and therefore if patients stop taking treatment then alternatives must be sought. In general oral alendronic acid and risedronate sodium are the preferred therapies but if intolerant of bisphosphonates consider denosumab as the preferred next option (contact the Rheumatology Department if you wish to use denosumab).
- Potential treatment failure is defined as a fracture despite at least 1 year of persistence with therapy. Patients should then be re-referred to the rheumatology clinic for further investigations and selection of alternative medication.

FIRST CHOICE: ALENDRONIC ACID + ADCAL-D₃®

ALENDRONIC ACID tablets 10mg, 70mg; effervescent tablets 70mg (contain 602mg sodium per tablet)
Dose: Treatment of postmenopausal osteoporosis and osteoporosis in men, 10mg daily or (in postmenopausal osteoporosis) 70mg once weekly on the same day each week. The effervescent tablets should only be used in patients who are unable to swallow tablets. Prophylaxis of glucocorticoid-induced osteoporosis in postmenopausal women not receiving HRT, 10mg daily.
RISEDRONATE SODIUM tablets 5mg, 35mg
Dose: Treatment and prevention of osteoporosis, including corticosteroid-induced osteoporosis, in postmenopausal women, 5mg daily or in the treatment of postmenopausal osteoporosis to reduce risk of vertebral or hip fractures, 35mg once weekly on the same day each week. Treatment of osteoporosis in men, 35mg weekly dose.

Other drugs for osteoporosis

S DENOSUMAB solution for injection 60mg/1mL; 120mg/1.7mL
Dose: Treatment of postmenopausal osteoporosis, by subcutaneous injection, 60mg every 6 months. Refer to information on Rheumatology webpage on Intranet.

S ZOLEDRONIC ACID infusion 5mg/100mL
Dose: By intravenous infusion, treatment of postmenopausal osteoporosis and osteoporosis in men (including corticosteroid-induced osteoporosis), 5mg annually as a single dose infused over 15 to 30 minutes, correct any vitamin D deficiency or hypocalcaemia prior to infusion, refer to protocol on Rheumatology webpage on Intranet. In general this is given annually for 3 years. Treatment of Paget’s disease of bone, 5mg as a single dose infused over at least 15 minutes; treat with Adcal D₃® for at least 10 days following infusion.

S TERIPARATIDE injection, pre-filled pen, 600 micrograms/2.4mL
Dose: By subcutaneous injection, 20 micrograms daily. Maximum duration of treatment is 24 months.

Bisphosphonates used in malignant disease

Refer to ‘NHS Highland Cancer Centre Guidelines for use of Bisphosphonates’ and Scottish Palliative Care Guidelines.

S PAMIDRONATE DISODIUM dry powder and solvent for solution for infusion 15mg, 90mg

S DENOSUMAB® (Xgeva®) solution for injection 120mg/1.7mL

S IBANDRONIC ACID tablets 50mg, concentrate for solution for infusion 2mg/2mL, 6mg/6mL

S SODIUM CLODRONATE tablets 800mg

S ZOLEDRONIC ACID solution for infusion 4mg/5mL
For reduction of bone damage in advanced malignancies involving bone and hypercalcaemia of malignancy.

6.7 OTHER ENDOCRINE DRUGS

Dopaminergic drugs

CABERGOLINE tablets 500 micrograms
Dose: For the treatment of hyperprolactinaemia following investigation, initially 250 micrograms twice weekly taken with food before retiring to bed, increasing to a maintenance dose of 500 micrograms twice weekly after 2 to 3 weeks; refer to BNF for cautions. For use in suppression of lactation see section 7.1.

Gonadorelin analogues

FIRST CHOICE: TRIPTORELIN
**TRIPTORELIN ACETATE** (Decapeptyl® SR) powder for suspension for injection vial 3mg, 11·25mg

**Dose:** 3mg injection, endometriosis and reduction in size of uterine fibroids, *by intramuscular injection*, 3mg every 4 weeks starting during first 5 days of menstrual cycle; for uterine fibroids continue treatment for at least 3 months; maximum duration of treatment 6 months (not to be repeated); 11·25mg injection, endometriosis, *by intramuscular injection*, 11·25mg every 3 months for maximum 6 months (not to be repeated) starting during first 5 days of menstrual cycle. The vials include an overage to allow administration of the dose.

**GOSERELIN** implant, pre-filled disposable injection 3·6mg

**Dose:** *By subcutaneous injection*, endometriosis, 3·6mg every 28 days, maximum duration of treatment 6 months (do not repeat). Before surgery in women who have anaemia due to uterine fibroids, 3·6mg every 28 days, maximum duration of treatment 3 months.
<table>
<thead>
<tr>
<th>Insulin type</th>
<th>Insulin sub-type</th>
<th>Insulin brand</th>
<th>Available formulations</th>
<th>Injection device</th>
<th>Insulin manufacturer</th>
<th>Injection in relation to meals</th>
<th>Onset of action</th>
<th>Peak of action</th>
<th>Duration of action</th>
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<tbody>
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<td>Autopen® / HumaPen® Savvio</td>
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<td>30 to 60mins</td>
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<td>1 to 2hrs</td>
<td>4 to 5hrs</td>
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### Review diet, exercise and adherence to medication before making dose adjustments or prescribing additional therapy

**HbA1c target individualised as agreed eg ≤58mmol/mol**

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<th><strong>Patient factors</strong></th>
<th><strong>&lt;25kg/m² OR Weight loss/ osmotic symptoms of hyperglycaemia</strong></th>
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<th><strong>Diet and exercise</strong></th>
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<th><strong>3 months</strong></th>
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<th><strong>First-line oral therapy (monotherapy)</strong></th>
<th><strong>SULFONYLUREA (SU)</strong></th>
<th><strong>METFORMIN (MET)</strong></th>
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<tr>
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<th><strong>MET + ONE of the following:</strong></th>
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<td><strong>Choose if BMI &gt;30kg/m² and hypos are a concern.</strong>*</td>
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<td><strong>SGLT2</strong></td>
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<td><strong>Choose if BMI &gt;30kg/m² and hypos are a concern.</strong>*</td>
<td><strong>SU</strong></td>
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<thead>
<tr>
<th><strong>GLP-1 therapy</strong></th>
<th><strong>Not appropriate</strong></th>
<th><strong>Licensed combinations include:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dual therapy - GLP-1 + [MET or SU or PIO (not with liraglutide)]</strong></td>
<td><strong>Triple therapy - [GLP-1 + MET + SU] or [GLP-1 + MET + PIO]</strong></td>
<td><strong>GLP1 may also be used with INS (see below)</strong></td>
</tr>
<tr>
<td><strong>stop DPP-4</strong></td>
<td><strong>consider reduction of SU dose on initiation</strong></td>
<td><strong>refer to GLP-1 protocol for further information.</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Insulin therapies</strong></th>
<th><strong>Insulin monotherapy or licensed combinations include:</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INS + MET + SU + SGLT2</strong></td>
<td><strong>INS + MET + PIO + Exenatide standard preparation or Dulaglutide.</strong></td>
</tr>
<tr>
<td><strong>INS + Liraglutide or Dulaglutide</strong></td>
<td><strong>specialist input required with all INS treatments refer to patient pathways for insulin therapy guidance note increased risk of oedema with PIO + INS.</strong></td>
</tr>
</tbody>
</table>

* Falls in the elderly, driving, occupation, alcohol consumption.

**SU – sulfonylurea; MET – metformin; PIO – pioglitazone; SGLT2 – sodium-glucose co-transporter 2 inhibitor; DPP-4 – Dipeptidylpeptidase-4 inhibitor; GLP-1 – Glucagon-like peptide-1 analogue; INS – insulin; SMBG – self-monitoring of blood glucose.**
<table>
<thead>
<tr>
<th>Medication</th>
<th>Gliclazide</th>
<th>Glipizide</th>
<th>Metformin (std prep)</th>
<th>Pioglitazone</th>
<th>Linagliptin</th>
<th>Sitagliptin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initiation dose</strong></td>
<td>40 to 80mg before breakfast</td>
<td>2.5 to 5mg before breakfast</td>
<td>500mg with breakfast for 1 week then 500mg twice daily</td>
<td>15mg once daily if elderly or on concomitant insulin</td>
<td>5mg once daily</td>
<td>100mg once daily</td>
</tr>
<tr>
<td><strong>Dose titration increment</strong></td>
<td>40 to 80mg</td>
<td>2.5 to 5mg</td>
<td>500mg to 1 gram</td>
<td>15mg</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Titration interval</strong></td>
<td>3 monthly (if using SMBG &lt;3 monthly)</td>
<td>3 monthly (if using SMBG &lt;3 monthly)</td>
<td>3 monthly</td>
<td>Elderly or on insulin – @3 months if no ADRs</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Maximum dose</strong></td>
<td>160mg twice daily before meals</td>
<td>20mg daily as divided doses with meals</td>
<td>1 gram twice daily</td>
<td>45mg daily</td>
<td>5mg daily</td>
<td>100mg daily</td>
</tr>
<tr>
<td><strong>Treatment failure criteria</strong></td>
<td>&lt;5-5mmol/mol reduction in HbA1c in 6 months</td>
<td>&lt;5-5mmol/mol reduction in HbA1c in 6 months</td>
<td>&lt;5-5mmol/mol reduction in HbA1c in 6 months</td>
<td>&lt;5-5mmol/mol reduction in HbA1c in 6 months</td>
<td>&lt;5-5mmol/mol reduction in HbA1c in 6 months</td>
<td></td>
</tr>
<tr>
<td><strong>Renal impairment</strong></td>
<td>&lt;50mL/min initially</td>
<td>&lt;50mL/min initially</td>
<td>Avoid if &lt;30mL/min Caution if 30 to 45mL/min</td>
<td>Dose as in normal renal function</td>
<td>Dose as in normal renal function</td>
<td>&gt;30 &lt;50mL/min 50mg once daily &lt;30mL/min - 25mg once daily</td>
</tr>
<tr>
<td><strong>Hepatic impairment</strong></td>
<td>Reduce dose</td>
<td>Reduce dose</td>
<td>Withdraw if tissue hypoxia likely</td>
<td>Avoid</td>
<td>Dose as in normal hepatic function</td>
<td>Use with caution in severe hepatic impairment</td>
</tr>
<tr>
<td><strong>Notes</strong></td>
<td>• weight gain • SMBG at higher doses</td>
<td>• weight gain • SMBG at higher doses</td>
<td>• low risk of hypo</td>
<td>• avoid in any degree of LV dysfunction • weight gain • takes 4 to 5 months to alter HbA1c • small increased risk of bladder Ca • consider fracture risk</td>
<td>• weight neutral • low risk of hypo</td>
<td>• weight neutral • low risk of hypo</td>
</tr>
</tbody>
</table>

*Unless at individualised target. If treatment failure criteria not met on maximum tolerated dose consider withdrawal of medication, substitution or addition of another medication.*
<table>
<thead>
<tr>
<th>Medication</th>
<th>Dapagliflozin</th>
<th>Empagliflozin</th>
<th>Exenatide (daily)</th>
<th>Exenatide (weekly)</th>
<th>Liraglutide</th>
<th>Dulaglutide</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initiation dose</strong></td>
<td>10mg once daily</td>
<td>10mg once daily (only initiate if CrCl ≥60mL/min)</td>
<td>5 micrograms twice daily (refer to GLP-1 analogues guidance on p179)</td>
<td>2mg once weekly (refer to GLP-1 analogues guidance)</td>
<td>600 micrograms once daily</td>
<td>750 micrograms once weekly (refer to GLP-1 analogues guidance)</td>
</tr>
<tr>
<td></td>
<td>(5mg if severe hepatic impairment)</td>
<td>Not recommended if &gt;85 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not recommended if &gt;75 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dose titration increment</strong></td>
<td>NA</td>
<td>Increase to 25mg once daily</td>
<td>5 micrograms twice daily</td>
<td>NA</td>
<td>600 micrograms once daily</td>
<td>If add-on therapy, 750 micrograms once weekly</td>
</tr>
<tr>
<td><strong>Titration interval</strong></td>
<td>NA</td>
<td>If no side-effects</td>
<td>1 month at initiation dose then titrate if no side-effects</td>
<td>NA</td>
<td>1 to 2 weeks at initiation dose then titrate if no side-effects</td>
<td>If no side-effects</td>
</tr>
<tr>
<td><strong>Maximum dose</strong></td>
<td>10mg daily</td>
<td>25mg daily</td>
<td>10 micrograms twice daily</td>
<td>2mg once weekly</td>
<td>Usually 1-2mg once daily, exceptionally</td>
<td>1-5mg once weekly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1-8mg once daily</td>
<td></td>
</tr>
<tr>
<td><strong>Treatment failure criteria</strong>&lt;sup&gt;2&lt;/sup&gt;</td>
<td>&lt;5-5mmol/mol reduction in HbA1c in 6 months</td>
<td>&lt;5-5mmol/mol reduction in HbA1c in 6 months</td>
<td>&lt;11mmol/mol reduction in HbA1c ± &lt;3% reduction in weight in 6 months</td>
<td>&lt;11mmol/mol reduction in HbA1c ± &lt;3% reduction in weight in 6 months</td>
<td>&lt;11mmol/mol reduction in HbA1c ± &lt;3% reduction in weight in 6 months</td>
<td></td>
</tr>
<tr>
<td><strong>Renal impairment</strong></td>
<td>Avoid if eGFR &lt;60mL/min</td>
<td>If CrCl falls to 45-60mL/min, 10mg daily. Avoid if &lt;45mL/min</td>
<td>Avoid if &lt;30mL/min</td>
<td>Avoid if &lt;50mL/min.</td>
<td>Avoid if &lt;30mL/min</td>
<td>Avoid if &lt;30mL/min</td>
</tr>
<tr>
<td><strong>Hepatic impairment</strong></td>
<td>5mg daily, increase according to response</td>
<td>Avoid in severe hepatic impairment</td>
<td>Dose as in normal hepatic function</td>
<td>Dose as in normal hepatic function</td>
<td>Avoid</td>
<td>No dosage adjustment required in patients with hepatic impairment</td>
</tr>
<tr>
<td><strong>Notes</strong></td>
<td>• promotes weight loss</td>
<td>• promotes weight loss</td>
<td>• promotes weight loss</td>
<td>• promotes weight loss</td>
<td>• promotes weight loss</td>
<td>• promotes weight loss</td>
</tr>
<tr>
<td></td>
<td>• low risk of hypo</td>
<td>• low risk of hypo</td>
<td>• diabetes &lt;10yrs</td>
<td>• diabetes &lt;10yrs</td>
<td>• diabetes &lt;10yrs</td>
<td>• diabetes &lt;10yrs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• BMI ≥30kg/m²</td>
<td>• BMI ≥30kg/m²</td>
<td>• BMI ≥30kg/m²</td>
<td>• BMI ≥30kg/m²</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>• effect may continue up to 10 weeks after discontinuation</td>
<td></td>
<td>• effect may continue for at least 3 weeks after discontinuation</td>
</tr>
</tbody>
</table>

*Unless at individualised target. If treatment failure criteria not met on maximum tolerated dose consider withdrawal of medication, substitution or addition of another medication.
Current diagnosis of or history of bladder cancer?

NO

Does the patient have symptoms or a history of heart failure (NYHA stages I to IV) or any degree of LV dysfunction?

YES

Evidence of macroscopic haematuria?

NO

Is the patient over 65 years?

NO

Benefits of pioglitazone likely to outweigh the risks of use.

YES

Exclude bladder cancer before prescribing. Encourage patients to report haematuria, dysuria and urinary urgency promptly if then treated with pioglitazone.

Current diagnosis of or history of bladder cancer?

YES

AVOID: risks of pioglitazone outweigh the benefits of use.

Treatment failure criteria* = <5.5mmol/mol reduction in HbA1c in 6 months.

*Unless at individualised target. If treatment failure criteria met on maximum tolerated dose consider withdrawal of medication, substitution or addition of another medication.

Initiate at 30mg daily and recheck HbA1c at 6 months. Consider titration to 45mg daily if HbA1c not at target.

Does the patient have symptoms or a history of heart failure (NYHA stages I to IV) or any degree of LV dysfunction?

YES

Initiate at 15mg daily for 3 months, if no ADRs then increase to 30mg daily and recheck HbA1c at 6 months from initiation. Consider titration to 45mg daily if HbA1c not then at target.

Initiate at 30mg daily and recheck HbA1c at 6 months. Consider titration to 45mg daily if HbA1c not at target.
PROTOCOL FOR USE OF GLUCAGON-LIKE PEPTIDE-1 (GLP-1) ANALOGUES
Glucagon-like peptide-1 analogues (GLP-1) analogues

GLP-1 analogues:

FIRST-LINE: Liraglutide
SECOND-LINE: Exenatide
THIRD-LINE: Dulaglutide

Prescribing information:

S LIRAGLUTIDE injection 18mg/3mL pre-filled pen
Dose: by subcutaneous injection, 600 micrograms once daily, at the same time each day, independent of meals. The dose may be increased if necessary at an interval of at least 1 week to 1·2mg. In exceptional circumstances a maximum dose of 1·8mg once daily may be used.

S EXENATIDE injection, pre-filled pen 5 micrograms/dose, 10 micrograms/dose; modified-release injection 2mg/pre-filled pen
Dose: by subcutaneous injection

Normal release: initially 5 micrograms twice daily within 1 hour before 2 main meals (at least 6 hours apart), increased if necessary after at least 1 month to maximum 10 micrograms twice daily. Some oral medications should be taken at least 1 hour before or 4 hours after exenatide injection; consult product literature for details.

Modified-release: for use in patients with compliance problems, needle phobia or where weekly administration by the district nurse etc would be advantageous. By subcutaneous injection, 2mg once weekly on the same day each week. To be administered at any time of day, with or without meals. The day of weekly administration can be changed if necessary as long as the next dose is administered at least 24 hours after the next dose is due. Effect may continue for up to 10 weeks after discontinuation.

S DULAGLUTIDE injection, pre-filled pen 0·75mg/dose, 1·5mg/dose
Dose: by subcutaneous injection

As monotherapy when metformin is inappropriate, 750 micrograms once weekly.

As add on therapy, 1·5mg once weekly, however consider a starting dose of 750 micrograms once weekly for potentially vulnerable populations such as those aged 75 years or over. If adding to existing metformin and/or pioglitazone therapy, continue the current dose of metformin/pioglitazone. If adding to existing therapy of a sulfonylurea or insulin, consider a lower dose of sulfonylurea/insulin to reduce the risk of hypoglycaemia.

Indications:

• For use in individuals with type 2 diabetes of less than 10 years duration and BMI 30kg/m² or over
• Third-line agent in addition to (metformin + sulfonylurea) OR (metformin + pioglitazone) OR (metformin + dapagliflozin)* OR (metfomin + insulin)# OR (pioglitazone + insulin)# where HbA1c is above target of 58mmol/mol
• Fourth-line agent in addition to (metformin + pioglitazone + insulin)# OR (metformin + dapagliflozin + insulin)*.
*Licence for dapagliflozin. #Licence for exenatide.

Contra-indications:

• Insulin deficiency or ketoacidosis
• Pregnancy, breast-feeding and children under 18 years
• Severe gastro-intestinal disease including gastroparesis and inflammatory bowel disease
• Previous history of pancreatitis.
**Considerations for clinical review:**

Review effect of therapy after 6 months using traffic-light table below:

**Clinical review:**

- Review effect of therapy after 6 months
- Expected beneficial effects:

  **HbA1c:** Reduction of 11mmol/mol (1%) OR treatment target of <59mmol/mol met

  **Weight:** Reduction of 3% of initial weight

**Further review:**

- Consider other factors which may preclude the use of insulin – for example occupation, social situation and ability to cope with insulin.

**Further information:**

- It is expected that contra-indications and interactions as per the BNF will be assessed for patients on an individual basis prior to prescribing any medication.

---

**Renal impairment:**

**LIRAGLUTIDE**
- Avoid if eGFR less than 30mL/min

**EXENATIDE**
- Use in caution in patients aged 70 years or over if eGFR 30 to 50mL/min
- Avoid if eGFR less than 30mL/min (standard preparation). Avoid if eGFR <50mL/min (weekly preparation).

**DULAGLUTIDE**
- Avoid if eGFR less than 30mL/min.
GUIDELINE FOR BLOOD GLUCOSE MONITORING

Inappropriate blood glucose monitoring should be changed in line with the guidance below and stopped if it is not required.

<table>
<thead>
<tr>
<th>Patients who should monitor blood glucose</th>
<th>Patients who do not need to monitor blood glucose (HbA\textsubscript{1c} is adequate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• individuals with insulin treated diabetes or being considered for insulin</td>
<td>Patients with type 2 diabetes managed with:</td>
</tr>
<tr>
<td>• individuals with type 2 diabetes at risk of hypoglycaemia, ie patients on a sulfonylurea</td>
<td>• diet and exercise</td>
</tr>
<tr>
<td>• individuals who require to undertake blood glucose monitoring under DVL:A regulations (<a href="http://www.gov.uk/diabetes-driving">www.gov.uk/diabetes-driving</a>)</td>
<td>• combinations of metformin, pioglitazone, dapagliflozin, DPP-4 inhibitors (sitagliptin, linagliptin) and GLP-1 analogues (liraglutide, exenatide) in the absence of medication known to cause hypoglycaemia, ie sulfonylureas and insulin.</td>
</tr>
<tr>
<td>• pregnant women with diabetes.</td>
<td></td>
</tr>
</tbody>
</table>

How often should patients test blood glucose levels?

Testing 1 to 4 times per day is appropriate for:

• patients with type 2 diabetes using or being considered for insulin injectable therapy
• patients with well-controlled type 1 diabetes
• children
• patients advised on an individual basis by an appropriate health care professional.

Testing more frequently than 4 times daily may be required:

• if there is evidence of impaired hypoglycaemia awareness
• during pregnancy (including gestational diabetes)
• for patients managed with a continuous subcutaneous insulin infusion (CSII by pump)
• if control is poor or unstable; reduce testing frequency again when control is improved
• in other selected circumstances, eg for occupational reasons.

Which blood glucose monitoring meter and test strips?

The different meters on the market all require different testing strips. Stocking many types of meter is potentially wasteful and can be confusing for patients and health-care professionals. The guidance given below is intended to help match blood glucose meters to individual requirements bearing in mind that many of the type 2 diabetes population do not require a multi-function meter therefore it is suggested that the following meters listed below be used in NHS Highland.

All meters are subject to inaccuracies arising from:

• **Poor technique**: Lack of hand washing can lead to contaminated samples giving an inaccurate result.
• **Insufficient blood on the test strip**: All of the advised meters use a capillary fill system so the strip ‘sucks up’ the blood rather than it being applied to the top of the strip. If the blood is incorrectly applied the meter will not work.
• **Temperature**: Meters and strips are designed to be most accurate at room temperature. If the meter is too cold it may not function.
• **Humidity** will also affect test strips. They should be stored in the container with the top closed and used within manufacturers’ recommended time after opening.
<table>
<thead>
<tr>
<th>TEST STRIPS</th>
<th>SETTING</th>
<th>SYSTEM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>COMMUNITY</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>GlucoRx Nexus</strong></td>
<td>For community adult testing of blood glucose</td>
<td>Nexus</td>
</tr>
<tr>
<td></td>
<td>Preferred choice for patients with Type 2 diabetes who need to test blood glucose</td>
<td>Nexus Mini</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nexus Voice talking meter for visually impaired</td>
</tr>
<tr>
<td>Performa</td>
<td>For children as advised by Paediatric Diabetes Team</td>
<td>Accu-Chek Performa Nano</td>
</tr>
<tr>
<td>Aviva</td>
<td>For children as advised by Paediatric Diabetes Team</td>
<td>Aviva Expert meter</td>
</tr>
<tr>
<td></td>
<td>For adults who use a Roche insulin pump or bolus adviser meter</td>
<td>Accu-chek combi pump handset</td>
</tr>
<tr>
<td>OneTouch Verio</td>
<td>For community use by adults whose self management includes pre- and post-meal tagging and trend monitoring</td>
<td>OneTouch Verio</td>
</tr>
<tr>
<td>GlucoMen Areo sensors</td>
<td>For community use by adults who test both blood glucose and blood ketones</td>
<td>GlucoMen Areo2K meter</td>
</tr>
<tr>
<td>GlucoMen Areo ketone sensors</td>
<td>For ketone testing in adults and children (not for use in neonates)</td>
<td>GlucoMen Areo2K meter</td>
</tr>
<tr>
<td>Accuchek mobile test cassette</td>
<td>For community use by adults who cannot use test strips or who find test strips inconvenient</td>
<td>Roche Accu-Chek Mobile</td>
</tr>
<tr>
<td>CONTOUR® NEXT</td>
<td>For adults and children who use a Medtronic Insulin Pump and those who download their meter results</td>
<td>CONTOUR® NEXT LINK</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CONTOUR® NEXT USB</td>
</tr>
<tr>
<td><strong>HOSPITAL</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Precision Pro</td>
<td>Blood glucose monitoring: all hospital locations</td>
<td>Precision Pro</td>
</tr>
<tr>
<td>Blood glucose test strips</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood ketones test strips</td>
<td>Blood ketone monitoring :specialist areas only</td>
<td></td>
</tr>
</tbody>
</table>
Who should be offered HRT?

- Peri- and postmenopausal women with symptoms attributable to the menopause.
- Follicle-stimulating hormone (FSH) measurements are not indicated prior to HRT treatment but may be considered to diagnose menopause only in women aged 40 to 45 years with menopausal symptoms or in women under 40 in whom menopause is suspected.
- Adopt an individualised approach at all stages of diagnosis, investigation and management of menopause.

Should first choice be oral or transdermal?

- Oral treatment is cost-effective and is well tolerated.
- Start with lower dose regimes and reappraise need on an annual basis. Do not change preparation before an adequate trial has been completed, as side-effects are common in the first 3 months but usually subside.
- The risk of VTE associated with HRT is greater for oral than transdermal preparations. The risk associated with transdermal HRT given at standard therapeutic doses is no greater than baseline population risk.
- Consider transdermal rather than oral HRT for menopausal women who are increased risk of VTE, including those with a BMI over 30kg/M².

When can bleed-free regimes be used?

- Women who have had no periods for at least 1 year prior to starting HRT or after 2 years on a sequential regime.

What are the contra-indications to HRT?

- Active arterial or venous thromboembolic disease.
- Unexplained vaginal bleeding.
- Oestrogen-dependent tumours, eg breast, uterus.
- Recent myocardial infarction and/or active coronary heart disease.

Risks of HRT

- HRT does not increase cardiovascular risk when started in women aged under 60 years. Cardiovascular risk factors are not a contraindication to HRT as long as they are optimally managed.
- Oral HRT (not transdermal) is associated with a small increase in the risk of stroke although the baseline population risk of stroke in women aged under 60 years is very low.
- Risk of VTE is increased by oral HRT compared to baseline population. If HRT is to be used by women at increased risk of thromboembolism, use a transdermal preparation.
- HRT with oestrogen and progestogen can be associated with an increase risk in breast cancer but any increase is related to the treatment duration and reduces on stopping HRT. HRT with oestrogen alone is associated with little or no change in the risk of breast cancer.
- If 1000 women age 50 to 59 used combined HRT for 5 years, it is estimated that an extra 3 breast cancers will be diagnosed.
- If HRT is commenced at a young age then the use of HRT up to age 50 does not increase breast cancer risk any more than in a woman who continues to have periods up to age 50.

General points

- HRT is not contraceptive. See guidance from the FSRH on Contraception for Women over 40 years (https://www.fsrh.org/documents/cec-ceu-guidance-womenover40-jul-2010/).
- Mirena® is licensed for use as progestogen phase of HRT but should be replaced within 5 years.

Discontinuing HRT

There is no clear consensus on how to discontinue HRT, and symptoms may recur regardless of whether HRT is stopped slowly or suddenly. It is not usually appropriate to start women over the age of 60 on HRT but it does not mean that those who have started it earlier need to stop it on reaching 60.

Alternatives to HRT for menopausal symptoms

- Do not routinely offer SSRI or SNRI type drugs or clonidine as first-line treatment for vasomotor symptoms alone. There is no clear evidence for SSRI or SNRI to ease low mood in menopausal women who have not been diagnosed with depression.
- Consider HRT to alleviate low mood that arises from the menopause.
• Relaxation therapy, mindfulness-based therapies and CBT may alleviate low mood and anxiety arising as a result of the menopause.
• There is some evidence that isoflavones or black cohosh may relieve vasomotor symptoms but safety is uncertain and interactions with other medicines have been reported.

Atrophic vaginitis
• Vaginal oestrogen effectively treats urogenital atrophy (including those on systemic HRT (see section 7.2). Continue treatment for as long as needed to relieve symptoms.
• Vaginal oestrogens may be considered in women in whom systemic HRT is contra-indicated.
• Non-hormonal options such as moisturisers and lubricants can be used alone or in addition to vaginal oestrogens.

Access to further information
For further information on issues around the menopause refer to www.menopausematters.co.uk or www.thebms.org.uk.
<table>
<thead>
<tr>
<th>HRT</th>
<th>TABLETS/OTHER</th>
<th>PATCHES</th>
<th>HINTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sequential preparations</td>
<td><strong>Elleste-Duet®</strong> estradiol 1 or 2mg norethisterone 1mg (C19)</td>
<td><strong>Evorel® Sequi</strong> estradiol 50 micrograms norethisterone 170 micrograms (C19)</td>
<td>Consider patches if liver disease or previous history of DVT/PE (see overleaf major caution).</td>
</tr>
<tr>
<td>For women with intact uterus</td>
<td><strong>Femoston®</strong> estradiol 1 or 2mg dydrogesterone 10mg (C21)</td>
<td><strong>Femseven® Sequi</strong> estradiol 50 micrograms levonorgestrel 10 micrograms (C19)</td>
<td>Switch from C19 to C21 progestogens if PMS-like symptoms and/or androgenic side-effects*.</td>
</tr>
<tr>
<td>- perimenopausal</td>
<td><strong>Cyclo-progynova®</strong> estradiol 2mg tablets and estradiol2mg/norgestrel 500 micrograms tablets</td>
<td></td>
<td>For persistent oestrogenic side-effects** reduce dose, change preparation or move to transdermal preparation.</td>
</tr>
<tr>
<td>- under age 54 with less than one year amenorrhoea</td>
<td></td>
<td></td>
<td>If switching from a sequential regimen try to keep to same ‘type/hormones’ where possible.</td>
</tr>
<tr>
<td>Always start on lower dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continuous combined preparations (period-free HRT)</td>
<td><strong>Premique® Low Dose</strong> conjugated oestrogen (equine) 300 micrograms, medroxyprogesterone acetate 1.5mg (C21)</td>
<td><strong>Evorel® Conti</strong> estradiol 50 micrograms norethisterone 170 micrograms (C19)</td>
<td>Consider patches if liver disease or previous history of DVT/PE (see overleaf major caution).</td>
</tr>
<tr>
<td>For women</td>
<td><strong>Klofem®</strong> estradiol 2mg norethisterone 1mg (C19)</td>
<td><strong>Femseven® Conti</strong> estradiol 50 micrograms levonorgestrel 7 micrograms (C19)</td>
<td>For persistent oestrogenic side-effects** reduce dose, change preparation or move to transdermal preparation.</td>
</tr>
<tr>
<td>- over age 54</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>or</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- more than one year since last menstrual period</td>
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<td></td>
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<tr>
<td>or</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>- after 2 years on sequential regime</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Always start on lower dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oestrogen only</td>
<td><strong>Elleste-Solo®</strong> estradiol 1 or 2mg</td>
<td><strong>Evorel®</strong> estradiol 25 or 50 or 75 or 100 micrograms (start on 50 microgram patch then adjust to lowest effective dose)</td>
<td>Consider patches if liver disease or previous history of DVT/PE (see overleaf major caution).</td>
</tr>
<tr>
<td>For women without a uterus</td>
<td><strong>Premarin®</strong> conjugated oestrogens (equine) 300 micrograms, 625 micrograms or 1.25mg</td>
<td><strong>Estraderm MX®</strong> estradiol 25 or 50 or 75 or 100 micrograms (start on 50 microgram patch then adjust to lowest effective dose)</td>
<td>For persistent oestrogenic side-effects** reduce dose, change preparation or move to transdermal preparation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Always start on lower dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topical oestrogen***</td>
<td>Estradiol (Vagifem®) vaginal tablets 10 micrograms or Estriol cream 0.01%</td>
<td>Review at 3 to 6 month intervals. Vagifem 10 micrograms has good long-term endometrial safety data.</td>
<td></td>
</tr>
<tr>
<td>To relieve vaginal symptoms only</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use minimum effective amount to control symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Progestogen</td>
<td><strong>Mirena®</strong> (releasing levonorgestrel 20 micrograms/24 hours) intra-uterine system</td>
<td>Lowest progestogenic side-effects. Potentially lowest breast cancer risk, as with oestrogen only HRT.</td>
<td></td>
</tr>
<tr>
<td>For the prevention of endometrial hyperplasia during oestrogen replacement therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*C19 (testosterone derivatives) eg norethisterone, levonorgestrel, norgestrel and C21 (progesterone derivatives) eg dydrogesterone, medroxyprogesterone. C19 progestogens may lead to bloating, mastalgia, depression, irritability and skin changes in a minority of women. **Oestrogenic side-effects include breast tenderness, bloating, leg cramps, nausea and headaches, and usually settle within 3 months. ***refer to section 7.2.

Lead reviewer: Obstetrics & Gynaecology Review Group
Approved by: Formulary Subgroup of NHS Highland ADT
Date: June 2016 (amended March 2017)
Review date: June 2018
Version: 7
Warning: document uncontrolled when printed
TUMOUR-INDUCED HYPERCALCAEMIA (TIH)*

**Step 1:** Hydrate overnight.

**Step 2:** If still hypercalcaemic after adequate hydration administer intravenous pamidronate. Dose according to corrected serum calcium below; dose may need to be higher if TIH is resistant to lower dose. Discuss with Consultant.

<table>
<thead>
<tr>
<th>Adjusted serum calcium (mmol/L)</th>
<th>Pamidronate dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 3*</td>
<td>30mg</td>
</tr>
<tr>
<td>3 to 3·5*</td>
<td>60mg</td>
</tr>
<tr>
<td>3·6 or greater</td>
<td>90mg</td>
</tr>
</tbody>
</table>

* in some patients it may be more appropriate to treat the hypercalcaemia more aggressively and use the 90mg dose.

**Notes**
1. Corrected calcium falls significantly within 1 to 2 days and normalisation is usually achieved within 3 to 7 days. Unless otherwise indicated recheck U+E, calcium and albumin after 4 to 5 days.
2. Check renal function; in renal impairment slow the rate of infusion as indicated below.
3. If corrected serum calcium continues to rise or has not returned to reference range within 5 days discuss future management with the Consultant.
4. If Consultant recommends rescue therapy, administer zoledronic acid.

**MULTIPLE MYELOMA (MM)**

- asymptomatic patients with no significant osteoporosis or lytic lesions – observe.
- patients with normal renal function – zoledronic acid 4mg every 4 weeks (with Adcal-D₃® one tablet daily).
- Patients with renal impairment – zoledronic acid dosing as in table below.

Review treatment after 2 years and in the absence of a stringent complete response continue sodium clodronate indefinitely.

**OTHER TUMOUR TYPES**

Requests for use in patients with neither breast cancer, TIH or MM with a life expectancy of at least 6 months must be approved by the NHS Highland non-Formulary request process before prescribing. The best data are available for zoledronic acid 4mg.

**BREAST CANCER**

for prevention of skeletal-related events

<table>
<thead>
<tr>
<th>Breast cancer with bone metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Severe pain OR Widespread skeletal involvement OR Oral compliance problems OR Unable to tolerate oral bisphosphonates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Oral ibandronic acid 50mg daily for 2 years with Adcal-D₃® – one tablet daily</th>
</tr>
</thead>
</table>

**Notes**
1. Only initiate therapy in patients with a life expectancy of at least 6 months (except for use in severe pain).
2. Review prescription annually.
3. Assessment does not justify use of routine bone scans.
4. For doses in renal impairment see below.

**BONE PAIN**

Consider bisphosphonates as part of therapeutic regimen. Treat with pamidronate 90mg every 4 weeks, or every 3 weeks to coincide with chemotherapy.

**DENTAL ASSESSMENT PRIOR TO STARTING BISPHOSPHONATE TREATMENT**

Due to the risk of osteonecrosis any major dental work that is required should be undertaken prior to starting treatment. Advise patients to contact their dentist for a check up appointment. Patients without a dentist should be referred directly to the Dental Manager requesting an oral health assessment.

**ADMINISTRATION AND MONITORING**

**RENAI IMPAIRMENT** Check renal function before initiating bisphosphonates – seek specialist advice for GFR less than 30mL/min.

**Disodium pamidronate:** GFR less than 30mL/min – not recommended; GFR 30 to 60mL/min – reduce infusion rate to 20mg/hour.

**Zoledronic acid:** GFR greater than 60mL/min – 4mg; GFR 50 to 60mL/min – 3·5mg; GFR 40 to 49mL/min – 3·3mg; GFR 30 to 39mL/min – 3mg; GFR less than 30mL/min – not recommended.

**Ibandronic acid (oral):** GFR less than 30mL/min – reduce dose to 50mg ONCE weekly.

**Sodium clodronate:** GFR 10 to 30mL/min – half the dose; GFR less than 10mL/min – contra-indicated.

**ADMINISTRATION**

Disodium pamidronate: infuse at a maximum rate of 1mg/minute.

Zoledronic acid: infuse 4mg over 15 minutes. No special precautions apply so can be given in the community setting.

Ibandronic acid (oral): advise patients to take on an empty stomach at least 1 hour before breakfast (or another oral medicine), swallow tablets whole with plenty of water while sitting or standing then stand or sit upright for at least 1 hour afterwards.

Sodium clodronate: avoid food for 1 hour before and after treatment, particularly calcium-containing products, iron and mineral supplements and antacids. Maintain adequate fluid intake.

**MONITORING**

Intravenous bisphosphonates (other than TIH) – monthly U+E, creatinine, corrected calcium. Do not repeat dose within 7 days to avoid hypercalcaemia.

Oral bisphosphonates – monitor U+E, creatinine and corrected calcium every 3 months at clinic appointments unless renal impairment.

Review medication that affects renal function (eg NSAIDs, diuretics, ACE inhibitors).

* see also guidance on hypercalcaemia in palliative care at [www.palliativecareguidelines.scot.nhs.uk](http://www.palliativecareguidelines.scot.nhs.uk).

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Lead reviewer: Jude Madeleine, Dr Chris Lush

Approved by: Formulary Subgroup of NHS Highland ADTC

Date: January 2015 (amended August 2017)

Review date: October 2017

Version: 6a

Warning: document uncontrolled when printed
CHAPTER 7 OBSTETRICS, GYNAECOLOGY, AND URINARY-TRACT DISORDERS

7.1 DRUGS USED IN OBSTETRICS

Guidance on the use of the following obstetric drugs is to be found in each obstetric department in NHS Highland and is posted on the Maternity and Gynaecology Services webpage on Intranet.

- **CARBOPROST** injection 250 micrograms/1mL
- **DINOPROSTONE** vaginal tablets 3mg
- **ERGOMETRINE** injection 500 micrograms/1mL
- **SYNTOMETRINE®** (ergometrine 500 micrograms, oxytocin 5 units/1mL) injection
- **OXYTOCIN** injection 5 units/1mL, 10 units/1mL
- **MIFEPRISTONE** tablets 200mg
  Only supplied to NHS hospitals and premises approved under the Abortion Act 1967.
- **MISOPROSTOL** tablets 100 micrograms [unlicensed], 200 micrograms [off-label].
  See NICE ESUOM11 ([www.nice.org.uk](http://www.nice.org.uk)). For protocols on use, see above.
- **ATOSIBAN** injection 6.75mg/0.9mL; concentrate for intravenous infusion 37.5mg/5mL
  May be considered for the inhibition of uncomplicated premature labour between 24 and 33 weeks of gestation; refer to guidance on Intranet and SPC. See also NICE ESUOM11 ([www.nice.org.uk](http://www.nice.org.uk)).
- **TERBUTALINE** injection 500 micrograms/1mL
- **RANITIDINE** tablets 150mg, injection 50mg/2mL
  Refer to guidance on antacid prophylaxis on Intranet.
- **CABERGOLINE** tablets 500 micrograms
  **Dose:** For the prevention of lactation, during first day postpartum, 1mg as a single dose; suppression of established lactation, 250 micrograms every 12 hours for 2 days: refer to BNF for cautions.

**Prophylaxis of neonatal respiratory distress syndrome**

Refer to guidance on antenatal corticosteroids at [www.rcog.org.uk](http://www.rcog.org.uk) and to Patient Group Direction on intranet. Depending on availability, either betamethasone or dexamethasone may be used.

- **BETAMETHASONE** injection 4mg/1mL (as sodium phosphate)
  **Dose:** by intramuscular injection, 2 doses of 12mg, given 24 hours apart [off-label].

- **DEXAMETHASONE** injection 3.3mg/1mL, 6.6mg/2mL (as sodium phosphate)
  **Dose:** by intramuscular injection, 2 doses of 12mg, given 24 hours apart [off-label].

7.2 TREATMENT OF VAGINAL AND VULVAL CONDITIONS

Refer to table.
HRT for vaginal atrophy

Hormonal preparations for vaginal atrophy

**ESTRADIOL** (Vagifem®) vaginal tablets 10 micrograms
**Dose:** Insert 1 vaginal tablet daily for 2 weeks then reduce to 1 tablet twice weekly. May be used long-term; systemic absorption is minimal.

**Note:** Estriol 0·01% intravaginal cream:
- patients who are allergic to peanuts or soya should avoid the 0·01% cream which contains arachis (peanut) oil.
- contact between latex contraceptive diaphragms or condoms and the 0·01% cream must be avoided because the rubber may be damaged by this preparation.

**ESTRIOL** intravaginal cream 0·01%, 0·1%
**Dose:** Insert 1 applicatorful (cream 0·01%) daily, preferably in evening; reduced to 1 applicatorful (cream 0·01%) twice weekly, attempts to reduce or discontinue should be made at 3 to 6 month intervals with re-examination. The 0·1% cream is used in hospital.

Non-hormonal preparations for vaginal atrophy

In certain situations a vaginal moisturiser such as Hyalofemme®, Sylk® or Replens MD® may be helpful.

Vaginal and vulval fungal infections

Refer to ‘Genital-tract infections’ guidance.

**FLUCONAZOLE**OTC capsules 150mg
**Dose:** 150mg as a single dose.

**CLOTRIMAZOLE**OTC pessary 100mg, 500mg; intravaginal cream 10%; cream 1%
**Dose:** Pessary, by vagina, 500mg at night as a single dose, vulvovaginal candidiasis in pregnancy, 100mg at night for 6 nights; intravaginal cream 10%, by vagina 5 gram applicatorful at night as a single dose; cream 1%, apply to anogenital area 2 to 3 times daily.

Other vaginal infections

Refer to ‘Genital-tract infections’ guidance.

**METRONIDAZOLE** vaginal gel 0·75%
**Dose:** Insert 5 gram applicatorful at night for 5 nights.

**CLINDAMYCIN** vaginal cream 2%
**Dose:** Insert 5 gram applicatorful at night for 7 nights.

For recurrent bacterial vaginosis alternative, non-antimicrobial vaginal gels such as Balance Activ BV® and Relactagel® may be useful.

Vulval lichen sclerosus

Topical clobetasol propionate (Dermovate®) (section 13.4) should be used as first-line in women with vulval skin changes in keeping with lichen sclerosus. Apply once nightly for 4 weeks for flares, reducing to alternate nights for 4 weeks and then continuing twice-weekly use as maintenance indefinitely. Most women will have a swift improvement in symptoms; referral for biopsy is not
necessary if there is a good response to treatment. No more than 30 grams should be used every 3 to 6 months. Recommend washing the area with Zerobase® cream (section 13.2). Refer to British Association of Dermatology guidance and patient information leaflets.

7.3 CONTRACEPTIVES

The effectiveness of both combined and progestogen-only oral contraceptives can be considerably reduced by interaction with drugs that induce hepatic enzyme activity; refer to BNF for further information. Consider barrier methods of contraception where appropriate in association with contraception to prevent infection. For information on the use of co-cyprindiol in acne refer to section 13.6.

Refer to:
- further information on contraceptive methods at https://www.fsrh.org/standards-and-guidance/current-clinical-guidance/
- medical eligibility criteria for contraceptive use: https://www.fsrh.org/standards-and-guidance/uk-medical-eligibility-criteria-for-contraceptive-use-ukmec/

**Combined hormonal contraceptives**

**Note:** Contraceptives containing desogestrel or gestodene may be considered for women unable to tolerate other progestogens. Advise patients that desogestrel and gestodene have been associated with an increased risk of venous thromboembolism.

**Oral (standard strength)**

**FIRST CHOICE:** RIGEVIDON®

RIGEVIDON® (levonorgestrel 150 micrograms, ethinylestradiol 30 micrograms) tablets (equivalent to Microgynon 30®)

MICROGYNON 30 ED® (levonorgestrel 150 micrograms, ethinylestradiol 30 micrograms) tablets, with 7 inactive tablets

LOESTRIN 30® (norethisterone acetate 1·5mg, ethinylestradiol 30 micrograms) tablets

CILIQUE® (norgestimate 250 micrograms, ethinylestradiol 35 micrograms) tablets (equivalent to Cilest®)

GEDAREL® 30/150 (desogestrel 150 micrograms, ethinylestradiol 30 micrograms) tablets (equivalent to Marvelon®)

MILLINETTE® 30/75 (gestodene 75 micrograms, ethinylestradiol 30 micrograms) tablets (equivalent to Femodene®)

TRIREGOL® (ethinylestradiol 30 micrograms, levonorgestrel 50 micrograms; ethinylestradiol 40 micrograms, levonorgestrel 75 micrograms; ethinylestradiol 30 micrograms, levonorgestrel 125 micrograms) tablets (equivalent to Logynon®)
Oral (low strength)

**FIRST CHOICE:** LOESTRIN 20®
**SECOND CHOICE:** GEDAREL 20/150®

LOESTRIN 20® (norethisterone acetate 1mg, ethinylestradiol 20 micrograms) tablets

GEDAREL 20/150® (desogestrel 150 micrograms, ethinylestradiol 20 micrograms) tablets (equivalent to Mercilon®)

Transdermal (standard strength)


$EVRA®$ (releasing ethinylestradiol approximately 33.9 micrograms/24 hours and norelgestromin approximately 203 micrograms/24 hours) patches

Oral progestogen-only contraceptives

Desogestrel is the oral progestogen-only method of choice. It is also less androgenic and may be more effective due to its effect on preventing ovulation.

**FIRST CHOICE:** DESOGESTREL

DESOGESTREL tablets 75 micrograms

Parenteral progestogen-only contraceptives

DEPO-PROVERA® (medroxyprogesterone acetate 150mg/1mL) injection (aqueous suspension)


Note: Sayana Press® is administered by the subcutaneous route. Rather than attending a clinic every 13 weeks for an injection, a woman can choose to self-administer Sayana Press® at home. Women must be trained in the technique and supervised by an appropriately trained health care professional (HCP) administering the first dose. Up to three injections may be given to take home with review at one year. Access to a HCP should be available if any problems arise. Give patients written information detailing administration instructions, potential side-effects and symptoms that should prompt medical review. Systems should be in place for the provision and disposal of sharps. Further information for HCP is available at [www.sayanapress.co.uk](http://www.sayanapress.co.uk). There is also a patient-specific website ([www.sayanaanswers.co.uk](http://www.sayanaanswers.co.uk)) which offers a text service to remind women when their next injection is due.

SAYANA PRESS® (medroxyprogesterone acetate 104mg/0.65mL) suspension for injection

Dose: by subcutaneous injection, 104mg within first 5 days of cycle, the second and subsequent doses should be given at 13 week intervals; for further information refer to SPC.

NEXPLANON® (containing etonogestrel 68mg in each flexible rod) implant

Nexplanon® provides effective contraception for up to 3 years. The contraceptive effect of Nexplanon® is rapidly reversed on removal of the implant; recommend an alternative method of

**Intra-uterine progestogen-only system**

**FIRST CHOICE: MIRENA®**

MIRENA® (releasing levonorgestrel 20 micrograms/24 hours) intra-uterine system

For use in contraception, Mirena® is effective for 5 years. If used in women over 45 years of age, can remain effective for 7 years, or longer, if patient remains amenorrhoeic [off-label]: refer to https://www.fsrh.org/standards-and-guidance/documents/fsrh-guidance-contraception-for-women-aged-over-40-years-2017/

JAYDESS® (releasing levonorgestrel 13·5mg/24 hours) intra-uterine system

For use in contraception, Jaydess® is effective for 3 years.

**Spermicidal contraceptives**

GYGEL® OTC nonoxinol ’9’ 2%

Regular use of nonoxinol ’9’ may increase risk of HIV transmission in at risk patients.

**Intra-uterine contraceptive devices (IUCD)**

Refer to the BNF for information on intra-uterine contraceptive devices. The TT 380® SlimLine is the preferred choice due to its 10 year use; the Nova-T® 380 with its 5 year use is a suitable alternative. Fertility declines with age and therefore any copper IUCD fitted in a woman over 40 may remain in the uterus until the menopause.

**Emergency contraception**

Refer to Emergency Contraception algorithm. Further information is available at https://www.fsrh.org/standards-and-guidance/current-clinical-guidance/emergency-contraception/

**FIRST CHOICE: INTRA-UTERINE DEVICE**

**SECOND CHOICE: ULIPRISTAL**

Insertion of an intra-uterine device is more effective than hormonal methods of emergency contraception, preventing 99% of expected pregnancies:

- a device such as the TT 380 SlimLine® or Nova-T® 380 can be inserted up to 120 hours (5 days) after unprotected sexual intercourse.
- if intercourse has occurred more than 5 days previously, the device can still be inserted up to 5 days after the earliest likely calculated ovulation (ie within the minimum period before implantation).
- Mirena® is unsuitable for emergency contraception.

Hormonal emergency contraception may be used if the IUCD is unsuitable or an oral preparation is preferred (also refer to Emergency Contraception algorithm):

- trial data has shown that the pregnancy rate is significantly lower with ulipristal than with levonorgestrel.
- for further information contact Highland Sexual Health, tel: 01463 704000 (for Argyll and Bute, contact Helensburgh SRH clinic tel: 01436 655000 or Dunoon SRH clinic tel: 01369 708359, or clinicians and patients can contact the Sandyford Initiative, tel: 0141 2118130).
- for missed pill advice see guidance.
ULIPRISTAL (EllaOne®) tablets 30mg

**Dose:** 30mg between 0 and 120 hours (5 days) after intercourse.

- if vomiting occurs within 3 hours of taking the ulipristal tablet, take another tablet.
- do not use ulipristal more than once in a cycle or concomitantly with levonorgestrel.
- women taking liver enzyme-inducing medicines should be advised not to use ulipristal during or within 28 days of stopping treatment.
- advise women not to use ulipristal if they are currently taking drugs that increase gastric pH (e.g., antacids, histamine H₂ receptor antagonists and proton pump inhibitors).
- avoid breast-feeding for at least 1 week after taking ulipristal.
- avoid hormonal contraception for 5 days after Ulipristal as studies have shown that this reduces the efficacy of ulipristal – refer to [https://www.fsrh.org/documents/ceustatementquickstartingafterupa/](https://www.fsrh.org/documents/ceustatementquickstartingafterupa/).

LEVONORGESTREL OTC tablets 1·5mg

**Dose:** 1·5mg as soon as possible after unprotected sexual intercourse (preferably within 12 hours but no later than after 72 hours).

- repeat if patient vomits within 2 hours.
- if on enzyme inducing drugs and certain antiretroviral drugs, take 2 tablets as a single dose if IUD is unacceptable. [off-label], refer to [BNF](https://www.gov.uk/government/organisations/national-health-service-bnf).

### 7.4 DRUGS FOR GENITO-URINARY DISORDERS

#### Drugs for urinary retention

**Alpha-blockers**

Doxazosin is the most cost-effective alpha-blocker and has a low incidence of side-effects.

**FIRST CHOICE: DOXAZOSIN**

**DOXAZOSIN** tablets 1mg, 2mg, 4mg

**Dose:** Initially 1mg daily; dose may be doubled at intervals of 1 to 2 weeks according to response, up to maximum 8mg daily; usual maintenance 2 to 4mg daily.

If patients have co-existing hypertension, doxazosin is an appropriate choice. Use of doxazosin m/r tablets is not recommended.

**TAMSULOSIN** m/r capsules 400 micrograms

**Dose:** 400 micrograms daily.

Prescribe the lower cost generic tamsulosin m/r capsules in preference to the higher cost m/r tablets which are non-Formulary.

**Note:** Alpha-blockers may cause intraoperative floppy iris syndrome; current or past use of alpha-blockers should be made known to the ophthalmic surgeon in advance of surgery.

#### Drugs for urinary frequency, enuresis and incontinence

Patients’ response to drugs within this class is idiosyncratic. It may be necessary to try different drugs before a response occurs. Mirabegron is the first beta-3 adrenoceptor agonist to treat symptoms of overactive bladder and offers an alternative where anticholinergics are either not tolerated or are ineffective. For guidance on the management of urinary incontinence in women refer to [www.nice.org.uk](http://www.nice.org.uk). For local continence care guidance and continence products formulary see Continence Care webpage on [Intranet](https://www.gov.uk/government/organisations/national-health-service-bnf).
**FIRST CHOICE:** TOLTERODINE (as immediate-release tablets)  
**SECOND CHOICE:**  
- SOLIFENACIN  
- MIRABEGRON

<table>
<thead>
<tr>
<th>Drug</th>
<th>Formulation</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOLTERODINE</td>
<td>Tablets 1mg, 2mg; m/r capsules 4mg</td>
<td>Tablets (immediate-release), 2mg twice daily, reduce to 1mg twice daily to minimise side-effects. Modified-release capsules, 4mg once daily, reduce to 1mg twice daily (as tablets) if necessary to reduce side-effects (modified-release dose form inappropriate for hepatic or severe renal impairment (eGFR less than 30mL/min/m²)).</td>
</tr>
<tr>
<td>SOLIFENACIN</td>
<td>Tablets 5mg, 10mg</td>
<td>5mg daily, increased if necessary after 3 to 4 weeks to 10mg once daily.</td>
</tr>
</tbody>
</table>

**MHRA:** Mirabegron is contra-indicated with severe uncontrolled hypertension; measure blood pressure before starting treatment and regularly during treatment – refer to [www.gov.uk](http://www.gov.uk).

**MIRABEGRON** m/r tablets 25mg; 50mg  
**Dose:** 50mg once daily. For dosing in patients with renal or hepatic impairment in the absence or presence of strong cytochrome P450 inhibitors such as itraconazole, ketoconazole, ritonavir, or clarithromycin, refer to [SPC](http://www.gov.uk).

**Note:** Oxybutynin  
- side-effects limit the use of oxybutynin but may be reduced by starting at a lower dose  
- do not use oxybutynin in those aged over 70 years or those with cognitive impairment.

**OXYBUTYNIN** tablets 2.5mg, 5mg; m/r tablets 5mg, 10mg  
**Dose:** Tablets, initially 2.5 to 5mg 2 to 3 times daily increased if necessary to maximum 5mg 4 times daily; modified-release tablets, 5mg daily, adjusted according to response in 5mg steps at weekly intervals, maximum 20mg daily taken as a single dose. The modified-release preparation has fewer side-effects but is not always as effective as the immediate-release preparation.

**Drugs used for nocturnal enuresis**

**DESMOPRESSIN** tablets 200 micrograms; oral lyophilisates (DesmoMelt®), 120 micrograms, 240 micrograms  
**Dose:** Primary nocturnal enuresis (with normal urine concentrating ability), adult (under 65 years) and child over 5 years, tablets, 200 micrograms at bedtime, only increased to 400 micrograms if lower dose ineffective; oral lyophilisates, sublingually 120 micrograms at bedtime, only increased to 240 micrograms if lower dose ineffective. Withdraw for at least 1 week for reassessment after 3 months. Refer to [BNF](http://www.gov.uk) for cautions.

**Ureteric colic**

**Note:** Abscesses and local necrosis at the injection site have been reported with diclofenac intramuscular injection. Always consider alternative routes of administration and follow manufacturers’ instructions for intramuscular administration with care.

**DICLOFENAC** suppositories 50mg, 100mg; injection 75mg/3mL  
**Dose:** Ureteric colic, by rectum, 50 to 100mg; by deep intramuscular injection, 75mg then a further 75mg after 30 minutes if necessary. Administer intramuscular injections by deep intragluteal injection into the upper outer quadrant. If 2 injections daily are required, use the alternate buttock for the second injection. Alternatively, 1 ampoule of 75mg can be combined with other dosage forms of diclofenac (tablets or suppositories) up to the maximum daily dose of 150mg.
Oral ibuprofen and diclofenac (section 10.1) may also be used in ureteric colic.

Bladder instillations

Interstitial cystitis/Painful bladder syndrome

Intravesical preparations such as sodium hyaluronate (Cystistat®) or hyaluronic acid and chondroitin sulfate (iAluRil®) are useful in the treatment of painful bladder syndrome. Initiation of treatment is restricted to urologists or specialist urology nurses. Where patients are stable, treatment may be continued in primary care with regular review by specialist urology nurses.

Urological surgery

SODIUM CHLORIDE solution for irrigation 0·9%, 3 litres
Used for all post transurethral resection of prostate (TURP) patients.

GLYCINE solution for irrigation 1·5%, 3 litres
Used during resection, then changed over to sodium chloride solution.

Catheter patency solutions

See guidance on the use of catheter patency solutions.
• Catheter patency solutions are licensed medical devices rather than medicines; initiation can therefore be undertaken by either a prescriber or registered nurse or midwife with the appropriate training and level of competence; such initiation by a registered nurse or midwife should simply be recorded within the patient’s notes and/or care plan.
• As they are not licensed medicines they need only be prescribed if a supply is required in the community or where prescribers initiate treatment to be given by others.
• See also ‘Community Catheter Formulary and Prescribing Notes’ on Intranet.

FIRST CHOICE: SODIUM CHLORIDE

Sodium chloride solution for irrigation 0·9%, 100mL is used to wash debris (blood, mucous, pus) from the catheter. It will not dissolve crystal formation. Solution G and Solution R are suitable for use in limited circumstances, see guidance.

Drugs for erectile dysfunction

Sildenafil has a duration of action of around 6 hours and its onset of effect may be delayed if taken with food. Tadalafil has a longer duration of action (up to 30 hours) and may be preferred for patients for whom this represents a significant advantage. Its onset of action is unaffected by food.

Serum testosterone should be measured on an early morning sample to exclude hypogonadism. Both tadalafil and sildenafil should be tried at their maximum doses on several occasions before referring the patient to Urology for consideration of other therapies, eg transurethral or intra-cavernosal alprostadil or vacuum devices. Psychosexual counselling should also be considered.

For further guidance see ‘Advice on management of erectile dysfunction’ on Intranet.

Note: Drug treatments for erectile dysfunction:
• May only be prescribed on the NHS under certain circumstances and the prescription must be endorsed SLS; refer to the BNF for further details.
• Most patients are not eligible under current NHS rules for NHS treatment. Where private prescriptions are issued, GPs may wish to advise patients that sildenafil is now very low cost and may be the preferable option.
**FIRST CHOICE: SILDENAFIL**

**SILDENAFIL** tablets 25mg, 50mg, 100mg  
**Dose:** Initially 50mg (older people, 25mg) approximately 1 hour before sexual activity, subsequent doses adjusted according to response to 25 to 100mg as a single dose as needed; maximum 1 dose in 24 hours (maximum single dose 100mg).

**TADALAFIL** tablets 2.5mg, 5mg, 10mg, 20mg  
**Dose:** Initially 10mg approximately 30 minutes to 12 hours before sexual activity, subsequent doses adjusted according to response to 20mg as a single dose; maximum 1 dose in 24 hours. The 2.5mg and 5mg tablets are recommended for specialist initiation only, for example after total prostatectomy; refer to ‘Managing erectile dysfunction after prostatectomy’ on Intranet.

**Note:** Sildenafil and tadalafil are contra-indicated in patients receiving nitrates and nicorandil. Use with caution in patients on alpha-blockers, eg doxazosin, tamsulosin. If prescribing after myocardial infarction/acute coronary syndrome, advise re-introduction at 1 month after cardiac event if patient is pain-free and does not require nitrates or nicorandil.

**S ALPROSTADIL** urethral application (MUSE®) 250 micrograms, 500 micrograms, 1mg; intracavernosal injection 5 micrograms, 10 micrograms, 20 micrograms, 40 micrograms; double chamber cartridge 10 micrograms, 20 micrograms

Vacuum pumps are available and prescribable in primary care following assessment and recommendation at a urology clinic.
**MISSED COMBINED ORAL CONTRACEPTIVE PILLS**

If one pill has been missed (more than 24 hours and up to 48 hours late)

**Continuing contraceptive cover**
- take the missed pill as soon as it is remembered
- continue the remaining pills at the usual time.

**Minimising the risk of pregnancy**

Emergency contraception (EC) is not usually required but may need to be considered if pills have been missed earlier in the packet or in the last week of the previous packet.

- If pills are missed in the first week (pills 1-7)
  - Consider EC if unprotected sex occurred in the pill-free interval or in the first week of pill-taking.

- If pills are missed in the second week (pills 8-14)
  - No indication for EC if the pills in the preceding 7 days have been taken consistently and correctly (assuming the pills thereafter are taken correctly and additional contraceptive precautions are used).

- If pills are missed in the third week (pills 15-21)
  - OMIT THE PILL-FREE INTERVAL by finishing the pills in the current pack (or discarding any placebo tablets) and starting a new pack the next day.

If two or more pills have been missed (more than 48 hours late)

**Continuing contraceptive cover**
- take the most recent missed pill as soon as possible
- continue the remaining pills at the usual time
- use condoms or avoid sex until seven consecutive active pills have been taken. This advice may be overcautious in the second and third weeks, but the advice is a backup in the event that further pills are missed.

**Minimising the risk of pregnancy**


Adapted with permission from Faculty of Sexual and Reproductive Healthcare Clinical Effectiveness Unit Statement (May 2011).

Lead reviewer: Obstetrics & Gynaecology Review Group
Date: June 2016
Version: 3

Approved by: Formulary Subgroup of NHS Highland ADTC
Review date: June 2018
Warning: document uncontrolled when printed
EMERGENCY CONTRACEPTION

Client requesting emergency contraception (EC)

- take full contraceptive, sexual and menstrual history, including sexually transmitted infection (STI) risk assessment
- exclude existing pregnancy and medical contra-indications to various EC methods
- check current/recent use of enzyme-inducing drugs, severe asthmatic or if breast-feeding
- check whether client has used oral hormonal emergency contraception in this cycle already and which type
  - establish:
    - number of episodes of unprotected sexual intercourse (UPSI) in this cycle
    - timing of earliest and most recent UPSI in relation to last menstrual period (LMP)
    - timing of intercourse in relation to incorrect contraception use, including in pill/patch/ring-free week
    - earliest possible date of ovulation (= 14 days before period, based on shortest possible cycle)
    - timing of earliest and most recent UPSI in relation to earliest possible date of ovulation.

Reassurance

EC not required

Less than 5 days since earliest UPSI

Discuss: copper intrauterine device is most effective EC compared to oral hormonal EC. Oral EC unlikely to be effective after ovulation.

EC required

More than 5 days since earliest UPSI but no later than 5 days after earliest date of ovulation

Copper-IUD preferred/more suitable

Oral hormonal EC preferred option

UPA-EC: Ulipristal (ellaOne®) (1st Choice)

- 0 to 120 hours since earliest UPSI
- no LNG-EC taken in the last 7 days
- not on liver enzyme-inducing drugs
- not suitable if severe asthma controlled on oral glucocorticoids.

May be used more than once per cycle

LNG-EC: Levonorgestrel (Levonelle® 1500)

- If UPA-EC is contra-indicated
  - 0 to 72 hours since earliest UPSI
  - no UPA-EC taken in last 5 days.

May use more than once in cycle

- may be inserted up to 5 days after first UPSI
- if timing of ovulation can be estimated copper-IUD may be inserted beyond 5 days of UPSI, as long as it does not occur beyond 5 days of earliest possible date of ovulation
- most effective EC method and provision of ongoing contraception
- if separate appointment for insertion (or referral to HSH/GP) needed, give interim hormonal EC
- if immediate need and out of hours, refer to Gynaec on call
- consider prophylactic azithromycin if STI risk
- if requested remove copper-IUD with next period or when no pregnancy risk and start alternative contraception.

All EC methods

- full consultation, including side-effects, action to be taken if vomiting within 2 to 3 hours (hormonal EC only)
- provide written information
- accurate documentation
- consider STI testing
- follow-up as appropriate.

CATHETER PATENCY SOLUTIONS FOR LONG-TERM INDWELLING URINARY CATHETERS
(see also ‘Community Catheter Formulary and Prescribing Notes’ on Intranet)

Clinical evidence for the use of catheter patency solutions is limited. The decision to use a catheter maintenance solution must therefore involve careful consideration of the potential risks and benefits of such an intervention for each individual patient and include the patient’s consent.

Potential benefits
Use of the appropriate catheter maintenance solution can:
- reduce the build up of mineral deposits or remove debris to reduce the frequency of catheter blockage and the need for re-catheterisation.
- minimise urothelial damage by removing encrustation prior to catheter removal.

Potential risks
- there is evidence that all catheter maintenance solutions cause mucosal trauma in the bladder due to the physical process of administration. Damage may be worse if the solution is acidic or if force is used during administration, eg via a syringe.
- the risk of infection increases each time the closed catheter system is broken into.
- catheter maintenance solutions may be employed when re-catheterisation is indicated, increasing the interventions and delaying appropriate treatment.
- pain and discomfort on administration.

Minimising the risks in practice
- exclude other causes of catheter-related problems, eg constipation, kinked tubing, inappropriate catheter choice, bladder overactivity.
- only utilise catheter maintenance solutions where there is a clear indication (see table below) and the benefit outweighs the risk of introducing infection.
- pre-warm solutions by immersion in lukewarm water, connect to the catheter using aseptic technique and administer by gravity.
- to minimise pain on administration consider using a smaller volume rather than the full 50 to 100mL. Only 15 to 20mL is required to bathe the lumen and tip of the catheter and can be repeated.
- halt treatment if the patient experiences pain or discomfort on administration.

Choice of solution

<table>
<thead>
<tr>
<th>Solution</th>
<th>Licensed indication</th>
<th>Recommended regimen</th>
<th>Practice notes/cautions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium chloride 0.9%</td>
<td>To remove debris (including blood clots) and mucous.</td>
<td>As required.</td>
<td>Provides a mechanical flush. Will not remove encrustation due to mineral deposits.</td>
</tr>
<tr>
<td>Solution G (contains citric acid 3.23%) (pH 4)</td>
<td>Dissolution of encrustation due to mineral deposits.</td>
<td>Once-weekly to a maximum of twice-daily depending on severity of the case. Instil for 15 to 20 minutes.</td>
<td>Charting of urinary pH over time will allow development of an individual catheter care plan but should not be used as a diagnostic tool in isolation.</td>
</tr>
<tr>
<td>Solution R (contains citric acid 6%) (pH 2)</td>
<td>For more persistent crystallisation particularly prior to catheter removal.</td>
<td>Once-weekly to maximum twice-daily depending on severity. Instil for 15 to 20 minutes. If complete blockage instil for 20 to 30 minutes with bag held in a raised position (eg at patient’s thigh level).</td>
<td>Strongly acidic, high potential for mucosal irritation. Minimise use as far as possible.</td>
</tr>
</tbody>
</table>

Note: Magnesium ammonium phosphate (struvite) and calcium phosphate crystals can form on the catheter tip, lumen and balloon under alkaline conditions (pH 7.5 to 9.5). Encrustation due to build up of these insoluble mineral deposits is associated with high urinary pH. Raised pH can help predict which patients would benefit from the use of catheter maintenance solutions. A prophylactic regimen can be utilised if the patient has a high urinary pH plus regular catheter blockage plus presence of encrustation in blocked catheter.

Note: Chlorhexidine is of limited value in preventing or treating common infecting organisms and is therefore not recommended. Some of these organisms exist in a biofilm which resists surface washing of antibiotics. Use of this solution is likely to lead to emergence of resistant organisms.

Initiation:
- Catheter patency solutions are licensed medical devices rather than medicines; initiation can therefore be undertaken by either a prescriber or registered nurse or midwife with the appropriate training and level of competence; such initiation by a registered nurse or midwife should simply be recorded within the patient’s notes and/or care plan.
- As they are not licensed medicines they need only be prescribed if a supply is required in the community or where prescribers initiate treatment to be given by others.
- All treatment should follow the guidance above.
CHAPTER 8   MALIGNANT DISEASE AND IMMUNOSUPPRESSION

Drugs listed in Chapter 8 should only be initiated by hospital specialists with appropriate expertise. All cytotoxic drugs in section 8.1 (with the exception of methotrexate, cyclophosphamide, mercaptopurine and hydroxycarbamide) and also rituximab and alemtuzumab in section 8.2 should only be prescribed by a hospital specialist with appropriate expertise, following an agreed protocol.

- For information on dosage, refer to Cancer Chemotherapy protocols in the Policies Library on the Intranet or treatment protocols available at department or ward level.
- When oral cytotoxics are used for the treatment of malignant disease, the whole course will be dispensed by the hospital pharmacy. The prescription should only be repeated on the explicit instruction of a specialist. Refer to ‘Guidelines for the safe use of cytotoxic chemotherapy’.
- For information on the administration and use of bisphosphonates in malignant disease refer to section 6.6 and the Cancer Centre guideline.
- Some of the medicines listed in this chapter can be used for more than one condition. Where use was established before 2002 and the medicine is listed then it is recommended for all its licensed indications in NHS Highland (unless specifically excluded). From 2002 onwards within NHS Highland the advice of SMC and NICE/Healthcare Improvement Scotland is being followed and is listed with each medicine used for malignant disease; this advice outlines approved and excluded indications.
- Liquid injection vial sizes change frequently for this group of drugs therefore for liquid injections only drug concentration is stated and no vial sizes are given. A number of these injections are presented in unlicensed pre-filled syringes; those which are available at present are marked with an asterisk (*).
- For information on intrathecal cytotoxics refer to the ‘Policy for the prescribing, dispensing, storage and administration of intrathecal systemic anti-cancer therapy (SACT) for adult patients’.

Refer to:
- ‘Guidelines for infection prophylaxis in adult haematology and oncology patients’.
- ‘Guidelines for the use of GCSF in adult patients receiving systemic anti-cancer treatment (SACT)’.
- ‘Immunotherapy toxicity management guidelines: ipilimumab, nivolumab and pembrolizumab’.

Note: Clinicians with any concerns on any issues regarding their patient’s cytotoxic drug therapy should contact the prescribing specialist before continuing therapy.

8.1 CYTOTOXIC DRUGS

Treatment for cytotoxic-induced side-effects

S CALCIUM FOLINATE tablets 15mg

S DISODIUM FOLINATE injection 50mg/mL

S MESNA tablets 400mg; solution for injection 100mg/mL

Alkylating drugs

S BENDAMUSTINE powder for concentrate for solution for infusion 25mg, 100mg
See SMC advice 694/11.
Also for selected patients with indolent (FCC, MCL, MZL, SLL, LPC) non-Hodgkin’s lymphoma.

S BUSULFAN tablets 2mg
CHAPTER 8 MALIGNANT DISEASE AND IMMUNOSUPPRESSION

**S CHLORAMBUCIL** tablets 2mg

**S CYCLOPHOSPHAMIDE** tablets 50mg; powder for solution for injection* 1 gram

**S IFOSFAMIDE** powder for concentrate for solution for injection 1 gram, 2 grams

**S LOMUSTINE** capsules 40mg

**S MELPHALAN** tablets 2mg

Cytotoxic antibiotics

**S BLEOMYCIN** powder for solution for injection 15000 units

**S DACTINOMYCIN** powder for solution for injection 500 micrograms

**S DAUNORUBICIN** powder for solution for infusion 20mg

**S DOXORUBICIN** solution for injection* 2mg/mL

**S DOXORUBICIN, PEGYLATED LIPID FORMULATION** (Caelyx®) concentrate for solution for infusion 2mg/mL
See SMC advice [84/03](https://www.nice.org.uk/ta/ta091) and NICE guidance [TA091](https://www.nice.org.uk/ta/ta091).

**S EPIRUBICIN** solution for infusion* 2mg/mL

**S IDARUBICIN** capsules 5mg, 10mg; powder for solution for injection 10mg

**S MITOMYCIN** powder for solution for injection 10mg, 20mg, 40mg
Mitomycin 40mg is given as a bladder instillation.

**S MITOXANTRONE** concentrate for solution for infusion 2mg/mL

Antimetabolites

**S AZACITIDINE** powder for suspension for injection 100mg
See SMC advice [589/09](https://www.nice.org.uk/ta/ta091).

**S CAPECITABINE** tablets 150mg, 500mg
See SMC advice [34/03](https://www.nice.org.uk/ta/ta091), [193/05](https://www.nice.org.uk/ta/ta091), [401/07](https://www.nice.org.uk/ta/ta091), [507/08](https://www.nice.org.uk/ta/ta091) and NICE guidance [TA61](https://www.nice.org.uk/ta/ta091), [CG81](https://www.nice.org.uk/ta/ta091), [TA100](https://www.nice.org.uk/ta/ta091).

**S CLADRIBINE** solution for subcutaneous injection 2mg/mL
See SMC advice [537/09](https://www.nice.org.uk/ta/ta091).

**S CYTARABINE** intrathecal injection 20mg/mL; injection 100mg/mL

**S FLUDARABINE** tablets 10mg; powder for solution for injection or infusion 50mg
See SMC advice [176/05](https://www.nice.org.uk/ta/ta091) and NICE guidance [TA29](https://www.nice.org.uk/ta/ta091).

**S FLUOROURACIL** solution for infusion 25mg/mL, 50mg/mL; cream 5%

**S GEMCITABINE** concentrate for solution for infusion* 200mg, 1 gram
See SMC advice [154/05](https://www.nice.org.uk/ta/ta091) and NICE guidance [TA25](https://www.nice.org.uk/ta/ta091), [CG121](https://www.nice.org.uk/ta/ta091).
**SMERCAPTOPURINE** tablets 50mg; oral suspension 100mg/5mL
See SMC advice 798/12.

**SMETHOTREXATE** oral solution 10mg/5mL; solution for injection* 25mg/mL, 100mg/mL; intrathecal injection 50mg/2mL.

**SPEMETREXED** injection, powder for concentrate for solution for infusion 100mg, 500mg
See SMC advice 192/05, 268/06, 342/07, 531/09, 770/12.

**SRAHLTITREXED** powder for solution for infusion 2mg
See NICE guidance CG131.

**STEGAFUR WITH GIMERACIL AND OTERACIL** (Teysuno®) capsules
15mg/4-35mg/11.8mg, 20mg/5.8mg/15.8mg
See SMC advice 802/12.

**STRIFLURIDINE AND TIPIRACIL** (Lonsurf®) tablets 15mg/6.14mg, 20mg/8.19mg
See SMC advice 1221/17.

**Vinca alkaloids and etoposide**

**SETOPOSIDE** capsules 50mg, 100mg; concentrate for solution for infusion 20mg/mL

**Note:** Vinca alkaloids must **ONLY** be given by **INTRAVENOUS** injection.

**SVINBLASTINE** solution for injection 10mg

**SVINCRISTINE** solution for injection* 1mg/mL

**SVINDESINE** powder for solution for injection 5mg

**SVINORELBIN** capsules 20mg, 30mg; concentrate for solution for infusion 10mg/mL
See SMC advice 179/05, 324/06 and NICE guidance CG81.

**Other antineoplastic drugs**

**SAFLIBERCEPT** concentrate for solution for infusion 25mg/mL
See SMC 878/14.

**SAMSAACRINE** injection 50mg/mL [unlicensed]

**SBEVACIZUMAB** solution for infusion 25mg/mL
See SMC 878/14, 1063/15, 1135/16.

**SBORTEZOMIB** powder for solution for injection 3.5mg
See SMC advice 126/04, 302/06, 822/12, 927/13, 1075/15.
For administration by subcutaneous or intravenous injection.

**SBRENTUXIMAB VEDOTIN** powder for concentrate for solution for infusion 50mg
See SMC advice 845/12.

**SCETUXIMAB** solution for infusion 5mg/mL
See SMC advice 155/05, 279/06, 543/09, 1012/14.

**SDARATUMUMAB** concentrate for solution for infusion 20mg/mL
See SMC advice 1205/17.

S **CRISANTASPASE** powder for solution for injection 10 000 units. Crisantaspase is the enzyme asparaginase produced by *Erwinia chrysanthemi*.

S **DACARBAZINE** injection 200mg, 500mg

S **TEMOZOLOMIDE** capsules 5mg, 20mg, 100mg, 250mg
See SMC advice 244/06 and NICE guidance TA23.

S **HYDROXYCARBAMIDE** capsules 500mg

S **IPILIMUMAB**^▼^ concentrate for solution for infusion 5mg/mL
See SMC advice 779/12, 997/14.

S **NIVOLUMAB**^▼^ concentrate for solution for infusion 10mg/mL
See SMC advice 1120/16, 1144/16, 1180/16, 1240/17.

S **OLAPARIB**^▼^ capsules 50mg
See SMC advice 1047/15.

S **PEMBROLIZUMAB**^▼^ powder for concentrate for solution for infusion 50mg
See SMC advice 1086/15, 1204/17, 1239/17.

S **PANITUMUMAB** concentrate for intravenous infusion 20mg/mL
See NICE MTA 439.

S **PENTOSTATIN** powder for solution for injection 10mg

S **CARBOPLATIN** concentrate for solution for infusion 10mg/mL
See NICE guidance CG121.

S **CISPLATIN** concentrate for solution for infusion 1mg/mL
See NICE guidance CG121.

S **OXALIPLATIN** concentrate for solution for infusion 5mg/mL
See SMC advice 211/05 and NICE guidance CG131, TA100.

S **PROCARBAZINE** capsules 50mg

S **AXITINIB** tablets 1mg, 5mg
See SMC advice 855/13. For use after failure of prior treatment with sunitinib or pazopanib [off-label] or a cytokine.

S **BOSUTINIB**^▼^ tablets 100mg, 500mg
See SMC advice 910/13.

S **CERITINIB**^▼^ capsules 150mg
See SMC advice 1097/15.

S **CRIZOTINIB**^▼^ capsules 200mg, 250mg
See SMC advice 865/13, 1152/16.

S **DABRAFENIB**^▼^ capsules 50mg, 75mg
See SMC advice 1023/15.
**CHAPTER 8  MALIGNANT DISEASE AND IMMUNOSUPPRESSION**

**S DASATINIB** tablets 20mg, 50mg, 80mg, 100mg, 140mg
See SMC advice **370/07**.

**S ERLOTINIB** tablets 100mg, 150mg
See SMC advice **220/05**.

**S EVEROLIMUS** tablets 2·5mg, 5mg, 10mg
See SMC advice **595/10, 872/13**.

**S IBRUTINIB**\(^\text{▼}\) capsules 140mg
See SMC advice **1150/16, 1151/16**.

**S IDELALISIB**\(^\text{▼}\) tablets 100mg, 150mg
See SMC advice **1026/15, 1039/15**.

**S IMATINIB** tablets 100mg, 400mg
See SMC advice **91/02, 08/02, 26/02, 584/09** and NICE guidance **TA70, TA86**. For use in adult patients with Philadelphia chromosome-positive acute lymphoblastic leukaemia (Ph+ALL).

**S LENVATINIB**\(^\text{▼}\) capsules 4mg, 10mg
See SMC advice **1179/16**.

**S NILOTINIB** capsules 150mg, 200mg
See SMC advice **440/08, 709/11**.

**S NINTEDANIB**\(^\text{▼}\) (Vargetef\(^\text{®}\)) capsules 100mg, 150mg
See SMC advice **1027/15**.

**S PAZOPANIB** tablets 200mg, 400mg
See SMC advice **676/11**.

**S PONATINIB**\(^\text{▼}\) tablets 15mg, 45mg
See SMC advice **1032/15**.

**S REGORAFENIB**\(^\text{▼}\) tablets 40mg
See SMC advice **1031/15**.

**S RUXOLITINIB** tablets 5mg, 10mg, 15mg, 20mg
See SMC advice **867/13**.

**S SUNITINIB** capsules 12·5mg, 25mg, 50mg
See SMC advice **275/06** and NICE guidance **TA169**.

**S SORAFENIB** tablets 200mg
See SMC advice **482/08**.

**S TRAMETINIB**\(^\text{▼}\) tablets 500 micrograms, 2mg
See SMC advice **1161/16**.

**S VEMURAFENIB** tablets 240mg
See SMC advice **792/12**.

**S CARFILZOMIB**\(^\text{▼}\) powder for solution for infusion 10mg, 30mg, 60mg
See SMC advice **1242/17**.
8.2 DRUGS AFFECTING THE IMMUNE RESPONSE

Immunoglobulins

Intravenous infusion of normal immunoglobulin (section 14.5) may be considered under specialist neurology advice for use in Guillain Barré syndrome, chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), myasthenia gravis and other immune mediated neurological disorders; refer to guidance at http://www.nsd.scot.nhs.uk/Documents/clinimmumoMarch12.pdf.

Antiproliferative immunosuppressants

S AZATHIOPRINE tablets 25mg, 50mg
Azathioprine is also used in:
- inflammatory bowel disease (section 1.5)
- rheumatic disease (section 10.1)
myasthenia gravis (section 10.2); see also ‘Myasthenia gravis: association of British neurologists’ management guidelines’ at http://pn.bmj.com/content/15/3/199.full

eczema (section 13.5).

For advice on monitoring azathioprine refer to Appendix 2: ‘Universal requirements for monitoring of conventional DMARDS in primary care’.

MHRA: Be aware of the risk of pulmonary complications (bronchiectasis, pulmonary fibrosis) with mycophenolate.

**S** MYCOPHENOLATE MOFETIL capsules 250mg; tablets 500mg; oral suspension 1 gram/5mL; powder for solution for infusion 500mg

Mycophenolate mofetil is also used in rheumatic disease (section 10.1). For advice on monitoring mycophenolate mofetil refer to Appendix 2: ‘Universal requirements for monitoring of conventional DMARDS in primary care’.

**S** MYCOPHENOLIC ACID (as mycophenolate sodium) e/c tablets (Myfortic®) 180mg, 360mg

Mycophenolic acid is also used in rheumatic disease (section 10.1). For advice on monitoring mycophenolic acid refer to Appendix 2: ‘Universal requirements for monitoring of conventional DMARDS in primary care’.

Other immunosuppressants

MHRA/CHM advice: Prescribe and dispense ciclosporin and tacrolimus by brand name; only switch formulations under the close supervision of a transplant specialist (www.gov.uk).

**S** CICLOSPORIN capsules (Neoral®) 10mg, 25mg, 50mg, 100mg; oral solution (Neoral®) 500mg/5mL; concentrate for intravenous infusion (oily) (Sandimmun®) 50mg/mL

Ciclosporin is also used in inflammatory bowel disease (section 1.5) and rheumatic disease (section 10.1). For advice on monitoring ciclosporin refer to Appendix 2: ‘Universal requirements for monitoring of conventional DMARDS in primary care’.

**S** TACROLIMUS capsules (Prograf®) 500 micrograms, 1mg, 5mg; capsules (Adoport®) 500 micrograms, 750 micrograms, 1mg, 2mg, 5mg; m/r capsules (Advagraf®) 500 micrograms, 1mg, 3mg,5mg; granules for oral suspension (Modigraf®) 200 micrograms, 1mg; concentrate for intravenous infusion 5mg/1mL

For advice on monitoring tacrolimus refer to Appendix 2: ‘Universal requirements for monitoring of conventional DMARDS in primary care’.

Anti-lymphocyte monoclonal antibodies

**S** OFATUMUMAB concentrate for solution for infusion 20mg/mL

See SMC advice 1037/15.

**S** RITUXIMAB solution for subcutaneous injection 120mg/mL

See SMC advice 33/03, 135/04, 330/06, 591/09, 675/11, 975/14 and NICE guidance TA137, TA065. Also for selected patients with CD 20+ B-cell lymphomas/lymphoproliferative and haematological autoimmune disorders [off-label].

Immunomodulating drugs used in the treatment of multiple sclerosis

**Note: Monitoring of immunomodulating drugs used in the treatment of multiple sclerosis**

With each drug, be aware of the potential risks and the need for monitoring. Information and advice is available from the Multiple Sclerosis Specialist Nurses, Raigmore Hospital. Further information and patient information letters are available for each drug at www.medicines.org.uk.
Drugs used in the treatment of multiple sclerosis

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<tr>
<th>First-line</th>
<th>Second-line: highly active multiple sclerosis</th>
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<tbody>
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<td>Peginterferon beta</td>
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<tr>
<td>Dimethyl fumarate</td>
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<td>Teriflunamide</td>
<td>Daclizumab</td>
</tr>
<tr>
<td>Glatiramer</td>
<td></td>
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</tbody>
</table>

**INTERFERON BETA** solution for injection beta-1a 22 micrograms (Rebif®), 44 micrograms (Rebi®), 30 micrograms (Avonex®); beta-1b 300 micrograms (Betaferon®, 300 micrograms (Extavia®)

**PEGINTERFERON BETA** (beta-1a; Plegridy®) solution for injection in pre-filled syringes 63 micrograms, 94 micrograms, 125 micrograms See SMC 1018/14.

**DIMETHYL FUMARATE** e/c capsules 120mg, 240mg See SMC advice 886/13. For advice on monitoring during and following treatment refer to SPC.

**TERIFLUNOMIDE** tablets 14mg See SMC advice 940/14.

**GLATIRAMER** solution for injection 20mg/mL; solution for injection, pre-filled syringe 20mg/mL, 40mg/mL

**FINGOLIMOD** capsules 500 micrograms See SMC advice 763/12.

**NATALIZUMAB** solution for intravenous infusion 20mg/mL See SMC advice 329/06. See also shared care protocol for the administration of natalizumab on Intranet.

**ALEMTUZUMAB** concentrate for solution for infusion 10mg/mL See SMC advice 959/14.

**OBINUTUZUMAB** concentrate for solution for infusion 25mg/mL See SMC advice 1008/14.

**DACLIZUMAB** solution for injection, pre-filled syringe 150mg; solution for injection, pre-filled pen 150mg See SMC advice 1216/17.

Other immunomodulating drugs

**INTERFERON ALFA** (alfa-2a (rbe); Roferon-A®) injection pre-filled syringe 3 million units/0.5mL, 4.5 million units/0.5mL, 6 million units/0.5mL, 9 million units/0.5mL See NICE guidance TA75.

**PEGINTERFERON ALFA** (alfa-2a; Pegasys®) solution for injection pre-filled syringe 180 micrograms

**BACILLUS CALMETTE-GUÉRIN** bladder instillation 12.5mg, 81mg For urology use.

**LENALIDOMIDE** capsules 2.5mg, 5mg, 7.5mg, 10mg, 15mg, 20mg, 25mg
CHAPTER 8 MALIGNANT DISEASE AND IMMUNOSUPPRESSION

See SMC advice 441/08, 942/14, 1096/15.

S POMALIDOMIDE \capsules 1mg, 2mg, 3mg, 4mg
See SMC advice 972/14.

S THALIDOMIDE (Thalidomide Celgene\®) capsules 50mg
See SMC advice 525/08.

8.3 SEX HORMONES AND HORMONE ANTAGONISTS IN MALIGNANT DISEASE

Oestrogens

S DIETHYLSTILBESTROL tablets 1mg

Progestogens

S MEDROXYPROGESTERONE ACETATE (Provera\®) tablets 100mg, 200mg

S MEGESTROL tablets 160mg

S NORETHISTERONE tablets 5mg

Hormone antagonists

The choice and initiation of tamoxifen or aromatase inhibitor (anastrozole, exemestane or letrozole) will be determined by the Breast Surgeon or Oncologist. Refer to 'Strategy for the use of Adjuvant Aromatase Inhibitors (AI) and Tamoxifen'. It is recommended that:

- all patients switching from tamoxifen to an AI should have a DXA scan shortly afterwards
- blood lipids are checked around 4 to 6 months after switching.

In patients with metastatic breast cancer the use of bisphosphonates may prevent skeletal complications of bone metastases; see Cancer Centre guidance.

S ANASTROZOLE tablets 1mg
See SMC advice 90/04, 198/05, NICE guidance TA112.

S EXEMESTANE tablets 25mg
See SMC advice 210/05, NICE guidance TA112.

S LETROZOLE tablets 2·5mg
See SMC advice 152/05, NICE guidance TA112.

Note: Tamoxifen can increase the risk of thromboembolism particularly during and immediately after major surgery or periods of immobility (see SPC). Advise patients of the symptoms of thromboembolism and to report sudden breathlessness and any pain in the calf of one leg.

S TAMOXIFEN tablets 20mg; oral solution 10mg/5mL

Prostate cancer: gonadorelin analogues, and gonadotrophin-releasing hormone antagonists

The gonadorelin analogues have similar efficacy in reducing testosterone levels and similar side-effect profiles. Leuprorelin (Prostap DCS\®) is recommended as first-choice in NHS Scotland.

FIRST CHOICE: LEUPRORELIN (PROSTAP DCS\®)
**LEUPROLELIN** injection 3.75mg, 11.25mg (Prostap DCS®)
*Dose:* *By subcutaneous injection,* 3.75mg every month, 11.25mg every 3 months.

**TRIPTORELIN** injection (as pamoate) 11.25mg, 22.5mg
*Dose:* *By intramuscular injection,* 11.25mg every 3 months or 22.5mg every 6 months.

Each vial includes an overage to allow administration of the dose.

The gonadotrophin-releasing hormone antagonist degarelix will be initiated by specialists in selected patients with advanced, hormone-naïve prostate cancer.

**DEGARELIX** injection 80mg, 120mg
See degarelix shared care guidance on Formulary webpage of *Intranet.*

### Prostate cancer: anti-androgens

Bicalutamide should be considered first choice in preference to cyproterone.

**BICALUTAMIDE** tablets 50mg, 150mg
*Dose:* 50mg daily in combination with gonadorelin analogue, 150mg once daily as monotherapy.

**MEDROXYPROGESTERONE ACETATE** (Provera®) tablets 10mg

**CYPROTERONE** tablets 50mg, 100mg
*Dose:* Anti-androgen, 100mg twice daily. Progestogen, 50mg daily.

**ENZALUTAMIDE** capsules 40mg
*Dose:* 160mg once daily. See SMC advice 911/13, 1066/15.

**ABIRATERONE** tablets 500mg
*Dose:* 1 gram once daily. See SMC advice 764/12, 873/13.

### Note:
Abiraterone is included in the Highland Formulary for use with prednisolone for the treatment of metastatic castration-resistant prostate cancer in adult men whose disease has progressed on or after a docetaxel-based chemotherapy regimen:
- in accordance with the SMC 764/12 restriction for use in patients who have received only one prior chemotherapy regimen
- the small cohort of patients in NHS Highland who have received second-line chemotherapy since abiraterone received its UK marketing authorisation
- in patients who have received only one prior chemotherapy regimen in the castrate refractory period but have received chemotherapy in the castrate sensitive phase within a clinical trial.

### Breast cancer and gonadorelin analogues

**GOSERELIN** implant 3.6mg

### Somatostatin analogues

**OCTREOTIDE** injection 50 micrograms/mL, 100 micrograms/mL, 500 micrograms/mL; injection (microsphere powder for aqueous suspension) 10mg, 20mg, 30mg

**LANREOTIDE** (Somatuline Autogel®) solution for injection pre-filled syringe 60mg, 90mg, 120mg
**STRATEGY FOR THE USE OF ADJUVANT AROMATASE INHIBITORS (AI) AND TAMOXIFEN**

The results for oestrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor-2 (HER2) testing should be available on all patients as soon as possible after surgery and before any decisions are made on the most appropriate adjuvant therapy. For patients already on treatment and reaching the 2 to 3 year and 5 year time frames, it is essential that retrospective testing of PR and HER2 is available in a timely manner to allow provision of recognised best management.

**POSTMENOPAUSAL?**

**Definitions:**
Postmenopausal at time of diagnosis of breast cancer defined as:
- Amenorrhoea >2 years duration and age >50 years
If amenorrhoea <2 years duration and/or age <55 years check LH/FSH/estradiol before chemotherapy

**CHEMOTHERAPY-INDUCED AMENORRHOEA DOES NOT EQUAL POSTMENOPAUSAL**
*NB: Ovarian function tests are unreliable post-chemotherapy/hormonal therapy*

If premenopausal before chemotherapy with persisting chemotherapy-induced amenorrhoea following chemo then at the time of considering an AI:
- >55 years class as postmenopausal
- 50 to 55 years use assessment of menopausal status before chemotherapy
- <50 years old = premenopausal unless ovarian ablation.

---

**Any One Of:**

- Grade 3
- Node +ve
- ER poor*
- HER2 +ve
- Path size ≥5cm (T3 & T4)
- Prev. neoadj AI with response

**Yes**

**Aromatase inhibitor**
5 years duration

**Yes**

**Tamoxifen**
5 years duration

**Extended adjuvant**
5 years tamoxifen + 3 years AI
OR
Switch
2.5 years tamoxifen + 2.5 years AI

**ALL THE REST, ie:**
- Grade 2 node -ve size <5cm
- Grade 1 node -ve size 2 to 5cm

**No**

Ineligible for AI, consider tamoxifen

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*The individual AI, letrozole, anastrozole or exemestane, will be chosen based on the prevailing licences.

**Immediate AI:** Anastrozole 1mg once daily (first choice) or letrozole 2-5mg once daily (second choice)

**Switch AI:** Exemestane 25mg once daily

**Extended AI:** Letrozole 2-5mg once daily

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*Micrometastases defined as 0-2mm to 2mm = node positive, isolated tumour cells defined as <0-2mm = node negative

*ER poor defined as Allred 3 to 5**

---

It is recommended that:
- all patients switching from tamoxifen to an AI should have a DXA scan shortly after that switch
- the patient's GP should check blood lipids around 4 to 6 months after that switch
- patients receiving tamoxifen should be made aware of the symptoms of thromboembolism and advised to report sudden breathlessness and any pain in the calf in one leg.
CHAPTER 9  NUTRITION AND BLOOD

9.1 ANAEMIAS AND SOME OTHER BLOOD DISORDERS

Iron-deficiency anaemias

Iron deficiency should be regarded as a symptom. Investigation of the underlying cause is vital. Haemoglobin should rise by approximately 20 grams/litre (2 grams/100mL) over 3 to 4 weeks. Once it has reached reference range, continue treatment for a further 3 months in order to replenish iron stores, and then stop. Failure to respond as predicted suggests other underlying factors may be contributing to the anaemia. Gastric irritation is the most common side-effect of iron therapy and is related to the content of elemental iron. A gradual increase in dose can help prevent some gastric side-effects. Modified-release preparations are not recommended as they deliver most of their iron to the small intestine where it is poorly absorbed. A range of oral iron preparations is available over the counter. Iron absorption is increased when taken on an empty stomach and 1 tablet of ferrous sulfate/fumarate once daily is usually adequate for prophylaxis. Where more frequent dosing is given it is important to allow at least 8 hours between doses.

FERROUS SULFATE\textsuperscript{OTC} (dried) tablets 200mg (65mg iron)
Dose: Prophylactic, 1 tablet daily; therapeutic, 1 tablet 2 to 3 times daily.

FERROUS FUMARATE\textsuperscript{OTC} tablets 210mg (68mg iron); syrup 140mg (45mg iron)/5mL
Dose: Prophylactic, 1 tablet 1 to 2 times daily or 5mL syrup twice daily; therapeutic, 1 tablet 2 to 3 times daily or 10mL syrup twice daily.

SODIUM FEREDETATE\textsuperscript{OTC} (Sytron\textsuperscript{®}) elixir 190mg (27.5mg iron)/5mL
Dose: Therapeutic, 5mL increasing gradually to 10mL 3 times daily.

Parenteral iron

Note: Only give iron parenterally if oral iron therapy is not tolerated.

- **Parenteral iron** can cause serious allergic or anaphylactoid reactions therefore administer treatment where cardiopulmonary resuscitation can be carried out. Check SPC for contraindications/cautions in the first trimester of pregnancy; can be used in the second and third trimesters and during lactation if the level of anaemia is considered to put mother or foetus at risk.
- Iron sucrose can be given by slow intravenous infusion or injection into a dialyser; it is too irritant to be given by intramuscular or subcutaneous routes. Iron isomaltoside is given by high-dose intravenous infusion; refer to the SPC for further information on infusion times.

\textsuperscript{S} IRON ISOMALTOSIDE 1000\textsuperscript{V} (Monofer\textsuperscript{®}) injection 100mg/1mL, 500mg/5mL, 1 gram/10mL
Dose: refer to SPC for information on dose calculation and administration.

\textsuperscript{S} FERRIC CARBOXYMALTOSIDE\textsuperscript{V} (Ferinject\textsuperscript{®}) injection 100mg/2mL, 500mg/10mL, 1 gram/20mL
Dose: refer to SPC for information on dose calculation and administration.

\textsuperscript{S} IRON SUCROSE\textsuperscript{V} (Venofer\textsuperscript{®}) injection 100mg/5mL
Dose: refer to SPC for information on dose calculation and administration.

\textsuperscript{S} IRON DEXTRAN\textsuperscript{V} (CosmoFe\textsuperscript{®}) injection 100mg/2mL
For intramuscular use in selected frail elderly patients where the risk of harm of repeated failed intravenous access is greater than the risk of intramuscular iron, or where due to frailty patients are unable to travel to a centre which provides intravenous therapy.

**Drugs used in megaloblastic anaemias**

**HYDROXOCOBALAMIN** injection 1mg/1mL
*Dose:* By intramuscular injection, pernicious anaemia and other irreversible causes of $B_{12}$ deficiency, initially 1mg, up to 3 times a week for 2 weeks then 1mg every 3 months for life.

**FOLIC ACID** tablets 400 micrograms*OTC*, 5mg; syrup 2·5mg/5mL
*Dose:* See note.

**Note:**
- **Folic acid** 5mg daily is used in folate-deficient megaloblastic anaemia. Most megaloblastic anaemias result from a lack of *either* vitamin $B_{12}$ or folate. It is essential to establish in every case which deficiency is present and the underlying cause before initiating treatment. For prophylaxis in chronic haemolytic states it is sufficient to give folic acid 5mg daily or even weekly, depending on the diet and the rate of haemolysis.
- Never give folic acid alone in the treatment of pernicious anaemia and other vitamin $B_{12}$ deficiency states because it may precipitate the onset of subacute combined degeneration of the spinal cord. If in doubt discuss with haematologist.
- Folic acid is also given at a dose of 400 micrograms daily to prevent the first occurrence of neural tube defects. It should be started as soon as pregnancy is planned or confirmed and continued until week 12 of pregnancy. To prevent the recurrence of neural tube defects give one 5mg tablet daily up to week 12 of pregnancy.
- Women wishing to become pregnant, with coeliac disease or diabetes or if taking antiepileptic medicines should be advised to take 5mg folic acid supplementation daily, starting at least one month before conception and continuing up to week 12 of pregnancy. For more information on nutrition in pregnancy see local Maternal and Child Nutrition Best Practice Guidance and pre-pregnancy, antenatal and postnatal care guidance for women with obesity, on Intranet.
- For advice on use of folic acid with methotrexate in inflammatory bowel disease see section 1.5, in rheumatic disease see section 10.1 and in dermatological conditions see section 13.5.

**Drugs used in hypoplastic, haemolytic and renal anaemias**

**FIRST CHOICE:** DARBEPOETIN ALFA

**S DARBEPOETIN ALFA** injection (Aranesp®) pre-filled syringe 10 micrograms/0·4mL, 15 micrograms/0·375mL, 20 micrograms/0·5mL, 30 micrograms/0·3mL, 40 micrograms/0·4mL, 50 micrograms/0·5mL, 60 micrograms/0·3mL, 80 micrograms/0·4mL, 100 micrograms/0·5mL, 130 micrograms/0·65mL, 150 micrograms/0·3mL, 300 micrograms/0·6mL; injection (Aranesp® SureClick) pre-filled disposable injection device 20 micrograms/0·5mL, 40 micrograms/0·4mL, 60 micrograms/0·3mL, 80 micrograms/0·4mL, 100 micrograms/0·5mL, 150 micrograms/0·3mL.

Renal and haematology patients on darbepoetin will have their treatment prescribed, supplied and monitored by their clinical speciality but outwith these areas the relevant clinical speciality should be contacted for advice if required. For renal patients contact the anaemia co-ordinator for supply.

**S EPOETIN BETA** (NeoRecormon®) injection pre-filled syringe 2000 units, 3000 units, 4000 units, 6000 units, 10 000 units, 20 000 units

Reco-Pen® injection devices and needles are available from Raigmore Hospital pharmacy.
Iron overload

**S** DEFERASIROX tablets 90mg, 180mg, 360mg

**S** DEFERIPRONE tablets 500mg

**S** DESFERRIOXAMINE injection 500mg, 2 grams

Drugs used in platelet disorders

**S** ELTROMBOPAG tablets 25mg, 50mg

**S** ROMIPLOSTIM injection 250 micrograms

**S** ANAGRELIDE capsules 500 micrograms

Drugs used in neutropenia

**FIRST CHOICE: **LENOGRASTIM

**S** LENOGRASTIM injection 13-4 million units (105 micrograms), 33-6 million units (263 micrograms)

**S** FILGRASTIM solution for injection 30 million units (300 micrograms/1mL) (Neupogen®), solution for injection pre-filled syringe 30 million units (300 micrograms/0.5mL) (Zarzio®), solution for injection pre-filled syringe 48 million units (480 micrograms/0.5mL) (Neupogen®, Zarzio®) Filgrastim should be prescribed by brand name.

**S** LIPEGFILGRASTIM injection 10mg/mL; injection pre-filled syringe 6mg/0.6mL

Drugs used to mobilise stem cells

**S** PLERIXAFOR injection 24mg/1.2mL

9.2 FLUIDS AND ELECTROLYTES

Refer to guidance on the treatment of hyponatraemia, hypokalaemia and hypomagnesaemia on Intranet (see summary guidance).

Oral potassium

**POTASSIUM CHLORIDE** effervescent tablets (Sando-K®) (12mmol potassium, 8mmol chloride/tablet); syrup (Kay-Cee-L®) (1mmol/mL each of potassium and chloride)

**Dose:** Refer to BNF. Advise patients to take with or after food.

Oral potassium supplementation is recommended only where there is proven depletion and is preferably given as a liquid (or effervescent) preparation; see summary guidance. The use of potassium-sparing diuretics is discussed in section 2.2.

Management of hyperkalaemia

Refer to guidance on the emergency management of hyperkalaemia on Intranet.

**CALCIUM POLYSTYRENE SULPHONATE** (Calcium Resonium®) powder

**Dose:** By mouth, 15 grams 3 to 4 times daily in water (not fruit squash, which has a high potassium content) or as a paste; by rectum, as an enema, 30 grams in methylcellulose solution, retained for 9 hours followed by irrigation to remove resin from colon.
Oral sodium

**SODIUM CHLORIDE** (Slow Sodium®) m/r tablets 600mg (approximately 10mmol each of sodium and chloride)

**Dose:** Prophylaxis of sodium chloride deficiency, 4 to 8 tablets daily with water (in severe depletion up to maximum 20 tablets daily). Chronic renal salt wasting, up to 20 tablets daily with appropriate fluid intake.

Oral rehydration therapy

**ORAL REHYDRATION SALTS** oral powder sachets OTC

**Dose:** According to fluid loss, usually 200 to 400mL of solution after every loose bowel motion. Child, 200mL after every loose bowel motion. Oral rehydration therapy is recommended for mild to moderate diarrhoea in children. In short bowel syndrome seek specialist advice on the treatment of diarrhoea with oral rehydration salts.

Oral bicarbonate

**SODIUM BICARBONATE** capsules 500mg (approximately 6mmol each of sodium and bicarbonate)

**Dose:** Refer to BNF.

**Intravenous sodium, glucose and potassium**

**Sodium chloride intravenous infusion**
- Sodium chloride 0·9%* (sodium 150mmol/L)
- Sodium chloride 0·18% (sodium 30mmol/L)
- Sodium chloride 0·45% (sodium 75mmol/L)
- Sodium chloride 1·8% (sodium 300mmol/L)
- Sodium chloride 2·7% (sodium 450mmol/L)

**Sodium chloride intravenous infusion with other ingredients**
- Sodium chloride 0·9%, glucose 5% (sodium 150mmol/L)
- Sodium lactate, compound

**Glucose intravenous infusion**
- Glucose 5%*
- Glucose 10%
- Glucose 20%

**Potassium chloride and glucose intravenous infusion**
- Potassium chloride 0·15%, glucose 5% (potassium 20mmol/L)
- Potassium chloride 0·3%, glucose 5% (potassium 40mmol/L)
- Potassium chloride 0·15%, glucose 10% (potassium 20mmol/L)
- Potassium chloride 0·3%, glucose 10% (potassium 40mmol/L)

**Potassium chloride and sodium chloride intravenous infusion**
- Potassium chloride 0·15%, sodium chloride 0·9% (potassium 20mmol/L, sodium 150mmol/L)
- Potassium chloride 0·3%, sodium chloride 0·9% (potassium 40mmol/L, sodium 150mmol/L)

**Potassium chloride, sodium chloride and glucose intravenous infusion**
- Potassium chloride 0·15%, sodium chloride 0·18%, glucose 4% (potassium 20mmol/L, sodium 30mmol/L)
- Potassium chloride 0·3%, sodium chloride 0·18%, glucose 4% (potassium 40mmol/L, sodium 30mmol/L)
- Potassium chloride 0·15%, sodium chloride 0·45%, glucose 5% (potassium 20mmol/L, sodium 75mmol/L)
- Potassium chloride 0·3%, sodium chloride 0·45%, glucose 5% (potassium 40mmol/L, sodium 75mmol/L)
- Potassium chloride 0·15%, sodium chloride 0·9%, glucose 5% (potassium 20mmol/L, sodium 150mmol/L)
- Potassium chloride 0·3%, sodium chloride 0·9%, glucose 5% (potassium 40mmol/L, sodium 150mmol/L)

**Potassium chloride concentrate injection** – only to be used where ready mixed solutions are unavailable; it is handled as a controlled drug in inpatient areas
- Potassium chloride 15% (potassium 20mmol/L, sodium 150mmol/L)

**Potassium chloride and sodium chloride intravenous infusion** – for use in Intensive Care and high dependency areas only
- Potassium chloride 3%, sodium chloride 0·9% (potassium 40mmol, sodium 15mmol/100mL)

*May be supplied on a GP10 prescription form on a ‘pay and report’ basis if required for patients cared for outside a hospital setting; for further information contact your local Lead Pharmacist or Hospital Pharmacist.
CHAPTER 9    NUTRITION AND BLOOD

Bicarbonate

**SODIUM BICARBONATE** infusion 1·26%, 4·2%, 8·4%; injection 4·2%, 8·4% 10mL; injection (Minijet®) 8·4% 50mL

Water

**WATER FOR INJECTIONS**

Plasma and plasma substitutes

° ALBUMIN solution 5% (500mL) (Alburex®), 20% (100mL)
See Blood Products information on Formulary webpage on Intranet.

GELASPAN® infusion

9.3    INTRAVENOUS NUTRITION

Order total parenteral nutrition (TPN) from Raigmore Hospital Pharmacy Department using the TPN prescriptions proforma provided. The standard TPN regimes are outlined in ‘Total parenteral nutrition regimes’. Information on prescribing TPN in Raigmore Hospital is available in the General Surgery Foundation Year Doctors’ Handbook or from Pharmacy Production staff, tel: 01463 704000 (switchboard).

Infusion fluids

° SYNTHAMIN 9 infusion

° SYNTHAMIN 9 EF infusion

° SYNTHAMIN 14 infusion

° SYNTHAMIN 14 EF infusion

° SYNTHAMIN 17 EF infusion

° PRIMENE 10% infusion 100mL (for neonatal use)

Lipid products

° LIQUID EMULSION 20% (ClinOleic® 20%, Intralipid® 20%)

Additives

° ADDITRACE® solution

° PEDITRACE® solution

° CERNEVIT® solution

° SODIUM ACETATE solution (sodium 11mmol/5mL)

° SODIUM CHLORIDE 30% solution (sodium 50mmol/10mL)
SOLIVITO N® solution

S VITLIPID N® INFANT emulsion

Ready to use bags

S NUTRIFLEX® PERI 1250mL, 2500mL

S NUTRIFLEX® PLUS 1875mL, 2500mL

S NUTRIFLEX® SPECIAL 1875mL

S NUTRIFLEX® SPECIAL EF 2500mL

S STRUCTOKABIVEN® (electrolyte-free) 986mL (for intradialytic parenteral nutrition)

9.4 ORAL NUTRITION

Foods for special diets

Always consider the most cost-effective and clinically appropriate product when recommending oral nutritional supplements (ONS). Prescribers are advised:

For new patients:
- only consider initiating ONS following ‘Food First’ dietary intervention and on the recommendation of a Dietitian where available.
- check the BNF for any drug nutrient interactions, e.g. warfarin.
- prescribe supplements as per table below only for ACBS approved indications and endorse prescriptions ‘ACBS’; social or financial reasons do not qualify for ONS prescription.
- powdered ONS should be used as a first-line product in community settings, unless contraindicated.
- always choose items indicated below as ‘First choice’ in preference as these are purchased on contract guaranteeing significant savings to the NHS; other choices are indicated only in the event of patients disliking the ‘First choice’ option.
- usually prescribe 28 days supply on acute prescription for a maximum of 3 months; further supply should only be on the advice of a Dietitian.
- refer to ‘Oral nutritional supplements (MUST)’ guidance on Intranet for further information.
- anyone requiring ONS as a sole source of nutrition should be referred to a Dietitian due to ONS having either deficiencies or excess of nutrients.

For existing patients who have received ONS prescriptions for more than 3 months:
- continue the prescription where a Dietitian has provided a detailed nutritional assessment and is closely following up the patient as detailed in dietetic correspondence.
- review all other patients as per ‘Oral nutritional supplements (MUST)’ guidance on Intranet.

<table>
<thead>
<tr>
<th>Recommended oral nutritional supplements (ONS)</th>
<th>Pack size</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Milk-based</strong></td>
<td></td>
</tr>
<tr>
<td>First choice</td>
<td>Aymes® Shake (or Aymes® Complete if dexterity problems)</td>
</tr>
<tr>
<td>Second choice</td>
<td>Ensure® Shake</td>
</tr>
<tr>
<td>Third choice</td>
<td>Fortisip® Compact</td>
</tr>
<tr>
<td><strong>Milk-based with higher protein content</strong></td>
<td></td>
</tr>
<tr>
<td>First choice</td>
<td>Fortisip® 2Kcal</td>
</tr>
<tr>
<td>Second choice</td>
<td>Ensure® TwoCal</td>
</tr>
</tbody>
</table>
Coeliac disease: gluten-free products

Refer to NHS Highland gluten-free foods formulary on Intranet.

Enteral nutrition

Enteral feeding may be justified for patients unable to meet their nutritional requirements orally. This may be via a nasoenteric tube (eg NG), gastrostomy tube (eg PEG) or jejunostomy tube. There are a number of nutritionally complete feeds available and the Dietitian will recommend a feed to meet the patient’s nutritional requirement. Information on how the different types of enteral feeding tubes available affect drug administration is available at www.medicinesresources.nhs.uk.

9.5 MINERALS

See guidance in ‘Treatment of low electrolytes’ on Intranet (summary guidance).

Calcium supplements

Calcium supplements are usually only required where dietary calcium is inadequate and are best taken apart from food to avoid a phosphate-binding action (see guidance in ‘Treatment of low electrolytes’ on Intranet (summary guidance). Those at risk of osteoporosis should maintain an adequate intake of calcium and vitamin D and any deficiency should be corrected by increasing dietary intake or taking supplements.

**CALCIUM** syrup (Alliance® Calcium) (calcium 2.5mmol or 102mg/5mL) [unlicensed].

**CALCIUM** effervescent tablets (Sandocal®-1000) (calcium 1 gram or 25mmol/tablet)

**CALCIUM GLUCONATE** injection 10% (calcium 8.4mg or 225 micromol/mL)

**CALCIUM CHLORIDE** injection 14.7% (calcium 40mg or 1mmol/mL); Minijet® 10% (calcium 27.3mg or 680 micromol/mL)

Hypercalcaemia

Refer to section 6.6 and NHS Highland Cancer Centre guidelines for the use of bisphosphonates in hypercalcaemia of malignancy.

**CALCITONIN (SALMON)** injection 100 units/1mL

Dose: Emergency treatment of hypercalcaemia, by slow intravenous infusion, 5 to 10 units/kg over at least 6 hours.

**S CINACALCET** tablets 30mg, 60mg, 90mg

Dose: Treatment of secondary hyperparathyroidism in patients with end-stage renal disease on maintenance dialysis therapy, initially 30mg once daily adjusted every 2 to 4 weeks to maximum 180mg daily.
Magnesium

See guidance in ‘Treatment of low electrolytes’ on Intranet (summary guidance).

**MAGNESIUM HYDROXIDE** mixture BP 1.325grams/5mL (magnesium 173mg or 7mmol/5mL)

**Dose:** *By mouth,* 5mL (7mmols) 3 times daily. Continue treatment for 48 hours after magnesium levels have returned to normal [off-label].

**MAGNESIUM GLYCEROphosphate** chewable tablets (magnesium 4mmol or 97mg/tablet) (Neomag®)

**Dose:** Initially 1 to 2 tablets 3 times daily; adjust dose according to serum total magnesium level.

**MAGNESIUM ASPARTATE DIHYDRATE** (Magnaspartate®) oral powder sachets 6.5 grams (magnesium 243mg or 10mmol/sachet)

**Dose:** One to two sachets daily, dissolved in water, tea or orange juice.

**MAGNESIUM SULFATE** injection 50% 1 gram/2mL (magnesium approx 2mmol /mL)

**Phosphate supplements**

See guidance in ‘Treatment of low electrolytes’ on Intranet (summary guidance).

**S ADDIPhOS**® injection solution (phosphate 40mmol, potassium 30mmol, sodium 30mmol/20mL)

**S DISODIUM HYDROGEN PHOSPHATE** injection solution (phosphate 6mmol, sodium 12mmol /10mL) [unlicensed].

**GLYCOPHOS**® **STERILE CONCENTRATE** injection solution (phosphate 20mmol, sodium 40mmol/20mL)

**PHOSPHATE-SANDOZ**® effervescent tablets (phosphate 16·1mmol, sodium 20·4mmol, potassium 3·1mmol/tablet)

**Phosphate-binding agents**

All patients receiving phosphate-binding agents should be assessed by a Renal Dietitian.

**CALCIUM CARBONATE** (Calcichew®) tablets 1·25 grams (calcium 500mg or 12.5mmol/tablet)

**Dose:** Initially 1 to 2 tablets 3 times daily with meals, then adjusted according to plasma-phosphate concentration.

**CALCIUM ACETATE** (Phosex®) tablets 1 gram (calcium 250mg or 6.2mmol/tablet)

**Dose:** Initially 1 tablet 3 times daily with meals, then adjusted according to plasma phosphate concentration. Tablets can be broken to aid swallowing, but not chewed (bitter taste).

**LANTHANUM** tablets 500mg, 750mg, 1 gram; powders 750mg, 1 gram

**Dose:** Initially 750mg daily in divided doses with meals or immediately after meals, then adjusted according to plasma phosphate concentration every 2 to 3 weeks.

**SEVELAMER** tablets 800mg

**Dose:** Initially 1 to 2 tablets 3 times daily with meals, then adjusted according to plasma-phosphate concentration.

**SUCROFERRIC OXYHYDROXIDE**® chewable tablets 500mg

**Dose:** Initially 1·5 grams daily in 3 divided doses, dose to be taken with meals, then adjusted in steps of 500mg every 2 to 4 weeks, dose adjusted according to serum-phosphate concentration; maintenance 1·5 to 2 grams daily in divided doses, maximum 3 grams per day.
Fluoride

**SODIUM FLUORIDE** (Duraphat®) toothpaste 0.619% (2800ppm), 1.1% (5000ppm)
For dentate patients undergoing head and neck radiotherapy, usually initiate on the 2800ppm strength. The 5000ppm strength is reserved for the most severe radiotherapy-induced caries.

Zinc supplements

**ZINC SULFATE** effervescent tablets 125mg (45mg zinc/tablet)
Dose: 1 tablet in water 1 to 3 times daily after food.

9.6 VITAMINS

Vitamin B group

All patients undergoing alcohol detoxification should be given parenteral vitamins B and C (Pabrinex®) as prophylaxis for Wernicke's encephalopathy in addition to oral thiamine. Due to the concern of long-term brain injury, and the low risk and cost of treatment, the index of suspicion for considering Wernicke's in these patients should be high and the threshold for considering the treatment recommendations low. Refer to section 4.10 and ‘Guidelines for administration of Pabrinex®/thiamine in alcohol detoxification’.

**THIAMINE (VITAMIN B₁)** tablets 50mg, 100mg
Dose: Mild deficiency, 25mg daily; severe deficiency 200mg to 300mg daily in divided doses. Patients with alcohol dependence should be prescribed oral thiamine 200mg to 300mg daily in divided doses (see guidance):
- before planned withdrawal of alcohol
- during acute withdrawal of alcohol
- for up to 12 months after acute withdrawal of alcohol, indefinitely in some cases
- for patients not undergoing alcohol withdrawal but at high risk of developing Wernicke's encephalopathy.

**PYRIDOXINE (VITAMIN B₆)** tablets 10mg, 50mg
Dose: Deficiency states, 20 to 50mg up to 3 times daily. Isoniazid induced neuropathy, prophylaxis 10mg daily; treatment, 50mg 3 times daily. Idiopathic sideroblastic anaemia, 100 to 400mg daily in divided doses.

The use of pyridoxine in premenstrual syndrome [off-label] is of doubtful value. Overdosage induces toxic effects.

**PARENTERAL VITAMINS B AND C** (Pabrinex®) high potency injection, *intravenous, intramuscular*
Dose: Refer to ‘Guidelines for administration of Pabrinex®/thiamine in alcohol detoxification’. For the administration of intramuscular Pabrinex® in primary care settings refer to the PGD.

Vitamin C

**ASCORBIC ACID** tablets 200mg, 500mg
Dose: Therapeutic, at least 250mg daily in divided doses.

Vitamin D

Following recommendation from the Scientific Advisory Committee on Nutrition, Scottish Government advice on vitamin D supplementation for all age groups has been updated. The advice is available, along with links to information leaflets for the public, health professionals and parents, at [http://www.gov.scot/Topics/Health/Healthy-Living/Food-Health/vitaminD](http://www.gov.scot/Topics/Health/Healthy-Living/Food-Health/vitaminD).
All pregnant women in NHS Highland are provided with Healthy Start maternal tablets for the duration of their pregnancy via their Midwifery antenatal contacts. These tablets contain vitamin D, folic acid and vitamin C and are provided free of charge.

Vitamin D (as colecalciferol) should usually only be prescribed:
- in line with local ‘Guidance for the identification and treatment of vitamin D deficiency’
- for patients receiving bone-active therapy for osteoporosis who are intolerant of Adcal D₃®/Calci-D®, see section 6.6.

**COLECALCIFEROL** capsules 20 micrograms (800 units), 80 micrograms (3200 units), 500 micrograms (20 000 units); tablets 20 micrograms (800 units); oral solution 2400 units/mL (InVita D₃® Oral Drops), 25 000 units/mL (InVita D₃®)

**Dose:** Refer to ‘Guidance for the identification and treatment of vitamin D deficiency’ on the Intranet. Patients with peanut allergy should avoid the capsules which may contain arachis (peanut) oil. The tablets and oral solution do not contain arachis (peanut) oil and are suitable for those with peanut allergy.

**ALFACALCIDOL** capsules 250 nanograms, 500 nanograms, 1 microgram; oral drops 100 nanograms/drop; injection 1 microgram/0·5mL

**Dose:** In renal osteodystrophy, 250 to 500 nanograms daily, then titrate according to response.

**Vitamin E**

**ALPHA TOCOPHERYL** capsules (VitaE®) 75 units (50mg), 200 units (134mg) [unlicensed]; suspension 500mg/5mL

**Dose:** Malabsorption in cystic fibrosis, 50 to 200mg daily.

**Vitamin K**

**MENADIOL** tablets 10mg

**Dose:** Malabsorption syndromes, 10mg daily.

**Note:** Konakion® MM Paediatric can be administered by intramuscular, intravenous or oral route.

**PHYTOMENADIONE** injection, in a mixed micelles vehicle (Konakion® MM Paediatric) 2mg/0·2mL, (Konakion® MM) 10mg/1mL

**Dose:** For reversal of warfarin anticoagulation seek advice from Consultant Haematologist. Vitamin K is used in patients with abnormal coagulation due to vitamin K deficiency or in patients on warfarin who are bleeding or who have a high INR. It may take up to 6 to 12 hours to act. The dose and route of administration depends on the indication; if in doubt, discuss with the Consultant Haematologist. Prothrombin complex is used in addition to vitamin K in patients who are bleeding and on warfarin or who are anticoagulated and requiring urgent surgery. It provides temporary but immediate reversal of anticoagulation and can be obtained from the Blood Transfusion Service on the authorisation of a Haematologist.

**Multivitamin preparations**

**FORCEVAL®** capsules

**Dose:** As an adjunct to synthetic diets, 1 capsule daily.

**KETOVITE®** tablets; liquid

**Dose:** As an adjunct to synthetic diets, 1 tablet 3 times daily, 5mL liquid daily. Use tablets and liquid together for complete vitamin supplementation.

**ABIDEC®** drops
Dose: Under 1 year, 0.3mL daily; 1 to 12 years, 0.6mL daily. The drops contain arachis (peanut) oil; avoid in children with peanut allergy.

**RENAVIT®** tablets
**Dose:** One tablet daily, swallowed not chewed.
This is a borderline substance which is prescribable for the dietary management of water-soluble vitamin deficiency in adults with renal failure on dialysis. Endorse script ACBS (Advisory Committee on Borderline Substances).

**S DEKAS PLUS®** chewable tablets; paediatric liquid; softgel capsules [unlicensed]
Only for use in patients with cystic fibrosis.

### 9.8 METABOLIC DISORDERS

**Wilson's disease**

**PENICILLAMINE** tablets 125mg, 250mg
**Dose:** 1.5 to 2 grams daily in divided doses before food. Maintenance 750mg to 1 gram daily for 1 year. Maximum 2 grams daily.
## TOTAL PARENTERAL NUTRITION REGIMES

<table>
<thead>
<tr>
<th>COMPONENTS</th>
<th>Reg 1</th>
<th>Reg 2</th>
<th>Reg 3</th>
<th>Reg 4</th>
<th>Reg 5</th>
<th>Reg 6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Peripheral OR</td>
<td>Peripheral OR</td>
<td>Central (NuTRIflex Lipid Peri 1250mL)</td>
<td>Central</td>
<td>Central</td>
<td>Central</td>
</tr>
<tr>
<td>TOTAL Nitrogen (g)</td>
<td>5-7</td>
<td>11-4</td>
<td>10-2</td>
<td>13-6</td>
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<td>20</td>
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<tr>
<td>TOTAL Glucose (g)</td>
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<td>160</td>
<td>225</td>
<td>300</td>
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<td>TOTAL Lipid (g)</td>
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<td>TOTAL (Kcal)</td>
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<td>1890</td>
<td>2515</td>
<td>1890</td>
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<tr>
<td>Sodium (mmol)</td>
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<tr>
<td>Potassium (mmol)</td>
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<td>52-5</td>
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<td>70-5</td>
<td>60</td>
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<td>Calcium (mmol)</td>
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<td>6</td>
<td>8</td>
<td>7-95</td>
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<tr>
<td>Magnesium (mmol)</td>
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<td>Phosphate (mmol)</td>
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<td>Cernevit (1vial)</td>
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<tr>
<td>Additrace (10mL)</td>
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<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Infusion rate mL/hour over 24 hours</td>
<td>52</td>
<td>104</td>
<td>78</td>
<td>104</td>
<td>78</td>
<td>106</td>
</tr>
</tbody>
</table>

### Out of hours supply
Raiigmore Hospital holds emergency stocks of NuTRIflex Lipid Peri 1250mL. This bag is highlighted in grey above, however bags taken from emergency stock will **not** contain Cernevit and Additrace. If TPN is required outside Pharmacy opening hours, this is the only bag which may be used. The NuTRIflex 1250mL bag can be administered via both a central line and a peripheral cannula. The NuTRIflex Lipid 1250mL TPN bag should be prescribed on the fluid chart with the rate of administration added. The flow rate should be 26mL/hour for the first 48 hours for patients starting TPN or until the patient has been assessed by a Dietitian. Refer these patients to a Dietitian as soon as possible.
GUIDELINES FOR ADMINISTRATION OF PABRINEX®/THIAMINE IN ALCOHOL DETOXIFICATION

Parenteral Pabrinex®

Alcohol dependent individuals requiring detoxification should be offered Pabrinex®.

Patients detoxifying in the community should be given Pabrinex® if they present with features which put them at risk of Wernicke’s encephalopathy (WE) (those with diarrhoea, vomiting, physical illness, weight loss, poor diet). There is a PGD for the administration of intramuscular Pabrinex® in primary care settings on Intranet.

For guidance on use of Pabrinex® see below.

- Always give Pabrinex® and thiamine BEFORE the administration of carbohydrate or glucose fluids to avoid precipitation of WE.
- See also ‘The Royal College of Physicians report on alcohol: guidelines for managing Wernicke’s encephalopathy in the Accident and Emergency department’ at: http://alcalc.oxfordjournals.org/content/37/6/513.full.pdf+html

A presumptive diagnosis of WE should be made with a history of alcohol abuse or current intoxication and one or more of the following unexplained symptoms:

- acute confusion
- ophthalmoplegia/nystagmus
- ataxia
- memory disturbance
- comatose/unconscious, hypotension and hypothermia.

If there is no response to parenteral Pabrinex®, seek specialist advice to rule out alternative diagnoses.

*Parenteral Pabrinex® – two formulations exist, ensure you are using the appropriate formulation for the route prescribed.

| Intramuscular Pabrinex® (store in refrigerator) | Preferred in settings where there are difficulties with intravenous access. | Dose: If symptom(s) present, ONE pair of ampoules twice daily for 3 days then if a response, one pair of ampoules once daily for 5 days, or for as long as improvement continues. If no symptoms present, ONE pair of ampoules once daily for 5 days. |
| Intravenous Pabrinex® (store at room temperature) | May offer a more rapid response than intramuscular and is therefore preferred in emergency cases. Prepare by diluting one pair of ampoules in 50 to 100mL sodium chloride 0·9% and administer by intravenous infusion over 30 minutes. | Dose: If symptom(s) present, TWO pairs of ampoules (BNF allows up to 3 pairs) 3 times daily for two days followed by ONE pair of ampoules once daily for up to 5 days, or for as long as improvement continues. If no symptoms present ONE pair of ampoules once daily for 3 to 5 days. |

Note: The risk of anaphylaxis is very small with Pabrinex®, however, in accordance with MHRA/CHM guidance, administration of Pabrinex® should only take place when appropriate resuscitation facilities are available. The clinical decision as to when to use intramuscular or intravenous preparation should be based on the local skills, facilities and patient group.

Oral thiamine

High dose oral thiamine: 200mg to 300mg daily in divided doses.

Two regimes are in use in NHS Highland:

- 50mg 4 times daily
- 100mg 3 times daily.

ALL alcohol dependent individuals requiring detoxification should be prescribed high dose oral thiamine along with Pabrinex®.

Consider prescribing high dose oral thiamine for all heavy drinkers.

There is clear consensus that oral thiamine cannot treat WE and may not prevent WE in patients at high risk of WE. In such patients all the guidance is consistent in advising that parenteral thiamine should be employed.

In the longer term, adherence with regimes requiring more than twice daily administration of medication is poor. Some thiamine is probably better than none after the acute phase, if adherence with multiple divided doses is problematic.
<table>
<thead>
<tr>
<th>Electrolyte</th>
<th>Level</th>
<th>Initial prescribing action</th>
<th>Monitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphate</td>
<td>Greater than 0·5 to 0·8mmol/L</td>
<td>No supplementation is required if dietary intake adequate.</td>
<td>Check phosphate after 24 hours.</td>
</tr>
<tr>
<td></td>
<td>0·3 to 0·5mmol/L</td>
<td>Asymptomatic patients may not need to be treated. Oral: 2 Phosphate Sandoz® tablets daily. Via enteral feeding tube: dissolve tablet(s) in 50mL water. Stopping feed is not required. Intravenous: peripheral administration – 10mL Glycophos® diluted in 250mL glucose 5% or sodium chloride 0·9%. Infuse over 12 hours. <strong>Half above doses in patients with eGFR ≤ 30mL/min.</strong></td>
<td>Check potassium, phosphate and adjusted calcium every 24 hours.</td>
</tr>
<tr>
<td></td>
<td>Less than 0·3mmol/L</td>
<td>Intravenous: peripheral administration – 20mL Glycophos® diluted in 500mL glucose 5% or sodium chloride 0·9%. Infuse over 12 hours. <strong>Half above dose in patients with eGFR less than 30mL/min.</strong></td>
<td>Check adjusted calcium, phosphate, sodium, magnesium and potassium every 12 hours.</td>
</tr>
<tr>
<td>Magnesium</td>
<td>0·5 to 0·7mmol/L</td>
<td>Oral: 5mL magnesium hydroxide mixture 3 times daily. Via enteral feeding tube: 1 to 2 magnesium glycerophosphate tablets 3 times daily. Crush tablets and dissolve in 50mL water. <strong>Half above dose in adults with eGFR less than 30mL/min.</strong></td>
<td>Check magnesium levels daily.</td>
</tr>
<tr>
<td></td>
<td>Less than 0·5mmol/L</td>
<td>Intravenous: peripheral administration – 10mL magnesium sulfate 50% injection in 250mL glucose 5% over 3 hours. Give 3 doses at 12 hour intervals. <strong>If eGFR less than 30mL/min – 10mmol (5mL) magnesium sulfate 50% (2mmol/mL) in 250mL glucose 5% over 6 hours. Give 3 doses at 12 hour intervals.</strong></td>
<td>Monitor BP, heart rate, respiratory rate, urine output and for signs of hypermagnesaemia during infusion. Check magnesium 6 hours after third infusion ends unless eGFR&lt;30mL/min. <strong>eGFR&lt;30mL/min see full guidance on Intranet.</strong></td>
</tr>
<tr>
<td>Adjusted calcium</td>
<td>2·0 to 2·25mmol/L</td>
<td>Oral: Sandocal® 1000, 1 to 2 tablets daily. Prescribe out with mealtimes. Via enteral feeding tube: dissolve Sandocal® 1000, 1 to 2 tablets daily in 30 to 50mL water. Consider alfacalcidol if patient has renal failure.</td>
<td>Recheck adjusted calcium after 24 hours.</td>
</tr>
<tr>
<td></td>
<td>Less than 2·0mmol/L</td>
<td>Intravenous: 50mL (11·25mmol) calcium gluconate 10% injection in 500mL sodium chloride 0·9% or glucose 5%. Infuse over 6 hours. <strong>If eGFR less than 30mL/min – 10mL calcium gluconate 10% injection. IV bolus over 5 minutes THEN 50mL (11·25mmol) calcium gluconate 10% in 500mL sodium chloride 0·9% or glucose 5%. Infuse over 4 hours.</strong></td>
<td>Check adjusted calcium and magnesium 60 minutes after infusion ends.</td>
</tr>
<tr>
<td>Potassium</td>
<td>3·0 to 3·5mmol/L</td>
<td>Oral: Sando-K® 2 tablets 3 times daily.</td>
<td>Monitor potassium after 2 days treatment then twice weekly until stable.</td>
</tr>
<tr>
<td></td>
<td>2·5 to 2·9mmol/L and low risk of complications</td>
<td>Oral: Sando-K® 3 tablets 3 times daily.</td>
<td>Monitor potassium daily until plasma K⁺ &gt;2·9mmol/L and then monitor as for 3·0 to 3·5mmol/L.</td>
</tr>
</tbody>
</table>
CHAPTER 10  MUSCULOSKELETAL AND JOINT DISEASE

10.1  DRUGS USED IN RHEUMATIC DISEASES AND GOUT

Non-steroidal anti-inflammatory drugs (NSAIDs)

Refer to local guidance on NSAIDs before initiating therapy:

- ‘Non-steroidal anti-inflammatory drugs (NSAIDs)’

**FIRST CHOICE**: IBUPROFEN (1-2 GRAMS/DAY OR LESS) or NAPROXEN

**IBUPROFEN** tablets 200mg\(^{\text{OTC}}\), 400mg\(^{\text{OTC}}\), 600mg; oral suspension 100mg/5mL\(^{\text{OTC}}\)

**Dose**: Initially 600mg to 1·8 grams daily in 3 to 4 divided doses, preferably after food; higher doses may be necessary in rheumatoid arthritis or gout; maximum of 2·4 grams daily. For OTC use the maximum dose is 1·2 grams daily. All risks increase above 1·2 grams daily. Maintenance dose of 600mg to 1·2 grams daily may be adequate.

**NAPROXEN** tablets 250mg\(^{\text{OTC}}\), 500mg; oral suspension 250mg/5mL

**Dose**: 500mg to 1 gram daily in 1 to 2 divided doses. Acute musculoskeletal disorders, 500mg initially, then 250mg every 6 to 8 hours as required, maximum dose after first day 1 gram daily. Acute gout, 750mg initially, then 250mg every 8 hours until attack has passed.

**CELECOXIB** capsules 100mg, 200mg

**Dose**: Osteoarthritis, 200mg daily in 1 to 2 divided doses, increased if necessary to maximum 200mg twice daily. Rheumatoid arthritis, 200 to 400mg daily in 2 divided doses; older people, initially 200mg daily in 2 divided doses; maximum 200mg twice daily.

**Note**: Diclofenac is associated with an increased risk of thrombotic events.

**DICLOFENAC** e/c tablets 25mg, 50mg; m/r tablets 75mg, 100mg; suppositories 12·5mg, 25mg, 50mg, 100mg; injection 75mg/3mL

**Dose**: By mouth, 75 to 150mg daily in 2 to 3 divided doses, preferably after food; by rectum, 75 to 150mg daily in divided doses; by injection see section 7.4. Maximum of 150mg daily by any route.

Corticosteroids

Systemic corticosteroids

**PREDNISOLONE** tablets 1mg, 5mg, 25mg; soluble tablets 5mg

**Dose**: Dose varies according to condition. Refer to BNF. If possible, avoid use of the high-cost prednisolone tablets 25mg and soluble tablets 5mg.

Do not use oral prednisolone or injectable corticosteroid prior to referral of a patient with suspected inflammatory joint disease. Corticosteroids are used, along with disease modifying therapy in the induction of remission of inflammatory arthritis once baseline prognostic factors have been assessed and treatment stratification allocated. Refer to SIGN guideline 123 for ‘Early Rheumatoid Arthritis’. For polymyalgia rheumatica, the majority of patients should respond to prednisolone 10 to 15mg daily. If patients fail to respond within 2 weeks cease treatment and review the diagnosis. Treatment is usually required for a minimum of 18 months; consider densitometry and bone protection at commencement (see section 6.6). Further advice is available on the Department of Rheumatology home page on Intranet. Larger doses of prednisolone are used to treat connective tissue disease and temporal arteritis.
Local corticosteroid injections

**Note:** Generally, no more than 3 joints to be injected on one day and no more than 3 injections per joint per year. If failure to respond, refer for specialist advice.

**HYDROCORTISONE** (as acetate) injection (aqueous suspension) 25mg/1mL
*Dose:* By *intra-articular or intrasynovial injection*, 5 to 50mg according to size of joint.

**METHYLPREDNISOLONE** (as acetate) injection (aqueous suspension) 40mg/1mL
*Dose:* By *intra-articular or intrasynovial injection*, 4 to 80mg according to size of joint.

**TRIAMCINOLONE** (as acetonide) injection (aqueous suspension) 10mg/1mL, 40mg/1mL
*Dose:* By *intra-articular injection or intrasynovial injection*, 2.5 to 40mg according to size of joint; total maximum 80mg.

**DEPO-MEDRONE® WITH LIDOCAINE** (methylprednisolone acetate 40mg, lidocaine 10mg/1mL) injection (aqueous suspension)
*Dose:* By *intra-articular or intrasynovial injection*, 4 to 80mg (of methylprednisolone) according to size of joint.

Drugs that modify the rheumatic disease process

All the drugs listed in this section should be initiated only on the advice of a Consultant Rheumatologist. **Regular monitoring is required for all drugs in this section**, which may include urine testing, full blood counts, liver enzymes and blood pressure monitoring. British Society for Rheumatology (BSR) guidance is generally followed; any variation in therapy will be specified on the Department of Rheumatology home page. For advice on monitoring refer to Appendix 2: Universal requirements for monitoring of conventional DMARDS in primary care.

For GP and patient advice on individual drugs and combination therapy, which is now the norm, refer to Department of Rheumatology home page and to product information (SPC).

Gold

**Note:** Sodium aurothiomalate
Warn patient to tell prescriber immediately if diarrhoea, sore throat, fever, infection, non-specific illness, unexplained bleeding and bruising, purpura, mouth ulcers, metallic taste, or rashes develop; also ask patients to report immediately any breathlessness or cough. Monitor urine tests and full blood counts before each dose.

**SODIUM AUROTHIOMALATE** injection 10mg/0.5mL, 50mg/0.5mL
*Dose:* Refer to Department of Rheumatology GP information leaflet for sodium aurothiomalate.

Antimalarials

**Note:** Hydroxychloroquine
Pre-treatment and annual eye checks are essential; refer to advice from Royal College of Ophthalmologists.

**HYDROXYCHLOROQUINE** tablets 200mg
Refer to Department of Rheumatology GP information leaflet for hydroxychloroquine.
Drugs affecting the immune response

Immunisation is actively promoted in patients with immune disorders, particularly if treated with immune-modulators; refer to Department of Rheumatology guidance ‘Vaccinations in the immunocompromised person’.

**AZATHIOPRINE** tablets 25mg, 50mg
Refer to Department of Rheumatology [GP information leaflet](#) for azathioprine. Monitor in accordance with ‘Universal requirements for monitoring of conventional DMARDs in primary care’ in Appendix 2.

**CICLOSPORIN** capsules (Neoral®) 25mg, 50mg, 100mg
Refer to Department of Rheumatology [GP information leaflet](#) for ciclosporin. Monitor in accordance with ‘Universal requirements for monitoring of conventional DMARDs in primary care’ in Appendix 2.

**CYCLOPHOSPHAMIDE** tablets 50mg, injection 1 gram
Refer to Department of Rheumatology [GP information leaflet](#) for cyclophosphamide; note the requirement for antibiotic prophylaxis for some patients.

**LEFLUNOMIDE** tablets 10mg, 15mg, 20mg
Refer to Department of Rheumatology [GP information leaflet](#) for leflunomide. Monitor in accordance with ‘Universal requirements for monitoring of conventional DMARDs in primary care’ in Appendix 2.

**METHOTREXATE** tablets 2.5mg; injection pre-filled pen (Metoject®) 7.5mg/0.15mL, 10mg/0.2mL, 12.5mg/0.25mL, 15mg/0.3mL, 17.5mg/0.35mL, 20mg/0.4mL, 22.5mg/0.45mL, 25mg/0.5mL, 27.5mg/0.55mL, 30mg/0.6mL; injection pre-filled syringes (Zlatal®) 7.5mg/0.3mL, 10mg/0.4mL, 12.5mg/0.5mL, 15mg/0.6mL, 17.5mg/0.7mL, 20mg/0.8mL, 22.5mg/0.9mL, 25mg/1mL
Refer to Department of Rheumatology GP information leaflets for oral methotrexate and parenteral methotrexate and to the shared care protocol for subcutaneous methotrexate. Monitor in accordance with ‘Universal requirements for monitoring of conventional DMARDs in primary care’ in Appendix 2.

**MYCOPHENOLATE MOFETIL** capsules 250mg; tablets 500mg; oral suspension 1 gram/5mL
Refer to Department of Rheumatology [GP information leaflet](#) for mycophenolate. Monitor in accordance with ‘Universal requirements for monitoring of conventional DMARDs in primary care’ in Appendix 2.

**MYCOPHENOLIC ACID** (as mycophenolate sodium) e/c tablets (Myfortic®) 180mg, 360mg
Monitor in accordance with ‘Universal requirements for monitoring of conventional DMARDs in primary care’ in Appendix 2.

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**Note: Ciclosporin**
Due to differences in bioavailability, specify the brand of oral ciclosporin to be dispensed.

**Note: Oral methotrexate**
- Pay attention to the strength of methotrexate tablets prescribed and the frequency of dosing; methotrexate is always given weekly. Prescribing and dispensing errors have caused fatalities.
- Folic acid ([section 9.1](#)) may lessen some toxic side-effects of methotrexate, eg nausea and mucositis (see dose advice in GP leaflet on Intranet) but continued monitoring of the full blood count, liver and renal function tests and a close watch for other untoward symptoms are required.
Cytokine modulators

See local prescribing advice on Rheumatology home page on Intranet.

\textbf{S Adalimumab} solution for injection, pre-filled syringe 40mg/0.4mL; pre-filled pen 40mg/0.4mL
Refer to Department of Rheumatology GP information leaflet for adalimumab.

\textbf{S Certolizumab Pegol} solution for injection, pre-filled syringe 200mg/1mL

\textbf{S Etanercept} solution for injection 25mg vial (Enbrel®); pre-filled syringe (Enbrel®, Benepali®) 25mg, 50mg; pre-filled pen 25mg (Enbrel®), 50mg (Enbrel®, Benepali®)
Prescribe etanercept by brand name.
Refer to Department of Rheumatology GP information leaflet for etanercept.

\textbf{S Infliximab} (Remicade®, Inflectra®) powder for concentrate for solution for infusion 100mg
Prescribe infliximab by brand name.

\textbf{S Baricitinib} (Olumiant®) tablets 2mg, 4mg
Refer to Department of Rheumatology GP information leaflet for baricitinib.

\textbf{S RituXimab} (Truxima®) concentrate for solution for infusion 100mg/10mL, 500mg/50mL
Prescribe rituximab by brand name.
Refer to Department of Rheumatology GP information leaflet for rituximab.

\textbf{S Tocilizumab} concentrate for solution for intravenous infusion 80mg/4mL, 200mg/10mL, 400mg/20mL; solution for injection, pre-filled syringe 162mg/0.9mL
Refer to Department of Rheumatology GP information leaflet for subcutaneous tocilizumab.

\textbf{S Secukinumab} solution for injection, pre-filled syringe 150mg
Refer to Department of Rheumatology GP information leaflet for secukinumab (Cosentyx®).

Phosphodiesterase-4 (PDE4) inhibitors

\textbf{S Apremilast} tablets in treatment initiation pack 10mg, 20mg, 30mg; tablets 30mg
Refer to Department of Rheumatology GP information leaflet for apremilast.

Sulfasalazine

\textbf{CSM advice: Sulfasalazine}
Advise patients receiving sulfasalazine to report any unexplained bleeding, bruising, purpura, sore throat, fever or malaise that occurs during treatment. Perform a blood count and stop the drug if there is suspicion of a blood dyscrasia.
Note that enteric-coated sulfasalazine tablets are preferred in rheumatoid arthritis patients because they cause less nausea and fewer gastrointestinal side-effects than standard tablets.

\textbf{S Sulfasalazine} e/c tablets 500mg; suspension 250mg/5mL
Refer to Department of Rheumatology GP information leaflet for sulfasalazine. Monitor in accordance with ‘Universal requirements for monitoring of conventional DMARDs in primary care’ in Appendix 2.

Gout and cytotoxic-induced hyperuricaemia

Refer to ‘Management of gout’ guidance on the Department of Rheumatology page on the intranet.
Acute attacks

For the management of acute gout consider:

- intra-articular methylprednisolone injection if one accessible joint affected.
- high-dose NSAIDs (used in the majority of patients) – the choice is based on GI bleeding risk and patient preference; naproxen may be used in place of indometacin (non-Formulary).
- oral prednisolone 20 to 40mg daily tapered over 2 weeks may be useful if above unsuitable.
- colchicine is an alternative, but can cause renal impairment and should be used with caution in GI disease. It is useful in heart failure and in those taking oral anticoagulants.

**COLCHICINE** tablets 500 micrograms
**Dose:** Refer to Department of Rheumatology guidance on the management of acute and chronic gout.

Long-term control of gout

<table>
<thead>
<tr>
<th>FIRST CHOICE:</th>
<th>ALLOPURINOL</th>
</tr>
</thead>
<tbody>
<tr>
<td>SECOND CHOICE:</td>
<td>FEBUXOSTAT</td>
</tr>
</tbody>
</table>

Consider allopurinol for long-term control in patients with acute attacks of gouty arthritis:

- with more than one episode in a year
- if attempts to reduce risk factors have failed
- with tophi, clinical or radiological signs of chronic gouty arthritis
- with recurrent uric acid renal stones.

Co-prescription with NSAIDs or colchicine 500 micrograms twice daily is often required for 6 months to 1 year. Febuxostat may be used for those with intolerance to allopurinol or mild to moderate renal impairment (caution with febuxostat if eGFR less than 30mL/min/1·73m²). Refer to ‘Management of gout’ guidance on the Rheumatology home page on the intranet.

**ALLOPURINOL** tablets 100mg, 300mg
**Dose:** Introduce allopurinol after the acute attack has settled, starting with a dose of 100mg/day after food, adjusted at fortnightly intervals to achieve serum urate less than 0·36 mmol/L. Usual maintenance dose: in mild conditions, 100 to 200mg daily; in moderately severe conditions, 300 to 600mg daily; in severe conditions, 700 to 900mg daily. Doses of over 300mg daily should be given in divided doses of up to 300mg. Monitor renal function in ‘at risk’ patients. Do not use allopurinol in patients with eGFR <30mL/min/1·73m².

**Note: Febuxostat**

- may be used when treatment with allopurinol is inadequate, not tolerated or contra-indicated
- aim to achieve serum urate levels less than 0·36mmol/L
- consider for patients with mild to moderate renal impairment (use febuxostat with caution if eGFR less than 30mL/min/1·73m²)
- avoid in patients with ischaemic heart disease or congestive heart failure
- check liver function prior to initiation and every 6 months thereafter
- febuxostat can cause serious skin conditions, see www.mhra.gov.uk.

**FEBUXOSTAT** tablets 80mg, 120mg
**Dose:** Initially 80mg once daily, if after 2 to 4 weeks the serum uric acid is greater than 0·36mmol/L then increase to 120mg once daily.

Hyperuricaemia associated with cytotoxic drugs

Allopurinol and rasburicase are used to prevent, and rasburicase is also used to treat, hyperuricaemia associated with cytotoxic drugs.
CHAPTER 10 MUSCULOSKELETAL AND JOINT DISEASE

**RASBURICASE** intravenous infusion 1.5mg, 7.5mg

### 10.2 DRUGS USED IN NEUROMUSCULAR DISORDERS

**Drugs that enhance neuromuscular transmission**

Neostigmine, pyridostigmine and immunosuppressants, eg prednisolone (section 6.3), azathioprine (section 8.2), are used to treat myasthenia gravis, whereas edrophonium is used in the diagnosis.

**PYRIDOSTIGMINE** tablets 60mg  
**Dose:** By mouth, 30 to 120mg at suitable intervals throughout day. Doses exceeding 360mg daily should only be prescribed in consultation with a specialist. Gastro-intestinal side-effects are common and can be treated with the antimuscarinic propantheline bromide (non-Formulary).

**EDROPHONIUM** injection 10mg/1mL [unlicensed]  
Stock is held in Raigmore Hospital emergency drug cupboard.

**NEOSTIGMINE** injection 2.5mg/1mL

**Spasticity**

***Note:***  
- Management of spasticity involves attention to posture; pain; bowel and bladder function as well as the use of medication.  
- All antispasticity drugs can cause tiredness and affect performance of skilled tasks, eg driving. Care is needed in patients with weakness and spasticity as they may be relying on the muscle tone to maintain posture.  
- Relaxation of the external bladder sphincter may contribute to urinary incontinence.  
- For specialist advice contact Rehabilitation Medicine.

**FIRST CHOICE:** **BACLOFEN**

**CSM advice:** Baclofen  
Serious side-effects can occur on abrupt withdrawal of baclofen. Discontinue by gradual dose reduction over at least 1 to 2 weeks (longer if symptoms occur).

**BACLOFEN** tablets 10mg; oral solution 5mg/5mL  
**Dose:** By mouth, 5mg 3 times daily, preferably with or after food, gradually increased; maximum 100mg daily (discontinue if no benefit within 6 weeks).

***Note:** Prescribers should be aware of the abuse potential with Sativex® and the risk of diversion.

**CANNABIS EXTRACT** (Sativex®) oromucosal spray containing dronabinol 27mg/mL and cannabidiol 25mg/mL  
Sativex® can be used in the treatment of spasticity and symptoms of neuropathic pain [off-label] in multiple sclerosis where first-line treatments have failed to control the symptoms. There is limited evidence for its effectiveness and due to non-submission of evidence, it is not recommended by SMC. Use of Sativex® should be closely controlled and only through, and under review of, the shared care protocol on Intranet. See also www.gov.uk.
### CHAPTER 10 MUSCULOSKELETAL AND JOINT DISEASE

#### 10.3 DRUGS FOR RELIEF OF SOFT-TISSUE DISORDERS AND TOPICAL PAIN RELIEF

**Enzymes**

* **COLLAGENASE** injection 900 micrograms
  For Hand Surgeon use only.

* **HYALURONIDASE** injection 1500 units
**Dose:** Extravasation, for use according to the ‘Extravasation Policy’ available in wards or departments where chemotherapy is administered. Hypodermoclysis, 1500 units dissolved in 1mL of water for injections or 0·9% sodium chloride injection, administered by subcutaneous injection before start of 500 to 1000mL infusion fluid.

**Topical NSAIDs and counter-irritants**

There is some evidence that topical NSAIDs have an effect in acute conditions like strains and sprains and in chronic conditions like arthritis and rheumatism. Simple analgesics or topical rubefacients may provide symptomatic relief and may be considered as an alternative. Generally unsuitable for children. Patient packs carry a warning to avoid during pregnancy or breast-feeding. A range of topical NSAIDs and rubefacients, including ibuprofen gel, is available to the public for self-medication from pharmacies and retail outlets. The cooling effect of levomenthol on the skin may be helpful.

**Note: Topical NSAIDs**

- Topical application of large amounts of NSAIDs may result in systemic effects including hypersensitivity and asthma (renal disease has also been reported).
- Giving NSAIDs by multiple routes has an additive effect, eg oral and topical.

**IBUPROFEN** topical gel 5%\textsuperscript{Otc}

**Dose:** Apply up to 3 times daily; review therapy after 14 days (or after 28 days for osteoarthritis).

**Note: Capsaicin**

Caution; wash hands immediately after use. Avoid contact with eyes and inflamed or broken skin.

**CAPSAICIN** cream 0·025%, 0·075%

**Dose:** 0·025%, for symptomatic relief in osteoarthritis, apply a small amount 4 times daily. 0·075%, for post-herpetic neuralgia (important: after lesions have healed) apply sparingly 3 to 4 times daily for 8 weeks then review. Watch carefully for broken skin and pressure sores in the feet and advise patients to stop treatment and seek help if there is any break in the skin or increasing irritation.

**LEVOMENTHOL CREAM 1%** (menthol 1% in aqueous cream; Arjun\textsuperscript{®})

Apply 1 to 2 times daily. See section 13.2 for use as an antipruritic.
NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS)

GENERAL CONSIDERATIONS

- **Peri-operative period**: refer to ‘Acid suppression therapy’ (p110) in Department of Surgery and Urology *Junior Doctor Handbook*.

- Prescribe only **one** NSAID at any one time (excluding low-dose aspirin). This includes topical preparations.

- Upper gastro-intestinal bleeding and ulceration occurs irrespective of the route of administration. The first indication of damage may be life-threatening complications. The risk of bleeding markedly increases after 5 days of treatment, especially in older people.

- Consider other methods of management before resorting to NSAIDs, eg intra-articular corticosteroid for acute *gout*, lifestyle advice and simple analgesics for osteoarthritis.

- There is no league table of efficacy or strength of NSAID and response seems to vary between individuals. Toxicities however do vary between preparations:
  - ibuprofen in low dose (up to 1-2 grams/day) has the lowest risk of gastro-intestinal toxicity compared to naproxen, diclofenac and indometacin.
  - celecoxib is associated with reduced gastro-intestinal risk relative to most NSAIDs at equivalent doses.
  - all NSAIDs, including cyclo-oxygenase-2-selective (COX-2) inhibitors, are relatively contra-indicated in those with previous peptic ulcer disease.
  - diclofenac can cause alteration in liver function tests and even hepatic necrosis; periodic checks of liver function are therefore required. Diclofenac should be withdrawn in cases of elevation of hepatic enzymes even when thought to be due to other therapy, eg DMARDs.

- The use of modified-release preparations is not recommended as sustained high levels may be associated with increased gastro-intestinal toxicity, similar to the effect of NSAIDs with a long half-life. They are only recommended when compliance is in doubt and could be improved by once-daily dosing.

- Review the continued use of NSAIDs on a regular basis – when inflammatory arthritis is in remission or a state of low disease activity then a trial of withdrawal of NSAID should always be attempted.

- Withdraw NSAIDs if patients develop worsening renal impairment. When NSAIDs are commenced in patients with pre-existing renal impairment check U&Es 1 to 2 weeks after initiation and periodically thereafter.

- Where possible avoid the concomitant use of NSAID and ACE inhibitor or angiotensin-II receptor antagonist. In this scenario U&Es should be checked 1 to 2 weeks after initiation and periodically thereafter.

- NSAIDs may lead to hypertension and increase cardiovascular risk. All NSAIDs, both unselective and cyclo-oxygenase-2-selective (COX-2) inhibitors, have a similar risk although naproxen and low-dose ibuprofen (up to 1-2 grams/day) appear to have a lower thrombotic risk than other NSAIDs, or COX-2 inhibitors. Diclofenac is associated with an increased risk of thrombotic events.

- There is a two-fold risk of hospitalisation for congestive cardiac failure when using NSAIDs in older people or those with existing heart failure.
### CONTRA-INDICATIONS

- known sensitivity to aspirin or other NSAID
- recent history of peptic ulcer disease
- patients with poorly-controlled asthma (including patients requiring oral steroids)
- moderate to severe renal impairment (eGFR less than 30)
- severe congestive cardiac failure requiring high-dose diuretics
- poorly-controlled hypertension
- bleeding problems, eg low platelets, known coagulopathy, on heparin infusion or high-dose enoxaparin
- severe liver dysfunction
- poorly-controlled diabetes
- pregnancy
- severe pregnancy-induced hypertension with proteinuria
- avoid in patients taking certain drugs, eg mifepristone.

### USE WITH CAUTION*

- mild to moderate renal impairment (eGFR less than 60)
- if eGFR less than 45 seek senior medical advice before use
- renal transplant patients with good function
- older patients (over 65 years)
- diabetes
- patients with inflammatory bowel disease (flare can be induced)
- peripheral vascular disease or treated cardiac failure
- after hepatobiliary, renal or major vascular surgery
- patients taking:
  - diuretics, especially potassium-sparing
  - ACE inhibitors, angiotensin-II receptor antagonists
  - ciclosporin
  - lithium – lithium toxicity may occur
  - see BNF for other drug interactions.
  - see ‘Sick day rule’ card
- correct dehydration, hypovolaemia and large blood losses prior to starting NSAIDs.

*In all of these patients where caution is advised, consider reducing the frequency of the NSAID and monitor renal function regularly. Any increasing trend in plasma urea, creatinine or potassium is an indication for stopping the NSAID.

### Gastroprotection

The following patients are at increased risk of GI complications. If an NSAID is considered absolutely necessary they should be co-prescribed lansoprazole or omeprazole (section 1.3):

- age over 75 years
- concomitant use of medicines known to increase risk of GI bleeds (ie anticoagulants, aspirin, corticosteroids, SSRIs, venlafaxine, duloxetine)
- history of GI ulcer/bleeding
- excessive alcohol/smoking.
CHAPTER 11 EYE

In General Practice discard eye drop bottles 28 days after opening and in hospitals discard after 7 days unless otherwise stated.

When patients are administering more than one preparation for the eye at the same time of the day, advise them to allow a five minute interval before administering the next drug.

Be aware of the potential for systemic side-effects of topically administered drugs (eg beta-blockers such as timolol).

In general, doses given are for adults unless a child’s dose is specified. Doses, indications and durations specified may differ from those for preparations available over the counter (OTC).

Patients on long-term eye drops may develop sensitivity reactions which may be to active ingredients or to preservative systems. They should be switched to unpreserved preparations. For information on preservatives and potential sensitisers in ocular preparations refer to the SPC; GPs may also refer to the table on www.mims.co.uk.

For patients who have difficulty handling eye dropper bottles consider use of compliance aids; refer to Eye Products section of Part 3 of Scottish Drug Tariff.

For information on unlicensed ophthalmic products refer to the ‘Unlicensed and off-label medicines list’ on the Intranet and to Royal College of Ophthalmologist guidance at www.rcophth.ac.uk.

11.3 ANTI-INFECTIVE EYE PREPARATIONS

Antibacterials

If asked to treat cases of conjunctivitis in patients aged 2 years and over, recommend simple eye cleansing measures (eg remove lash debris) in preference to chloramphenicol which has been shown to be no better than placebo. If there is no improvement after a few days consider a trial of chloramphenicol. Viral conjunctivitis is common and is self-limiting but may take several days to weeks to resolve. For the management of blepharitis encourage regular eyelid hygiene.

Chloramphenicol eye drops are well-tolerated and the recommendation that they should be avoided because of an increased risk of aplastic anaemia is not well-founded. Fusidic acid viscous eye drops can be administered twice daily, however they have a narrower spectrum of action than chloramphenicol and are significantly more expensive.

**FIRST CHOICE:** CHLORAMPHENICOL
**SECOND CHOICE:** FUSIDIC ACID

CHLORAMPHENICOL eye drops 0.5% OTC; preservative-free eye drops 0.5%; eye ointment 1% OTC

*Dose:* *Eye drops,* apply 1 drop at least every 2 hours then reduce frequency as infection is controlled and continue for 48 hours after healing; *eye ointment,* apply either at night (if drops used during the day) or 4 times daily (if eye ointment used alone). Chloramphenicol eye drops and ointment are available for the counter for adults and for children over the age of 2 years for a maximum of 5 days treatment; see Appendix 5 Minor Ailments Service Formulary.

FUSIDIC ACID eye drops 1% (in gel basis)

*Dose:* Apply twice daily and continue for 48 hours after healing.
GENTAMICIN drops 0·3%, 1·5%
Dose: Apply 1 drop at least every 2 hours then reduce frequency as infection is controlled and continue for 48 hours after healing.
High strength gentamicin eye drops 1·5% [unlicensed] are available from special-order manufacturers; for information contact Medicines Information.

S OFLOXACIN eye drops 0·3%
Dose: Apply 1 drop at least every 2 hours then reduce frequency as infection is controlled and continue for 48 hours after healing. Treat for a maximum of 10 days.

S LEVOFLOXACIN eye drops 5mg/mL
Dose: Apply 1 drop every 2 hours (maximum 8 times daily) for the first 2 days, then 4 times daily for 3 days.

S CEFUROXIME preservative-free eye drops 5% [unlicensed]
Available from special-order manufacturers; for information contact Medicines Information.

Antivirals

ACICLOVIR eye ointment 3%
Dose: Apply 5 times daily (continue for at least 3 days after complete healing, maximum 14 days).

GANCICLOVIR eye gel 0·15%
Dose: Apply 5 times daily (continue for at least 3 days after complete healing, maximum 14 days).

11.4 CORTICOSTEROIDS AND OTHER ANTI-INFLAMMATORY PREPARATIONS

Corticosteroids

Topical corticosteroids should normally only be used under expert supervision for the short-term treatment of local inflammation. Prescribers must be certain of the diagnosis before prescribing topical corticosteroids as their use may aggravate dendritic ulcers caused by herpes simplex and, in patients predisposed to simple glaucoma, a ‘steroid glaucoma’ may be produced. Fluorometholone is less likely to cause ‘steroid glaucoma’.

S BETAMETHASONE drops 0·1%; eye ointment 0·1%
Dose: Eye drops, apply 1 drop 4 times daily; uncontrolled inflammation up to every hour until controlled then reduce frequency.

S DEXAMETHASONE eye drops 0·1%; preservative-free eye drops 0·1%
Dose: Apply 1 drop 4 to 6 times daily; severe conditions every 30 to 60 minutes until controlled then reduce frequency.

S FLUOROMETHOLONE eye drops 0·1%
Dose: Apply 1 drop 2 to 4 times daily. Contains polyvinyl alcohol 1·4%.

S PREDNISOLONE eye drops 0·5% (as sodium phosphate), 1% (as acetate); preservative-free eye drops 0·5% (as sodium phosphate)
Dose: Apply 1 drop 4 to 6 times daily; severe conditions every 30 to 60 minutes until controlled then reduce frequency.

Corticosteroids with antibacterials

S BETAMETHASONE WITH NEOMYCIN (betamethasone 0·1%, neomycin 0·5%) eye drops
Dose: Apply 1 drop up to 6 times daily.
S MAXITROL® (dexamethasone 0.1%, neomycin 3500 units/gram, polymyxin B 6000 units/mL) eye drops; eye ointment
Dose: Eye drops, apply 1 drop 4 times daily or up to every 2 hours if required; eye ointment, if used alone, apply twice daily.

Intravitreal corticosteroids

S DEXAMETHASONE intravitreal implant 700 micrograms
See SMC 652/10. Also for specialist treatment of inflammation of the posterior segment of the eye presenting as non-infectious uveitis.

Other anti-inflammatory preparations

Sodium cromoglycate is first choice for the management of allergic eye conditions. Second choice options are nedocromil sodium, olopatadine, Otrivine-Antistin® and lodoxamide; base selection on patient response and preference.

**FIRST CHOICE: SODIUM CROMOGLICATE**

SODIUM CROMOGLICATE OTC eye drops 2%
Dose: Apply 1 drop 4 times daily for allergic eye conditions.

NEDOCROMIL SODIUM eye drops 2%
Dose: Apply 1 drop twice daily for allergic eye conditions, increased if necessary to 4 times daily; maximum 12 weeks treatment. May be useful for patients with allergic or seasonal conjunctivitis who have had an inadequate response to sodium cromoglicate.

LOLOPATADINE eye drops 1mg/mL
Dose: Apply 1 drop twice daily for allergic eye conditions.

Resultado-Antistin® (antazoline 0.5%, xylometazoline 0.05%) eye drops
Dose: Apply 1 drop two to three times daily for allergic eye conditions.

LODOXAMIDE eye drops 0.1%
Dose: Apply 1 drop four times daily for allergic eye conditions.

Ciclosporin (section 11.8) may be used under specialist advice as an anti-inflammatory.

Anti-inflammatory analgesics

DICLOFENAC preservative-free eye drops 0.1%
May be useful for short-term pain relief in large corneal abrasion or welder’s flash injuries.

S KETOROLAC eye drops 0.5%

**11.5 MYDRIATICS AND CYCLOPLEGICS**

Tropicamide is appropriate for diagnostic use to dilate the pupil for examination of the fundus. Dilation usually takes 20 minutes and lasts for approximately 3 hours although this is variable. Only use atropine according to an Ophthalmologist’s advice.

TROPICAMIDE preservative-free eye drops 1%
Dose: Apply 1 drop as necessary.
CYCLOPENTOLATE eye drops 0.5%, 1%; preservative-free eye drops 0.5%, 1%
Dose: In adults, refer to SPC, in children refer to BNF for Children.

S ATROPINE preservative-free eye drops 1%

PHENYLEPHRINE preservative-free eye drops 2.5%

11.6 TREATMENT OF GLAUCOMA

The use of drugs in this section will be guided by specialist advice. It is known that compliance is improved with simplification of the dosing regime. If specialist recommendation is for a combination agent then this should be continued in the community.

Beta-blockers

| Note: Systemic absorption of timolol and betaxolol may induce bronchospasm in sensitive individuals; do not use in patients with asthma. Eye drops containing beta-blockers are also contra-indicated in patients with bradycardia, heart block or heart failure. |

S TIMOLOL eye drops 0.25%, 0.5%; long-acting eye drops 0.25%, 0.5% (Timoptol®-LA); preservative-free long-acting eye gel 0.1% (Tiopex®)
Dose: Standard eye drops, apply 1 drop twice daily; long-acting eye gel/drops, apply 1 drop once daily.

S BETAXOLOL eye drops 0.25%, 0.5%
Dose: Apply 1 drop twice daily.

Prostaglandin analogues

Generic preparations should be used. Rarely, patients switched from branded products may be sensitive to excipients in the generic forms, in which case discuss alternative generic options with the pharmacist. If unsuccessful, a branded version may be re-prescribed. Bimatoprost preparations may be used in latanoprost non-responders. Combination eye drops may be useful if compliance is likely to be a problem.

FIRST CHOICE: LATANOPROST

S LATANOPROST eye drops 50 micrograms/mL; preservative-free eye drops 50 micrograms/mL
Dose: Apply 1 drop once daily, preferably in the evening.

S LATANOPROST WITH TIMOLOL (latanoprost 50 micrograms/mL, timolol 5mg/mL) eye drops
Dose: Apply 1 drop once daily.

S BIMATOPROST eye drops 100 micrograms/mL; preservative-free eye drops 300 micrograms/mL
Dose: Apply 1 drop once daily, preferably in the evening. May be useful in latanoprost non-responders.

S BIMATOPROST WITH TIMOLOL (bimatoprost 300 micrograms/mL, timolol 5mg/mL) eye drops; preservative-free eye drops
Dose: Apply 1 drop once daily.
TAFLUPROST
preservative-free eye drops 15 micrograms/mL
Dose: Apply 1 drop once daily, preferably in the evening.

TAFLUPROST WITH TIMOLOL
(tafluprost 15 micrograms/mL, timolol 5mg/mL) preservative-
free eye drops
Dose: Apply 1 drop once daily.

Sympathomimetics

BRIMONIDINE
eye drops 0.2%
Dose: Apply 1 drop twice daily.

APRACLONIDINE
eye drops 0.5%; preservative-free eye drops 1%

Carbonic anhydrase inhibitors and systemic drugs

ACETAZOLAMIDE
tablets 250mg; m/r capsules 250mg; injection 500mg
Dose: 250mg to 1 gram daily in divided doses.

DORZOLAMIDE
eye drops 2%; preservative-free eye drops 2%
Dose: Used alone, apply 1 drop 3 times daily; with topical beta-blocker, apply 1 drop twice daily.

DORZOLAMIDE WITH TIMOLOL
(dorzolamide 2%, timolol 0.5%) eye drops; preservative-
free eye drops
Dose: Apply 1 drop twice daily.

BRINZOLAMIDE
eye drops 10mg/mL
Dose: Apply 1 drop twice daily increased to 3 times daily if necessary.
May be useful where there is intolerance to dorzolamide eye drops due to stinging.

BRINZOLAMIDE WITH TIMOLOL
(brinzolamide 10mg/mL, timolol 5mg/mL) eye drops
Dose: Apply 1 drop twice daily.

BRINZOLAMIDE WITH BRIMONIDINE
(brinzolamide 10mg/mL, brimonidine tartrate
2mg/mL) eye drops
Dose: Apply 1 drop twice daily.

Miotics

PILOCARPINE
eye drops 1%, 2%, 4%; preservative-free eye drops 2%
Dose: Apply 1 drop up to 4 times daily.

11.7 LOCAL ANAESTHETICS

Proxymetacaine should only be used for diagnostic and operative procedures such as removal of
foreign bodies but not for continued pain relief as it can delay healing of the corneal epithelium.
Cyclopentolate (section 11.5) dilates the pupil which can relieve pain in conditions such as anterior
uveitis and painful corneal lesions.

PROXYMETACAINE
preservative-free eye drops 0.5%
Dose: To be applied as required.
11.8 MISCELLANEOUS OPHTHALMIC PREPARATIONS

Tear deficiency, ocular lubricants, and astringents

For advice on the prescribing and use of tear substitutes, refer to table below and ‘Dry eye syndrome’ guidance on the Intranet.

- many of these products are available over the counter (see also Appendix 5)
- base the choice of tear substitute on patient acceptability and cost
- acetylcysteine is a mucolytic and is useful for patients with painful eyes due to mucous keratopathy.

### TOPICAL LUBRICANTS/TEAR SUBSTITUTES

See also general guidance on the management of dry eye syndrome on the Intranet.

<table>
<thead>
<tr>
<th>1st line</th>
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<tbody>
<tr>
<td>hypromellose eye drops 0.5% (Isopto Plain\textsuperscript{®}) or 1% (Isopto Alkaline\textsuperscript{®})</td>
<td>polyvinyl alcohol eye drops 0.4% (Sno Tears\textsuperscript{®}, Liquifilm\textsuperscript{®})</td>
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<tr>
<td>2nd line</td>
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<tr>
<td>carbomer gel 0.2% (Viscottears\textsuperscript{®})</td>
<td>consider ointment at night, eg Xailin Night\textsuperscript{®} or VitA-POS\textsuperscript{®}</td>
</tr>
<tr>
<td>3rd line</td>
<td>Rapid breakdown preserved agents; may be suitable in preservative intolerance; suitable for contact lens wearers:</td>
</tr>
<tr>
<td>Blink\textsuperscript{®} Intensive Tears (sodium hyaluronate eye drops 0.2%)</td>
<td>(10mL)</td>
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<tr>
<td>Oxyal\textsuperscript{®} (sodium hyaluronate eye drops 0.15%)</td>
<td>(10mL)</td>
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<tr>
<td>Systane\textsuperscript{®} (hydroxypropyl guar eye drops)</td>
<td>(10mL)</td>
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<tr>
<td>4th line/preservative-free (PF)</td>
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<tr>
<td>sodium hyaluronate eye drops (PF) 0.1% to 0.2%</td>
<td></td>
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<tr>
<td>o Vismed\textsuperscript{®} Multi 0.18% (10mL – shelf life 1 month after opening)</td>
<td></td>
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<tr>
<td>o Hylo-Tears\textsuperscript{®} 0.1% (10mL – shelf life 6 months after opening)</td>
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<tr>
<td>o Hylo-Forte\textsuperscript{®} 0.2% (10mL – shelf life 6 months after opening)</td>
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Note: with frequent use many patients will require more than 10mL per month.

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<tbody>
<tr>
<td>sodium hyaluronate eye drops (PF) 0.4%</td>
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<tr>
<td>o Clinitas\textsuperscript{®} 0.4% (single use 30 units)</td>
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<tr>
<td>carmellose eye drops 0.5% (Celluvisc\textsuperscript{®} 0.5% single use 30 units)</td>
<td></td>
</tr>
<tr>
<td>carmellose eye drops 1% (Celluvisc\textsuperscript{®} 1% single use 30 units)</td>
<td></td>
</tr>
<tr>
<td>polyvinyl alcohol eye drops (PF) 0.4% (Liquifilm\textsuperscript{®} PF single use 30 units)</td>
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**HYPROMELLOSE** \textsuperscript{OTC} eye drops 0.3%, 0.5% (Isopto Plain\textsuperscript{®}), 1% (Isopto Alkaline\textsuperscript{®})

**Dose:** Apply 1 drop 3 to 4 times daily, may need to increase frequency to hourly for adequate relief. The higher strength preparations may be more effective and are lower cost; it is recommended that new patients are started on the 0.5% strength.

**POLYVINYL ALCOHOL** \textsuperscript{OTC} eye drops 1.4% (Sno Tears\textsuperscript{®}, Liquifilm Tears\textsuperscript{®})

**Dose:** Apply 1 drop 4 times daily, increasing to every hour if required.

**CARBOMERS** \textsuperscript{OTC} eye drops 0.2% (Viscottears\textsuperscript{®})

**Dose:** Apply 1 drop 3 to 4 times daily or as required. Carbomers are useful and they are low cost.

**XAILIN NIGHT\textsuperscript{®}** eye ointment (contains liquid paraffin plus excipients)

**Dose:** Apply at night or if required up to 4 times daily throughout the day.

**VITA-POS\textsuperscript{®}** eye ointment (contains liquid paraffin plus excipients)
Dose: Apply at night or if required up to 4 times daily throughout the day.

**SODIUM HYALURONATE** eye drops 0.15% (Oxyal®), 0.2% (Blink® Intensive Tears)
**Dose:** Apply as required. Usually initiate therapy with 0.1% to 0.2% and consider higher strength if unsatisfactory response.

**SYSTANE®** (polyethylene glycol 400 0.4%, propylene glycol 0.3%, hydroxypropyl guar) eye drops  **Dose:** Apply as required.

**S ILUBE®** (acetylcysteine 5%, hypromellose 0.35%) eye drops  **Dose:** Apply 1 drop 3 to 4 times daily.

**Preservative-free tear substitutes**

For further advice on preservative-free tear substitutes, refer to ‘Guidelines for dry eye syndrome’ on the Intranet.

**CARBOMERS OTC** preservative-free eye gel 0.2% (Xailin® Gel multidose unit)
**Dose:** Apply 3 to 4 times daily or as required. The sodium perborate preservative is converted to water and oxygen on contact with tear film.

**CARMELLOSE OTC** preservative-free eye drops 0.5%, 1% (Celluvisc® single use units)
**Dose:** Apply 1 drop 4 times daily, increasing to every hour if required.

**XAILIN NIGHT®** eye ointment (contains liquid paraffin plus excipients)
**Dose:** Apply at night or if required up to 4 times daily throughout the day.

**VITA-POS®** eye ointment (contains liquid paraffin plus excipients)
**Dose:** Apply at night or if required up to 4 times daily throughout the day.

**POLYVINYL ALCOHOL OTC** preservative-free eye drops 1.4% (Liquifilm Tears® single use units)
**Dose:** Apply 1 drop 4 times daily, increasing to every hour if required.

**SODIUM HYALURONATE** preservative-free eye drops 0.1% (Hylo-Tear® multidose unit), 0.18% (Vismed® Multi multidose unit), 0.2% (Hylo-Forte® multidose unit), 0.4% (Clinitas® single use units)
**Dose:** Apply as required. Usually initiate therapy with 0.1% to 0.2% and consider higher strength if unsatisfactory response.

**SYSTANE® ULTRA** (polyethylene glycol 400 0.4%, propylene glycol 0.3%, hydroxypropyl guar, sorbitol) preservative free eye drops, single use units
**Dose:** As required.

**SODIUM CHLORIDE** preservative-free eye drops 0.9% OTC

**Ocular diagnostic, peri-operative and specialist-use preparations**

**S CICLOSPORIN** preservative-free eye drops 0.1% (Ikervis®)
**Dose:** Apply 1 drop at bedtime.

**FLUORESCEIN SODIUM** preservative-free eye drops 1%, 2%; solution for injection 10%

**S MIOCHOL-E®** (acetylcholine 1%, mannitol 3%) solution for intra-ocular irrigation
**AFLIBERCEPT** solution for intravitreal injection 4mg/0·1mL

**RANIBIZUMAB** solution for intravitreal injection 1·65mg/0·165mL prefilled syringe, 2·3mg/0·23mL vial

**BEVACIZUMAB** intravitreal injection, pre-filled syringe 5mg/0·2mL [unlicensed].

**ADALIMUMAB** solution for injection, pre-filled syringe 40mg/0·8mL, pre-filled pen 40mg/0·8mL. For specialist treatment of sight threatening, non-infectious, inflammatory eye disease [off-label].

**OCRIPLASMIN** concentrate for solution for intravitreal injection 500 micograms/0·2mL vial

**CEFUROXIME** (Aprokam®) powder for solution for injection 50mg

**SODIUM CHLORIDE** eye drops 4-5% [unlicensed] Available for specialist use from special-order manufacturers; for information contact Medicines Information.

**POVIDONE IODINE** solution for intra-ocular irrigation 5% in balanced salt solution [unlicensed]

Botulinum toxin type A (section 4.9) is also used under specialist advice for blepharospasm.

**Miscellaneous eye products**

For those having difficulty administering eye drops, a range of eye drop dispensers are available from the Hospital Supplies Department and are prescribable in primary care; refer to Eye Products section of Part 3 of Scottish Drug Tariff.

For other eye preparations approved for use in NHS Highland refer to 'Highland unlicensed and off-label medicines list' on Intranet (chlorhexidine, fluorouracil, hexamidine, polihexanide).
CHAPTER 12 EAR, NOSE AND OROPHARYNX

12.1 DRUGS ACTING ON THE EAR

Otitis externa

There is a lack of evidence to prove the efficacy of one product over another in this section. The choice of preparation should be governed by patient acceptability, tolerance to ingredients, and cost. Both Sofradex® ear drops and flumetasone with clioquinol ear drops contain antibacterials which are not used systemically. Gentamicin with hydrocortisone ear drops are recommended for resistant infections. Otomize® spray is recommended for use in older patients or those with dexterity problems. Acetic acid 2% spray may be useful in recurrent and recalcitrant cases of otitis externa; a proprietary preparation EarCalm® spray is on sale to the public. These preparations should be used for up to a maximum of 7 days to prevent fungal overgrowth and the potential for ototoxicity. The appropriateness of administering drops should be carefully considered beforehand because the skin of the ear canal is very sensitive.

Corticosteroid

BETAMETHASONE drops 0·1%
Dose: Apply 2 to 3 drops every 2 to 3 hours (Betnesol®), every 3 to 4 hours (Vistamethasone®); reduce frequency when relief obtained.

Corticosteroid with antibacterial

BETAMETHASONE WITH NEOMYCIN (betamethasone 0·1%, neomycin 0·5%) drops
Dose: Apply 2 to 3 drops into the ear every 3 to 4 hours; reduce frequency when relief obtained.

SOFRADEX® (dexamethasone 0·05%, framycetin 0·5%, gramicidin 0·005%) drops
Dose: Apply 2 to 3 drops into the ear 3 to 4 times daily.

FLUMETASONE WITH CLIOQUINOL (flumetasone 0·02%, clioquinol 1%) ear drops
Dose: Apply 2 to 3 drops into the ear twice daily for up to 7 days.

GENTAMICIN WITH HYDROCORTISONE (hydrocortisone 1%, gentamicin 0·3%) ear drops
Dose: Apply 2 to 4 drops into the ear 3 to 4 times daily and at night.

OTOMIZE® (dexamethasone 0·1%, neomycin 3250 units/mL, glacial acetic acid 2%) ear spray
Dose: Apply 1 metered spray into the ear 3 times daily.

CILODEX® (ciprofloxacin 3mg/mL, dexamethasone 1mg/mL) ear drops
Dose: Apply 4 drops twice daily for 7 days.

Anti-infective preparations

CLOTrimazole solution 1%
Dose: Apply into ear 2 to 3 times daily continuing for at least 14 days after infection disappears.

ACETIC ACID spray 2%
Dose: One metered dose into ear at least 3 times daily.

Removal of ear wax

The patient should lie with the affected ear uppermost for 5 to 10 minutes after a generous amount of the softening remedy has been introduced into the ear.
OLIVE OIL OTC ear drops
Dose: If the wax is hard and impacted use twice daily for a few days before syringing. Allow to warm to room temperature before use.

SODIUM BICARBONATE OTC ear drops 5%
Dose: If the wax is hard and impacted use twice daily for a few days before syringing.

12.2 DRUGS ACTING ON THE NOSE

Drugs used in nasal allergy

In seasonal allergic rhinitis (e.g. hay fever), treatment should begin 2 to 3 weeks before the season commences and may have to be continued for several months. Nasal preparations containing corticosteroids have a useful role in the treatment of allergic rhinitis. If monotherapy with antihistamine or corticosteroid is insufficient, consider a 2 month trial of Dymista® for the relief of symptoms of moderate to severe seasonal and perennial allergic rhinitis.

The risk of systemic effects may be greater with nasal drops than metered nasal sprays; drops are administered incorrectly more often than sprays. Fluticasone nasal drops may be considered for the treatment of severe nasal polyps and severe rhinitis [off-label] on the advice of an ENT specialist. Refer to guidance on ‘Nasal blockage’ and ‘Nasal discharge’ on Intranet.

Nasal sprays

**FIRST CHOICE: BECLOMETASONE**

BECLOMETASONE OTC nasal spray 50 micrograms/metered spray
Dose: Apply 100 micrograms (2 sprays) into each nostril twice daily or 50 micrograms (1 spray) into each nostril 3 to 4 times daily; maximum total 400 micrograms (8 sprays) daily; when symptoms controlled, reduce dose to 50 micrograms (1 spray) into each nostril twice daily.

MOMETASONE nasal spray 50 micrograms/metered spray
Dose: Apply 100 micrograms (2 sprays) into each nostril once daily, increased if necessary to maximum 200 micrograms (4 sprays) into each nostril once daily; when control achieved reduce to 50 micrograms (1 spray) into each nostril once daily.

FLUTICASONE FUROATE (Avamys®) nasal spray 27.5 micrograms/metered spray
Dose: Apply 55 micrograms (2 sprays) into each nostril once daily; when control achieved reduce to 27.5 micrograms (1 spray) into each nostril once daily.

DYMISTA® (fluticasone propionate 50 micrograms, azelastine 137 micrograms/metered spray)
Dose: Moderate to severe seasonal and perennial allergic rhinitis if monotherapy with antihistamine or corticosteroid is insufficient, 1 spray into each nostril twice daily. Discontinue after 2 months if no benefit.

Nasal drops

S FLUTICASONE PROPIONATE nasal drops 400 micrograms/0.4mL unit
Dose: Severe nasal polyps, apply 200 micrograms (approximately 6 drops) into each nostril once or twice daily; consider alternative treatment if no improvement after 4 to 6 weeks.

Topical nasal decongestants

XYLOMETAZOLINE OTC paediatric nasal drops 0.05%; nasal spray 0.1%
Dose: Paediatric nasal drops, instil 1 to 2 drops into each nostril once or twice daily when required; maximum duration 5 days; nasal spray, apply 1 spray into each nostril 1 to 3 times daily when required; maximum duration 7 days.

Sodium chloride 0.9% given as nasal drops and available over the counter, may relieve nasal congestion by helping to liquefy mucous secretions and may be useful for infants under 3 months.

Topical nasal decongestants often cause rebound congestion; use for no longer than 7 days. Avoid sympathomimetics, such as xylometazoline, in patients taking monoamine-oxidase inhibitors (Section 4.3).

Nasal preparations for infection and epistaxis

Note: Naseptin cream contains arachis (peanut) oil; avoid in patients with peanut allergy.

NASEPTIN® (chlorhexidine 0.1%, neomycin 0.5%) cream
Dose: For eradication of nasal carriage of staphylococci, apply to nostrils 4 times daily for 10 days; for preventing nasal carriage of staphylococci, apply to nostrils twice daily.

Naseptin® is also used for the treatment of epistaxis and following minor procedures [off-label]. Refer to guidance on ‘Nose bleed – acute and chronic’ on Intranet.

MUPIROCIN nasal ointment 2%
Dose: For eradication of nasal carriage of MRSA only, apply 3 times daily to the inner surface of each nostril. Continue each course of treatment for 5 days, with sampling 2 days or more after completing the course. The course may be repeated once, after which further treatment should be discussed with the Infection Control Team.

12.3 DRUGS ACTING ON THE OROPHARYNX

Refer to guidance on mouth care in Scottish Palliative Care Guidelines and ‘Saliva management: sialorrhoea in palliative care’ in Appendix 7.

Drugs for oral ulceration and inflammation

Benzydamine is effective at relieving oral discomfort including irradiation mucositis.

BENZYDAMINE OTC mouthwash 0.15%; oromucosal spray 0.15%
Dose: Mouthwash, rinse or gargle, using 15mL (diluted with water if stinging occurs), every 1½ to 3 hours as required, usually for up to 7 days; spray, 4 to 8 sprays onto affected area every 1½ to 3 hours.

HYDROCORTISONE OTC oromucosal tablets 2.5mg
Dose: 1 tablet 4 times daily, allowed to dissolve slowly in the mouth in contact with the ulcer.

BETAMETHASONE soluble tablets 500 micrograms
Dose: Oral ulceration [off-label], 500 micrograms dissolved in 20mL water and rinsed around the mouth 4 times daily; do not swallow.

Toothache

CLOVE OIL BP 100% v/v (10mL)
For dental out of hours use in adults and children over 4 years of age with toothache.
Oropharyngeal anti-infective drugs

For guidance on treating oral thrush in infants refer to ‘Policy on treatment of breast thrush while breastfeeding’ on Intranet.

**FIRST CHOICE: NYSTATIN**

**NYSTATIN** oral suspension 100 000 units/mL  
**Dose:** 100 000 units (1mL) 4 times daily after food usually for 7 days (continued for 48 hours after lesions have resolved), divide administration of the dose between both sides of the mouth.

**Mouthwashes**

**CHLORHEXIDINE**<sup>OTC</sup> mouthwash 0·2%, dental gel 1%  
**Dose:** *Mouthwash,* rinse the mouth with 10mL for about 1 minute twice daily; *dental gel,* brush on the teeth or apply to affected areas once or twice daily.

Chlorhexidine mouthwash causes a reversible brown staining of the teeth and may be incompatible with some toothpastes; leave an interval of at least 30 minutes between using mouthwash and toothpaste.

**Treatment of dry mouth**

Saliveze<sup>®</sup> oral spray is the lowest cost preparation. It has Advisory Committee on Borderline Substances (ACBS) approval for prescribing only for patients suffering from dry mouth as a result of having (or having undergone) radiotherapy, or sicca syndrome whereas Biotène Oralbalance<sup>®</sup> gel and Xerotin<sup>®</sup> oral spray can be used for any condition giving rise to a dry mouth. Endorse Saliveze<sup>®</sup> prescriptions as ‘ACBS’.

**SALIVEZE**<sup>®</sup> oral spray  
**Dose:** ACBS: patients suffering from dry mouth as a result of having (or having undergone) radiotherapy, or sicca syndrome, 1 spray onto oral mucosa as required.

**BIOTÈNE ORALBALANCE**<sup>®</sup> saliva replacement gel  
**Dose:** Symptomatic treatment of dry mouth, apply to gums and tongue as required.

**XEROTIN**<sup>®</sup> oral spray  
**Dose:** Symptomatic treatment of dry mouth, spray onto oral mucosa as required.
CHAPTER 13  SKIN

Refer to the extensive clinical guidelines at the end of the chapter. For NHS Highland guidance on the treatment of head lice and scabies refer to NHS Highland Intranet.

The National Dermatology Patient Pathways (http://www.dermatology.nhs.scot/dermatology-pathways/introduction/ and via the NHS Highland Intranet under Shared Clinical Guidelines) should be used in association with drug recommendations and guidance in this chapter to inform the management of acne, alopecia, atopic eczema, benign skin lesions, generalised and local pruritus, hand and foot eczema, molluscum contagiosum, nail dystrophy, non-melanoma skin cancers, psoriasis, rosacea, scabies, solar (actinic) keratoses and Bowen’s Disease, suspicious pigmented lesions, urticaria, and viral warts. Also refer to the British Association of Dermatologists Clinical Guidelines at www.bad.org.uk.

For use of dermatologicals in children, refer to BNF for Children.

13.1 MANAGEMENT OF SKIN CONDITIONS

Vehicles

Choice of vehicle is very personal; it can mean the difference between treatment success and failure. Skin treatments are ‘worn’, like clothes. Patients will not use a topical therapy that irritates their skin, and will be reluctant to use one that does not ‘feel right’.

Ointments are recommended as the first choice of formulation for most skin diseases and are particularly useful for dry, scaly conditions. Ointments are greasy and generally insoluble in water so can be difficult to wash off; they do not suit all patients and may be less acceptable to some patients.

Creams, emulsions of oil and water, often contain an antimicrobial preservative and are therefore more likely to cause both irritant and allergic reactions. For this reason creams are often best avoided as first-line treatment, but can be better than ointments for some acute conditions due to a cooling effect as they evaporate. Creams may be more cosmetically acceptable for some patients in some body sites and are often the agents of choice for moist, flexural areas such as axillae.

Lotions also have a cooling effect, and may be preferable to treat hairy sites. They can be made up in either water or alcohol. Alcoholic lotions will sting if applied to broken or acutely inflamed skin.

Gels have a high water content, and are especially suitable for the face and scalp; however, gels may irritate in some circumstances.

Refer to guidance on ‘Adverse reactions to topical therapy’.

13.2 EMOLLIENT AND BARRIER PREPARATIONS

Refer to guidance on the ‘Use of emollients’.

Emollients

Base the choice of emollient on patient preference to optimise compliance, preparation cost, site of application and whether it is for use only as an emollient or also as a soap substitute.
FIRST CHOICE:  
ZEROBASE® CREAM  
or  
DIPROBASE® CREAM  
SECOND CHOICE:  
ZERODERM® OINTMENT  
or  
EPADERM® OINTMENT

ZEROBASE® OTC cream  
The cream is available as a 50 gram tube and a 500 gram pump dispenser. The pump dispenser is particularly suitable for long-term use and as a soap substitute.

DIPROBASE® OTC cream; ointment  
The cream is available as a 50 gram tube and a 500 gram pump dispenser. The pump dispenser is particularly suitable for long-term use and as a soap substitute.

ZERODERM® OTC ointment  

EPADERM® OTC ointment  

HYDROMOL® OTC ointment

DOUBLEBASE® OTC gel

DERMOL® 500 lotion (contains benzalkonium chloride 0·1% and chlorhexidine hydrochloride 0·1%)  
Antiseptic emollient. Particularly useful for hand eczema.

**Note:** Aqueous cream has been removed from the Highland Formulary as an emollient because it commonly irritates the skin. It was not designed to be left on the skin and should only be used as a soap substitute if at all. Newer, less irritant emollients such as Zerobase®/Diprobase® cream and Zeroderm®/Epaderm® ointment should be recommended to patients; for further information refer to guidance on the ‘Use of emollients’.

**DERMATONICS® ONCE HEEL BALM** cream (urea 25%)  
For use in patients with diabetes as part of an individually-tailored foot management plan in conjunction with podiatry care.

**Useful for scaly conditions**

**LIQUID AND WHITE SOFT PARAFFIN OINTMENT 50/50 OTC** [unlicensed]

**YELLOW SOFT PARAFFIN OTC**

**OLIVE OIL OTC**  
With very scaly or crusted conditions (eg plaque psoriasis), application of lukewarm olive oil to scaly areas, after bathing and drying, and before applying emollients or other topical treatments, can gently remove scale or crusts and be very soothing.

**Emollient bath additives**

FIRST CHOICE:  
OILATUM®

OILATUM® OTC emollient bath additive; junior emollient bath additive (fragrance-free)

BALNEUM® OTC bath oil
The preferred choice for older patients as it is less slippery.

**AVEENO® OTC** bath and shower oil
This is a borderline substance which is only prescribable for specified conditions (refer to BNF). Endorse script ACBS (Advisory Committee on Borderline Substances). It can be very soothing for some patients, especially those with eczema.

**Emollient bath additives with antimicrobials**

**EMULSIDERM® OTC** liquid emulsion (benzalkonium chloride 0.5%)
Best added to bath water and applied to scaly/broken areas, lesions and flexural staphylococcal carrier sites, after bathing/showering and before drying. First choice for minor skin infections, including impetigo, infected eczema etc and for hospital use.

**OILATUM® PLUS** emollient bath additive
For use in accordance with policy for methicillin-resistant *Staphylococcus aureus* on Intranet.

**Emollient shower gels**

**FIRST CHOICE: DERMOL® 200**

**DERMOL® 200 OTC** shower emollient (benzalkonium chloride 0.1% and chlorhexidine hydrochloride 0.1%)

**OILATUM® OTC** shower emollient gel

**Barrier preparations**

There is very little evidence to support the use of barrier preparations in any condition, other than incontinence dermatitis and nappy rash. Refer to guidance.

For advice on caring for the skin surrounding a wound, refer to guidance in the NHS Highland Wound Management Guidelines and Formulary on the Intranet.

**FIRST CHOICE: CONOTRANE® CREAM**

**CONOTRANE® OTC** cream (benzalkonium chloride 0.1% and dimeticone '350' 22%, cetostearyl alcohol, fragrance)

**SUDOCREM® OTC** cream (benzyl alcohol 0.39%, benzyl benzoate 1.01%, benzyl cinnamate 0.15%, wool fat hydrous (hypoallergenic lanolin) 4%, zinc oxide 15.25%)
Apply Sudocrem® sparingly.

**13.3 ANTIPRURITICS**

Refer to guidance on ‘Management of pruritus’ and information on scabies in section 13.10, and National Patient Pathways. For oral antihistamines refer to section 3.4.

**FIRST CHOICE:** **LEVOMENTHOL CREAM 1%**

or **BALNEUM PLUS® CREAM**

**LEVOMENTHOL** cream 1% (menthol 1% in aqueous cream; Arjun®)
BALNEUM PLUS®OTC bath oil; cream

CROTAMITON OTC cream 10%
Useful for scabetic pruritus.

13.4 TOPICAL CORTICOSTEROIDS

Refer to guidance on ‘Use of topical corticosteroids’ and ‘Management of eczema/dermatitis’. Prescribe by generic name whenever possible.

Mildly potent

Usually sufficient for children and safer for flexural and facial inflammatory conditions.

**FIRST CHOICE: HYDROCORTISONE 1%**

HYDROCORTISONE cream 0.5%, 1%OTC; ointment 0.5%, 1%OTC
Refer to BNF for OTC restrictions.

FLUOCINOLONE ACETONIDE (Synalar 1 in 10 Dilution®) cream 0.0025%

Moderately potent

**FIRST CHOICE: CLOBETASONE BUTYRATE (EUMOVATE®)**

CLOBETASONE BUTYRATE (Eumovate®) cream 0.05%OTC; ointment 0.05%
Refer to BNF for OTC restrictions.

BETAMETHASONE VALERATE (1 in 4 dilution: Betnovate-RD®, Audavate-RD®) cream 0.025%; ointment 0.025%

FLUOCINOLONE ACETONIDE (Synalar 1 in 4 Dilution®) cream 0.00625%; ointment 0.00625%

Potent

**FIRST CHOICE: BETAMETHASONE VALERATE (BETNOVATE®)**

BETAMETHASONE VALERATE (full strength®) cream 0.1%; ointment 0.1%; lotion 0.1%; scalp application 0.1%; foam scalp application (Bettamousse®) 0.12%

HYDROCORTISONE BUTYRATE (Locoid®) cream 0.1%; lipocream 0.1%; ointment 0.1%

FLUOCINOLONE ACETONIDE (Synalar®) cream 0.025%; ointment 0.025%; gel 0.025%

MOMETASONE FUROATE (Elocon®) cream 0.1%; ointment 0.1%

DIPROSALIC® (salicylic acid 3%, betamethasone dipropionate 0.05%) ointment

DIPROSALIC® (salicylic acid 2%, betamethasone dipropionate 0.05%) scalp application

Very potent

CLOBETASOL PROPIONATE (Dermovate®, ClobaDerm®) cream 0.05%; ointment 0.05%
Not recommended for first-line use. Avoid in children. Use must be reviewed by prescriber at least monthly, it should never be on repeat prescription except for use in special circumstances, eg vulval lichen sclerosus; see section 7.2 and guidance on use of topical corticosteroids.

Corticosteroids with added antimicrobial agents

Do not use in preference to topical corticosteroids alone, unless there is overt infection, see guidance. Refer to antimicrobial guidance. They should only be on repeat prescription when recommended by a specialist.

Mildly potent

CANESTEN HC® OTC ( clotrimazole 1%, hydrocortisone 1%) cream
Refer to BNF for OTC restrictions.

DAKTACORT® (miconazole 2%, hydrocortisone 1%) cream OTC, ointment
Refer to BNF for OTC restrictions.

FUCIDIN H® ( fusidic acid 2%, hydrocortisone acetate 1%) cream
Limited indications: use ONLY for short periods of time (up to 10 days) to prevent bacterial resistance. It should only be on repeat prescription when recommended by a specialist.

Moderately potent

TRIMOVATE® ( oxytetracycline 3%, nystatin 100 000 units/gram, clobetasone butyrate 0-05%) cream

Potent

BETAMETHASONE WITH CLIOQUINOL (clioquinol 3%, betamethasone valerate 0-1%) cream; ointment

SYNALAR C® (clioquinol 3%, fluocinolone acetonide 0-025%) cream; ointment

S FUCIBET® ( fusidic acid 2%, betamethasone valerate 0-1%) cream
Limited indications: use ONLY for short periods of time (up to 10 days) to prevent bacterial resistance. It should never be on repeat prescription.

Very potent

S CLOBETASOL PROPIONATE WITH NEOMYCIN AND NYSTATIN ( clobetasol propionate 0-05%, neomycin 0-5%, nystatin 100 000 units/gram) cream; ointment
To be used under specialist recommendation.

13.5 PREPARATIONS FOR ECZEMA AND PSORIASIS

Preparations for eczema

Refer to guidance on ‘Management of eczema/dermatitis’, National Patient Pathways and SIGN.

ICHTHAMMOL 1% ZINC OXIDE BP 15% IN YELLOW SOFT PARAFFIN paste
Requires extemporaneous preparation [unlicensed].

ZINC PASTE AND ICHTHAMMOL bandages
Preparations for psoriasis

Refer to guidance on ‘Management of psoriasis’, National Patient Pathways and SIGN.

Topical preparations for psoriasis

Vitamin D and analogues

**CALCITRIOL** (Silkis®) ointment 3 micrograms/gram
Dose: Apply twice daily, up to 35% of body surface area to be treated daily. Maximum dose, 30 grams daily.

**CALCIPOTRIOL** ointment 50 micrograms/gram
Dose: Apply twice daily. Maximum dose, 100 grams weekly.

**TACALCITOL** (Curatoderm®) ointment 4 micrograms/gram
Dose: Apply daily, preferably at bedtime. Maximum dose, 10 grams daily.

**CALCIPOTRIOL WITH BETAMETHASONE** (betamethasone dipropionate 0·05%, calcipotriol 50 micrograms/gram) ointment; gel (Dovobet®); cutaneous foam (Enstilar®)
Dose: Ointment, see BNF. Gel can be used on all areas including the scalp; for scalp psoriasis apply 1 to 4 grams to scalp once daily, shampoo off after leaving on scalp overnight or during day. To remove gel from the scalp, apply shampoo while the hair is still dry. The recommended gel treatment period is 4 weeks for scalp areas and 8 weeks for ‘non-scalp’ areas. Foam, apply once daily for 4 weeks – refer to SPC for advice on administration. The foam spray may be useful for patients who find alternative preparations difficult to apply.

Coal tar preparations

For coal tar shampoos refer to section 13.9.

**FIRST CHOICE: COAL TAR (EXOREX®)**

**COAL TAR** OTC (Exorex®) lotion 5%
Dose: Apply 2 to 3 times daily (avoid mucosa and broken skin).

**COCOIS® OTC** scalp ointment (coal tar solution 12%, salicylic acid 2%, precipitated sulfur 4%)
Dose: Apply to scalp lesions for 1 hour then shampoo off. Use daily for 3 to 7 days then once weekly as necessary.

**COAL TAR IN YELLOW SOFT PARAFFIN** 10%
Dose: Apply twice daily. Available from special-order manufacturers [unlicensed]; for information contact Medicines Information.

**S COAL TAR POMADE** 6% (coal tar solution 6%, salicylic acid 2% in emulsifying ointment)
Available from special-order manufacturers [unlicensed]; for information contact Medicines Information.

Coal tar preparations with corticosteroid

**S COAL TAR IN BETNOVATE RD** ointment (coal tar 5%, 10%, with betamethasone 0·025%)
For hospital use only. Available from special-order manufacturers [unlicensed]; for information contact Medicines Information.
Dithranol

**DITHRANOL** (Dithrocream®) cream 0·1%, 0·25%, 0·5%, 1%, 2%

**Dose:** Apply to skin or scalp for maximum 1 hour, then wash or shampoo off (‘short contact’ Dithrocream® regimen).

**DITHRANOL IN LASSAR’S PASTE** 0·1%, 0·5%, 1%, 2%, 5%, 8%

Usually used under hospital supervision. Contains salicylic acid. Requires extemporaneous preparation [unlicensed].

**Oral retinoids for psoriasis**

**S** ACITRETIN capsules 10mg, 25mg
For initiation and prescription by dermatological specialist.

**Drugs affecting the immune response**

Advise patients prescribed drugs in this section to avoid excessive exposure to UV light.

**S** AZATHIOPRINE tablets 50mg

For initiation by hospital specialist only. Refer to guidance on the safe and effective prescribing of azathioprine at [www.bad.org.uk](http://www.bad.org.uk). For advice on monitoring azathioprine refer to Appendix 2: ‘Universal requirements for monitoring of conventional DMARDS in primary care’.

**S** CICLOSPORIN (Neoral®) capsules 10mg, 25mg, 50mg, 100mg; oral solution 500mg/5mL
For initiation by hospital specialist only. For advice on monitoring ciclosporin refer to Appendix 2: ‘Universal requirements for monitoring of conventional DMARDS in primary care’.

**TACROLIMUS** (Protopic®) ointment 0·03%, 0·1%
Advise patients not to apply other topical preparations within 2 hours of application.

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**Note:** Methotrexate: pay attention to the frequency of dosing for safety:
- methotrexate is always given once weekly
- prescribing and dispensing errors have caused fatalities
- the 2·5mg tablet only is recommended for safety.

**S** METHOTREXATE tablets 2·5mg

For initiation by hospital specialist only. When methotrexate is prescribed for dermatological conditions it is usually used in conjunction with folic acid 5mg daily except on the day when methotrexate is taken. For advice on monitoring methotrexate refer to Appendix 2: ‘Universal requirements for monitoring of conventional DMARDS in primary care’.

**Other preparations for psoriasis**

For other preparations for psoriasis approved for use in NHS Highland refer to ‘Highland unlicensed and off-label medicines list’ on Intranet (5- and 8-methoxypsoralen).

**13.6 PREPARATIONS FOR ACNE AND ROSACEA**

Refer to guidelines and notes on ‘Management of acne’ and National Patient Pathways.

**Benzoyl peroxide**

**BENZOYL PEROXIDE**<sup>OTC</sup> aqueous gel 5%, 10%
**Topical antibacterials for acne**

**ZINERYT®** (erythromycin 40mg, zinc acetate 12mg/mL on reconstitution) topical solution  
**Dose:** Apply twice daily.

**CLINDAMYCIN** topical solution 1% (in aqueous alcoholic basis); gel 1% (contains propylene glycol)  
**Dose:** Used under specialist advice for the treatment of acneform rash associated with cancer chemotherapy [off-label], apply thinly once daily.

**Topical retinoids and related preparations for acne**

Avoid in pregnancy and breast-feeding; adequate contraception is essential for women of childbearing age.

**FIRST CHOICE:** ADAPALENE CREAM

**ADAPALENE** (Differin®) cream 0·1%  
**Dose:** Apply thinly at night after washing.

**EPIDUO®** (adapalene 0·1%, benzoyl peroxide 2·5%) gel  
**Dose:** Apply thinly once daily in the evening.

**Oral preparations for acne**

**FIRST CHOICE:** OXYTETRACYCLINE  
**SECOND CHOICE:** ERYTHROMYCIN

**OXYTETRACYCLINE** tablets 250mg  
**Dose:** 500mg twice daily, for at least 3 months.

**ERYTHROMYCIN** tablets 250mg  
**Dose:** 500mg twice daily, for at least 3 months.

**DOXYCYCLINE** capsules 100mg  
**Dose:** 100mg daily, for at least 3 months.

**Note:** Co-cyprindiol

- Co-cyprindiol carries an increased risk for venous thromboembolism. The risk increases with increasing BMI; avoid co-cyprindiol in patients with a BMI above 35kg/m². See CSM advice in **BNF** section 13.6.2 and [https://www.fsrh.org/documents/cec-ceu-statement-dianette-jun-2013/](https://www.fsrh.org/documents/cec-ceu-statement-dianette-jun-2013/).
- Co-cyprindiol provides effective contraception. An additional hormonal contraceptive should not be used in combination with co-cyprindiol.

**CO-CYPRINDIOL** (cyproterone acetate 2mg, ethinylestradiol 35 micrograms) tablets  
**Dose:** 1 tablet daily for 21 days starting on the first day of the menstrual cycle and repeated after a 7-day interval, usually for several months; withdraw treatment 2 menstrual cycles after acne has resolved (repeat courses may be given if recurrence).

**ISOTRETINOIN** capsules 5mg, 10mg, 20mg
Isotretinoin should only be prescribed by or under supervision of Physicians with expertise in the use of systemic retinoids for the treatment of severe acne and a full understanding of the risk of isotretinoin therapy and monitoring requirements.

**Topical preparations for rosacea**

Refer to:
- guidance on ‘Management of rosacea’
- section 13.10 for metronidazole (Rozex®) cream 0·75% used in rosacea.

**AZELAIC ACID** (Finacea®) gel 15%

**Dose:** Apply twice daily.

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**MHRA: Brimonidine gel; advice for healthcare professionals**

- Exacerbation of rosacea symptoms occurred in up to 16% of patients treated with brimonidine gel in clinical studies; in most cases, erythema and flushing resolve after stopping treatment.
- Initiate treatment with a small amount of gel (less than the maximum dose) for at least 1 week and increase the dose gradually, based on tolerability and response to treatment.
- Advise patients carefully on how to apply the gel and on the importance of not exceeding the maximum daily dose (which is 1 gram of gel in total weight, approximately 5 pea-sized amounts).
- Advise patients to stop treatment and consult a doctor if their symptoms worsen during treatment (increased redness or burning).
- For further information see [www.gov.uk](http://www.gov.uk).

**Risk of systemic cardiovascular effects**

- Cases of bradycardia, hypotension (including orthostatic hypotension), and dizziness after application of brimonidine gel have been reported, some of which required hospitalisation.
- Some cases were associated with application of brimonidine gel after laser procedures to the skin, which possibly caused increased absorption of the gel.
- Warn patients not to apply brimonidine gel to irritated or damaged skin, including after laser therapy to the skin.
- For further information see [www.gov.uk](http://www.gov.uk).

**BRIMONIDINE** (Mirvaso®) gel 0·33%

**Dose:** For patients with moderate to severe persistent facial erythema associated with rosacea, apply twice daily, initiate as per MHRA advice above.

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**13.7 PREPARATIONS FOR WARTS**

**Note:** No treatment may be required, especially in young children.

**SALICYLIC ACID**<sup>OTC</sup> gel 12%, 26%

**Dose:** For hand and plantar warts, apply daily. Salicylic acid should be applied for up to 4 months for persistent warts. Initially use the 12% preparation, but increase to the 26% if there is no improvement after the first pack is finished. Take care to avoid applying to surrounding healthy skin. Also refer to National Patient Pathways.

**Anogenital warts**

Refer to product literature for specific indications and dosing information. Liquid nitrogen therapy should also be considered if available. Avoid podophyllotoxin, podophyllum and imiquimod in pregnancy and breast-feeding. Imiquimod should be reserved for the treatment of resistant warts.
Patients with anogenital warts should normally be treated in collaboration with practitioners offering Sexual Health Services.

**PODOPHYLLOTOXIN** cream 0·15%; alcoholic solution 0·5%

*S PODOPHYLLUM* 25% in industrial methylated spirits
Requires extemporaneous preparation [unlicensed].

**IMIQUIMOD** (Aldara®) cream 5%

### 13.8 SUNSCREEN PREPARATIONS

**SUNSENSE ULTRA**<sub>OTC</sub> lotion SPF 50+
This is a borderline substance which is only prescribable for photosensitive patients. Endorse script ACBS (Advisory Committee on Borderline Substances).

**UVISTAT®**<sub>OTC</sub> cream SPF 30
This is a borderline substance which is only prescribable for photosensitive patients. Endorse script ACBS (Advisory Committee on Borderline Substances).

**Photodamage**

**DICLOFENAC** (Solaraze®) gel 3%
*Dose*: Actinic keratosis, apply thinly twice daily for 60 to 90 days. Maximum 8 grams daily.

### 13.9 SHAMPOOS AND OTHER PREPARATIONS FOR SCALP AND HAIR CONDITIONS

**Coal tar preparations**
(Refer also to section 13.5)

<table>
<thead>
<tr>
<th><strong>FIRST CHOICE: ALPHOSYL 2 IN 1® SHAMPOO</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ALPHOSYL 2 IN 1®</strong>&lt;sub&gt;OTC&lt;/sub&gt; (coal tar extract 5%) shampoo</td>
</tr>
<tr>
<td><strong>Dose</strong>: Seborrhoeic dermatitis, psoriasis and scaling; use up to 3 times weekly.</td>
</tr>
<tr>
<td><strong>CAPASAL®</strong>&lt;sub&gt;OTC&lt;/sub&gt; (coconut oil 1%, salicylic acid 0·5%, coal tar 1%) shampoo</td>
</tr>
<tr>
<td><strong>Dose</strong>: Seborrhoeic dermatitis, psoriasis, scaling and itching, use 3 times weekly.</td>
</tr>
</tbody>
</table>

**Antifungal shampoos**

**KETOCONAZOLE**<sub>OTC</sub> shampoo 2%
*Dose*: Seborrhoeic dermatitis and dandruff; apply to scalp twice weekly for 6 weeks initially, then as required. Pityriasis versicolor; as a topical treatment to skin, refer to **BNF** for regimen.

**Hirsutism**

A patient information leaflet on ‘Hirsutism’ is available at [www.bad.org.uk](http://www.bad.org.uk). For some women with facial hirsutism topical eflornithine offers advantages over oral co-cyprindiol (section 13.6) as it avoids the risks associated with systemic therapies.

*S EFLORNITHINE* (Vaniqa®) cream 11·5%
Dose: Apply thinly twice daily. Eflornithine is much more effective where physical methods of hair removal are being used simultaneously. In the absence of improvement after treatment for 4 months, discontinue eflornithine.

13.10 ANTI-INFECTIVE SKIN PREPARATIONS

Antibacterial preparations only used topically

Note: Mupirocin cream and ointment are not interchangeable – the prescription should specify the formulation required.

S MUPIROCIN (Bactroban®) cream 2%
Dose: For traumatic lesions secondarily infected with MRSA, apply 3 times daily for up to 10 days; re-evaluate if no response after 3 to 5 days.

S MUPIROCIN ointment 2%
Dose: For MRSA skin colonisation or infection, apply up to 3 times daily for up to 10 days. May sting.

Antibacterial preparations also used systemically

S SODIUM FUSIDATE cream 2%
Dose: Apply 3 to 4 times daily for up to 7 days.
Limited indications: staphylococcal skin infections, eg impetigo. Use ONLY for short periods of time (up to 10 days) to prevent bacterial resistance. Refer to ‘Management of infection’ guidance.

METRONIDAZOLE (Rozex®) cream 0·75%
Dose: Rosacea, apply thinly twice daily for up to 3 to 4 months (often very rapidly effective); avoid contact with eyes. Cream is preferable to gel. Refer to ‘Management of rosacea’ guidance.

METRONIDAZOLE (Anabact®) gel 0·75%
Dose: For malodorous tumours and skin ulcers, apply to clean wound once or twice daily and cover with non-adherent dressing. Unsuitable for use in rosacea.

Antifungal preparations

AMOROLFINE OTC nail lacquer 5%
Dose: Dermatophyte infection, apply to infected nails once or twice weekly for 6 months (fingers) or 12 months (toes).

CLOTRIMAZOLE OTC cream 1%; solution 1%
Dose: Apply 2 to 3 times daily, continuing for 14 days after lesions have healed.

TERBINAFINE OTC cream 1%
Dose: Apply thinly once or twice daily for up to 1 week in tinea pedis, 1 to 2 weeks in tinea corporis and tinea cruris, 2 weeks in cutaneous candidiasis and pityriasis versicolor; review after 2 weeks. Not recommended for children.

MICONAZOLE NITRATE spray powder 0·16%
Dose: For interdigital tinea pedis, apply twice daily, continuing for 10 days after lesions have healed.

Treatment of lice and scabies
Consult NHS Highland guidance and leaflets on the treatment of head lice and scabies prior to prescribing, available via Intranet. For further information contact the Health Protection Team on 01463 704886 and refer to National Patient Pathways.

**Head lice**

Never use insecticides as a preventative measure as this promotes resistance. They should only be used when living lice have been found on the head. A second treatment is always needed after 7 days to kill lice emerging from surviving eggs. Alcoholic formulations may be irritant; aqueous formulations are preferred. Dimeticone is a non-insecticide preparation available for head lice treatment. Nitcombs and the ‘Bug Buster Kit’, containing an illustrated guide and combs, are now available on prescription or OTC; only one kit is required for a family and it is reusable.

**DIMETICONE** OTC lotion 4%
**Dose:** Rub into dry hair and scalp, allow to dry naturally, shampoo after minimum 8 hours (or overnight). Repeat application after 7 days.

**MALATHION** OTC aqueous liquid 0·5%
**Dose:** Rub into dry hair and scalp, allow to dry naturally, remove by washing after 12 hours. Repeat application after 7 days.

**Scabies**

A second application is always needed after 7 days. Treat all members of household/close contacts simultaneously, once only.

**FIRST CHOICE: PERMETHRIN**

**PERMETHRIN** OTC cream 5%
**Dose:** Apply over whole body and wash off after 8 to 12 hours. If hands are washed with soap and water within 8 hours of application re-apply cream. Repeat application after 7 days.

**MALATHION** OTC aqueous liquid 0·5%
**Dose:** Apply over whole body and wash off after 24 hours. If hands are washed with soap within 24 hours they should be retreated. Repeat application after 7 days.

Alcoholic lotion is not recommended for scabies or crab lice because it is irritant.

**13.11 SKIN CLEANSERS AND ANTISEPTICS**

For information on the use of skin cleansers and antiseptics refer to the NHS Scotland National Infection Prevention and Control Manual, the MRSA Policy and other Infection Control Policies on Intrnernet. Also refer to emollients for hand eczema and emollient bath additives with antiseptics listed in section 13.2.

**POTASSIUM PERMANGANATE** solution tablets for preparation of topical solution 400mg
ADVERSE REACTIONS TO TOPICAL THERAPY

- Adverse reactions are due either to irritation or contact allergy. They can be difficult to differentiate clinically, although immediate stinging is likely to be irritant in nature.

- Irritant reactions can affect anyone, but are more likely in atopic patients who tend to have dry, sensitive skin. They are more common with creams, which contain preservatives, biocides and emulsifiers than with ointments. Irritant facial conditions, such as rosacea, are more commonly irritated by gel preparations, which often contain propylene glycol, than by creams.

- Allergic reactions are less common and usually involve the immune system via a Type IV delayed hypersensitivity reaction, which can be investigated by patch testing. They should be suspected if the skin condition worsens or extends to other areas while on treatment and usually take 3 to 4 days to develop.

- Any topical agent can cause an allergic reaction, although some are more likely to than others, particularly topical antihistamines, local anaesthetics, antibiotics and creams, rather than ointments. The reaction may be due to an active ingredient, eg hydrocortisone or neomycin, or to an excipient, eg a preservative or emulsifier: related agents may cross-react. All ingredients are listed in the Summary of Product Characteristics (emc.medicines.org.uk/).

- Consider reporting adverse reactions online at https://yellowcard.mhra.gov.uk/.
USE OF EMOLLIENTS
(refer to section 13.2)

- Emollients are an important part of the treatment of all inflammatory dermatoses. They soothe inflamed skin, give the necessary lubrication to protect against further damage from external agents and help reduce transdermal water loss. They should continue to be applied even when the skin appears to return to normal, as it will still be unstable and easily irritated for several months after the inflammation subsides.

- It is particularly important to use emollients regularly, repeatedly and in adequate quantities in dry skin conditions such as atopic dermatitis and on dry, older skin, to reduce scaling, itching and protect against environmental irritants.

- Many emollients can be directly applied and used in the bath/shower. It is helpful for patients to be shown how to do this properly by trained staff.

- Some emollients contain an antiseptic (eg Emulsiderm®). These may be especially useful where the inflammatory condition is at risk of secondary infection, eg when the skin is broken by scratching.

- Emollients can be applied at any time of the day but are particularly helpful after a bath or shower; many can also be used as a soap substitute for cleansing.

- There are many types of emollient available. The cheaper ones are often as effective as the more expensive however it is helpful to give patients a range of emollients to find which suits their skin best, as choice of preparation will vary from person to person. Some patients like to use a cream or gel (non-sticky) during the daytime, and an ointment at night.

- Aqueous cream is not recommended as an emollient because it commonly irritates. It was not designed to be left on the skin.

- The best emollient to use is that which suits the patient.

- When applying topical steroids and emollients allow one to dry in before applying the other.
INCONTINENCE DERMATITIS

General measures
- assess the incontinence - can the condition be improved?
- ensure adequate fluid intake and healthy diet
- exclude urinary-tract infection
- assess the requirement for incontinence pads
- avoid plastic pants.

Cleansing/washing
Avoid hot water, prolonged soaking, bubble baths, talcs and perfumed soaps and alcohol-based wipes. If the skin becomes wet with urine, washing with warm water may be adequate. Gently pat the skin dry; avoid rubbing. If no urine has been in contact with the skin, washing at every pad change is unnecessary. Emollients and foam cleansers can be beneficial for dry, scaly skin as a soap substitute and to remove old layers of cream.

Barrier preparations
There are many preparations available but little published evidence to inform a choice. Consider safety, efficacy, cost-effectiveness and patient acceptability. Barrier preparations should be applied sparingly to the affected area only; excessive use can cause maceration, increasing the risk of microbial infection. Creams should be used with caution or avoided when incontinence pads are required as they may impair absorption.

Treatment
Treatment of active inflammation usually includes a topical antifungal, eg clotrimazole 1%, perhaps combined with a topical steroid eg Canesten HC®. See section 13.4.

Nappy rash
Nappy rash is a form of incontinence dermatitis and the guidance above also applies in this condition. In particular the following measures should be taken:
- increase the frequency of nappy changing and cleansing the skin
- apply a barrier cream after every nappy change
- let the child spend as long as possible without a nappy on.
MANAGEMENT OF PRURITUS
(refer to section 13.3 and National Patient Pathways)

- It is important to look for and treat any primary skin disease, eg eczema.

- Look carefully for the burrows of scabies, refer to section 13.10, to local guidance available on Intranet and to National Patient Pathways.

- If the skin is dry, apply liberal quantities of emollient. An emollient may also help even when the skin does not feel dry. Refer to section 13.2 and to guidance.

- Keep the environment cool, as pruritus is temperature-dependent.

- Avoid hot baths/showers and use unperfumed cleansers. Balneum Plus® bath oil is a good antipruritic.

- Zerobase® cream is a good soap substitute.

- Menthol 1% in aqueous cream is a useful first-line topical antipruritic emollient.

- A sedating antihistamine may be used at night in intractable pruritus where sedation is desirable (see section 3.4).

- Crotamiton cream is useful for the itch of scabies, which may take some weeks to settle after successful treatment.

- In the absence of skin inflammation or lesions, consider:
  - renal disease (U&E profile)
  - diabetes (glucose)
  - liver disease/cholestatics (LFT profile)
  - iron deficiency (ferritin profile)
  - polycythaemia and other blood dyscrasias (FBC and ESR or plasma viscosity)
  - thyroid disease (over or underactive) (TFT profile)
  - lymphoma and solid tumours, especially breast and lung cancer (chest x-ray)
  - drug reaction
  - hyper/hypocalcaemia (calcium and phosphate profiles).

- Only use topical corticosteroids if there are visible signs of inflammatory skin disease.

- Application of a bland moisturiser, such as Zerobase® cream, is useful for the symptomatic relief of itch from chickenpox etc.
USE OF TOPICAL CORTICOSTEROIDS
(refer to section 13.4)

Topical corticosteroid preparations are used in the treatment of inflammatory skin conditions other than those due to an infection. They are not curative, and should be backed up with other measures, in particular irritant avoidance and regular emollients (see section 13.2).

- Apply topical steroids thinly, initially twice daily. When applying along with an emollient, it does not matter which agent is applied first; allow one to dry in before applying the other. As an eruption settles, taper application gradually to once daily then to every 2nd day before stopping, usually after 10 to 14 days.

- They should not be used indiscriminately for pruritus, urticaria, or in undiagnosed rashes. They are contra-indicated in rosacea, and care should be taken with regular review when treating delicate areas of skin (face, groin, axillae or breast) or an eruption where the diagnosis is unclear. Potent steroids should only be used in psoriasis (other than on the scalp) under regular supervision due to the risk of provoking a severe pustular flare. Potent steroids can be used in recalcitrant conditions such as palmoplantar pustulosis, lichen simplex and nodular prurigo, provided that patients are reviewed regularly to ensure treatment is appropriate.

- Choice of steroid strength will depend on the nature of the condition being treated, the age of the patient and the site of disease, the aim being to use the weakest preparation that will suppress the inflammation. Take particular care when treating the face and flexures of children (especially under wet wrap dressings). It is reasonable to supply 2 strengths for patients with chronic conditions, one to be used for maintenance and a stronger one for short-term use during flare-ups.

- Prolonged use of potent steroids will lead to skin atrophy with easy bruising and striae formation, and can suppress the pituitary-adrenal axis. Facial use may cause a rosacea-like papular eruption (perioral dermatitis). In general, potent steroid preparations should only be used on ‘tough’ areas of skin (trunk and limbs). Delicate areas such as face, groin and axillae should be treated with mildly potent steroid preparations.

- The very potent steroid, clobetasol propionate (Dermovate®, ClobaDerm®), should be used with great caution, for brief periods only (preferably no longer than 2 weeks) and reviewed by the prescriber at least monthly. It should never be on repeat prescription, other than in special circumstances, eg vulval lichen sclerosus, refer to section 7.2 and British Association of Dermatology guidance and patient information leaflet available at www.bad.org.uk.

- Compound preparations, which contain antimicrobial agents, are useful where there is overt secondary infection. Their use otherwise is debatable, although they are often used where there may be a microbial component present such as in flexures. Those containing fusidic acid should only be used for short periods of time (up to 10 days) to reduce the likelihood of developing bacterial resistance and provoking MRSA colonisation. They should never be on repeat prescription.

- In general, ointment preparations are preferable for dry, scaly conditions; creams for moist ‘steamy’ areas (eg axillae and groin) and gels/lotions for the scalp.

Fingertip units can be helpful when determining prescription quantities. One fingertip unit (approximately 500mg, which covers the distal phalanx of the forefinger when squeezed out of the tube) is sufficient to cover the area of both hands, approximately 2% of skin area in an adult.
MANAGEMENT OF ECZEMA/DERMATITIS
(refer to sections 13.4, 13.5, National Patient Pathways and SIGN)

The mainstay of eczema/dermatitis management should comprise:

1. irritant avoidance
2. regular emollients
3. careful use of topical steroid.

Eczema/dermatitis (the terms are synonymous) is no more a diagnosis than, say, ‘anaemia’. It simply describes the clinico-pathological characteristics of an inflammatory erythematousquamous rash, which may weep and blister in the acute stage, becoming scaly and subsequently thickened if repeatedly scratched or rubbed.

Sometimes there is only one cause for eczema, eg allergic contact dermatitis to nickel in earrings. Often, however, there are more than one and sometimes several contributory causes, eg a hairdresser with an atopic background who develops irritant hand eczema from shampoo, which can be secondarily infected, or further complicated by allergic contact dermatitis to protective rubber gloves. It is important to identify all contributory factors.

- Check diagnosis to exclude psoriasis, fungal infection or scabies.
- Determine whether there is an atopic background.
- Determine the potential role of irritants, which is almost inevitable. Zerobase® cream or Zeroderm® ointment are good soap substitutes (refer to section 13.2).
- Consider an allergic component, particularly in varicose, ear, genital, hand, foot or facial eczema.
- Consider the presence of infection. Differentiate, if possible, between bacterial (golden crust, pustules usually caused by Staph. aureus or Strep. pyogenes), herpetic (vesicles or pustules) or mycological causes. Send appropriate swabs or scrapings for mycological assessment when necessary. Severe infections may require parenteral therapy.
- In seborrhoeic dermatitis consider yeast infection and treat with Canesten HC® or Daktacort® ointment.
- Weeping or blistered skin can be washed once or twice daily in a bath containing Emulsiderm® emollient, which can also be applied directly to lesions before drying. Lukewarm olive oil applied after washing and drying can be soothing and helpful, especially to remove crust and scale.
- Wet wrap or paste bandages can be useful in children and adults with limb eczema.
- Sedative antihistamines can be helpful at night. For further information see section 3.4.

Phototherapy may be considered for more chronic, stubborn extensive disease.

MANAGEMENT OF PSORIASIS
(also refer to section 13.5, National Patient Pathways, SIGN and British Association of Dermatology patient information leaflets (www.bad.org.uk))

- Management of psoriasis with emollients only (refer to ‘Use of emollients’ guideline and section 13.2) may be adequate in mild or asymptomatic cases, as well as for maintenance between exacerbations.

- Localised plaque
  - an emollient is important to lubricate skin at all times
  - the addition of a tar preparation may be appropriate in mild cases
  - alternatively, use short contact dithranol or topical vitamin D analogue and steroid.

- Itchy plaques – consider alternating tar or calcitriol with moderately potent topical steroid (eg Betnovate-RD® ointment).

- Hyperkeratotic – salicylic acid preparation, eg Diprosalic® ointment (also contains betamethasone dipropionate), in combination with tar or calcitriol and lukewarm olive oil to soften crusts. Diprosalic® ointment is for short-term use only and should not be used as maintenance treatment.

- Flexural, facial, hair margin – if calcitriol irritates use a moderately potent topical steroid, eg clobetasone butyrate (Eumovate® ointment).

- Guttate – emollient plus coal tar preparation (Exorex® lotion). Consider excluding streptococcal infection and referral if not settling after 6 weeks.

- Scalp
  - application of lukewarm olive oil to scalp, leave at least 30 minutes to soften scale and wash out with tar-based shampoo (Alphosyl 2 in 1® or Capasal®). Refer to section 13.9.
  - if not itchy, use a descaling ointment such as Cocois® ointment, applied for 30 to 60 minutes before shampoo
  - if itchy, use short-term (up to 2 weeks) intermittent steroid lotion or scalp application.

Refer if:
- failure to respond adequately to above
- more than 20% skin involved
- stubborn guttate not responding to standard treatment after 6 weeks
- unstable (pustular or inflamed) psoriasis.

Phototherapy
Although phototherapy is a first-line treatment for moderate to severe psoriasis it does not help all cases of psoriasis and must be carefully monitored. For these reasons, sunbeds should not be used for treatment.
Always try a topical antibiotic preparation before prescribing oral antibiotics. Do not use antibiotics continuously for more than 6 months without a 3-week drug holiday during which a topical antiseptic, eg benzoyl peroxide, should be applied to help reduce bacterial resistance. Always combine oral antibiotics with a topical antiseptic (see algorithm).
THERAPEUTIC NOTES

- Acne can be broadly classified into the following categories:

  **Mild:** The disease consists of open and closed comedones with some superficial papules and pustules.
  
  **Moderate:** More frequent deeper papules and pustules with mild scarring.
  
  **Severe:** Includes all of the above plus nodular abscesses and leads to more extensive scarring.

- Refer to algorithm on previous page.

- All topical acne treatments should be applied to the whole area affected throughout the course, even during periods of relative quiescence and ‘drug holidays’ from oral antibiotics.

1. **Mild comedonal/non-inflammatory acne**

   **First choice:**
   - **Benzoyl peroxide** applied once or twice daily. Introduce gradually. Emphasise that there must be some skin peeling if treatment is going to work, if problematic reduce the frequency of application to alternate days.
   - or
   - **Adapalene** (as benzoyl peroxide and adapalene (Epiduo®) gel or adapalene cream) applied once daily, may be less irritant than retinoids (cream is less irritant than gel). Avoid retinoids and adapalene during pregnancy. Avoid or minimise exposure to sunlight of areas treated with topical retinoids or adapalene. When exposure cannot be avoided, use a sunscreen product and protective clothing.

2. **Mild inflammatory acne**

   **First choice:**
   - **Erythromycin and zinc acetate (Zineryt® topical solution)** applied once or twice daily.
   - or
   - **Adapalene** (as benzoyl peroxide and adapalene (Epiduo®) gel or adapalene cream) – see above.

3. **Oral antibiotics**

   **First choice:**
   - **Oxytetracycline 500mg** twice daily for at least 3 months
   - or
   - **Erythromycin 500mg** twice daily for at least 3 months

   Do not prescribe tetracyclines in children, pregnancy or breast-feeding mothers as they are deposited in growing teeth and bone. Avoid excess sun exposure when taking tetracyclines (dose-dependent phototoxic reaction).

   Take **oxytetracycline** tablets with clear fluids at least an hour before food or 2 hours after previous meals. Do not take with iron or antacid preparations which may reduce absorption. Avoid concomitant use of different systemic and topical antibiotics. Benzoyl peroxide will reduce the risk of bacterial resistance developing.

   Always try a topical antibiotic, antiseptic or retinoid-like preparation before prescribing oral antibiotics and continue to apply one during antibiotic treatment (they are synergistic). Do not use oral antibiotics continuously for more than 6 months without a 3 week drug holiday during which a topical antiseptic (eg benzoyl peroxide) should be applied to help reduce bacterial resistance.
4. **Contraception**

Current recommendations are that no additional contraceptive precautions are required when hormonal contraceptives are used with oral oxytetracycline, erythromycin or doxycycline for acne.

*Progestogen-only implant use may affect acne in some women. Acne has been shown to occur, improve or worsen with the use of a progestogen-only implant. Where acne fails to improve, consider switching to an oestrogenic contraceptive such as Gedarel 30/150® ([https://www.fsrh.org/documents/cec-ceu-guidance-young-people-mar-2010/](https://www.fsrh.org/documents/cec-ceu-guidance-young-people-mar-2010/)).*

5. **Check compliance**

If the acne does not show a satisfactory response after 3 months of antibiotic treatment, switch to an alternative antibiotic such as doxycycline 100mg daily for 3 months then re-assess response.

*Doxycycline* may be taken with food, this may help to reduce the incidence of GI irritation. Do not prescribe tetracyclines to children, pregnant women or breast-feeding mothers as they are deposited in growing teeth and bone. Avoid excess sun exposure when taking tetracyclines (dose-dependent phototoxic reaction).

6. **Co-cyprindiol**

Co-cyprindiol is no more effective than oral antibiotic therapy, but is useful in females who also wish to receive oral contraception. It is contra-indicated in pregnancy, so must be taken assiduously. A pregnancy test is mandatory prior to initiation.

It reduces sebum excretion, which is under androgen control, and so can also help in idiopathic hirsutism.

Co-cyprindiol carries an increased risk for venous embolism. The risk increases with increasing BMI and co-cyprindiol should not be used in patients with a BMI above 35kg/m². See CSM advice in BNF section 13.6.2 and [https://www.fsrh.org/documents/cec-ceu-statement-dianette-jun-2013/](https://www.fsrh.org/documents/cec-ceu-statement-dianette-jun-2013/).

Co-cyprindiol provides effective contraception. An additional hormonal contraceptive should not be used in combination with co-cyprindiol.

7. **Oral isotretinoin**

Oral isotretinoin side-effects include teratogenicity, hyperlipidaemia, dryness and irritation of skin and mucous membranes. Isotretinoin must only be prescribed by or under the supervision of Physicians with expertise in the use of systemic retinoids for the treatment of severe acne and a full understanding of the risk of isotretinoin therapy and monitoring requirements.
MANAGEMENT OF CHRONIC URTICARIA AND ANGIOEDEMA
(also refer to National Patient Pathways and British Association of Dermatology guidance and patient information leaflet (www.bad.org.uk)

Preparations used in the management of serious acute allergic emergencies are listed in section 3.4: for guidance on their use refer to Resuscitation Council algorithms.

Urticaria and angioedema are caused by similar mechanisms and their management is essentially the same. This section is the view of the Dermatology Department, Raigmore Hospital and only a brief guide to initial management.

Physical urticarias (eg cold urticaria) are less common than ‘ordinary’ urticaria, however patients with physical urticaria often suffer from ‘ordinary’ urticaria whealing and/or angioedema as well.

Urticaria is artificially divided into ‘acute’ and ‘chronic’; the former lasting less than 6 weeks, the latter longer.

Investigations and associations
A careful history is most important, particularly precise details of attacks, symptoms, signs, and general health and activities immediately before attacks. It is especially helpful to seek:

- a history of atopic problems
- a detailed drug history, including OTC and ‘alternative’ preparations (see triggering factors, below)
- effect of anxiety/stress, infections, arthritis/inflammatory disease, thyroid disease, menstruation.

Urticaria, especially chronic urticaria, is relatively rarely an ‘allergic’ phenomenon; a specific allergic cause is usually obvious from a careful history.

Once acute or episodic urticaria has resolved, investigation is unlikely to yield any useful information.

Investigations
- Undertake the following in all chronic urticaria patients: U&E, LFT, TFT, FBC, ESR, C-reactive protein, autoantibodies, complement profiles.
- The following tests are seldom appropriate and are expensive:
  - C1 esterase inhibitor is only helpful in cases of suspected ‘hereditary’ angioedema (very rare).
  - IgE and RAST profiles seldom yield useful information in the absence of clear clinical suspicion/evidence of a specific sensitivity. By definition, atopic patients nearly always have elevated IgE levels and often multiple positive RASTs to common inhalants and food atopens. Patch testing is inappropriate.

Triggering factors
The following often worsen/precipitate attacks in a non-specific, ‘pharmacological’ fashion, rather than being due to ‘allergy’:

- Alcohol, caffeine, aspirin and other related NSAIDs, codeine and other opiates and OTC preparations containing them. They should be sought in the history (above). Paracetamol is the analgesic of choice in urticaria patients and seldom causes problems.
- Junk foods containing preservatives, flavourings and colouring materials may cause ‘pseudo allergic’ flares of urticaria/angioedema, as can foods containing high levels of salicylates.
- Any prescriber looking after a patient with urticaria/angioedema should be informed of the presence of this reaction pattern. Exercise caution with exposure to the drugs/substances listed above and especially to opiates (including general anaesthetics) and some iodine-based
radiographic contrast media. Also avoid ACE inhibitors and angiotensin-II receptor antagonists until urticaria has settled for at least 6 months.

**Treatment**
- Start with a non-sedating antihistamine. Most agents help within 2 weeks but overall adequacy of control by an individual agent should not be judged for 6 weeks.

- The first-line non-sedating antihistamine in NHS Highland is cetirizine:
  - prescribe cetirizine if the response to treatment is unsatisfactory as advocated in national guidance [off-label]; see www.bad.org.uk.
  - if control is still inadequate after 6 weeks rotate to an alternative antihistamine.
  - if control is still poor after a further 6 weeks consider referral to Dermatology.

- Systemic steroids are **definitely** a third-line agent for severe urticaria/angioedema only and should be used in conjunction with antihistamines. They are often complicated by tachyphylaxis/rebound; always taper **slowly**. A sensible starting dose would be 20 to 30mg once daily, tapering by 2.5mg/day once or twice per week down to 10mg once daily then reducing at the rate of 2.5mg each week. If systemic steroids are required for more than 4 weeks consider referral. As with most inflammatory dermatoses, excessively fast withdrawal of systemic steroids is often followed by rebound which may be severe and worse than the original condition.

- Subcutaneous adrenaline (Epipen®) is only very rarely indicated.

**Natural history**
- Chronic idiopathic urticaria and physical urticarias usually run a waxing/waning course of months to years before settling spontaneously, usually after 9 months to 2 years.

- Treatment is aimed at control, not necessarily eradication.

- Classical triggers (listed above) should be avoided in all cases, however a specific ‘allergy’ or an associated problem is usually not found.

- Disease impact studies in recent years have shown that chronic urticaria is as disabling/upsetting to patients as moderate to severe angina.
MANAGEMENT OF ROSACEA
(also refer to section 13.6, National Patient Pathways and British Association of Dermatology patient information leaflet (www.bad.org.uk))

Reduce triggering factors such as:

- hot drinks like tea and coffee, alcohol etc.
- hot and spicy food
- excessive heat, direct sunshine, hot showers etc.
- topical steroids.

Topical treatment (refer to section 13.6):

For mild papular/pustular rosacea:

- metronidazole (Rozex®) 0·75% cream or gel
- azelaic acid 15% cream.

For moderate to severe persistent redness/erythema:

- brimonidine gel 0·33% can be used (note MHRA advice below).

Oral treatment:

For moderate rosacea or not responding to topical treatment:

- a tetracycline, eg oxytetracycline or doxycyline
- erythromycin is an alternative
- review treatment in 6 to 8 weeks and if improvement the dose of antibiotics can be reduced, or change to topical.

For severe rosacea or not responding to oral antibiotics refer to Dermatology Department at Raigmore Hospital.

MHRA: Brimonidine gel: advice for health professionals:

- Exacerbation of rosacea symptoms occurred in up to 16% of patients treated with brimonidine gel in clinical studies; in most cases, erythema and flushing resolve after stopping treatment.
- Initiate treatment with a small amount of gel (less than the maximum dose) for at least 1 week and increase the dose gradually, based on tolerability and response to treatment.
- Advise patients carefully on how to apply the gel and on the importance of not exceeding the maximum daily dose (which is 1 gram of gel in total weight, approximately 5 pea-sized amounts).
- Advise patients to stop treatment and consult a doctor if their symptoms worsen during treatment (increased redness or burning).
- For further information see www.gov.uk.

Risk of systemic cardiovascular effects

- Cases of bradycardia, hypotension (including orthostatic hypotension), and dizziness after application of brimonidine gel have been reported, some of which required hospitalisation.
- Some cases were associated with application of brimonidine gel after laser procedures to the skin, which possibly caused increased absorption of the gel.
- Warn patients not to apply brimonidine gel to irritated or damaged skin, including after laser therapy to the skin.
- For further information see www.gov.uk.
For guidance regarding the use of any vaccine consult ‘Immunisation against infectious disease’ ('the Green Book'), available at https://www.gov.uk/government/organisations/public-health-england/series/immunisation-against-infectious-disease-the-green-book (most chapters have been amended since publication in 2006 and prescribers should always consult the electronic version). General information about immunisation is available at: http://www.immunisationscotland.org.uk. Those who prescribe vaccines regularly may find it useful to subscribe to Scottish Vaccine Update which has a useful summary of current issues (www.hps.scot.nhs.uk).

The NHS Highland ‘Immunisation procedure’ and the ‘Policy for staff immunisation’ are available on the intranet. Advice on any aspect of immunisation is available from the Health Protection Team, tel: 01463 704000 (switchboard).

14.4 VACCINES AND ANTISERA

Vaccines for UK immunisation schedule

All vaccines provided as part of the UK immunisation schedule are supplied by the NHS.

<table>
<thead>
<tr>
<th>Vaccine components</th>
<th>Brands available*</th>
<th>Additional information (see also BNF for Children)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria, tetanus, pertussis (acellular, component) and poliomyelitis (inactivated) vaccine (adsorbed, reduced antigen(s) content)</td>
<td>Boostrix-IPV®</td>
<td>For pregnant women. Ideally to be immunised between 28 and 32 weeks of pregnancy. For further details see: <a href="http://www.sehd.scot.nhs.uk/cmo/CMO(2012)09.pdf">http://www.sehd.scot.nhs.uk/cmo/CMO(2012)09.pdf</a></td>
</tr>
<tr>
<td>Diphtheria, tetanus, pertussis (acellular, component), hepatitis b (rDNA), poliomyelitis (inactivated), and Haemophilus influenzae type b conjugate (adsorbed), child (DTPa/HBV/IPV/ Hib)</td>
<td>Infanrix-Hexa®</td>
<td>For primary immunisation in children 8 weeks to 10 years of age.</td>
</tr>
<tr>
<td>Adsorbed diphtheria, tetanus, pertussis (acellular, component) and poliomyelitis (inactivated), child (DTaP/IPV)</td>
<td>Infanrix-IPV®</td>
<td>For boosting in children 3 years to 10 years of age.</td>
</tr>
<tr>
<td>Adsorbed diphtheria (low-dose), tetanus, pertussis (acellular, component) and poliomyelitis (inactivated), child (DTaP/IPV)</td>
<td>Repevax®</td>
<td>For boosting in children 3 years to 10 years of age.</td>
</tr>
<tr>
<td>Adsorbed diphtheria (low-dose), tetanus and poliomyelitis (inactivated), adults and children over 10 years (Td/IPV)</td>
<td>Revaxis®</td>
<td>For primary immunisation and boosting in individuals aged 10 years and over.</td>
</tr>
<tr>
<td>Haemophilus influenzae type b and Meningococcal group C conjugate, child (Hib/MenC)</td>
<td>Menitorix®</td>
<td>For boosting in children 1 year to 10 years of age.</td>
</tr>
<tr>
<td>Human papillomavirus</td>
<td>Cervarix® Gardasil®</td>
<td>For girls in national programme Gardasil® is supplied via vaccine holding centres. Young women aged 18 years and over for whom there is a clinical indication for HPV vaccination may be prescribed vaccine on GP10.</td>
</tr>
<tr>
<td>Measles/mumps/rubella live (MMR)</td>
<td>Priorix® MMRvaxPro®</td>
<td>For primary immunisation.</td>
</tr>
<tr>
<td>Meningococcal group C conjugate</td>
<td>Menjugate Kit® NeisVac-C®</td>
<td>One dose at 3 months for primary immunisation.</td>
</tr>
<tr>
<td>Meningococcal group B vaccine</td>
<td>Bexsero®</td>
<td>For primary immunisation at 2 and 4 months. Booster at 12 months. For guidance on the prevention of sepsis in asplenic patients refer to Intranet.</td>
</tr>
<tr>
<td>Meningococcal A, C, W135 and Y conjugate</td>
<td>Menveo® Nimenrix®</td>
<td>One dose routinely given in S3. From 1 August 2015 to Easter 2016 – urgent</td>
</tr>
</tbody>
</table>
For guidance on the prevention of sepsis in asplenic patients refer to Intranet. Consult Green Book for appropriate use in cases of complement deficiency.

**Vaccines/antitoxin for specific risk groups**


<table>
<thead>
<tr>
<th>Vaccine components</th>
<th>Brands available</th>
<th>Prescription status (NHS or private) and additional information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacillus Calmette-Guérin (BCG) (intradermal)</td>
<td>SSI®</td>
<td>NHS • for administration to those in risk groups in accordance with the procedure on Intranet for the identification and treatment of individuals in Highland who require tuberculin skin testing and/or BCG • may also be prescribed by clinicians when contacts of cases are referred by Public Health.</td>
</tr>
<tr>
<td>Botulism antitoxin</td>
<td></td>
<td>NHS • for use on the advice of Microbiology.</td>
</tr>
<tr>
<td>Hepatitis A single component</td>
<td>Avaxim® Havrix Monodose® Havrix Junior Monodose® Vaqta® Paediatric Vaqta® Adult</td>
<td>NHS • for use in accordance with the Highland BBV Managed Clinical Network Hepatitis A and Hepatitis B Vaccination Strategy.</td>
</tr>
<tr>
<td>Hepatitis A and hepatitis B (combined)</td>
<td>Ambirix® Twinrix®</td>
<td>NHS • for use in accordance with the Highland BBV Managed Clinical Network Hepatitis A and Hepatitis B Vaccination Strategy.</td>
</tr>
<tr>
<td>Hepatitis B single component</td>
<td>Engerix B® Fendrix® HBvaxPRO®</td>
<td>NHS • for individuals in high-risk groups (see Green Book) • excludes travellers and those immunised for occupational risk • employer (not employee) to be charged for occupational immunisation • the 40 micrograms dose is used for chronic haemodialysis patients – see policy at <a href="http://intranet.nhsh.scot.nhs.uk/PoliciesLibrary/Documents/Blood%20Borne%20Virus%20Protocol.pdf">http://intranet.nhsh.scot.nhs.uk/PoliciesLibrary/Documents/Blood%20Borne%20Virus%20Protocol.pdf</a>.</td>
</tr>
<tr>
<td>Influenza inactivated (split virion, surface antigen, virosomal)</td>
<td>Seasonal influenza</td>
<td>NHS • for risk groups as defined in annual CMO letter.</td>
</tr>
<tr>
<td>Influenza, live attenuated</td>
<td>Fluenz® Tetra</td>
<td>NHS • 2014/15 for all pre-school children from 2 years, and children in P1 to P7 at school • To be rolled out to all children 2 to 17 years.</td>
</tr>
<tr>
<td>Meningococcal A, C, W135 &amp; Y</td>
<td>Menveo®</td>
<td>NHS</td>
</tr>
<tr>
<td>Conjugate</td>
<td>Nimenrix&lt;sup&gt;®&lt;/sup&gt;</td>
<td>• only when advised by Health Protection Team as part of the public health management of cases of infection.</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>----------------------</td>
<td>-----------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Meningococcal B</td>
<td>Bexsero&lt;sup&gt;®&lt;/sup&gt;▼</td>
<td>For use in patients with asplenia, hyposplenia and complement disorders – see Green Book and policy on Intranet.</td>
</tr>
<tr>
<td>Palivizumab (see Chapter 5)</td>
<td>Synagis&lt;sup&gt;®&lt;/sup&gt;</td>
<td>NHS • to protect specified groups of infants at risk of serious Respiratory Syncytial Virus (RSV) infection (see SGHD/CMO(2010)22).</td>
</tr>
<tr>
<td>Pneumococcal polysaccharide (23 valent) (PPV)</td>
<td>Pneumococcal Polysaccharide Vaccine Sanofi Pasteur MSD</td>
<td>NHS • not recommended for children under 2 years of age • for guidance on the prevention of sepsis in asplenic patients refer to Intranet.</td>
</tr>
<tr>
<td>Rabies</td>
<td>Rabies vaccine Rabipur&lt;sup&gt;®&lt;/sup&gt;</td>
<td>NHS For pre-exposure prophylaxis in high-risk occupational groups and post-exposure prophylaxis following the advice of the Health Protection Team.</td>
</tr>
<tr>
<td>Tuberculin PPD RT 23 SSI 2 units/0.1mL for routine use, and 10 units/0.1mL</td>
<td>SSI&lt;sup&gt;®&lt;/sup&gt;</td>
<td>NHS • for Mantoux Test; refer to procedure (as for BCG) on Intranet • [unlicensed].</td>
</tr>
<tr>
<td>Varicella-zoster live</td>
<td>Varilrix&lt;sup&gt;®&lt;/sup&gt; Varivax&lt;sup&gt;®&lt;/sup&gt;</td>
<td>NHS Only for risk groups as per chapter 34 of the Green Book.</td>
</tr>
</tbody>
</table>

### 14.5 IMMUNOGLOBULINS

See information on the supply and use of the following products on the Formulary webpage on Intranet. Formulary accepted indications are "red" and "blue" indications in the NHS Scotland Clinical Guidelines for Immunoglobulin Use 2012. See also section 8.2.

S **NORMAL IMMUNOGLOBULIN** solution for intravenous infusion 100mg/mL (Kiovig<sup>®</sup>, Octagam<sup>®</sup>); solution for subcutaneous injection 160mg/mL (Subgam<sup>®</sup>), 200mg/mL (Hizentra<sup>®</sup>)

S **ANTI-D (RH<sub>O</sub>) IMMUNOGLOBULIN** 250 units, 500 units, 1500 units

S **ANTIHEPATITIS B IMMUNOGLOBULIN** intramuscular injection 500 units

S **ANTITETANUS IMMUNOGLOBULIN** intramuscular injection 250 units

S **ANTIVARICELLA-ZOSTER IMMUNOGLOBULIN** intramuscular injection 250 units

S **ANTIRABIES IMMUNOGLOBULIN** intramuscular injection
GUIDANCE ON PRESCRIBING VACCINES AND MEDICINES FOR TRAVEL

Information on vaccines and medicines for travel is available from Health Protection Scotland at [www.hps.scot.nhs.uk](http://www.hps.scot.nhs.uk), from [www.travax.nhs.uk](http://www.travax.nhs.uk), from the National Travel Health Network and Centre [www.nathnac.org](http://www.nathnac.org) and from [Medicines Information](http://www.medicinesinformation.org.uk). Patients can also be directed to [www.fitfortravel.nhs.uk](http://www.fitfortravel.nhs.uk). Advice for GPs on travel immunisations is available at [www.bma.org.uk](http://www.bma.org.uk).

### VACCINES

<table>
<thead>
<tr>
<th>Vaccine components</th>
<th>Brands available</th>
<th>Prescription status (NHS or private) and additional information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacillus Calmette-Guérin (BCG) (intradermal)</td>
<td>SSI®</td>
<td>NHS For those under 16 years of age who are going to live with local people for more than 3 months in a high-risk country – refer to procedure as above on Intranet.</td>
</tr>
<tr>
<td>Cholera&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td>Dukoral® (oral suspension)</td>
<td>NHS No longer recommended for routine use. It can be offered to humanitarian aid and relief workers, and travellers with remote itineraries in areas of cholera outbreaks who have limited access to safe water and medical care.</td>
</tr>
<tr>
<td>Diptheria (adsorbed diptheria (low-dose), tetanus and poliomyelitis (inactivated), adults and children over 10 years)</td>
<td>Revaxis®</td>
<td>NHS For individuals aged 10 years and over.</td>
</tr>
<tr>
<td>Hepatitis A single component</td>
<td>Avaxim® Havrix Monodose® Havrix Junior Monodose® Vaqtä® Paediatric Vaqtä® Adult</td>
<td>NHS</td>
</tr>
<tr>
<td>Hepatitis A and hepatitis B (combined)</td>
<td>Ambrix® Twinrix®</td>
<td>NHS</td>
</tr>
<tr>
<td>Hepatitis A with typhoid polysaccharide&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Hepatyrix® ViATIM®</td>
<td>NHS</td>
</tr>
<tr>
<td>Hepatitis B single component</td>
<td>Engerix B® Fendrix® HBvaxPRO®</td>
<td>Private</td>
</tr>
<tr>
<td>Japanese encephalitis&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td>Ixiaro®</td>
<td>Private</td>
</tr>
<tr>
<td>Meningococcal A, C, W135 and Y polysaccharide&lt;sup&gt;1&lt;/sup&gt;</td>
<td>ACWY Vax®</td>
<td>Private</td>
</tr>
<tr>
<td>Meningococcal A, C, W135 and Y conjugate</td>
<td>Menvec® Nimenrix®</td>
<td>Private</td>
</tr>
<tr>
<td>Poliomyelitis (adsorbed diptheria (low-dose), tetanus and poliomyelitis (inactivated), adults and children over 10 years)</td>
<td>Revaxis®</td>
<td>NHS</td>
</tr>
<tr>
<td>Rabies</td>
<td>Rabies vaccine Rabipur®</td>
<td>Private</td>
</tr>
<tr>
<td>Tetanus (adsorbed diptheria (low-dose), tetanus and poliomyelitis (inactivated), adults and children over 10 years)</td>
<td>Revaxis®</td>
<td>NHS</td>
</tr>
<tr>
<td>Tick-borne encephalitis&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td>TicoVac® TicoVac preparations</td>
<td>Private</td>
</tr>
<tr>
<td>Typhoid&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Typherix® Typhim Vi® Vivotif® live oral</td>
<td>NHS</td>
</tr>
<tr>
<td>Yellow fever&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td>Stamari®</td>
<td>Private Only from yellow fever vaccination centres.</td>
</tr>
</tbody>
</table>

---

1. Not stocked in Highland Hospitals  
2. Non-Formulary
Hospital pharmacies do not stock or supply vaccines solely used as travel vaccines. Any vaccines for use outwith the UK immunisation programme must be supplied on a GP10 (or private prescription if applicable) and not taken from the stock provided for the childhood programme or supplied on stock order forms (GP10A) as these forms are intended only for items for immediate use.

Advise patients that travel vaccinations aim to minimise risk and not eliminate it. Few vaccines offer 100% protection against disease.

Many travellers do not allow a sufficient time period for the full and licensed vaccination schedule to be administered. In many cases, a shortened or rapid schedule can be given and offers more protection than no vaccination at all. If there has been a deviation from the licensed vaccination schedule, it is recommended that practices obtain a signed recognition and consent from the patient stating that they have been made aware of the increased risk as a result.

**MEDICINES**

Increasing numbers of people are travelling from the UK to exotic and remote destinations, and health professionals giving advice on travel health must be competent to do so.

All General Practices should be registered users of Travax (www.travax.nhs.uk). For nursing staff, the Royal College of Nursing has published ‘Travel health nursing: career and competence development’ (2012), which can be accessed at www.rcn.org.uk.

**Malaria prophylaxis**

National decisions on prescription status are based on the balance of personal risk versus population risk. Antimalarials should not be prescribed for prophylaxis on the NHS; a private prescription must be issued. If preferred, community pharmacies can advise on and sell non-prescription antimalarial medicines over the counter. Community pharmacies can also advise on other issues related to travel medicine. In addition to Travax, additional information is available at www.fitfortravel.nhs.uk.

**Taking medicines out of the UK**

Patients requiring regular repeat medication for a stable pre-existing illness may be supplied with an NHS prescription for a maximum of three months treatment, to provide treatment for the journey and until further supplies can be secured at the destination.

If patients are to be out of the UK for longer than this then they may require on-going medical review and it would be more appropriate to provide a letter detailing the patient’s medicines until they can make arrangements to get further supplies of medicines at their destination.

Advice for patients requesting medicines for taking on extended holidays and for taking prescribed controlled drugs outside the UK is available at http://www.nhs.uk/chq/Pages/1074.aspx?CategoryID=70&SubCategoryID=175.

**Prophylactic medication**

A person is not entitled to NHS provision of drugs where there is no existing condition. Any requests for items to be prescribed in case of illnesses contracted whilst travelling abroad (eg ciprofloxacin or oral rehydration sachets for diarrhoea) are a private transaction.
CHAPTER 15 ANAESTHESIA

Refer to Raigmore Hospital ‘Acute Pain Manual’, ‘Non-steroidal anti-inflammatory drugs (NSAIDs)’, ‘Acute pain – adult oral/rectal analgesic step ladder’ on Intranet and local guidance on the assessment of patients pre-admission and pre-operation. The majority of drugs listed in Chapter 15 are for use by clinicians with appropriate expertise. See guidance on ‘Local anaesthetic toxicity’.

15.1 GENERAL ANAESTHESIA

SODIUM CITRATE oral solution 300mmol/L (0.3 Molar)

Intravenous anaesthetics

ETOMIDATE solution for injection 20mg/10mL

KETAMINE CD2 solution for injection 200mg/20mL, 500mg/10mL

PROPOFOL emulsion for injection 1% 200mg/20mL, 500mg/50mL; emulsion for injection 1% pre-filled syringe 500mg/50mL; emulsion for injection 2% 1 gram/50mL

THIOPENTAL powder for solution for injection 500mg

Inhalational anaesthetics

DESFLURANE inhalation vapour 1mL/1mL

ISOFLURANE inhalation vapour 1mL/1mL

SEVOFLURANE inhalation vapour 1mL/1mL

NITROUS OXIDE inhalation gas 1mL/1mL

NITROUS OXIDE 50% AND OXYGEN 50% inhalation gas

Antimuscarinic drugs

ATROPINE solution for injection 600 micrograms/1mL

GLYCOPYRRONIUM solution for injection 600 micrograms/3mL

Benzodiazepines

DIAZEPAM tablets 2mg, 5mg, 10mg; oral solution 2mg/5mL; emulsion for injection 10mg/2mL; rectal solution 2.5mg/1.25mL, 5mg/2.5mL, 10mg/2.5mL

LORAZEPAM tablets 1mg; solution for injection 4mg/1mL [licensed and unlicensed preparations]

MIDAZOLAM CD3 oromucosal solution 50mg/5mL (Epistatus® CD3) [unlicensed]; solution for injection 10mg/2mL, 5mg/5mL; solution for infusion 50mg/50mL

The 10mg/2mL injection is used in Palliative Care as a subcutaneous bolus injection; refer to Scottish Palliative Care Guidelines.
MIDAZOLAM WITH LIDOCAINE CD3 (midazolam 20mg, lidocaine 10mg/0.5mL) nasal solution [unlicensed]
For use by anaesthetists only, for the sedation of patients for whom traditional methods of sedation
(oral or intravenous) are contraindicated or unsuitable.

TEMAZEPAM CD3 tablets 10mg; oral solution 10mg/5mL

Non-opioid analgesics

S PARECOXIB powder and solvent for solution for injection 40mg

Opioid analgesics

ALFENTANIL CD2 solution for injection 1mg/2mL; intensive care solution for injection 5mg/1mL

FENTANYL CD2 solution for injection 100 micrograms/2mL, 500 micrograms/10mL (ITU only); nasal spray (PecFent®) 100 micrograms/metered spray, 400 micrograms/metered spray

REMIFENTANIL CD2 powder for concentrate for solution for injection 2mg, 5mg

Other drugs for sedation

DEXMEDETOMIDINE injection 200 micrograms/2mL

Muscle relaxants

Non-depolarising muscle relaxants

ATRACURIUM solution for injection 25mg/2.5mL, 250mg/25mL

MIVACURIUM solution for injection 10mg/5mL, 20mg/10mL

ROCURONIUM solution for injection 50mg/5mL

Depolarising muscle relaxants

SUXAMETHONIUM solution for injection 100mg/2mL

Anticholinesterase with glycopyrronium used in anesthesia

NEOSTIGMINE WITH GLYCOPYRRONIUM (neostigmine 2.5mg, glycopyrronium 500 micrograms/1mL) solution for injection

Other drugs for reversal of neuromuscular blockade

SUGAMMADEX solution for injection 200mg/2mL, 500mg/5mL
For immediate reversal of rocuronium-induced neuromuscular blockade; see SMC advice.

Antagonists for central and respiratory depression

FLUMAZENIL solution for injection 500 micrograms/5mL

NALOXONE solution for injection 400 micrograms/1mL; solution for injection pre-filled syringe
400 micrograms/1mL (Minijet®), 2mg/2mL (for use in A&E)
**Drugs for malignant hyperthermia**

**DANTROLENE** powder for solution for injection 20mg  
Dantrolene is held within theatres at each hospital. Refer to [BNF](https://www.gov.uk/government/collections/bnf) for further information on use.

**15.2 LOCAL ANAESTHESIA**

The maximum safe local anaesthesia doses are as follows:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Maximum safe dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lidocaine</td>
<td>3mg/kg</td>
</tr>
<tr>
<td>Lidocaine (with adrenaline/epinephrine)</td>
<td>7mg/kg</td>
</tr>
<tr>
<td>Bupivacaine</td>
<td>2mg/kg</td>
</tr>
<tr>
<td>Bupivacaine (with adrenaline/epinephrine)</td>
<td>2mg/kg</td>
</tr>
<tr>
<td>Levobupivacaine</td>
<td>2mg/kg</td>
</tr>
</tbody>
</table>

Refer to information on [local anaesthetic toxicity](https://www.gov.uk/government/collections/bnf).

**LIDOCAINE** solution for injection 1% (50mg/5mL, 100mg/10mL, 200mg/20mL), 2% (100mg/5mL)

**LIDOCAINE WITH ADRENALINE** (Xylocaine®) solution for injection (lidocaine 1%, adrenaline 1 in 200 000), (lidocaine 2%, adrenaline 1 in 200 000)

**BUPIVACAINE** infusion (epidural) 250mg/250mL (0·1%) in sodium chloride 0·9%

**BUPIVACAINE WITH GLUCOSE** (Marcain Heavy®) (bupivacaine 20mg, glucose 320mg/4mL) solution for injection for spinal anaesthesia

**LEVOBUPIVACAINE 0·1% WITH FENTANYL 2 MICROGRAMS/ML** infusion in sodium chloride 0·9% (250mL) [unlicensed]

**LEVOBUPIVACAINE** solution for injection 25mg/10mL, 50mg/10mL, 75mg/10mL; epidural infusion 250mg/200mL (0·125%)

**PRILOCAINE** solution for injection 1% 500mg/50mL

**ADRENALINE WITH ARTICAINE** injection (adrenaline 1 in 100 000 (22 micrograms), articaine 88mg/2·2mL cartridge)

**MEPIVACAINE** solution for injection cartridge 3%

**For surface anaesthesia**

**LIDOCAINE** topical solution 4%; ointment 5%; spray 10%

**LIDOCAINE WITH PRILOCAINE** (lidocaine 2·5%, prilocaine 2·5%) (EMLA®) cream

**LIDOCAINE WITH CHLORHEXIDINE** (lidocaine 2%, chlorhexidine 0·25%) gel

**LIDOCAINE WITH PHENYLEPHRINE** (lidocaine 5%, phenylephrine 0·5%) topical solution

**TETRACAINE** (Ametop®) gel 4%  
Tetracaine is an effective local anaesthetic for topical application; Ametop® gel is preferred to EMLA® cream.
For dental use

LIDOCAINE WITH ADRENALINE (lidocaine 2%, adrenaline 1 in 80 000) solution for injection cartridge

PRILLOCAINE WITH FELYPRESSIN (prilocaine 3% (60mg), felypressin 0·066 unit/2·2mL) solution for injection cartridge; self-aspirating cartridge
LOCAL ANAESTHETIC TOXICITY

Local anaesthetic toxicity is rare but life-threatening. Most deaths from local anaesthetic toxicity have been due to the inadvertent intravenous injection of a toxic dose of local anaesthetic. Rapid recognition and appropriate treatment saves lives.

<table>
<thead>
<tr>
<th>Early signs and symptoms:</th>
<th>Late signs and symptoms:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• tinnitus</td>
<td>• tonic-clonic convulsions</td>
</tr>
<tr>
<td>• flushed face</td>
<td>• profound hypotension</td>
</tr>
<tr>
<td>• circum-oral numbness</td>
<td>• drowsiness</td>
</tr>
<tr>
<td>• lightheadedness</td>
<td>• coma</td>
</tr>
<tr>
<td></td>
<td>• respiratory arrest</td>
</tr>
</tbody>
</table>

**MANAGEMENT OF LOCAL ANAESTHETIC TOXICITY**

Treatment of local anaesthetic toxicity is likely to have a good outcome if toxicity is recognised and basic resuscitation is started early. The basic tenets of treatment are:

- prevent hypoxia which will cause brain damage and make fitting or arrhythmias more difficult to control
- treat hypotension and arrhythmias early
- ensure that fits are adequately treated
- most reactions are short-lived if the above advice is followed.

<table>
<thead>
<tr>
<th>A. Airway</th>
<th>Ensure an adequate airway and give oxygen.</th>
</tr>
</thead>
<tbody>
<tr>
<td>B. Breathing</td>
<td>Ensure that the patient is breathing adequately. Ventilation with or without intubation may be required.</td>
</tr>
</tbody>
</table>
| C. Circulation     | Treat circulatory failure with intravenous fluids and vasopressors:  
                    | • ephedrine hydrochloride solution for injection 3mg/mL, by slow intravenous injection 3 to 6 mg every 3 to 4 minutes (maximum per dose 9mg), adjusted according to response. Maximum 30mg per course.  
                    | • adrenaline may be used cautiously intravenously in boluses of 0.5 to 1mL of 1:10 000 if ephedrine is either unavailable or ineffective.  
                    | • treat arrhythmias.  
                    | • start chest compressions if cardiac arrest occurs or there is an arrhythmia with no output. |
| D. Drugs           | Treat convulsions. Do not allow fits to continue as this will cause hypoxia.  
                    | • diazepam 0.2 to 0.4mg/kg intravenously slowly over 5 minutes, repeated after 10 minutes if required, or 2-5mg to 10mg rectally.  
                    | • buccal midazolam 10mg [unlicensed].  
Reduce the myocardial local anaesthetic concentration with lipid emulsion 20% (ClinOleic® 20%, Intralipid® 20%) [off-label].  
• give 1mL/kg bolus.  
• give 2 further doses every 3 to 5 minutes.  
• start an infusion at 0.25mL/kg/min until 500mL given.  
After successful resuscitation admit the patient to a high dependency area or Intensive Care Unit.

Central nervous system toxicity

Respiratory arrest
Coma
Convulsions
Loss of consciousness
Muscle twitching
Slurred speech
Tinnitus
Lightheadedness
Tingling tongue/lips

Plasma lidocaine concentration (microgram/mL)

Cardiovascular system toxicity

Ventricular arrest
Cardiac arrhythmias
Myocardial depression

DEATH

25
20
15
10
5
0

Lead reviewer: Anaesthetics Review Group
Date: August 2016
Version: 1
Approved by: Formulary Subgroup of NHS Highland ADTC
Review date: August 2018
Warning: document uncontrolled when printed
## APPENDIX 1  
### THERAPEUTIC DRUG MONITORING SUMMARY

For information on features and management of overdose contact the UK National Poisons Information Service 0844 892 0111 or access TOXBASE ([www.toxbase.org](http://www.toxbase.org)) available in A&E or Acute Medical Admissions Unit, Raigmore Hospital. For further information on therapeutic drug monitoring contact Medicines Information. For laboratory information refer to the [Blood Sciences](#) and [Microbiology](#) pages on Intranet.

<table>
<thead>
<tr>
<th>DRUG</th>
<th>TIME TO STEADY STATE</th>
<th>IDEAL SAMPLING TIME</th>
<th>TARGET RANGE</th>
<th>COMMENTS</th>
</tr>
</thead>
</table>
| CARBAMAZEPINE | 2 to 3 weeks (initiation)  
At least 2 to 4 weeks after dose change | Before dose (not critical) | 4 to 12mg/L | Induces its own metabolism (peaks 3 weeks after initiation).  
Check drug interactions especially with other antiepileptics and drugs with narrow therapeutic index.  
Sampling is only useful if toxicity or poor compliance suspected. |
| CICLOSPORIN | 2 to 4 days | TROUGH (12 hours post-dose) |  | Red EDTA tube to be sent to Blood Sciences for analysis on Tuesdays and Thursdays. |
| DIGOXIN | 7 to 10 days (initiation and after dose change) | Before dose or over 6 hours after dose | 0.5 to 2 micrograms/L | Dose requirements lower in renal impairment and older people. Question the need to take levels unless signs of toxicity or suspect non-compliance; measurement only usually necessary for confirmation of toxic dosage or where problems occur with maintenance therapy, including a possible lack of compliance. |
| GENTAMICIN | 1 day (depends on renal function) | Use with caution in oliguric patients who are critically unwell.  
For high-dose regimen 6 to 14 hours after start of infusion.  
Use nomogram for timing of subsequent doses. | See [nomogram on prescription chart](#) or [online gentamicin calculator](#) | For all regimens dose interval depends on renal function, monitor more frequently if renal function changes or is unstable.  
For high-dose regimen monitor once at initiation then every 2 or 3 days if renal function is stable. If renal function is unstable, monitor levels after every dose. |
| LITHIUM | 5 days (initiation and after dose change) | 12 hours after dose | 0.4 to 1 mmol/L (narrower range may be advised by psychiatrist) | Dose depends on renal function.  
Check lithium level 4 to 7 days after initiation and 7 days after a dose change.  
Monitor weekly until stabilised then every 3 months.  
Monitor more regularly if renal function changes.  
Monitor thyroid and renal function every 6 months.  
Check drug interactions.  
Check lithium levels when interacting medication is started or stopped. |

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**Lead reviewer:** Therapeutic Drug Monitoring Review Group  
**Date:** October 2016  
**Approved by:** Formulary Subgroup of NHS Highland ADTC  
**Review date:** October 2018  
**Version:** 7  
**Warning:** document uncontrolled when printed
<table>
<thead>
<tr>
<th>DRUG</th>
<th>TIME TO STEADY STATE</th>
<th>IDEAL SAMPLING TIME</th>
<th>TARGET RANGE</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHENYTOIN</td>
<td>2 to 3 weeks (initiation and after dose change)</td>
<td>Before dose (not critical)</td>
<td>10 to 20mg/L</td>
<td>Check phenytoin level 3 days after initiating treatment to confirm the patient’s metabolism is not remarkably different from the norm. Care with increase in dose – non-linear rise in level. Care if hypoalbuminaemia, liver or renal failure. Check for drug interactions.</td>
</tr>
<tr>
<td>SIROLIMUS*</td>
<td>2 to 4 days</td>
<td>TROUGH (24 hours post-dose)</td>
<td>For renal transplant patients the levels are individualised according to patient risk – contact a Renal Consultant for advice.</td>
<td>Red EDTA tube to be sent to Blood Sciences for analysis on Fridays.</td>
</tr>
<tr>
<td>TACROLIMUS</td>
<td>2 to 4 days</td>
<td>TROUGH (12 or 24 hours post-dose depending on preparation prescribed)</td>
<td>For renal transplant patients the levels are individualised according to patient risk – contact a Renal Consultant for advice.</td>
<td>Red EDTA tube to be sent to Blood Sciences for analysis on a Monday, Wednesday and Friday.</td>
</tr>
<tr>
<td>TEICOPLANIN</td>
<td>3 to 5 days if loading dose given</td>
<td>TROUGH</td>
<td>20 to 30mg/L</td>
<td>Troughs above 60mg/L associated with toxicity. Loading dose is required to achieve steady state. Serum levels sent to Bristol Laboratory on weekdays with turnaround time of 1 to 2 days.</td>
</tr>
<tr>
<td>TOBRAMYCIN</td>
<td>1 day (depends on renal function)</td>
<td>TROUGH (before dose) PEAK (1 hour after end of infusion)</td>
<td>TROUGH less than 2mg/L PEAK 6 to 10mg/L</td>
<td>Dose depends on renal function. Monitor more frequently if renal function changes. Alternative dosing regimens are used in patients with cystic fibrosis, seek advice from respiratory physicians.</td>
</tr>
<tr>
<td>THEOPHYLLINE</td>
<td>At least 5 days (initiation and after dose change) or immediate if given IV (aminophylline) with a loading dose</td>
<td>Oral: – 4 to 6 hours after dose (not critical) Intravenous no loading: – 4 to 8 hours after start of infusion Intravenous with loading: – 30 to 60 minutes Conversion from IV to oral: – over 24 hours after oral dose</td>
<td>10 to 20 mg/L (serum levels of aminophylline are expressed as theophylline)</td>
<td>Some clinicians use low oral dose as there is evidence of therapeutic effect at levels as low as 5mg/L. Aminophylline is theophylline in a formulation for intravenous administration. Monitoring is more important for intravenous therapy or suspected toxic reaction. Clearance altered by other drugs, smoking, hepatic dysfunction, cardiac disease and COPD, can be difficult to predict with any accuracy.</td>
</tr>
<tr>
<td>VALPROIC ACID</td>
<td>3 days</td>
<td>Pre-dose</td>
<td>50 to 100mg/L</td>
<td>Rarely useful. Poor correlation between concentration and effect. Sampling is only useful if toxicity or poor compliance suspected.</td>
</tr>
<tr>
<td>VANCOMYCIN</td>
<td>1 day if loading dose is given (depends on renal function)</td>
<td>TROUGH (before dose) PEAK (2 hours after end of infusion)</td>
<td>TROUGH 10 to 20mg/L depending on advice from Microbiology PEAK 18 to 26mg/L</td>
<td>Dose depends on renal function. Monitor more frequently if renal function changes. For deep-seated infections, troughs up to 20mg/L may be recommended by Microbiology.</td>
</tr>
</tbody>
</table>

* Non-Formulary drug
This table sets out the requirements for ongoing monitoring of conventional DMARDs (disease modifying anti-rheumatic drugs) in primary care. This guidance has been agreed across all specialities in NHS Highland. Some patients will require additional monitoring due to the severity of their condition or other specific factors: in these cases, the consultant will inform the GP of the specific monitoring required. **A consultant’s advice always takes precedence over this guidance.** More detailed patient and GP information leaflets may be available from the relevant specialities such as those produced by the Rheumatology team. This guidance does not cover baseline pre-screening for initiating DMARDs.

<table>
<thead>
<tr>
<th>Drug Combination</th>
<th>Initial monitoring until dose is stable for 6 weeks</th>
<th>Monitoring for next 3 months</th>
<th>Monitoring for next 9 months</th>
<th>Long-term monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azathioprine</td>
<td>FBC, LFTs, creatinine/eGFR</td>
<td>FBC, LFTs, creatinine/eGFR</td>
<td>FBC, LFTs, creatinine/eGFR</td>
<td>FBC, LFTs, creatinine/eGFR</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>Every 2 weeks</td>
<td>Every 1 month</td>
<td>Every 3 months</td>
<td>Every 3 months</td>
</tr>
<tr>
<td>Methotrexate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sulfasalazine/</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mesalazine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ciclosporin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mycophenolate</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tacrolimus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combination* of leflunomide &amp; methotrexate</td>
<td>Every 2 weeks</td>
<td>Every 1 month</td>
<td>Every 3 months</td>
<td>Except sulfasalazine/mesalazine: stop monitoring at 12 months</td>
</tr>
</tbody>
</table>

**Additional drug-specific testing required:**

1: Azathioprine  TPMT at baseline
2: Leflunomide  BP and weight at each attendance
3: Methotrexate  Dermatology only: procollagen III every 3 months
4: Ciclosporin  BP and blood glucose at each attendance
5: Tacrolimus  BP and blood glucose at each attendance

Hydroxychloroquine  Annual review by optometrist

*For all other combinations, follow the monitoring for the DMARD with the highest frequency of tests. No additional tests are needed.*

Key: FBC = full blood count, LFTs = liver function tests, eGFR = estimated glomerular filtration rate
APPENDIX 3 GOOD PRESCRIPTION WRITING GUIDELINES

**GENERAL** (also refer to ‘Prescription writing’ section in current BNF and General Medical Council guidance ‘Good practice in prescribing and managing medicines and devices’ at www.gmc-uk.org/guidance/ethical_guidance/14316.asp).

1. **HIGHLAND FORMULARY**
   - Please use/refer to the Highland Formulary or other relevant Highland formulary when choosing appropriate prescription.
   - Prescribers must be aware of the Formulary and license status of any medicine prescribed and must comply with all policies relating to the supply of non-Formulary medicines, see Formulary webpage on Intranet.

2. **WRITE LEGIBLY**
   - Prescriptions should be:
     - legible
     - in black ink
     - dated
     - include the full name and address of the patient and community health index (CHI) number
     - signed in black ink by the prescriber.

3. **AGE, DATE of BIRTH and CHI Number**
   - These must always be stated. In the case of prescription-only medicines, it is a legal requirement to state the age for children under 12 years of age.
   - For outpatient prescriptions, the PMS (Patient Management System) label should be used.

4. **DOSE**
   - The dose must be stated in the International System of Units (SI units).
   - Abbreviations for grams (g); milligrams (mg), millilitres (mL) and litres (L) may be used.
   - ‘Micrograms’, ‘nanograms’ and ‘units’ must be written in full.
   - State the dosage form, dose, route, timing and frequency.
   - ‘As required’ prescriptions should also specify the maximum dose per specified time period (eg day) and indication.

5. **FREQUENCIES and ROUTES OF ADMINISTRATION**
   - These should be written in full.
   - When an amendment to a medicine currently being prescribed is needed, eg frequency or dose change, a new entry must be made on the Kardex* and the original entry discontinued.

6. **DECIMAL POINTS**
   - Avoid unnecessary zeros, however always precede a decimal point with a zero where there is no other figure.
   - When unavoidable, decimal points should always have a number covering in front eg 0·5mL and not ·5mL.
   - Decimal points should be clear and, ideally, centred.
   - Whole numbers should be kept whole, eg 5mg and not 5·0 mg.
   - Quantities of 1 gram or more should be written as gram/grams.
   - Quantities less than 1 gram should be written as milligrams, eg 500mg.
   - Quantities less than 1mg should be written as micrograms, eg 100 micrograms, not 100μg or 0·1mg.

7. **AS DIRECTED**
   - Avoid writing ‘as directed’ unless clear written direction, which is signed by the prescriber, is provided separately.

8. **NON-PROPRIETARY (GENERIC) NAMES**
   - Recommended International Non-proprietary Names (ie generic names as they appear in the British National Formulary) should be used for a medicine and be written in full except for some combination products, some modified-release preparations and where bioavailability is a problem.

9. **ABBREVIATIONS**
   - Avoid abbreviations.

10. **WEIGHT OR SURFACE AREA**
    - Where the weight or surface area is required to calculate a dose, write this on the prescription.

11. **CONTROLLED DRUGS**
    - For advice on prescribing controlled drugs refer to current BNF and ‘GP Summary; a guide to good practice in the management of CDs in primary care’ at http://www.knowledge.scot.nhs.uk/media/CLT/ResourceUploads/4068524/A_Guide_to_Good_Practice_Summary_for_GPs_v.2.0_160915.doc
**HOSPITAL INPATIENT ‘DIRECTION TO ADMINISTER’ (additional advice)**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>1. ADMINISTRATION</strong></td>
<td>A medicine that is not correctly prescribed must not be administered if it is considered that following the prescribing instruction may be harmful to the patient. If the prescription is unclear or illegible this must be referred to the prescriber before any medicine is administered.</td>
</tr>
</tbody>
</table>
| **2. DRUG KARDEX** | The Drug Kardex must include the patient's  
- name  
- hospital number (and/or Community Health Index (CHI) number)  
- date of birth and weight must be recorded on the front of the Kardex, also surface area if a dosage requires it. |
| **3. PRESCRIBERS** | Medicines must be prescribed on all appropriate prescription sheets by a registered or provisionally registered medical practitioner, dentist, supplementary or independent non-medical prescriber. |
| **4. KARDEX PRESCRIPTIONS** | These must be dated and written legibly, typed or electronically produced in indelible black ink specifying the dosage form, dose, route, timing and frequency with the prescriber's signature and printed name for each item prescribed.  
- Take care to ensure correct section of form is used, eg ‘once only’ and ‘pre-med regular therapy’ or ‘as required therapy’.  
- Specify time using the 24-hour clock, eg 22:00 rather than 10pm. |
| **5. CAPITALS** | All written prescribing information on the Drug Kardex must be in capitals. |
| **6. AS REQUIRED MEDICINES** | For medicines prescribed on an 'as required' basis, abbreviations must not be used and dose, dosage interval and indication for the medicine should be clearly stated, eg 500mg every four hours for a headache when required.  
- Indicate the maximum dose in a given time period, if appropriate. |
| **7. DISCONTINUATION** | To discontinue a medicine, the prescriber must draw a clear Z through the prescription section and a clear diagonal line through every section of the record of administration areas with a vertical line right through the last recorded date of being given, enter the date in the 'stop date' box and initial it.  
- When an amendment to a medicine currently being prescribed is needed, eg dosage change, a new entry must be made on the Kardex and the original entry discontinued. |
| **8. PRESCRIPTION SHEETS** | Avoid using more than one Drug Kardex for each patient if at all possible. Old Kardexes must be cancelled by drawing two parallel diagonal lines across the front page and writing ‘cancelled’. It should be authorised by the prescriber's signature and date of cancellation.  
- A new Kardex should be used for each hospital admission. |
| **9. REWRITING** | If it is necessary to rewrite a Drug Kardex the original start date for each item must be used. |
| **10. SPECIAL SHEETS** | When special sheets (eg oral anticoagulants, insulin and continuous infusions) are in use, items must also be prescribed on the Drug Kardex with the dose stated as charted. |
| **11. PATIENT TRANSFER** | The Kardex should be signed and dated when a patient is transferred from one place to another and the same Kardex continued. |
| **12. ALLERGY SECTION** | An entry must always be made in the Allergy/Drug Sensitivity section.  
- Write either drug name or ‘nil known’. |

*refers to any form of (direction to administer) documentation.*
### PRIMARY CARE/HOSPITAL OUTPATIENT PRESCRIPTIONS (additional advice)

| 1. PATIENT’S DETAILS | The prescription should include as a minimum:  
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• name</td>
</tr>
<tr>
<td></td>
<td>• home address</td>
</tr>
<tr>
<td></td>
<td>• hospital number (and/or CHI number).</td>
</tr>
</tbody>
</table>

| 2. PRESCRIBER’S DETAILS | Prescriptions written by non-medical prescribers should state:  
|--------------------------|------------------------------------------------------------------|
|                          | • the type of prescriber, eg Nurse Supplementary/Independent Prescriber  
|                          | • the prescriber’s professional registration number, eg NMC PIN number  
|                          | • the prescriber’s contact details including telephone number where this is not pre-printed on the form.  
| For prescriptions to be dispensed by a community pharmacy/dispensing GP practice, the prescription should state the reference number of the GP practice with which the patient is registered to allow correct allocation of prescribing costs. |

| 3. CAPITALS | All handwritten prescribing information on prescriptions must be in capitals. |

| 4. NAME, PRESCRIBED ITEM, FORMULATION, STRENGTH, DOSE/FREQUENCY and QUANTITY | For prescribing in primary care and for patients whose prescriptions will be dispensed in the community, the prescription must contain the name of the prescribed item, formulation, strength (if appropriate), dosage and frequency, and quantity to be dispensed. The quantity should be appropriate to the patient’s treatment needs, bearing in mind the frequency of review and need to avoid waste.  
|                                                                       | • Some medicines are only available in patient packs (or multiples thereof) and special containers. In such cases complete packs (or multiple packs) should be prescribed, provided this is clinically and economically appropriate.  
|                                                                       | • Specify the quantity for solid preparations as number of dose units (number of tablets, patches, etc.), for liquid measures in millilitres (mL), for topical preparations by mass (grams, g), or volume (millilitres, mL).  
|                                                                       | • Do not use terms such as ‘1 pack’ or ‘1 OP’.  
|                                                                       | • Alternatively, for preparations to be given at a fixed dose and interval, the duration of treatment can be used in place of the quantity to be dispensed. |

| 5. NUMBER OF DAYS | The quantity to be supplied may be stated by indicating the number of days’ treatment required in the box provided on the NHS forms. In most cases, the exact amount will be supplied.  
|                   | • This cannot apply to items directed to be used ‘as required’ – if the exact dose and frequency are not given the quantity needs to be stated.  
|                   | • When several items are ordered on one form, the box can be marked with the number of days’ treatment, provided the quantity is added for any item for which the amount cannot be calculated. |

| 6. UNUSED SPACE | Block out unused space on the prescription form with, for example, a diagonal line (to prevent subsequent fraudulent addition of extra items). |

| 7. MORE THAN ONE/ MAXIMUM NUMBER | Where there is more than one item on a form, insert a line between each item for clarity. A maximum of three items is allowed on one prescription form. |

| 8. SIGNATURE | Prescriptions must be signed in the signature space, in black ink, before they are issued. |
COMPUTER GENERATED PRESCRIPTIONS (additional advice)

1. **PRINT OUT**
   The computer must **print out** the date, the patient’s surname, one forename, other initials, address and CHI number and may also print out the patient’s title and date of birth. The age of children under 12 years and of adults over 60 years must be printed in the box available; print the age of children under 5 years in years and months. A facility must also exist to print out the age of patients between 12 and 60 years.

2. **PRESCRIBER’S DETAILS**
   The prescriber’s name must be printed on the prescription (who will normally sign it). The surgery address, reference number, and Health Board are also necessary. In addition, print the surgery telephone number. Computer generated prescriptions issued by non-medical prescribers should also indicate the type of prescriber, eg Nurse Supplementary/Independent Prescriber, and their professional registration number, eg NMC PIN number.

3. **RESPONSIBLE PRINCIPAL**
   When prescriptions are to be signed by general practitioner registrars, assistants, locums or deputising doctors, the name of the doctor printed on the form must still be that of the **responsible principal**.

4. **COMPUTER MEMORY**
   Names of medicines must come from a dictionary held in the **computer memory** to provide a check on the spelling and to ensure that the name is written in full. The computer can be programmed to recognise both the non-proprietary and the proprietary name of a particular drug and to print out the preferred choice, but must not print out both names. For medicines not in the dictionary, separate checks are required – the user must be warned that no check was possible and the entire prescription must be entered in the lexicon.

5. **THE DICTIONARY**
   The dictionary may contain information on usual doses, formulations and pack sizes to produce standard pre-determined prescriptions for common preparations and provide a check on individual prescription validity on entry.

6. **DISPENSING**
   Checks may be incorporated to ensure that all the information required for **dispensing** a particular drug has been filled in. For instructions such as ‘as directed’ and ‘when required’, the maximum daily dose should normally be specified.

7. **NUMBERS/CODES**
   Numbers and codes used in the system for organising and retrieving data must never appear on the form.

8. **SUPPLEMENTARY WARNINGS/ADVICE**
   Write all supplementary warnings and advice in full. They should not interfere with the clarity of the prescription itself and should be in line with any warnings or advice in the Highland Formulary or BNF. Avoid numerical codes.

9. **UNUSED SPACE**
   A mechanism (such as printing a series of non-specific characters) should be incorporated to cancel out **unused space**, or wording such as ‘no more items on this prescription’ may be added after the last item. Otherwise, the prescriber should delete the space manually.

10. **AVOID FORGERY**
    To avoid forgery, the computer may print on the form the number of items to be dispensed (somewhere separate from the box for the pharmacist). There should be no more than three items on a prescription form.

11. **HANDWRITTEN ALTERATIONS**
    Handwritten alterations should only be made in exceptional circumstances – it is preferable to print out a new prescription. Any alterations must be made in the prescriber’s own handwriting and countersigned; update all computer records to fully reflect any alteration. Prescriptions for drugs used for contraceptive purposes (but which are not promoted as contraceptives) may need to be marked in handwriting with the symbol ♀ (or endorsed in another way to indicate that the item is prescribed for contraceptive purposes).

12. **THE PRESCRIPTION**
    The right hand side of the **prescription** is normally used as an ordering form for repeat prescriptions, but take care to avoid including confidential information. It may be advisable for the patient’s name to appear at the top, but this should be preceded by ‘confidential’.

13. **REPRINTING/ DUPLICATE**
    Prescription forms that are reprinted or issued as a duplicate should be labelled clearly as such.
APPENDIX 4  EMERGENCY TREATMENT OF POISONING

The following are the treatments for poisoning used in NHS Highland; stock in individual hospitals is held in agreement with Accident and Emergency consultant staff. Use will be in accordance with national guidance (www.toxbase.org) or in consultation with staff from the National Poisons Information Service (tel: 0344 892 0111).

REMOVAL AND ELIMINATION

$CHARCOAL, ACTIVATED (Activated charcoal) oral suspension 1 gram/5mL (Charcodote®), granules 50 grams (Carbomix®)

SPECIFIC DRUGS

$ACETYLCYSTEINE injection 2 grams/10mL

$ATROPINE injection 600 micrograms/1mL, 600 micrograms/1mL pre-filled syringe

$BOTULISM ANTITOXIN injection [unlicensed]

$CALCIUM CHLORIDE injection 10mmol/10mL

$CALCIUM GLUCONATE gel 2.5% [unlicensed], injection 10% (10mL)

$CLINOLEIC infusion 20% 500mL

$CYPROHEPTADINE HYDROCHLORIDE tablets 4mg

$DANTROLENE SODIUM injection 20mg

$DESFERRIOXAMINE injection 500mg

$DICOBALT EDETATE injection 300mg/20mL

$DIGOXIN-SPECIFIC ANTIBODY FRAGMENTS (F(ab)) (DigiFab®) powder for reconstitution for intravenous infusion 40mg/vial

$DISODIUM FOLINATE injection 400mg/8mL
The disodium salt of folinic acid is stocked in Raigmore hospital in preference to the calcium salt.

$EUROPEAN VIPER VENOM ANTISERUM (snake venom antiserum) injection [unlicensed]

$FLUMAZENIL injection 500 micrograms/5mL

$FOMEPIZOLE injection 1 gram/mL [unlicensed]

$GLUCAGON (GlucaGen® HypoKit) injection 1mg

$GLYCERYL TRINITRATE injection 5mg/5mL, 50mg/50mL

$HYDROXOCOBALAMIN (Cyanokit®) injection 5 grams

$IDARUCIZUMAB (Praxbind®) 2.5g/50mL solution for injection/infusion
MACROGOL 3350 WITH ANHYDROUS SODIUM SULFATE, POTASSIUM CHLORIDE, SODIUM BICARBONATE AND SODIUM CHLORIDE (Klean-Prep®) oral powder sachets, 69 grams/sachet

MESNA injection 1 gram/10mL

METHYLTHIONINIUM CHLORIDE (METHYLENE BLUE) injection 50mg/10mL

NALOXONE injection 400 micrograms/1mL

OCTREOTIDE injection 50 micrograms/1mL

PHENTOLAMINE injection 10mg/1mL [unlicensed]

PHYTOMENADIONE injection 10mg/1mL

PRASTICHOLINE injection 1 gram
Stock held in Raigmore Pharmacy Store.

PROCYCLIDINE injection 10mg/2mL

PRATAMINE SULFATE injection 50mg/5mL

SODIUM BICARBONATE infusion 1.26%, 8.4%

SODIUM THIOSULFATE injection 25% (250mg/mL)
### SUMMARY OF NHS HIGHLAND MINOR AILMENTS
#### SERVICE FORMULARY 8th EDITION

**Summary of Minor Ailment Service Formulary preparations by BNF classification**

The following medicines from the BNF can be provided on the Community Pharmacy Minor Ailments Service (MAS):

- pharmacy medicines (P) and general sales list medicines (GSL)
- selected items from Part 3 of the Scottish Drug Tariff

Medicines listed below are included in the NHS Highland MAS Formulary which is available on the NHS Highland Intranet and website and on the Community Pharmacy website page for Highland. The medicines in this NHS Highland MAS Formulary should meet the needs of the majority of patients under the MAS.

Some prescription-only medicines (POMs) may be provided using NHS Highland Patient Group Directions (PGDs) to enable the provision of the more cost-effective POM versions of chloramphenicol eye drops and fluconazole 150mg capsules under the MAS. These PGDs are distributed to all community pharmacies in NHS Highland and can be accessed on the Community Pharmacy Services section on NHS Highland Intranet at [http://intranet.nhsh.scot.nhs.uk/](http://intranet.nhsh.scot.nhs.uk/) or [https://nhsnss.org/services/practitioner/pharmacy/](https://nhsnss.org/services/practitioner/pharmacy/).

### 1. Antacids
- **Mucogel®** (Co-magaldrox SF) 195/220 suspension (500mL)
- Compound alginic acid preparations
  - *Gaviscon® Advance* chewable tablets (60)
  - *Peptac®* suspension (500mL)

### 2. Antispasmodics
- Mebeverine tablets 135mg (15)

### 3. Antisecretory drugs
- Ranitidine tablets 75mg (6 or 12)

### 4. Antimotility drugs
- Loperamide capsules 2mg (10)
- Oral rehydration salts, powder sachets (6)

#### 4.1 Bulk forming laxatives
- Ispaghula husk 3-5g/sachet (30)

#### 4.2 Stimulant laxatives
- Docusate sodium capsules 100mg (30)
- Docusate sodium solution 50mg/5mL (300mL)
- Glycerol suppositories 2g, 4g (12)
- Senna tablets 7-5mg (20)
- Senna syrup 7-5mg/5mL (150mL)

#### 4.3 Osmotic laxatives
- Macrogol oral powder compound sachets 13-125grams/sachet (*Laxido®*) (20)
- Lactulose solution 3-1 to 3-7g/5mL (300mL)

#### 4.4.1 Soothing haemorrhoidal preparations
- *Anusol®* cream (23g)
- *Anusol® ointment* (25g)
- *Anusol® suppositories* (12)

#### 4.4.2 Compound haemorrhoidal preparations with corticosteroids
- *Anusol Plus HC®* ointment (15g)
- *Anusol Plus HC®* suppositories (12)

### 3.4.1 Antihistamines
- Cetirizine tablets 10mg (30)
- Cetirizine oral solution 5mg/5mL (200mL)
- Loratadine tablets 10mg (30)
- Chlorphenamine tablets 4mg (28)
- Chlorphenamine SF oral solution 2mg/5mL (150mL)

### 4.6 Drugs used in nausea and vertigo
- Cinnarizine tablets 15mg (15)
- Promethazine tablets 25mg (10)
- Promethazine elixir 5mg/5mL (100mL)
- Hyoscine hydrobromide tablets 150 micrograms (12)
- Hyoscine hydrobromide tablets 300 micrograms (12)

### 4.7 Analgesics

#### Non-opioid analgesics
- Paracetamol tablets 500mg (32)
- Paracetamol SF suspension 120mg/5mL (100mL/200mL)
- Paracetamol SF suspension 250mg/5mL (100mL/200mL)

#### Migraine
- Sumatriptan tablets 50mg (2)

### 5.2 Antifungal drugs
- Fluconazole 150mg capsules (1) (for vaginal candidiasis only)

### 5.5.1 Drugs for threadworms
- *Ovex®* (Mebendazole) tablets 100mg (1 or 4)
- *Ovex®* (Mebendazole) suspension 100mg/5mL (30mL)

### 7.2.2 Vaginal and vulval infections
- Clotrimazole vaginal tablet 500mg (1)
- Clotrimazole cream 1% (20g)
- Clotrimazole vaginal cream 10% (5g)

### 9.1.2 Drugs used in megaloblastic anaemias
- Folic acid tablets 400 micrograms (90)
9.2.1.2 Oral rehydration therapy
  • Oral rehydration salts, powder sachets (6)

10.1.1 Non-steroidal anti-inflammatory drugs
  • Ibuprofen tablets 200mg (24)
  • Ibuprofen tablets 400mg (24)
  • Ibuprofen suspension 100mg/5mL (100mL)

10.3.2 Topical non-steroidals
  • Ibuprofen topical gel 5% w/w (30g)

11.1.1 Non-steroidal anti-inflammatory drugs
  • Ibuprofen tablets 200mg (24)
  • Ibuprofen tablets 400mg (24)
  • Ibuprofen suspension 100mg/5mL (100mL)

11.3.1 Antibacterials
  • Chloramphenicol eye drops 0-5% (10mL)
  • Chloramphenicol eye ointment 1% (4g)

12.1.3 Removal of ear wax
  • Olive oil ear drops (10mL)
  • Sodium bicarbonate ear drops 5% (10mL)

12.2.1 Nasal allergy
  • Beclometasone nasal spray 50 micrograms/spray (100 or 180 doses)

12.3.1 Emollient and barrier preparations
  • Liquid and white soft paraffin ointment 50/50 (250g)
  • Yellow soft paraffin (500g)
  • Diprobase® cream (50g, 500g)
  • Epaderm® ointment (125g, 500g)
  • Hydromol® ointment (125g, 500g)

13.2.1.1 Emollient bath additives
  • Oilatum® emollient (bath additive (250mL, 500mL)
  • Oilatum® Junior bath additive (250mL)
  • Bainem® bath oil (200mL, 500mL)
  • Emulsiderm® liquid emulsion (300mL)
  • Dermo® 200 shower emollient (200mL)

13.3 Topical local antipruritics
  • Arjuna® (Menthol 1% in aqueous cream) (100g)
  • Crotamiton cream 10% (30g)

13.4 Topical corticosteroids
  • Hydrocortisone ointment 1% (15g)
  • Hydrocortisone cream 1% (15g)

13.6.1 Topical preparations for acne
  • Benzoyl peroxide aqueous gel 5% (Acnecide®) (30g)
  • Benzoyl peroxide aqueous gel 10% (Panoxyl® Aquagel) (40g)

13.7 Preparations for warts and callouses
  • Bazuka® gel 12%, 26% (5g)

13.9 Shampoos and scalp preparations
  • Alphosyl 2 in 1® (coal tar extract 5%) shampoo (125mL)
  • Capasal® shampoo (250mL)
  • Ketoconazole shampoo 2% (60mL/100mL)

13.10.2 Antifungal preparations
  • Amorolfine nail lacquer 5% (3mL)
  • Clotrimazole cream 1% (20g)
  • Miconazole nitrate spray powder 0-16% (100g)
  • Terbinafine cream 1% (7-5g)

13.10.4 Parasiticidal preparations
  • Dimeticone lotion 4% (50mL/150mL)
  • Malathion aqueous liquid 0-5% (50mL/200mL)
  • Permethrin dermal cream 5% (30g)
  • Nitcomb (1)
  • Nitty Gritty NitFree (Steel Nit comb (1)
  • Bug Buster Kit (1)
APPENDIX 6 POLYPHARMACY: SUMMARY OF GUIDANCE FOR PRESCRIBING IN FRAIL ADULTS

The NHS Scotland *Polypharmacy Guidance 2015* supports all clinicians carrying out comprehensive medication reviews with patients and carers. It aims to help practitioners to get evidence into action for safe and effective, person-centred care, in a complex area of practice. The guidance is available as an app with desktop and mobile versions providing clinicians with guidance at their fingertips, in clinical settings or community. An overview of the '7-steps' process is shown below:

<table>
<thead>
<tr>
<th>Domain</th>
<th>Steps</th>
<th>Process</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aims</td>
<td>1. Identify objectives of drug therapy</td>
<td>Review diagnoses and identify therapeutic objectives with respect to: • Management of existing health problems • Prevention of future health problems.</td>
</tr>
<tr>
<td>Need</td>
<td>2. Identify essential drug therapy</td>
<td>Identify essential drugs (not to be stopped without specialist advice) • Drugs that have essential replacement functions eg levothyroxine • Drugs to prevent rapid symptomatic decline, eg drugs for Parkinson’s disease, heart failure.</td>
</tr>
<tr>
<td></td>
<td>3. Does the patient take unnecessary drug therapy?</td>
<td>Identify and review the (continued) need for drugs • with temporary indications • with higher than usual maintenance doses • with limited benefit in general for the indication they are used for • with limited benefit in the patient under review (see Drug efficacy and applicability (NNT) table in guidance).</td>
</tr>
<tr>
<td>Effectiveness</td>
<td>4. Are therapeutic objectives being achieved?</td>
<td>Identify the need for adding/intensifying drug therapy in order to achieve therapeutic objectives • To achieve symptom control • To achieve biochemical/clinical targets • To prevent disease progression/exacerbation.</td>
</tr>
<tr>
<td>Safety</td>
<td>5. Does the patient have ADR or is at risk of ADR?</td>
<td>Identify patient safety risks by checking for • drug-disease interactions • drug-drug interactions (see ADR table) • robustness of monitoring mechanisms for high-risk drugs • drug-drug and drug-disease interactions • risk of accidental overdosing. Identify adverse drug effects by checking for • specific symptoms/laboratory markers eg hypokalaemia) • cumulative adverse drug effects (see ADR table) • drugs that may be used to treat ADRs caused by other drugs.</td>
</tr>
<tr>
<td>Adherence/patient</td>
<td>7. Is the patient willing and able to take drug therapy as intended?</td>
<td>Identify risks to patient non-adherence by considering • Is the medicine in a form that the patient can take? • Is the dosing schedule convenient? • Is the patient able to take medicines as intended? • Might the patient benefit from the Chronic Medication Service (CMS)? • Is the patient’s pharmacist informed of changes to regimen? Ensure drug therapy changes are tailored to patient preferences by • Discuss with the patient/carer/welfare proxy therapeutic objectives and treatment priorities • Decide with the patient/carer/welfare proxies what medicines have an effect of sufficient magnitude to consider continuation or discontinuation.</td>
</tr>
</tbody>
</table>

NNT are a guide; they do not give exact figures for individual patients. Older people have increased absolute event rates, thus NNT to prevent one event may be lower in older people – conversely NNH are likely to be higher – see weighing the benefit/risk in NNT.
APPENDIX 7  PALLIATIVE CARE GUIDELINES

Scotland’s national guidelines for palliative care are available at: www.palliativecareguidelines.scot.nhs.uk.

The primary goal of these guidelines is to improve care by minimising inconsistencies in clinical practice through the provision of practical and readily usable, evidence-based or best-practice guidance on a range of common clinical issues. These guidelines have been developed for use by all healthcare professionals involved in the provision of palliative care to those with a life-limiting illness. The guidelines have been produced by collaboration between a multidisciplinary group of professionals working in community, hospital and specialist palliative care services across Scotland’s NHS (including NHS Highland) and third sector organisations.

National guidelines listed in the table below supersede previous local versions of palliative care guidance. The following local guidelines are not yet available in national guidelines and are included in this appendix:
1. Management of fungating tumours in palliative care in adults
2. Managing sleep disturbance in adults
3. Respiratory-tract secretions in palliative care in adults
4. Saliva management: sialorrhoea in adults
5. Management of diabetes in adults in palliative care
6. Antiemetics used in palliative care.

The local 24-hour Palliative Care advice line can be contacted at Highland Hospice, tel: 01463 243132 (or for internal calls from Raigmore Hospital speed dial 1333, and ask to speak to the Doctor on call).

The Palliative Care Advisory Service (PCAS) in Raigmore Hospital can be contacted by staff for advice 24 hours a day. For referral to PCAS between 9am and 5pm, Monday to Friday: 1) Obtain consent from the Consultant in charge of the patient’s care. 2) Contact at Raigmore Hospital, tel: 01463 704000.

<table>
<thead>
<tr>
<th>Scottish palliative care guidelines (<a href="http://www.palliativecareguidelines.scot.nhs.uk">www.palliativecareguidelines.scot.nhs.uk</a>)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pain</strong></td>
</tr>
<tr>
<td>Pain Assessment - Cognitive Impairment  (<a href="#">link</a>)</td>
</tr>
<tr>
<td>Pain Management  (<a href="#">link</a>)</td>
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<tr>
<td>Neuropathic Pain  (<a href="#">link</a>)</td>
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<tr>
<td>Choosing and Changing Opioids  (<a href="#">link</a>)</td>
</tr>
<tr>
<td>Anticipatory prescribing  (<a href="#">link</a>)</td>
</tr>
<tr>
<td><strong>Symptom Control</strong></td>
</tr>
<tr>
<td>Bowel Obstruction  (<a href="#">link</a>)</td>
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<tr>
<td>Breathlessness  (<a href="#">link</a>)</td>
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<tr>
<td>Constipation  (<a href="#">link</a>)</td>
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<tr>
<td>Cough  (<a href="#">link</a>)</td>
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<td>Delirium  (<a href="#">link</a>)</td>
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<td>Depression  (<a href="#">link</a>)</td>
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<td>Diarrhoea  (<a href="#">link</a>)</td>
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<td>Hiccups  (<a href="#">link</a>)</td>
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<tr>
<td>Mouth Care  (<a href="#">link</a>)</td>
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<td>Nausea and Vomiting  (<a href="#">link</a>)</td>
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<tr>
<td>Pruritus  (<a href="#">link</a>)</td>
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<tr>
<td>Sweating  (<a href="#">link</a>)</td>
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<tr>
<td>Weakness / Fatigue  (<a href="#">link</a>)</td>
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<tr>
<td>Syringe pumps  (<a href="#">link</a>)</td>
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<tr>
<td>Out of hours handover  (<a href="#">link</a>)</td>
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<tr>
<td><strong>Palliative Emergencies</strong></td>
</tr>
<tr>
<td><strong>Seizures</strong> (<a href="#">link</a>)</td>
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<tr>
<td>--------------------------</td>
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<tr>
<td>End of Life care</td>
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<tr>
<td></td>
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<td></td>
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<tr>
<td>Medicine Information sheets</td>
</tr>
</tbody>
</table>
1. MANAGEMENT OF FUNGATING TUMOURS IN PALLIATIVE CARE IN ADULTS

A fungating tumour is a primary or secondary cancer that has ulcerated the skin. The management of fungating tumours focuses on alleviating the distressing symptoms associated with the wound and providing emotional support to the patient and family/carers. They most commonly develop from cancer of the head and neck, breast, melanoma and soft tissue sarcoma. Treatment is directed towards control of bleeding, odour restriction, absorption of exudates, control of pain associated with the lesion and comfort/cosmetic appearance. This information is a guide and a comprehensive wound assessment should be undertaken.

If the wound is moist/dry and clean the primary dressing should be a non-adherent foam dressing (semi-permeable), eg Allevyn/Mepilex.

### Bleeding
- alginate dressing
- soak gauze in adrenaline (epinephrine) 1:1000 and apply to the wound for 10 minutes
- topical application of sucralfate paste (two 1g tabs crushed in 5mL of KY jelly) or suspension 1g/10mL
- tranexamic acid topically (500mg in 5mL injection ampoules)
- radiotherapy
- major haemorrhage (See guideline on 'Haemorrhage'.

### Odour control
- metronidazole: oral 200mg to 400mg three times daily or topical gel formulation twice a day, may be ongoing
- charcoal dressing, eg Clinisorb®
- silver dressings – not appropriate if radiotherapy is part of treatment plan
- deodorisers in the room/use of aromatherapy oils
- use of single room if appropriate.

### Absorption of exudates
- exclude wound infection as this can increase exudates
- absorbent dressing, eg hydrogel/hydrofibre
- control bacterial contamination
- honey dressings
- protect surrounding skin from excoriation and maceration with suitable barrier product such as Cavilon®
- surgical debridement.

### Pain
See section on 'Pain Management'. Topical opioids may be used on specialist recommendation only (off-label).

Secondary dressings consist of foam dressing +/- additional padding and tubifast to secure

For persistent difficult symptoms contact Highland Hospice/PCAS
Emotional support

The consequences of having a fungating lesion secondary to cancer can be far reaching and encompass physical, psychological, social, sexual and spiritual dimensions. Each patient will react in their own way and a sensitive, skilled approach to care is vital. Patients may experience depression, embarrassment, social isolation, fear, repulsion, shame, altered body image, and a constant reminder of advanced, incurable disease.

Health professionals need to establish trust with patients and family and use tact and sensitivity.

There are strategies for managing these psychosocial problems. Interventions should aim to boost patient confidence and improve their ability to socialise wherever possible.

- cosmetic appearance – dressings need to effectively manage odour and exudates but where possible restore body symmetry
- access to counselling services
- appropriate social support decreases stress and anxiety at home
- spiritual care according to individual’s beliefs
- involvement of the patient, family and carers in decisions about care
- open, honest communication of goals and decisions
- appropriate use of touch/physical contact
- access to complementary therapies.
2. MANAGING SLEEP DISTURBANCE IN ADULTS

Assess current difficulties:
- fear of sleeping
- number/length of wakening periods
- quality of sleep – dreams/nightmares
- daytime activity/sleepiness.

Physical symptom-related issues, eg:
- pain
- nausea/vomiting
- breathlessness/cough
- itch
- cramps
- continence issues – nocturia, incontinence, constipation.

Emotional issues
- anxiety
- depression
- fear
- spiritual distress.

Symptoms
- review symptom management
- review medication (Box 1)
- address underlying anxieties and fears, including spiritual issues and other unresolved issues.

Develop a sleep plan, taking into account:
- environment
- comfort – is bed harder now due to weight loss?
- daytime napping
- timing of drinks
- caffeine/alcohol intake especially late in the day
- exercise – but not within 2 hours of settling
- develop sleep rituals.

Education
- sleep rituals
- reduce stimulation approaching bed time
- relaxation/breathing techniques.

Complementary therapies
- aromatherapy
- acupuncture.
BOX 1

Review medication
- caffeine/alcohol/nicotine

Prescribed medication interrupting night-time sleep
- diuretics – taken after midday
- steroids – taken after midday
- sedative/hypnotic withdrawal
- opioid side-effects
- theophylline, methylphenidate, beta-blockers etc.

Medication causing daytime drowsiness
- night-time sedation
- sedative/hypnotic/anxiolytic drugs
- antihistamines.
3. RESPIRATORY-TRACT SECRETIONS IN PALLIATIVE CARE IN ADULTS

For full guidelines, resources and information:

Introduction
The patient has, or is at risk of developing, excessive respiratory tract secretions/noisy breathing near the end of life. On average, this occurs in about 50% of people who are dying, from a few hours up to 3 days before death. The patient is likely to be semi-conscious or unconscious and unlikely to be distressed. However, this symptom can be distressing for relatives, carers and others involved. Management takes account of this.

CAUSE
• fluid pooling in the hypopharynx and airways when the patient is too weak to expectorate or swallow
• build-up of saliva is the most common cause.

MANAGEMENT
Assessment
• exclude treatable causes (eg left ventricular failure, infection)
• assess patient’s level of consciousness and understanding
• assess relatives’ understanding and anxieties.

Non-drug management
• explanation of symptom control plan to patient if conscious or semi-conscious.
• explanations to family/carers and reassurance that patient is unlikely to be distressed if semi-conscious or unconscious. This may ease family’s distress and remove the need for drugs or other interventions.
• if possible position patient semi-prone to encourage postural drainage.
• Reduce risk by avoiding fluid overload; review any assisted hydration or nutrition (intravenous or subcutaneous fluids, feeding) if symptoms develop. Suction may also exacerbate secretions.

Drug treatments
• Intermittent subcutaneous injections often work well or medication can be given as a subcutaneous infusion. Be aware that conscious patients may be troubled by dry mouth on these medications.
  o First-line: hyoscine butylbromide subcutaneous 20mg, hourly as required (up to 120mg/24 hours).
  o Second-line: glycopyrronium bromide subcutaneous 200 micrograms, 6 to 8-hourly as required.
  o Third-line: hyoscine hydrobromide subcutaneous 400 micrograms, 2-hourly as required.

Patient has excessive respiratory-tract secretions

YES
1. Reposition patient (if possible).
2. **Prescribe** hyoscine butylbromide (Buscopan) 20mg subcutaneously **OR** glycopyrronium 200 micrograms subcutaneously as stat doses.
3. If effective but secretions recur then give further subcutaneous dose.
   Commence subcutaneous infusion, via syringe pump, of Buscopan 60mg over 24 hours. This can be increased to 80mg after 24 hours if symptoms persist. Bolus 20mg subcutaneously 4-hourly can be given as required up to a total overall maximum dose of Buscopan of 120mg in 24 hours.
   **OR** glycopyrronium 600 micrograms to 1200 micrograms subcutaneously over 24 hours via syringe pump. Bolus of 200 to 400 micrograms subcutaneously 4-hourly can be given as required up to a total overall dose of glycopyrronium of 2400 micrograms in 24 hours.

NO
1. **Prescribe anticipatory medication:** hyoscine butylbromide (Buscopan) 20mg subcutaneously 4-hourly as required.
   Maximum dose 120mg in 24 hours.

Supportive information:
Anticipatory prescribing in this manner will ensure that in the last hours/days of life there is no delay in responding to the symptom if it occurs.

For Raigmore based staff, if medication is ineffective and symptoms persist contact the Raigmore Hospital Palliative Care Advisory Service on ext. 5405/6340.

For all other staff, for further advice and for out of hours/weekends, contact Highland Hospice 24-hour helpline on 01463 243132.
4. SALIVA MANAGEMENT: SIALORRHOEA IN ADULTS

DESCRIPTION - drooling/sialorrhea
Drooling is the unintentional loss of saliva from the mouth. In the adult population it can be associated with neurological disorders such as Parkinson’s disease, motor neurone disease (MND) and stroke. Contrary to popular belief, drooling is rarely caused by hypersalivation but is more often related to neuromuscular and/or sensory dysfunction in the oral stage of the swallow.

CAUSES
Neuromuscular dysfunction/sensory dysfunction
Cognitive development disorder, cerebral palsy, Parkinson’s disease
(pseudo bulbar and bulbar palsy, stroke – less common)
Hypersecretion – usually controlled by increased swallowing
Inflammation (teething, dental caries, oral cavity infection, rabies)
Medication side-effects (tranquillisers, anticonvulsants)
Toxin exposure (mercury)

COMPLICATIONS
Drooling in the adult patient has various repercussions, ranging from physical difficulties such as dehydration, foul oral odour, perioral skin maceration and increased risk of aspiration pneumonia, to social ramifications such as embarrassment, isolation and increased dependency.

As such, drooling can have a negative effect on quality of life, so much so that many patients rate drooling as their worst symptom.

IDENTIFY PROBLEM

ASSESS:
• CAUSES
• SEVERITY
• FREQUENCY
• QUALITY OF LIFE IMPACT.

TREAT REVERSIBLE CAUSES, eg INFECTION
• DENTAL PROBLEMS (SEE DENTIST/DENTAL OFFICER) AND ORAL HYGIENE
• GASTRO-oesophageal reflux disease
• MEDICATION REVIEW (SEE PHARMACIST)

REMEMBER TO REVIEW AND REASSESS FOR POSITIVE OUTCOMES.

ACTIVITY: positioning
Encouraging small changes in positioning, such as:
• head position
• sitting position
• eating position
• sleeping position
• positioning during daily tasks in order to reduce the loss of saliva from the mouth
• etc.

ACTIVITY: sensory stimulation,
omotor exercises
Simple techniques to increase oral stimulation and promote regular swallowing:
• sips of iced, fizzy or citrus-flavoured fluids
• use of sugar-free chewing gum, boiled sweets to stimulate swallowing
• etc.
Exercises aimed at improving oral function:
• oro-motor exercises.

ACTIVITY: behavioural programme
A programme designed to remove or introduce particular behaviours for the purpose of reducing drooling, eg:
• regular swallows
• regular sips of fluid
• swallow reminder badge
• lip closure
• regular dabbing of chin
• etc.

MEDICATION (unlicensed or off-label use)
Anticholinergic medications – contra-indicated in glaucoma, obstructive uropathy, GI motility disorders, myasthenia gravis. Less well tolerated in older people.
• atropine 1% drops – apply 1 to 2 drops under the tongue up to four times a day. Side-effects: constipation, excessive oral dryness, urinary retention, blurred vision, tachycardia.
• glycopyrrolate 1 or 2mg tablets (non-formulary). Usual dose 500 micrograms up to 3 times a day titrated to effectiveness and tolerability. 20% drop out rate due to side-effects: constipation, excessive oral dryness, urinary retention, blurred vision, hyperactivity, irritability.
• hyoscine hydrobromide (scopolamine) 1-5mg patch. May require to be applied daily as opposed to licensed application rate of every 3 days. Urinary retention and blurred vision limit use, along with irritation at patch site, irritability, dizziness, glaucoma.

REFERRAL TO SPECIALIST REHABILITATION or RELEVANT PALLIATIVE SERVICE
TO CONSIDER: botulinum toxin, radiation, surgery
## Quality of life – how severely does this affect you?

<table>
<thead>
<tr>
<th>Patient name:</th>
<th>Please indicate (1 = low impact, 5 = high impact)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Little impact</td>
<td>Some impact</td>
</tr>
<tr>
<td><strong>1 Communication:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Face-to-face</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Over the phone</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Writing/computing</td>
<td></td>
</tr>
<tr>
<td><strong>2 Eating:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>At home</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Outside home</td>
<td></td>
</tr>
<tr>
<td><strong>3 Socialisation:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Socialising at home</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Going out</td>
<td></td>
</tr>
<tr>
<td><strong>4 Carrying out daily activities:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dressing</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Preparing food/drink</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Work around the house</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hobbies, eg gardening</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Driving</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other (please specify)</td>
<td></td>
</tr>
<tr>
<td><strong>5 How does this make you feel?</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Body image</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Role</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Self-esteem</td>
<td></td>
</tr>
</tbody>
</table>
Saliva rating scale – frequency and severity

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Points</th>
<th>Severity</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never drools (dry)</td>
<td>1</td>
<td>Dry (never drools)</td>
<td>1</td>
</tr>
<tr>
<td>Occasionally drools (not every day)</td>
<td>2</td>
<td>Mild (only the lips are wet)</td>
<td>2</td>
</tr>
<tr>
<td>Frequently drools (every day but not all the time)</td>
<td>3</td>
<td>Moderate (wet on lips and chin)</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Severe (clothes get damp and need changed)</td>
<td>4</td>
</tr>
<tr>
<td>Constantly drools (always wet)</td>
<td>4</td>
<td>Profuse (clothes, hands and objects become wet)</td>
<td>5</td>
</tr>
</tbody>
</table>

It is helpful to complete rating scales every day for 5 days, where possible at the end of the day. Longer measures (10 days) are particularly helpful if the individual’s drooling varies from day to day. It is helpful if two individuals in different settings, without discussion, can complete an assessment.

Drugs which may cause sialorrhoea: this is not necessarily a complete list, please check individual product specifications

<table>
<thead>
<tr>
<th>Drug</th>
<th>Drug</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam</td>
<td>Ketamine</td>
<td>Physostigmine</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Lamotrigine</td>
<td>Pilocarpine</td>
</tr>
<tr>
<td>Bethanechol</td>
<td>Levodopa</td>
<td>Risperidone</td>
</tr>
<tr>
<td>Buspirone</td>
<td>Lithium</td>
<td>Rivastigmine</td>
</tr>
<tr>
<td>Clozapine</td>
<td>Mefenamic acid</td>
<td>Sildenafil</td>
</tr>
<tr>
<td>Desflurane</td>
<td>Modafinil</td>
<td>Tacrine</td>
</tr>
<tr>
<td>Diazoxide</td>
<td>Neostigmine</td>
<td>Theophylline</td>
</tr>
<tr>
<td>Diazoxide</td>
<td>Neostigmine</td>
<td>Theophylline</td>
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<tr>
<td>Diazoxide</td>
<td>Neostigmine</td>
<td>Theophylline</td>
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<td>Diazoxide</td>
<td>Neostigmine</td>
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<td>Diazoxide</td>
<td>Neostigmine</td>
<td>Theophylline</td>
</tr>
<tr>
<td>Diazoxide</td>
<td>Neostigmine</td>
<td>Theophylline</td>
</tr>
<tr>
<td>Edrophonium</td>
<td>Nifedipine</td>
<td>Tobramycin</td>
</tr>
<tr>
<td>Galantamine</td>
<td>Olanzapine</td>
<td>Venlafaxine</td>
</tr>
<tr>
<td>Imipenem/cilastatin</td>
<td>Pentoxifylline</td>
<td></td>
</tr>
</tbody>
</table>
5. MANAGEMENT OF DIABETES IN ADULTS IN PALLIATIVE CARE

Pre-terminal disease will influence glycaemic control (Box 1)

- goal of treatment is to avoid hypoglycaemia and manage symptoms of hyperglycaemia (balance against burdens of additional treatment and monitoring)
- Type 1 diabetes has an absolute insulin requirement (wish to avoid diabetic ketoacidosis)
- little evidence to guide best practice
- individualised treatments, particularly in Type 2 diabetes.

Additional symptom burden to patients may include:

- **Hyperglycaemia**: dry mouth, thirst, lethargy, blurred vision, polyuria, recurrent infections
- **Hypoglycaemia**: sweating, hunger, trembling, blurred vision, headache, confusion and disorientation, drowsiness, unconsciousness/coma, seizures.

Potentially reversible issues: infection

- stop or limit drugs which adversely influence blood glucose (Box 2)
- avoid hyperosmotic hyperglycaemic states.

**Type 1 diabetes**

- monitor BM less frequently – ask why are you checking?
- relax blood glucose targets (aim >7 to <15 mmol/L as long as asymptomatic)
- **always continue basal insulin** – patient may have reduced insulin requirement (reduce by 30 to 50%)
- consider omitting doses of rapid-acting insulin if not eating.

Terminal phase – time is short (may be weeks)

**Type 1 diabetes**

Once-daily basal insulin (Lantus®, Detemir®, Insulatard®). If unsure use 50 to 70% normal basal dose. Avoid glucose-containing fluids. Don’t be afraid of stopping therapies:

- palliative care patients don’t die of hypoglycaemia
- palliative care patients don’t die of diabetic ketoacidosis
- palliative care patients WILL NOT die of hyperglycaemia.

See Box 3 for communication issues. Stop monitoring.

**Type 2 diabetes**

**Individualised treatment**

Consider:

- reduce or stop sulfonylurea
- stop metformin
- stop gliptin
- stop GLP-1
- stop dapagliflozin
- reduce pre-mix twice-daily insulin
- consider once-daily long-acting basal insulin instead (Lantus®, Detemir®, Insulatard®)
- reduce or stop short-acting insulin
- continue low-dose long-acting insulin.

**Terminal phase**

**Type 2 diabetes**

Stop all diabetes therapy

For persistent difficult symptoms contact Highland Hospice/PCAS or Diabetes Team
Box 1
Palliative care considerations for glycaemic control

- anorexia and cachexia
  - inability to take food or medicines
  - increased hypoglycaemia risk
- infection
- metastatic disease
  - increased risk of hypoglycaemia (liver, adrenals)
  - increased risk of lactic acidosis
- cirrhosis
  - hypoglycaemia risk
- tumour products
  - most promote insulin resistance
  - may induce hypoglycaemia
- cardiac failure
  - catecholamine excess leads to insulin resistance
- pancreatic cancer
  - pancreatic destruction may lead to Type 1 diabetes-like insulin deficiency
- nutritional status
  - supplements or nasogastric feeding cause hyperglycaemia.

Box 2
Drugs which may adversely affect blood glucose

- octreotide:
  - inhibits insulin secretion, causing hyperglycaemia
- steroids (given in the morning can cause late afternoon and evening hyperglycaemia)
  - orexigenic (stimulates appetite), may contribute to hyperglycaemia
  - induce insulin resistance, causing hyperglycaemia.
  (Insulin doses are often increased to accompany steroid therapy. If steroids are withdrawn patients are potentially at risk of hypoglycaemia if insulin is not altered quickly, or marked hyperglycaemia if all treatment including insulin is stopped and there are still steroids in the system).
- some diuretics
- some atypical antipsychotics may increase insulin resistance and cause hyperglycaemia.

Box 3
Communications with patients and families

Patients/families who have lived with diabetes over a long period of time may find a more relaxed attitude to diet and monitoring difficult to come to terms with. It is important that the addition of insulin therapy is not seen as adding to anxiety, or withdrawal perceived as abandonment of care.

Individualise monitoring based on patient factors, therapy and goals of care.
### 6. ANTIEMETICS USED IN PALLIATIVE CARE


<table>
<thead>
<tr>
<th>Receptor site affinities of selected antiemetics</th>
<th>$D_2$ antagonist</th>
<th>$H_1$ antagonist</th>
<th>Muscarinic antagonist (anticholinergic)</th>
<th>$5HT_2$ antagonist</th>
<th>$5HT_3$ antagonist</th>
<th>$NK_1$ antagonist</th>
<th>$5HT_4$ agonist</th>
<th>$CB_1$ agonist</th>
<th>GABA mimetic</th>
<th>Additional information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dompiredone $\dagger QT$</td>
<td>**</td>
<td></td>
<td></td>
<td>**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Caution in Parkinson’s disease. Avoid in complete GI obstruction.</td>
</tr>
<tr>
<td>Haloperidol $\dagger QT$</td>
<td>***</td>
<td></td>
<td></td>
<td>**/</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Avoid in Parkinson’s disease.</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>**</td>
<td></td>
<td></td>
<td>**</td>
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<td></td>
<td></td>
<td></td>
<td>Caution in Parkinson’s disease. Avoid in complete GI obstruction.</td>
</tr>
<tr>
<td>Cyclazine</td>
<td>**</td>
<td>**</td>
<td></td>
<td>**</td>
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<td></td>
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<td></td>
<td></td>
<td>Avoid in Parkinson’s disease. Avoid in complete GI obstruction.</td>
</tr>
<tr>
<td>Hyoscine Hydrobromide</td>
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<td></td>
<td></td>
<td>***</td>
<td>Avoid in severe heart failure.</td>
</tr>
<tr>
<td>Chlorpromazine $\dagger QT$</td>
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<td>***</td>
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<td>**</td>
<td>**</td>
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<td></td>
<td></td>
<td></td>
<td>Avoid in Parkinson’s disease.</td>
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<tr>
<td>Levomepromazine $\dagger QT$</td>
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<td>***</td>
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<td>**</td>
<td>**</td>
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<td></td>
<td></td>
<td></td>
<td>Avoid in Parkinson’s disease.</td>
</tr>
<tr>
<td>Olanzapine $\dagger QT$</td>
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<td>**</td>
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<td></td>
<td>**</td>
<td></td>
<td>Avoid in Parkinson’s disease.</td>
</tr>
<tr>
<td>Prochlorperazine $\dagger QT$</td>
<td>***</td>
<td>**</td>
<td></td>
<td>*</td>
<td></td>
<td>**</td>
<td>**</td>
<td></td>
<td></td>
<td>Avoid in Parkinson’s disease.</td>
</tr>
<tr>
<td>Promethazine $\dagger QT$</td>
<td><em>/</em>*</td>
<td>**</td>
<td></td>
<td>**</td>
<td>**</td>
<td></td>
<td>**</td>
<td></td>
<td></td>
<td>Avoid in Parkinson’s disease.</td>
</tr>
<tr>
<td>Lorazepam</td>
<td></td>
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<td></td>
<td></td>
<td>***</td>
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<tr>
<td>Nabilone</td>
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<td>**</td>
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<td></td>
<td>***</td>
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<tr>
<td>Aprepitant</td>
<td></td>
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</tr>
<tr>
<td>Ondansetron/Granisetron $\dagger QT$</td>
<td></td>
<td></td>
<td></td>
<td>**</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>***</td>
<td>Very constipating – co-prescribe laxatives.</td>
</tr>
</tbody>
</table>

Pharmacological activity: blank = none or insignificant; * = slight; ** = moderate; *** = marked.

Muscarinic antagonists (anticholinergic burden) – postural hypotension, risk of falls, urinary retention, sedation, dizziness.

$\dagger$ domperidone does not normally cross the blood-brain barrier; minimal risk of extrapyramidal effects, watch for interactions.

SCHEMATIC REPRESENTATION OF EMETOGENIC RECEPTOR LOCATIONS AND STIMULI IN PALLIATIVE CARE

Management options – block receptor or neurotransmitter OR block the vomiting centre.

Drugs
- Biochemistry
- Toxins

Chemoreceptor trigger zone

Cerebral cortex
- Anxiety, anticipation (anxiolytic)
- Pain (analgesic)
- Raised intracranial pressure (steroid)

Vestibular mechanism
- Pharynx

Gut viscera
- 5HT4 agonist
- Metoclopramide
- (prokinetic)
- D2 antagonist
- Metoclopramide
- Denperidone
- (antikinetic)
- (5HT3 – ondansetron)

Broad-spectrum antiemetic - levomepromazine

A. MacRobbie Final May 2015