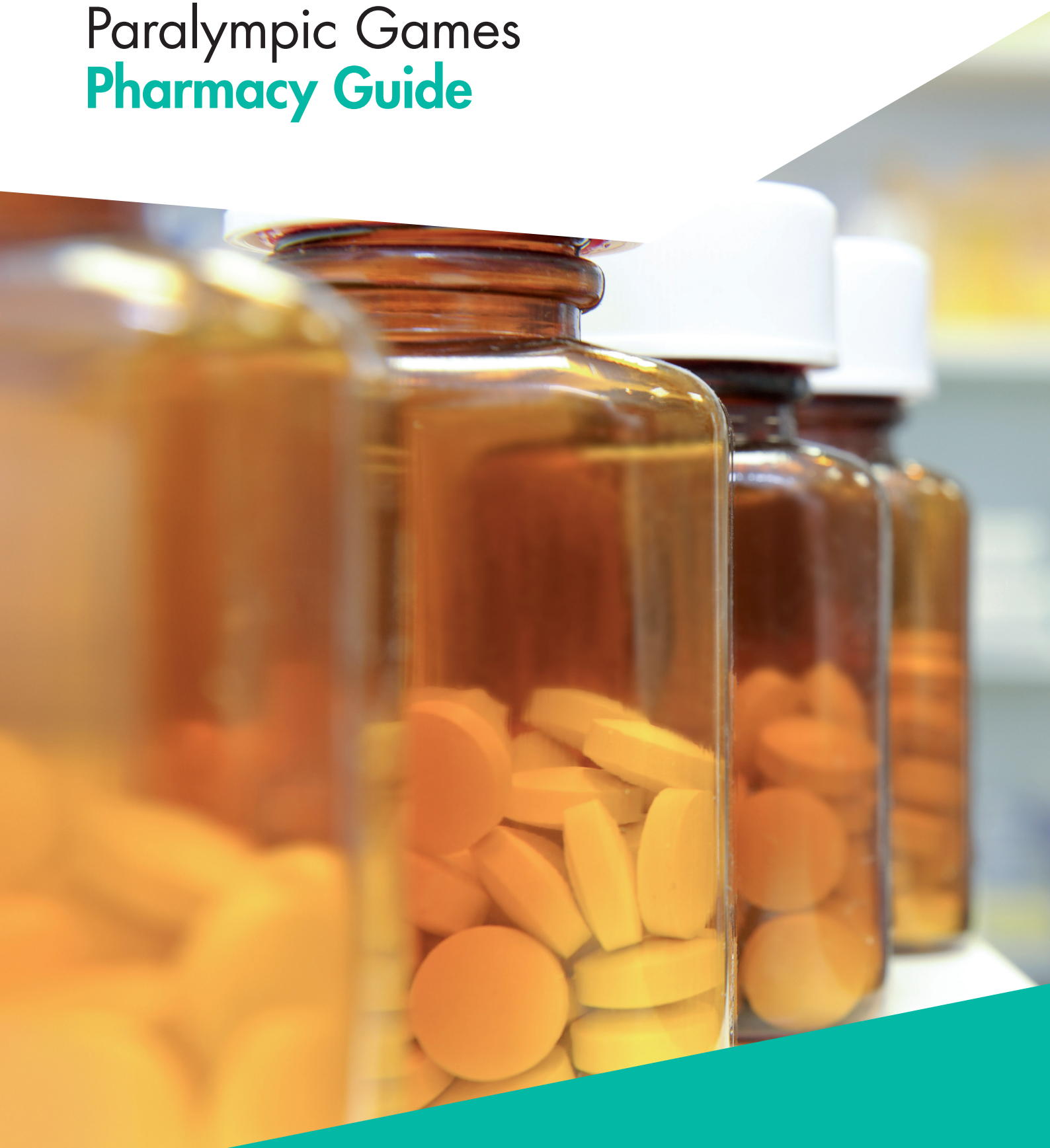
London 2012

Paralympic Games
Pharmacy Guide



About the Pharmacy Guide

All information contained in this Pharmacy Guide was correct at the time of publication in January 2012. However, please note that these details may change between now and the Games. All updates to this guide will be posted on The Exchange, LOCOG's secure extranet (https://theexchange.london2012.com), where they may be downloaded by NPCs.

Along with the Healthcare Guide, this edition of the Pharmacy Guide is initially being published in electronic form only. Printed versions of both guides will be distributed to NPC medical teams upon arrival at the Paralympic Village at Games time.

British National Formulary

The information in this guide has been adapted from the British National Formulary (BNF), editions 61 and 62. For more comprehensive prescribing and drug information, please refer to the complete current edition of the British National Formulary, which is available from the polyclinic pharmacies and clinical areas at competition venues or online at www.bnf.org.

The BNF is jointly owned by the Royal Pharmaceutical Society of Great Britain and the BMJ Publishing Group Ltd (jointly referred to as 'the Publisher'). The BNF provides UK healthcare professionals with authoritative and practical information on the selection and clinical use of medicines in a clear, concise and accessible manner. The BNF is designed for prescribers, pharmacists and other healthcare professionals, situated within the United Kingdom. The Publisher works to ensure that the information provided in the BNF is accurate and up-to-date as at the date of publication, but changes do regularly occur and the Publisher does not warrant that it is accurate.

The BNF is designed as a digest for rapid reference and it may not always include all information necessary for prescribing or dispensing. Also, less detail is given on certain specialties, since those involved are expected to have specialist knowledge and access to specialist literature. The BNF should be interpreted in light of professional knowledge and supplemented as necessary with specialist publications and by reference to product literature. Information is also available from medicines information services.

The fullest extent permitted by law, the Publisher assumes no responsibility for any aspect of healthcare administered with the aid of this information or any other use of this information. The Publisher does not exclude any liability for death or personal injury resulting from negligence, fraud, or any liability which cannot be excluded by applicable law.

Welcome

The London Organising Committee of the Olympic Games and Paralympic Games Ltd (LOCOG) has developed a medical services programme dedicated to providing comprehensive medical care during the London 2012 Olympic and Paralympic Games. This Pharmacy Guide contains the definitive list of medicines available from the polyclinic pharmacies, with comprehensive prescribing information for each drug and details of the procedures for the prescribing and supply of medicines to individuals requiring medical treatment.

The medicines listed in this guide will be provided to athletes and other accredited individuals free of charge. Medicines should be prescribed in quantities required for immediate and necessary care for the duration of the Games – the LOCOG Chief Medical Officer reserves the right to review each prescription with regard to an appropriate quantity. If a National Paralympic Committee (NPC) team doctor wishes to prescribe a medicine not included in this Pharmacy Guide, every effort will be made to facilitate the availability of the medicine. However, the prescription will be at the cost of the NPC.

The medicines listed in this guide are classified according to the World Anti-Doping Agency (WADA) 2012 Prohibited List in-competition as either:

– permitted
– prohibited
– prohibited in certain sports

Special procedures are in place for the prescribing of medicines to athletes that are classified as 'prohibited'. All athletes and healthcare professionals involved in prescribing or administering medicines should familiarise themselves with the World Anti-Doping Code and the WADA 2012 Prohibited List, online at www.wada-ama.org. The version of the 2012 Prohibited List available from the WADA website during the dates of the London 2012 Paralympic Games will apply.

Particular care should be taken when a prescription is written for a prohibited substance for an athlete. This requires a Therapeutic Use Exemption (TUE), which must be approved by the IPC Medical Committee (in accordance with the IPC Anti-Doping Code, article 4.4.2.2). Information on the prohibited or permitted status of any particular medicine can be found on the Global Drug Reference Online (Global DRO) website, www.globaldro.com.

Due to the nature of temporary registration, NPC doctors are restricted to caring for members of their own delegation, or to members of other specified delegations where a prior agreement in writing has been submitted to LOCOG.

We welcome you to the 2012 Games and trust you will have a safe and healthy experience.

Richard Budgett
Chief Medical Officer

Pamela Venning
Senior Medical Manager

Mark Stuart
Superintendent Pharmacist

London 2012 Paralympic Games Pharmacy Guide: Contents

Essential information

Village polyclinic pharmacies

Pharmacies will be located within the Paralympic Village, the Paralympic Sailing Village in Portland and the Paralympic Rowing Village in Egham. The pharmacies will be open from 07:00 to 23:00 daily. Emergency medicine access will be available outside these hours and may be arranged via the night duty Polyclinic Manager.

The pharmacies will provide the medicines listed in this Pharmacy Guide free of charge to individuals as part of the medical treatment for acute or the acute exacerbation of chronic medical conditions. Medicines will be dispensed on an immediate and necessary basis, by prescription only. Any individual with an existing medical condition is advised to bring enough medicine with them to cover the duration of their visit to the UK and their travel home.

A comprehensive medicines information service will be provided at the polyclinic pharmacies, and information on medicines will be available in languages other than English through an interpreter. The medicines information service may be accessed either in person or by telephone, and will offer information on topics such as:

– clinical drug information
– international or foreign medicines
– poisons and toxicology information
– prohibited status of drugs in sport
– prescribing procedures

All individuals accredited for the residential zones of the Villages will have access to the polyclinic pharmacies.

Minor ailments scheme for non-athletes

Pharmacists in the polyclinics at the Paralympic Village, the Paralympic Sailing Village and the Paralympic Rowing Village will offer a professional consultation service for non-athletes presenting with minor conditions. Over-the-counter medicines for a range of minor conditions can be recommended and supplied by the pharmacists to named and accredited individuals.

Over-the-counter medicines will only be supplied by pharmacists to the presenting patient. A medical encounter record will be completed by the issuing pharmacist at the time of the consultation, and the patient may be referred to a doctor or other appropriate healthcare professional if necessary. Over-the-counter medicines for athletes will only be issued upon presentation of a prescription from a doctor.

Medicines available at competition venues

A limited quantity of essential medicines will be available for immediate and emergency patient care in both athlete and spectator medical rooms at all competition venues. Medicines from these stocks will usually be issued only as a single dose or as an immediate treatment to the patient. The doctor may choose to write a prescription for subsequent doses for ongoing treatment, which may be dispensed in full by one of the pharmacies listed above.

Registration of NPC team doctors

A special registration process for NPC team doctors is in place for the London 2012 Paralympic Games. Team doctors may be registered with the General Medical Council (GMC) to practise from 22 August 2012 until 12 September 2012, the opening and closing dates of the Paralympic Village. This temporary, special-purpose registration will license doctors to treat only members of their own team (or other non-UK teams by special arrangement). **All NPC team doctors must be registered by 29 February 2012.**

Team doctors who are registered with the GMC may write prescriptions for members of their own delegation, or for members of other specified delegations where a prior written agreement between NPCs has been submitted to LOCOG. These prescriptions may be dispensed at Village polyclinic pharmacies (free of charge) or at any commercial pharmacy (where a fee will be payable).

Import and export of medicines

Full guidance on the import and export of stocks of medicines to meet the needs of teams competing in the Games, and the import and export of medicines for personal use, including the specific requirements for controlled drugs, is contained in the London 2012 Customs and Freight Forwarding Guide. The guide may be accessed through The Exchange, LOCOG's secure extranet for NPCs, at https://theexchange.london2012.com.

In most situations, UK medicines legislation does not impose restrictions on the import of medicines for personal use. However, for the purposes of team preparations leading up to and during the Olympic and Paralympic Games, the UK Medicines and Healthcare products Regulatory Agency (MHRA) is implementing a reasonable restriction on the import of medicines for personal use. The quantity of prescription-only medicines (POM) and pharmacy (P) non-controlled medicines that may be imported into and/or exported out of the UK will be restricted to a quantity that is equal to or less than three months' supply.

Any medicines brought into the UK will need to be taken out of the UK on departure or at the end of the Games. No export licences or documentation will be required unless the medicines are controlled drugs and the quantity constitutes more than three months' supply.

Declaration of medicines on arrival at the Paralympic Village

The MHRA requires the NPC Chief Medical Officer, or the designated head doctor accompanying a team, to provide a list of the medicines that the team are bringing into the UK, including dosages and amounts, and that are being kept within the Villages for use by members of their team. If medicines have been transferred from the Olympic delegation for use by the Paralympic delegation from the same country, they should be indicated on the list submitted to the LOCOG Medical Services team and annotated as 'transferred from NOC to NPC'. This list will constitute a statement on behalf of the NPC and will be kept by LOCOG Medical Services, and will be shared with the MHRA if requested.

The list must be provided via email to pharmacy@london2012.com before arrival in the Villages. In exceptional circumstances, the list may be provided to the polyclinic pharmacy within 24 hours of the first entry of the NPC Chief Medical Officer (or medicines) into the Village. Prescription pads will only be issued to NPC team doctors after the list has been submitted on behalf of their NPC.

The list must contain the following information:

Date:			
NPC country:			
Name of Chief Medical Officer or head doctor:			
Name of medicine	**Form**	**Strength**	**Quantity**
e.g. Diclofenac	tablets	50mg	200 tablets

A single statement on behalf of the NPC must be provided by the NPC Chief Medical Officer as verification that the medicines are for use by the healthcare professionals of their NPC.

Storage and safe use of team medicines
NPC healthcare personnel are responsible for the storage and safekeeping of their delegation's medicines and supplies. LOCOG is not responsible for, and shall have no liability relating to or arising out of, the storage or monitoring of the supplies and medicines by the NPC.

Medicines should be stored in a secure locked receptacle and kept in the original packaging until used, and may only be administered to members of the prescribing NPC doctor's delegation (unless a written agreement exists between two NPCs). NPC doctors should ensure that robust systems are in place to ensure the safe and secure handling of medicines in their possession.

Prescriptions

Prescription pads must be collected in person by the doctor who will use the prescription pad. Prescription pads will be available from polyclinic pharmacies in the Villages.

Prescription pads will only be issued to doctors who are registered with the GMC. All GMC registrations will be verified at the time of collection, and a sample signature from the collecting doctor must be provided on receipt of the prescription pad.

Medicines will only be dispensed from a polyclinic pharmacy when the details have been written on official LOCOG prescription forms, either by accredited LOCOG doctors or by accredited NPC doctors registered to prescribe in the UK. All prescriptions must be written in English.

Prescriptions may be generated electronically from the medical encounter system by LOCOG-accredited doctors with access to the system. In order to be validated as a legal prescription, these forms must be printed on paper and signed by hand. The prescription may then be handed to the pharmacy for dispensing. Instructions on how to generate a prescription this way may be found in the medical encounter system user guide.

NPC doctors are only permitted to prescribe medicines to members of their own delegation, unless a prior written agreement exists between NPCs and has been submitted in writing to LOCOG.

Up to seven days' supply, or a small complete pack of medicine, will generally be dispensed with a single prescription. Further supplies will normally require a subsequent prescription. Antibiotics may be prescribed in sufficient quantities to treat the medical condition.

The original signed prescription will be kept in the polyclinic pharmacy. Any duplicate copies will remain with the patient's record or with the NPC doctor.

All information on prescriptions must be clearly and legibly printed. Please avoid Latin and abbreviations; for example, use 'take one tablet orally twice daily'.

The following information must be included on the prescription:

– venue
– date
– prescriber's name, accreditation number, GMC number and a contact mobile telephone number
– patient's name, accreditation number and NPC
– name of medicine
– form of medicine (for example: tablet, capsule, suspension)
– unit strength
– quantity
– directions for use
– prohibited substances declaration where applicable (see below)

Prescribing a prohibited substance
Prohibited substances are drugs that, according to the WADA 2012 Prohibited List or each International Federation's (IF) rules for a particular sport, may not be used by athletes who will be competing in the Paralympic Games, unless a Therapeutic Use Exemption (TUE) has been granted by the appropriate authority or, in the case of an emergency during the Games period, a TUE application has been submitted to the IPC Medical Committee.

Prescribing prohibited substances for athletes should be avoided unless a TUE is obtained in advance, or in medical emergencies when an athlete's health takes absolute priority and a retroactive TUE should be obtained.

If a TUE has already been obtained from the appropriate authority before the prescription has been written, a copy of the TUE documentation should be presented to the dispensing pharmacist, who will then dispense the medicine for the athlete. In all other cases, it is the responsbility of the athlete to ensure compliance with the IPC Anti-Doping Code (article 4.4) and the WADA International Standard for Therapeutic Use Exemptions (ISTUE).

If the prohibited medicine is to be administered at a venue, the LOCOG Venue Medical Manager must notify LOCOG Medical Headquarters, which will notify the LOCOG Chief Medical Officer. If the medicine is to be administered or dispensed at a polyclinic, the administering doctor or polyclinic pharmacist will notify the Polyclinic Manager or the Superintendent Pharmacist, who will notify the LOCOG Chief Medical Officer. In both situations, the LOCOG Chief Medical Officer will then notify the Chair of the IPC Medical Committee. If an NPC team doctor prescribes the medicine, he/she must assist the athlete in the completion of an IPC TUE Application Form for submission to the Chair of the IPC Medical Committee in order to obtain a TUE before the administration of the prohibited substance (except in an emergency, when a retroactive TUE application should be submitted).

Prescription procedure for prohibited substances

– In an emergency, a doctor must treat an athlete, including using prohibited substances and methods if clinically necessary, and must inform and assist the athlete in the completion of a retroactive TUE application as soon as possible afterwards.

– If it is not an emergency, the prescribing doctor must explain to the athlete that a prohibited substance is being prescribed and must explain the consequences if a TUE is not obtained in advance. A TUE application should normally be submitted to the IPC Medical Committee and approval should be obtained before treatment.

– The prescribing doctor and the athlete who is receiving the medication must sign the prescription to confirm that they are aware of the status of the substance.

– The dispensing pharmacist must confirm with the prescribing doctor that the substance is a prohibited substance and must also confirm that they wish to proceed to prescribe the substance.

– The pharmacist should sign the prescription to verify that they have informed the prescribing doctor and the athlete that the substance is prohibited.

– If a prohibited substance is prescribed for an athlete by a LOCOG doctor, the duty senior Sports Medicine Team Leader's signature is required on the prescription.

– The dispensing pharmacist should stamp the prescription as 'prohibited' and label the dispensed medicine as 'prohibited'.

More detail on IPC TUE management during the London 2012 Paralympic Games may be found in the London 2012 Paralympic Games Doping Control Guide, available on The Exchange (https://theexchange.london2012.com).

How to use the London 2012 Paralympic Games Pharmacy Guide

The medicines included in this Guide are arranged according to therapeutic classification, in alphabetical order according to their generic name. Multi-ingredient preparations are listed by their brand name.

The following information is included:

– general prescribing information about the therapeutic class of the medicine
– drug name (common brand names are used for multi-ingredient preparations)
– indications
– cautions
– contra-indications
– available forms (including standard pack size; note that only seven days' supply will be dispensed from LOCOG pharmacies)
– dose
– side-effects
– status (according to the WADA 2012 Prohibited List)

The information in this guide has been adapted from the British National Formulary. For more comprehensive prescribing and drug information, please refer to the complete current edition of the British National Formulary, which is available at polyclinic pharmacies and clinical areas at competition venues or online at www.bnf.org.

1.0 Gastro-intestinal system

1.1 Dyspepsia and gastro-oesophageal reflux disease

1.1.1 Antacids

Antacids (usually containing aluminium or magnesium compounds) can often relieve symptoms in ulcer dyspepsia and in non-erosive gastro-oesophageal reflux. They are also sometimes used in functional (non-ulcer) dyspepsia, but the evidence of benefit is uncertain. Antacids are best given when symptoms occur or are expected, usually between meals and at bedtime, four or more times daily; additional doses may be required up to once an hour. Liquid preparations are more effective than tablet preparations. Simeticone (activated dimeticone) is added to an antacid as an antifoaming agent to relieve flatulence. Alginates, added as protectants, may be useful in gastro-oesophageal reflux disease.

Antacids preferably should not be taken at the same time as other drugs as they may impair absorption. Antacids may also damage enteric coatings designed to prevent dissolution in the stomach.

Drug: Asilone tablets®

Indications: dyspeptic symptoms including flatulence and associated abdominal distension, heartburn, oesophagitis

Cautions: see notes above

Contra-indications: none noted

Available forms: tablets containing aluminium hydroxide 500mg, activated dimeticone 270mg (24-tablet pack)

Dose: 1–2 tablets chewed or sucked before meals and at bedtime or when required

Side-effects: none noted

Status: permitted

Drug: Gaviscon Advance tablets®

Indications: gastro-intestinal reflux

Cautions: see notes above

Contra-indications: none noted

Available forms: tablets, sugar-free, sodium alginate 500mg, potassium bicarbonate 100mg, contains 2.25mmol Na+, 1mmol K+/tablet (20-tablet and 60-tablet packs)

Dose: 1–2 tablets to be chewed after meals and at bedtime

Side-effects: none noted

Status: permitted

Drug: Maalox Plus Suspension

Indications: dyspepsia

Cautions: see notes above

Contra-indications: none noted

Available forms: sugar-free, dried aluminium hydroxide 220mg, simeticone 25mg, magnesium hydroxide 195mg/5mL (low Na+) (500mL pack)

Dose: 5–10mL 4 times daily (after meals and at bedtime) or when required

Side-effects: none noted

Status: permitted

Drug: magnesium trisilicate mixture, BP

Indications: dyspepsia

Cautions: see notes above

Contra-indications: hypophosphataemia

Available forms: oral suspension, 5% each of magnesium trisilicate, light magnesium carbonate and sodium bicarbonate in a suitable vehicle with a peppermint flavour (200mL pack)

Dose: 10–20mL in water 3 times daily or as required

Side-effects: diarrhoea, belching due to liberated carbon dioxide; silica-based renal stones reported on long-term treatment

Status: permitted

Drug: Peptac Suspension®

Indications: gastro-intestinal reflux

Cautions: see notes above

Contra-indications: none noted

Available forms: suspension, sugar-free, sodium bicarbonate 133.5mg, sodium alginate 250mg, calcium carbonate 80mg/5mL, contains 3.1mmol Na+/5mL (500mL pack)

Dose: 10–20mL after meals and at bedtime

Side-effects: none noted

Status: permitted

1.1.2 H2-receptor antagonists

Histamine H2-receptor antagonists heal gastric and duodenal ulcers by reducing gastric acid output as a result of histamine H2-receptor blockade; they are also used to relieve symptoms of gastro-oesophageal reflux disease. H2-receptor antagonists should not normally be used for Zollinger-Ellison syndrome because proton pump inhibitors (see section 1.1.3, p16) are more effective. H2-receptor antagonists are used for the treatment of functional dyspepsia and for the treatment of uninvestigated dyspepsia in patients without alarm features.

Side-effects

Side-effects of the H2-receptor antagonists include diarrhoea, headache and dizziness. Rash (including erythema multiforme and toxic epidermal necrolysis) occurs less frequently. Other side-effects reported rarely or very rarely include hepatitis, cholestatic jaundice, bradycardia, psychiatric reactions (including confusion, depression and hallucinations), blood disorders (including leucopenia, thrombocytopenia and pancytopenia), arthralgia and myalgia. There are isolated reports of gynaecomastia and impotence with H2-receptor antagonists such as ranitidine.

Drug: ranitidine

Indications: benign gastric and duodenal ulceration, NSAID-associated ulceration, prophylaxis of NSAID-associated gastric or duodenal ulcer, chronic episodic dyspepsia, gastro-oesophageal reflux disease, prophylaxis of stress ulceration

Cautions: see notes above; also acute porphyria

Contra-indications: none noted

Available forms: tablets (as hydrochloride), 75mg (24-tablet pack) and 150mg (60-tablet pack); effervescent tablets (as hydrochloride), 150mg (60-tablet pack); injection (as hydrochloride), 25mg/mL (2mL ampoule)

Dose: according to indications as outlined below:

- benign gastric and duodenal ulceration, chronic episodic dyspepsia: 150mg twice daily or 300mg at night for 4–8 weeks in benign gastric and duodenal ulceration, up to 6 weeks in chronic episodic dyspepsia, and up to 8 weeks in NSAID-associated ulceration (in duodenal ulcer, 300mg can be given twice daily for 4 weeks to achieve a higher healing rate)
- prophylaxis of NSAID-associated gastric or duodenal ulcer (unlicensed dose): 300mg twice daily
- gastro-oesophageal reflux disease: 150mg twice daily or 300mg at night for up to 8 weeks or, if necessary, 12 weeks (moderate to severe, 600mg daily in 2–4 divided doses for up to 12 weeks); long-term treatment of healed gastro-oesophageal reflux disease 150mg twice daily
- by intramuscular injection: 50mg every 6–8 hours
  by slow intravenous injection: 50mg diluted to 20mL and given over at least 2 minutes; may be repeated every 6–8 hours

Side-effects: see notes above; less commonly blurred vision; also reported pancreatitis, involuntary movement disorders, interstitial nephritis, alopecia

Status: permitted

1.1.3 Proton pump inhibitors

Proton pump inhibitors are effective short-term treatments for gastric and duodenal ulcers. They can be used for the treatment of dyspepsia and gastro-oesophageal reflux disease and for the prevention and treatment of NSAID-associated ulcers. They can also be used to control the excessive secretion of gastric acid in Zollinger-Ellison syndrome.

Side-effects

Side-effects of the proton pump inhibitors include gastro-intestinal disturbances (including nausea, vomiting, abdominal pain, flatulence, diarrhoea and constipation) and headache. Less frequent side-effects include dry mouth, peripheral oedema, dizziness, sleep disturbances, fatigue, paraesthesia, arthralgia, myalgia, rash and pruritus. Other side-effects reported rarely or very rarely include taste disturbance, stomatitis, hepatitis, jaundice, hypersensitivity reactions (including anaphylaxis, bronchospasm), fever, depression, hallucinations, confusion, gynaecomastia, interstitial nephritis, hyponatraemia, blood disorders (including leucopenia, leucocytosis, pancytopenia, thrombocytopenia), visual disturbances, sweating, photosensitivity, alopecia, Stevens-Johnson syndrome and toxic epidermal necrolysis. By decreasing gastric acidity, proton pump inhibitors may increase the risk of gastro-intestinal infections (including Clostridium difficile infection).

Drug: omeprazole

Indications: benign gastric and duodenal ulcers, NSAID-associated duodenal or gastric ulcer and gastroduodenal erosions, Zollinger-Ellison syndrome, gastro-oesophageal reflux disease, acid-related dyspepsia

Cautions: see notes above

Contra-indications: none noted

Available forms: tablets, 10mg (7-tablet pack); capsules, 20mg (28-capsule pack)

Dose: according to indications as outlined below:

- benign gastric and duodenal ulcers: 20mg once daily, increasing to 40mg daily in severe or recurrent cases
- maintenance for recurrent duodenal ulcer: 20mg once daily
  prevention of relapse in duodenal ulcer: 10mg daily, increasing to 20mg once daily if symptoms return
- NSAID-associated duodenal or gastric ulcer and gastroduodenal erosions: 20mg once daily
- prophylaxis in patients with a history of NSAID-associated duodenal or gastric ulcers, gastroduodenal lesions, or dyspeptic symptoms who require continued NSAID treatment: 20mg once daily
- Zollinger-Ellison syndrome: initially 60mg once daily
- gastro-oesophageal reflux disease: 20mg once daily, 40mg once daily has been given for 8 weeks in gastro-oesophageal reflux disease refractory to other treatment; maintenance 20mg once daily
- acid reflux disease (long-term management): 10mg daily, increasing to 20mg once daily if symptoms return

Side-effects: see notes above; also agitation and impotence

Status: permitted

1.2 Antispasmodics

Antispasmodic drugs may be useful in irritable bowel syndrome and in diverticular disease. Antimuscarinic drugs (such as hyoscine butylbromide) reduce gut motility. Other antispasmodics such as mebeverine and peppermint oil are believed to be direct relaxants of intestinal smooth muscle and may relieve pain in irritable bowel syndrome and diverticular disease.

Drug: hyoscine butylbromide

Indications: symptomatic relief of gastro-intestinal or genito-urinary disorders characterised by smooth muscle spasm and bowel colic

Cautions: should be used with caution in gastro-oesophageal reflux disease, diarrhoea, ulcerative colitis, autonomic neuropathy, hypertension, conditions characterised by tachycardia and in individuals susceptible to angle-closure glaucoma

Contra-indications: antimuscarinics are contraindicated in myasthenia gravis (but may be used to decrease muscarinic side-effects of anticholinesterases), paralytic ileus, pyloric stenosis, toxic megacolon, prostatic enlargement

Available forms: tablets, 10mg (56-tablet pack)

Dose: smooth muscle spasm: 20mg, 4 times daily

Side-effects: include constipation, transient bradycardia (followed by tachycardia, palpitation and arrhythmias), reduced bronchial secretions, urinary urgency and retention, dilatation of the pupils with loss of accommodation, photophobia, dry mouth, flushing and dryness of skin. Side-effects that occur occasionally include confusion, nausea, vomiting, giddiness; very rarely, angle-closure glaucoma can occur

Status: permitted

Drug: mebeverine

Indications: adjunct in gastro-intestinal disorders characterised by smooth muscle spasm

Cautions: avoid in acute porphyria

Contra-indications: paralytic ileus

Available forms: tablets, 135mg (100-tablet pack); capsules, modified release 200mg (60-capsule pack)

Dose: 135mg 3 times daily or 200mg twice daily (modified release capsules), preferably 20 minutes before meals

Side-effects: allergic reactions (including rash, urticaria, angioedema) reported

Status: permitted

Drug: peppermint oil

Indications: relief of abdominal colic and distension, particularly in irritable bowel syndrome

Cautions: sensitivity to menthol

Contra-indications: none noted

Available forms: capsules, 0.2mL (84-capsule pack)

Dose: 1–2 capsules swallowed whole with water 3 times daily

Side-effects: heartburn, perianal irritation, rarely allergic reactions (including rash, headache, bradycardia, muscle tremor, ataxia)

Status: permitted

1.3 Acute diarrhoea

The priority in acute diarrhoea is the prevention or reversal of fluid and electrolyte depletion. For details of oral rehydration preparations, see section 8.1.2 (p85).

Antimotility drugs relieve symptoms of acute diarrhoea. They are used in the management of uncomplicated acute diarrhoea in adults; fluid and electrolyte replacement may be necessary in case of dehydration.

Antispasmodics (see section 1.2, p17) are occasionally of value in treating abdominal cramp associated with diarrhoea but should not be used for primary treatment. Antibacterial drugs are generally unnecessary in simple gastro-enteritis because the complaint usually resolves quickly without them, and infective diarrhoeas in the UK often have a viral cause. However, systemic bacterial infection does need appropriate systemic treatment; for drugs used in campylobacter enteritis, shigellosis and salmonellosis, see section 5.1 (p61).

1.3.1 Antimotility drugs

Drug: co-phenotrope

Indications: adjunct to rehydration in acute diarrhoea

Cautions: may give rise to atropine side-effects in susceptible individuals

Contra-indications: like antimuscarinics, may be contra-indicated in myasthenia gravis (but may be used to decrease muscarinic side-effects of anticholinesterases), paralytic ileus, pyloric stenosis, toxic megacolon, prostatic enlargement

Available forms: tablets, co-phenotrope 2.5/0.025 (diphenoxylate hydrochloride 2.5mg, atropine sulphate 25 micrograms) (100-tablet pack)

Dose: initially 4 tablets, followed by 2 tablets every 6 hours until diarrhoea controlled

Side-effects: potential to cause side-effects associated with opiate-based analgesics (see section 4.5.3, p56) and those associated with antimuscarinics (such as transient bradycardia, dilation of pupils with loss of accommodation, dry mouth, flushing) in susceptible individuals; also associated with abdominal pain, anorexia, fever

Status: permitted

Drug: loperamide

Indications: symptomatic treatment of acute diarrhoea, adjunct to rehydration in acute diarrhoea

Cautions: none noted

Contra-indications: conditions where inhibition of peristalsis should be avoided, where abdominal distension develops, or in conditions such as active ulcerative colitis or antibiotic-associated colitis

Available forms: capsules, 2mg (6-capsule and 30-capsule packs)

Dose: acute diarrhoea: 4mg initially followed by 2mg after each loose stool for up to 5 days; usual dose 6–8mg daily, maximum dose 16mg daily

Side-effects: abdominal cramps, dizziness, drowsiness; skin reactions including urticaria, paralytic ileus, abdominal bloating also reported

Status: permitted

1.4 Laxatives

It is important for those who complain of constipation to understand that their bowel habit can vary considerably in frequency without doing harm. A useful definition of constipation is the passage of hard stools less frequently than the patient's own normal pattern. Misconceptions about bowel habits have led to excessive laxative use. Abuse may lead to hypokalaemia. Laxatives may be divided into different types but this disguises the fact that some laxatives have a complex action.

Bulk-forming laxatives such as isphagula husk relieve constipation by increasing faecal mass that stimulates peristalsis; patients should be advised that the full effect may take some days to develop. They are of particular value in those with small hard stools but should not be required unless fibre cannot be increased in the diet. Adequate fluid intake must be maintained to avoid intestinal obstruction.

Stimulant laxatives such as senna increase intestinal motility and often cause abdominal cramp, and should be avoided in intestinal obstruction. Glycerol suppositories act as a rectal stimulant by virtue of the mildly irritant action of glycerol.

Osmotic laxatives such as lactulose increase the amount of water in the large bowel by drawing fluid from the body into the bowel. Lactulose produces an osmotic diarrhoea of low faecal pH.

Drug: glycerol

Indications: constipation

Cautions: see notes above

Contra-indications: none noted

Available forms: suppositories 4G (12-suppository pack)

Dose: 1 suppository moistened with water before use, when required

Side-effects: none noted

Status: permitted

Drug: isphagula husk

Indications: constipation

Cautions: adequate fluid intake should be maintained to avoid intestinal obstruction

Contra-indications: difficulty in swallowing, intestinal obstruction, colonic atony, faecal impaction

Available forms: buff, effervescent, sugar and gluten-free isphagula husk 3.5G/sachet (low Na+) (10-sachet and 30-sachet packs)

Dose: 1 sachet in water twice daily, preferably after meals

Side-effects: flatulence, abdominal distension, gastro-intestinal obstruction or impaction; hypersensitivity reported

Status: permitted

Drug: lactulose

Indications: constipation (may take up to 48 hours to act)

Cautions: lactose intolerance

Contra-indications: galactoaemia, intestinal obstruction

Available forms: solution, lactulose 3.1–3.7g/5mL with other ketoses (300mL pack)

Dose: 15mL twice daily, adjusted according to response

Side-effects: nausea (can be reduced by administering with water, fruit juice or with meals), vomiting, flatulence, cramps, abdominal discomfort

Status: permitted

Drug: senna

Indications: constipation

Cautions: see notes above

Contra-indications: see notes above

Available forms: tablets, total sennosides (calculated as sennoside B) 7.5mg (60-tablet pack)

Dose: 2–4 tablets usually at night; initial dose should be low then gradually increased; note: acts in 8–12 hours

Side-effects: none noted

Status: permitted

1.5 Local preparations for anal and rectal disorders

Anal and perianal pruritus, soreness and excoriation are best treated by the application of bland ointments and suppositories. These conditions occur commonly in patients suffering from haemorrhoids, fistulas and proctitis. Cleansing with attention to any minor faecal soiling, adjustment of the diet to avoid hard stools, the use of bulk-forming materials such as bran and a high residue diet are helpful. When necessary, topical preparations containing local anaesthetics or corticosteroids are used, provided perianal thrush has been excluded. Perianal thrush is treated with a topical antifungal preparation (see section 5.2, p71).

Drug: Anusol ointment®

Indications: haemorrhoids, pruritis ani, other ano-rectal conditions

Cautions: none noted

Contra-indications: none noted

Available forms: ointment (25g pack)

Dose: apply night and morning and after defaecation

Side-effects: none noted

Status: permitted

Drug: Anusol with hydrocortisone ointment (Anusol HC®)

Indications: haemorrhoids, ani pruritis

Cautions: prolonged use can cause atrophy of the anal skin

Contra-indications: suitable for occasional short-term use after exclusion of infections such as herpes simplex

Available forms: ointment (30g pack)

Dose: apply night and morning and after defaecation

Side-effects: prolonged use can cause atrophy of the anal skin

Status: permitted

2.0 Cardiovascular system

2.1 Positive inotropic drugs

Digoxin is a cardiac glycoside that increases the force of the myocardial contraction and reduces conductivity within the atrioventricular (AV) node. Digoxin is most useful for controlling ventricular response in persistent and permanent atrial fibrillation and atrial flutter. Unwanted effects depend both on the concentration of digoxin in the plasma and on the sensitivity of the conducting system or of the myocardium. It can sometimes be difficult to distinguish between toxic effects and clinical deterioration because the symptoms of both are similar.

Drug: digoxin

Indications: heart failure, supraventricular arrhythmias (particularly atrial fibrillation and atrial flutter)

Cautions: recent myocardial infarction; sick sinus syndrome; thyroid disease; reduce dose in the elderly; severe respiratory disease; hypokalaemia, hypomagnesaemia, hypercalcaemia, hypoxia (risk of digitalis toxicity); monitor serum electrolytes and renal function; avoid rapid intravenous administration (risk of hypertension and reduced coronary flow)

Contra-indications: intermittent complete heart block, second degree AV block; supraventricular arrhythmias associated with accessory conducting pathways (for example, Wolff-Parkinson-White syndrome); ventricular tachycardia or fibrillation; hypertrophic cardiomyopathy (unless concomitant atrial fibrillation and heart failure, but use with caution); myocarditis; constrictive pericarditis (unless to control atrial fibrillation or improve systolic dysfunction, but use with caution)

Available forms: tablets, digoxin 62.5 micrograms, 125 micrograms and 250 micrograms (28-tablet packs)

Dose: as follows:
- maintenance: for atrial fibrillation or flutter, by mouth, according to renal function and initial loading dose, usual range 125–250 micrograms daily
- heart failure (for patients in sinus rhythm): by mouth, 62.5–125 micrograms once daily

Side-effects: see notes above; also nausea, vomiting, diarrhoea; arrhythmias, conduction disturbances; dizziness; blurred or yellow vision; rash, eosinophilia; less commonly depression; very rarely anorexia, intestinal ischaemia and necrosis, psychosis, apathy, confusion, headache, fatigue, weakness, gynaecomastia on long-term use, thrombocytopenia

Status: permitted

2.2 Diuretics

Loop diuretics are used in pulmonary oedema due to left ventricular failure and in patients with chronic heart failure. Combination diuretic therapy may be effective in patients with oedema resistant to treatment with one diuretic.

Drug: furosemide

Indications: oedema, resistant hypertension

Cautions: hypovolaemia and hypotension should be corrected before initiation of treatment with loop diuretics; electrolytes should be monitored during treatment. Loop diuretics can exacerbate diabetes and gout. If there is an enlarged prostate, urinary retention can occur and an adequate urinary output should be established before initiating treatment

Contra-indications: loop diuretics should be avoided in severe hypokalaemia, severe hyponatraemia, anuria

Available forms: tablets, 20mg and 40mg; injection, 2mL ampoule containing 20mg

Dose: as follows:
- by mouth: oedema, initially 40mg in the morning, maintenance 20–40mg daily; resistant oedema, 80–120mg daily; resistant hypertension, 40–80mg daily
- by intramuscular or slow intravenous injection: initially 20–50mg, increased if necessary in steps of 20mg not less than every 2 hours; doses greater than 50mg should be given by intravenous infusion only

Side-effects: include mild gastro-intestinal disturbances, pancreatitis, hepatic encephalopathy, postural hypotension, temporary increase in serum cholesterol and triglyceride concentration, hyperglycaemia, acute urinary retention, electrolyte disturbances (including hyponatraemia, hypokalaemia, hypocalcaemia, hypomagnesaemia), metabolic alkalosis, blood disorders (including bone marrow depression, thrombocytopenia, leucopenia), hyperuricaemia, visual disturbances, tinnitus and deafness (usually with high parenteral doses and rapid administration, and in renal impairment), hypersensitivity reactions (including rash, photosensitivity, pruritis); can also cause intrahepatic cholestasis and gout

Status: prohibited

2.3 Drugs for arrhythmias

Anti-arrhythmic drugs can be classified clinically into those that act on supraventricular arrhythmias (for example, verapamil); those that act on both supraventricular and ventricular arrhythmias (for example, amiodarone); and those that act on ventricular arrhythmias (for example, lidocaine). Amiodarone is used in the treatment of arrhythmias, particularly when other drugs are ineffective or contra-indicated.

Drug: amiodarone

Indications: can be used for paroxysmal supraventricular, nodal and ventricular tachycardias, atrial fibrillation and flutter, ventricular fibrillation; can also be used for tachyarrhythmias associated with Wolff-Parkinson-White syndrome; should be initiated in hospital or under specialist supervision

Cautions: liver-function and thyroid-function tests required before treatment and then every 6 months; hypokalaemia (measure serum-potassium concentration before treatment); chest x-ray required before treatment; heart failure; elderly; severe bradycardia and conduction disturbances in excessive dosage; intravenous use may cause moderate and transient fall in blood pressure (circulatory collapse precipitated by rapid administration or overdosage) or severe hepatocellular toxicity (monitor transaminases closely); administration by central venous catheter recommended if repeated or continuous infusion required, but note that infusion via peripheral veins may cause pain and inflammation; ECG monitoring and resuscitation facilities must be available during intravenous use; acute porphyria

Contra-indications: except in cardiac arrest: sinus bradycardia, sino-atrial heart block; unless pacemaker fitted avoid in severe conduction disturbances or sinus node disease; thyroid dysfunction; iodine sensitivity; avoid intravenous use in severe respiratory failure, circulatory collapse or severe arterial hypotension; avoid bolus injection in congestive heart failure or cardiomyopathy

Available forms: tablets, 200mg (28-tablet pack); injection (6mL ampoule containing 50mg/mL)

Dose: as follows:

– by mouth: 200mg 3 times daily for 1 week, reduced to 200mg twice daily for a further week; maintenance: usually 200mg daily or the minimum required to control the arrhythmia
– by intravenous infusion (see Cautions above): initially 5mg/kg over 20–120 minutes with ECG monitoring; subsequent infusion given if necessary according to response up to maximum 1.2g in 24 hours

Side-effects: nausea, vomiting, taste disturbances, raised serum transaminases (may require dose reduction or withdrawal if accompanied by acute liver disorders), jaundice; bradycardia (see Cautions above); pulmonary toxicity (including pneumonitis and fibrosis); tremor, sleep disorders; hypothyroidism, hyperthyroidism; reversible corneal microdeposits (sometimes with night glare); phototoxicity, persistent slate-grey skin discoloration (see also notes above), injection-site reactions; less commonly onset or worsening of arrhythmia, conduction disturbances (see Cautions above), peripheral neuropathy and myopathy (usually reversible on withdrawal); very rarely chronic liver disease including cirrhosis, sinus arrest, bronchospasm (in patients with severe respiratory failure), ataxia, benign intracranial hypertension, headache, vertigo, epididymo-orchitis, impotence, haemolytic or aplastic anaemia, thrombocytopenia, rash (including exfoliative dermatitis), hypersensitivity including vasculitis, alopecia, impaired vision due to optic neuritis or optic neuropathy (including blindness), anaphylaxis on rapid injection; also hypotension, respiratory distress syndrome, sweating, hot flushes

Status: permitted

Drug: verapamil hydrochloride

Indications: supraventricular arrhythmias

Cautions: first-degree AV block; acute phase of myocardial infarction (avoid if bradycardia, hypotension, left ventricular failure); patients taking beta-blockers (important: see below); avoid grapefruit juice (may affect metabolism). Verapamil injections should not be given to patients recently treated with beta-blockers because of the risk of hypotension and asystole. The suggestion that when a verapamil injection has been given first, an interval of 30 minutes before giving a beta-blocker is sufficient has not been confirmed

Contra-indications: hypotension, bradycardia, second- and third-degree AV block, sick sinus syndrome, cardiogenic shock, sino-atrial block; history of heart failure or significantly impaired left ventricular function, even if controlled by therapy; atrial flutter or fibrillation associated with accessory conducting pathways (for example, Wolff-Parkinson-White syndrome); acute porphyria

Available forms: injection (2mL ampoule containing 2.5mg/mL)

Dose: by slow intravenous injection over 2 minutes (3 minutes in elderly), supraventricular arrhythmias (but see also Contra-indications above), 5–10mg (preferably with ECG monitoring); in paroxysmal tachyarrhythmias, a further 5mg after 5–10 minutes if required

Side-effects: constipation; less commonly nausea, vomiting, flushing, headache, dizziness, fatigue, ankle oedema; rarely allergic reactions (erythema, pruritus, urticaria, angioedema, Stevens-Johnson syndrome); myalgia, arthralgia, paraesthesia, erythromelalgia; increased prolactin concentration; rarely gynaecomastia and gingival hyperplasia after long-term treatment; after intravenous administration or high doses, hypotension, heart failure, bradycardia, heart block, asystole

Status: permitted

2.4 Beta-adrenoceptor blocking drugs

Beta-adrenoceptor blocking drugs (beta-blockers) block the beta-adrenoceptors in the heart, peripheral vasculature, bronchi, pancreas and liver. In clinical practice, they are used in the management of hypertension, angina, post-myocardial infarction, arrhythmias, heart failure, thyrotoxicosis and prophylaxis of migraine, and to alleviate some symptoms of anxiety.

Drug: propranolol

Indications: see Dose below

Cautions: avoid abrupt withdrawal, especially in ischaemic heart disease; first-degree AV block; portal hypertension (risk of deterioration in liver function); diabetes; history of obstructive airways disease (introduce cautiously and monitor lung function); myasthenia gravis; symptoms of hypoglycaemia and thyrotoxicosis may be masked; psoriasis; history of hypersensitivity – may increase sensitivity to allergens and result in more serious hypersensitivity response, and may also reduce response to adrenaline (epinephrine)

Contra-indications: asthma (but see notes above), uncontrolled heart failure, Prinzmetal's angina, marked bradycardia, hypotension, sick sinus syndrome, second- or third-degree AV block, cardiogenic shock, metabolic acidosis, severe peripheral arterial disease; phaeochromocytoma (apart from specific use with alpha-blockers, see below)

Available forms: tablets, containing propranolol hydrochloride 10mg and 40mg (28-tablet packs)

Dose: according to indications as outlined below:
- hypertension: initially 80mg twice daily, increased at weekly intervals as required; maintenance 160–320mg daily
- angina: initially 40mg 2–3 times daily; maintenance 120–240mg daily
  arrhythmias: hypertrophic cardiomyopathy, anxiety tachycardia and thyrotoxicosis (adjunct), 10–40mg 3–4 times daily
- anxiety with symptoms such as palpitation, sweating, tremor: 40mg once daily, increased to 40mg 3 times daily if necessary
- prophylaxis after myocardial infarction: 40mg 4 times daily for 2–3 days, then 80mg twice daily, beginning 5 to 21 days after infarction
- essential tremor: initially 40mg 2–3 times daily; maintenance 80–160mg daily
  migraine prophylaxis: 80–240mg daily in divided doses

Side-effects: gastro-intestinal disturbances; bradycardia, heart failure, hypotension, conduction disorders, peripheral vasoconstriction (including exacerbation of intermittent claudication and Raynaud's phenomenon); bronchospasm (see above), dyspnoea; headache, fatigue, sleep disturbances, paraesthesia, dizziness, vertigo, psychoses; sexual dysfunction; purpura, thrombocytopenia; visual disturbances; exacerbation of psoriasis, alopecia; rarely rashes, dry eyes (reversible on withdrawal)

Status: prohibited in certain sports (including Archery and Shooting)

2.5 Nitrates

Nitrates have a useful role in angina. Although they are potent coronary vasodilators, their principal benefit follows from a reduction in venous return that reduces left ventricular work. Unwanted effects such as flushing, headache and postural hypotension may limit therapy, especially when angina is severe or when patients are unusually sensitive to the effects of nitrates.

Sublingual glyceryl trinitrate is one of the most effective drugs for providing rapid symptomatic relief of angina, but its effect lasts only for 20–30 minutes; the 300-microgram tablet is often appropriate when glyceryl trinitrate is first used. The aerosol spray provides an alternative method of rapid relief of symptoms for those who find difficulty in dissolving sublingual preparations.

Drug: glyceryl trinitrate

Indications: prophylaxis and treatment of angina

Cautions: hypothyroidism; malnutrition; hypothermia; recent history of myocardial infarction; heart failure due to obstruction; hypoxaemia or other ventilation and perfusion abnormalities; susceptibility to angle-closure glaucoma

Contra-indications: hypersensitivity to nitrates; hypotensive conditions and hypovolaemia; hypertrophic cardiomyopathy; aortic stenosis; cardiac tamponade; constrictive pericarditis; mitral stenosis; toxic pulmonary oedema; head trauma; cerebral haemorrhage; cerebrovascular disease; marked anaemia

Available forms: sublingual tablets, glyceryl trinitrate 300 micrograms (100-tablet pack); aerosol spray, glyceryl trinitrate 400 micrograms/metered dose (200-dose unit pack)

Dose: sublingually 0.3–1mg, repeated as required; when using the aerosol spray, the dose is 1–2 doses under the tongue and then close mouth

Side-effects: postural hypotension, tachycardia (but paradoxical bradycardia also reported); throbbing headache, dizziness; less commonly nausea, vomiting, heartburn, flushing, syncope, temporary hypoxaemia, rash; very rarely angle-closure glaucoma

Status: permitted

2.6 Calcium channel blockers

Nifedipine relaxes vascular smooth muscle and dilates coronary and peripheral arteries. Short-acting formulations of nifedipine are not recommended for angina or long-term management of hypertension; their use may be associated with large variations in blood pressure and reflex tachycardia.

Drug: nifedipine

Indications: prophylaxis of angina; hypertension; Raynaud's phenomenon

Cautions: see notes above; also withdraw if ischaemic pain occurs or existing pain worsens shortly after initiating treatment; poor cardiac reserve; heart failure or significantly impaired left ventricular function (heart failure deterioration observed); severe hypotension; elderly; diabetes mellitus; avoid grapefruit juice (may affect metabolism); acute porphyria

Contra-indications: cardiogenic shock; advanced aortic stenosis; within 1 month of myocardial infarction; unstable or acute attacks of angina

Available forms: capsules, 10mg nifedipine (90-capsule pack)

Dose: as follows:
- angina prophylaxis (but not recommended; see notes above) and Raynaud's phenomenon: initially 5mg 3 times daily, adjusted according to response to 20mg 3 times daily
- hypertension: not recommended, therefore no dose stated

Side-effects: gastro-intestinal disturbance; hypotension, oedema, vasodilatation, palpitation; headache, dizziness, lethargy, asthenia; less commonly tachycardia, syncope, chills, nasal congestion, dyspnoea, anxiety, sleep disturbance, vertigo, migraine, paraesthesia, tremor, polyuria, dysuria, nocturia, erectile dysfunction, epistaxis, myalgia, joint swelling, visual disturbance, sweating, hypersensitivity reactions (including angioedema, jaundice, pruritus, urticaria, rash); rarely anorexia, gum hyperplasia, mood disturbances, hyperglycaemia, male infertility, purpura, photosensitivity reactions; also reported dysphagia, intestinal obstruction, intestinal ulcer, gynaecomastia, agranulocytosis, anaphylaxis

Status: permitted

2.7 Oral anticoagulants

The oral anticoagulants antagonise the effects of vitamin K. It takes at least 48–72 hours for the anticoagulant effect to develop fully; warfarin is the drug of choice. If an immediate effect is required, unfractionated or low molecular weight heparin must be given concomitantly. Oral anticoagulants should not be used in cerebral artery thrombosis or peripheral artery occlusion as first-line therapy; aspirin is more appropriate for the reduction of risk in transient ischaemic attacks.

Drug: warfarin

Indications: prophylaxis of embolisation in rheumatic heart disease and atrial fibrillation; prophylaxis after insertion of prosthetic heart valve; prophylaxis and treatment of venous thrombosis and pulmonary embolism; transient ischaemic attacks

Cautions: use with caution in patients with hepatic or renal impairment; also recent surgery; recent ischaemic stroke; history of gastro-intestinal bleeding; peptic ulcer; concomitant use of drugs that increase risk of bleeding; bacterial endocarditis (increased risk of bleeding; use only if warfarin otherwise indicated), avoid cranberry juice

Contra-indications: haemorrhagic stroke; significant bleeding; avoid use within 48 hours postpartum

Available forms: tablets, warfarin sodium 1mg (brown), 3mg (blue), 5mg (pink) (28-tablet packs)

Dose: depends on whether loading is required and the level of anticoagulation required, but the daily maintenance dose is usually 3–9mg (taken at the same time each day); for further information on dosing of warfarin, see the full edition of the British National Formulary (www.bnf.org)

Side-effects: haemorrhage (see the full edition of the British National Formulary; www.bnf.org); also nausea, vomiting, diarrhoea, jaundice, hepatic dysfunction, pancreatitis, pyrexia, alopecia, purpura, rash, 'purple toes', skin necrosis (increased risk in patients with protein C or protein S deficiency)

Status: permitted

2.8 Antiplatelet drugs

Antiplatelet drugs decrease platelet aggregation and inhibit thrombus formation in the arterial circulation because in faster-flowing vessels, thrombi are composed mainly of platelets with little fibrin.

Use of aspirin in primary prevention of cardiovascular events, in patients with or without diabetes, is of unproven benefit. Long-term use of aspirin, in a dose of 75mg daily, is of benefit in established cardiovascular disease (secondary prevention); unduly high blood pressure must be controlled before aspirin is given. If the patient is at a high risk of gastro-intestinal bleeding, a proton pump inhibitor (see section 1.1.3, p16) can be added.

Clopidogrel is licensed for the prevention of ischaemic events in patients with a history of symptomatic ischaemic disease. Clopidogrel, in combination with low-dose aspirin, is also licensed for acute coronary syndrome without ST-segment elevation and for acute myocardial infarction with ST-segment elevation.

Drug: aspirin (antiplatelet)

Indications: secondary prevention of thrombotic cerebrovascular or cardiovascular disease, and following by-pass surgery

Cautions: asthma; uncontrolled hypertension; previous peptic ulceration (but manufacturers may advise avoidance of low-dose aspirin in history of peptic ulceration); concomitant use of drugs that increase risk of bleeding; G6PD deficiency

Contra-indications: use other than as an antiplatelet in children and adolescents under 16 years (Reye's syndrome) active peptic ulceration; haemophilia and other bleeding disorders; hypersensitivity: aspirin and other NSAIDs are contra-indicated in history of hypersensitivity to aspirin or any other NSAID, which includes those in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by aspirin or any other NSAID

Available forms: dispersible tablets, aspirin, 75mg (28-tablet pack)

Dose: 75–300mg daily, depending on indication (see the full edition of the British National Formulary; www.bnf.org)

Side-effects: bronchospasm; gastro-intestinal irritation, gastro-intestinal haemorrhage (occasionally major), also other haemorrhage (for example, subconjunctival)

Status: permitted

Drug: clopidogrel

Indications: prevention of atherosclerotic events in peripheral arterial disease, or within 35 days of myocardial infarction, or within 6 months of ischaemic stroke; prevention of artherosclerotic events in acute coronary syndrome without ST-segment elevation (given with aspirin; see notes above) and in acute myocardial infarction with ST-segment elevation (given with aspirin; see notes above)

Cautions: patients at risk of increased bleeding from trauma, surgery or other pathological conditions; concomitant use of drugs that increase risk of bleeding; discontinue 7 days before elective surgery if antiplatelet effect not desirable

Contra-indications: active bleeding

Available forms: tablets, clopidogrel (as besilate or hydrochloride), 75mg (30-tablet pack)

Dose: according to indications as outlined below:
- prevention of artherosclerotic events in peripheral arterial disease or after myocardial infarction or ischaemic stroke: 75mg once daily
- acute coronary syndrome (without ST-segment elevation): initially 300mg then 75mg daily (with aspirin – see notes above)
- acute myocardial infarction (with ST-segment elevation): initially 300mg then 75mg daily (with aspirin; see notes above), initial dose omitted if patient over 75 years

Side-effects: dyspepsia, abdominal pain, diarrhoea; bleeding disorders (including gastro-intestinal and intracranial); less commonly nausea, vomiting, gastritis, flatulence, constipation, gastric and duodenal ulcers, headache, dizziness, paraesthesia, leucopenia, decreased platelets (very rarely severe thrombocytopenia), eosinophilia, rash, pruritus; rarely vertigo; very rarely colitis, pancreatitis, hepatitis, acute liver failure, vasculitis, confusion, hallucinations, taste disturbance, stomatitis, bronchospasm, interstitial pneumonitis, blood disorders (including thrombocytopenic purpura, agranulocytosis, pancytopenia), hypersensitivity-like reactions (including fever, glomerulonephritis, arthralgia, Stevens-Johnson syndrome, toxic epidermal necrolysis, lichen planus)

Status: permitted

2.9 Antifibrinolytic drugs and haemostatics

Fibrin dissolution can be impaired by the administration of tranexamic acid, which inhibits fibrinolysis. It can be used to prevent bleeding and in the management of menorrhagia. Tranexamic acid may also be used in hereditary angioedema and epistaxis.

Drug: tranexamic acid

Indications: see notes above

Cautions: massive haematuria (avoid if risk of ureteric obstruction); not for use in disseminated intravascular coagulation; irregular menstrual bleeding (exclude structural or histological causes of menorrhagia, or fibroids causing distortion of the uterine cavity, before initiating treatment); regular liver function tests in long-term treatment of hereditary angioedema

Contra-indications: thromboembolic disease

Available forms: tablets, tranexamic acid 500mg (60-tablet pack)

Dose: as follows:

- by mouth: local fibrinolysis, 1–1.5g (or 15–25mg/kg) 2–3 times daily; menorrhagia (initiated when menstruation has started): 1g 3 times daily for up to 4 days, maximum 4g daily
- hereditary angioedema: 1–1.5g 2–3 times daily
- epistaxis: 1g 3 times daily for 7 days

Side-effects: nausea, vomiting, diarrhoea (reduce dose); rarely disturbances in colour vision (discontinue), thromboembolic events, convulsions, allergic skin reactions; dizziness and hypotension on rapid intravenous injection

Status: permitted

3.0 Respiratory system

3.1 Bronchodilators

3.1.1 Selective beta$_2$ agonists

Selective beta$_2$ agonists produce bronchodilation. A short-acting beta$_2$ agonist is used for immediate relief of asthma symptoms, while some long-acting beta$_2$ agonists are added to an inhaled corticosteroid in patients requiring prophylactic treatment.

Mild to moderate symptoms of asthma respond rapidly to the inhalation of a selective short-acting beta$_2$ agonist such as salbutamol or terbutaline. If beta$_2$ agonist inhalation is needed more often than once daily, prophylactic treatment should be considered. Regular treatment with an inhaled short-acting beta$_2$ agonist is less effective than 'as required' inhalation and is not appropriate prophylactic treatment.

A short-acting beta$_2$ agonist inhaled immediately before exertion reduces exercise-induced asthma. However, frequent exercise-induced asthma probably reflects poor overall control and calls for reassessment of asthma treatment.

Formoterol (eformoterol) and salmeterol are longer-acting beta$_2$ agonists that are administered by inhalation. They should be used for asthma only in patients who regularly use an inhaled corticosteroid. They have a role in the long-term control of chronic asthma and they can be useful in nocturnal asthma. Salmeterol should not be used for the relief of an asthma attack: it has a slower onset of action than salbutamol or terbutaline. Formoterol is licensed for short-term symptom relief and for the prevention of exercise-induced bronchospasm; its speed of onset of action is similar to that of salbutamol.

Combination inhalers that contain a long-acting beta$_2$ agonist and a corticosteroid ensure that long-acting beta$_2$ agonists are not used without concomitant corticosteroids, but reduce the flexibility to adjust the dose of each component.

Cautions

Beta$_2$ agonists should be used with caution in hyperthyroidism, cardiovascular disease, arrhythmias, susceptibility to QT-interval prolongation and hypertension. Potentially serious hypokalaemia may result from beta$_2$ agonist therapy. Particular caution is required in severe asthma, because this effect may be potentiated by concomitant treatment with theophylline and its derivatives, corticosteroids and diuretics, and by hypoxia. Plasma-potassium concentration should therefore be monitored in severe asthma.

Side-effects

Side-effects of the beta$_2$ agonists include fine tremor (particularly in the hands), nervous tension, headache, muscle cramps and palpitation. Other side-effects include tachycardia, arrhythmias, peripheral vasodilation, myocardial ischaemia and disturbances of sleep and behaviour. Paradoxical bronchospasm (occasionally severe), urticaria, angioedema, hypotension and collapse have also been reported. High doses of beta$_2$ agonists are associated with hypokalaemia.

Drug: formoterol fumarate

Indications: reversible airways obstruction (including nocturnal asthma and prophylaxis of exercise-induced bronchospasm) in patients requiring long-term regular bronchodilator therapy, chronic obstructive pulmonary disease

Cautions: see notes above

Contra-indications: none noted

Available forms: Turbohaler® (dry powder inhaler), formoterol fumarate 6 micrograms/metered inhalation (60-dose unit)

Dose: by inhalation of powder: chronic asthma, 6–12 micrograms 1–2 times daily, increased up to 24 micrograms twice daily if necessary; for relief of bronchospasm, adult and child over 6 years: 6–12 micrograms; prophylaxis of exercise-induced bronchospasm, 12 micrograms before exercise; chronic obstructive pulmonary disease, 12 micrograms 1–2 times daily; for symptom relief, additional doses can be taken to a maximum total of 48 micrograms daily (maximum single dose of 24 micrograms)

Side-effects: see notes above; very rarely QT-interval prolongation, taste disturbances, nausea, dizziness, rash, pruritus also reported

Status: permitted for inhalation within normal dose regimen

Drug: salbutamol

Indications: asthma and other conditions associated with reversible airways obstruction

Cautions: see notes above

Contra-indications: none noted

Available forms: injection, salbutamol (as sulphate) 500 micrograms/mL (1mL ampoule); aerosol inhalation, salbutamol (as sulphate) 100 micrograms/metered inhalation (200-dose unit); nebuliser solution, salbutamol (as sulphate) 2mg/mL, 2.5mL unit-dose vials (5mg)

Dose: as follows:

- by aerosol inhalation: 100–200 micrograms (1–2 puffs); for persistent symptoms up to 4 times daily, prophylaxis of allergen- or exercise-induced bronchospasm, 200 micrograms (2 puffs)
- by inhalation of nebulised solution: adult and child over 5 years: 2.5–5mg, repeated up to 4 times daily or more frequently in severe cases
- by subcutaneous or intramuscular injection: 500 micrograms, repeated every 4 hours if necessary

Side-effects: see notes above

Status: permitted for inhalation within normal dose regimen; injection prohibited

Drug: salmeterol

Indications: reversible airways obstruction (including nocturnal asthma and prevention of exercise-induced bronchospasm) in patients requiring long-term regular bronchodilator therapy

Cautions: see notes above

Contra-indications: none noted

Available forms: Evohaler® aerosol inhalation, salmeterol (as xinafoate) 25 micrograms/metered inhalation (120-dose unit)

Dose: by inhalation, asthma, 50 micrograms (2 puffs) twice daily; up to 100 micrograms (4 puffs) twice daily in more severe airways obstruction

Side-effects: see notes above

Status: permitted

Drug: terbutaline

Indications: asthma and other conditions associated with reversible airways obstruction

Cautions: see notes above

Contra-indications: none noted

Available forms: Turbohaler® (dry powder inhaler), terbutaline sulphate 500 micrograms/metered inhalation (100-dose unit)

Dose: adult and child over 5 years: 500 micrograms (1 inhalation); for persistent symptoms, up to 4 times daily

Side-effects: see notes above

Status: prohibited

3.1.2 Antimuscarinic bronchodilators

Ipratropium can provide short-term relief in chronic asthma, but short-acting beta$_2$ agonists act more quickly and are preferred. Ipratropium by nebulisation can be added to other standard treatment in life-threatening asthma or if acute asthma fails to improve with standard therapy.

Drug: ipratropium

Indications: reversible airways obstruction

Cautions: antimuscarinic bronchodilators should be used with caution in patients with prostatic hyperplasia, bladder outflow obstruction, and those susceptible to angle-closure glaucoma. Acute angle-closure glaucoma reported with nebulised ipratropium, particularly when given with nebulised salbutamol (and possibly other beta$_2$ agonists); care needed to protect patient's eyes from nebulised drug or from drug powder

Contra-indications: none noted

Available forms: aerosol inhalation, ipratropium bromide 20 micrograms/metered inhalation (200-dose unit); nebuliser solution, isotonic, ipratropium bromide 250 micrograms/mL, 1mL unit-dose vials (20-unit dose pack)

Dose: as follows:
- by aerosol inhalation, 20–40 micrograms, 3–4 times daily
- by inhalation of nebulised solution, for acute bronchospasm, 500 micrograms repeated as necessary

Side-effects: dry mouth is the most common side-effect of antimuscarinic bronchodilators; also constipation, cough, paradoxical bronchospasm, headache, dizziness; less commonly nausea, tachycardia, palpitation, atrial fibrillation, urinary retention, angle-closure glaucoma, blurred vision occur; raised intra-ocular pressure has occurred rarely; also vomiting, diarrhoea, local irritation; rarely laryngospasm, eye pain, mydriasis

Status: permitted

3.2 Corticosteroids

Corticosteroids are effective in asthma as they reduce airway inflammation (and hence reduce oedema and secretion of mucus into the airway). An inhaled corticosteroid is used regularly for prophylaxis of asthma when patients require a beta$_2$ agonist more than twice a week, or if symptoms disturb sleep more than once a week, or if the patient has suffered exacerbations in the last two years requiring a systemic corticosteroid or a nebulised bronchodilator. Regular use of inhaled corticosteroids reduces the risk of exacerbation of asthma. Corticosteroid inhalers must be used regularly for maximum benefit; alleviation of symptoms usually occurs three to seven days after initiation.

Preparations that combine a corticosteroid with a long-acting beta$_2$ agonist may be helpful for patients stabilised on the individual components in the same proportion.

Cautions

The potential for paradoxical bronchospasm (calling for discontinuation and alternative therapy) should be borne in mind. Mild bronchospasm may be prevented by inhalation of a short-acting beta$_2$ agonist beforehand (or by transfer from an aerosol inhalation to a dry powder in inhalation). Doses for corticosteroid CFC-free pressurised metered-dose inhalers may be different from traditional CFC-containing inhalers and may be different between brands.

Side-effects

Candidiasis: the risk of oral candidiasis can be reduced by using a spacer device with the corticosteroid inhaler; rinsing the mouth with water (or cleaning teeth) may be helpful. For side-effects associated with prolonged use of high-dose treatment, see the full edition of the British National Formulary (www.bnf.org).

Drug: beclometasone dipropionate

Indications: prophylaxis of asthma

Cautions: see notes above

Contra-indications: none noted

Available forms: aerosol inhalation (Clenil Modulite®), beclometasone dipropionate 50 micrograms/metered inhalation, 100 micrograms/metered inhalation, 250 micrograms/metered inhalation (200-dose units)

Dose: by aerosol inhalation, 200–400 micrograms twice daily, adjusted as necessary up to 1mg twice daily

Side-effects: see notes above

Status: permitted

Drug: fluticasone propionate

Indications: prophylaxis of asthma

Cautions: see notes above

Contra-indications: none noted

Available forms: Evohaler® aerosol inhalation, fluticasone propionate 125 micrograms/metered inhalation (120-dose unit); 250 micrograms/metered inhalation (120-dose unit)

Dose: by aerosol inhalation, prophylaxis of asthma, adult and child over 16 years: 100–500 micrograms twice daily, increased according to severity of asthma; maximum 1mg twice daily

Side-effects: see notes above; also very rarely dyspepsia, hyperglycaemia and arthralgia

Status: permitted

3.2.1 Compound preparations

Cautions

Hyperthyroidism, cardiovascular disease, arrhythmias, susceptibility to QT-interval prolongation, and hypertension; $beta_2$ agonists should be used with caution in diabetes – monitor blood glucose (risk of ketoacidosis); systemic corticosteroid therapy may be required during periods of stress or when either airways obstruction or mucus prevent drug access to smaller airways. Potentially serious hypokalaemia may result from $beta_2$ agonist therapy. Particular caution is required in severe asthma, because this effect may be potentiated by concomitant treatment with theophylline and its derivatives, corticosteroids and diuretics, and by hypoxia. Plasma-potassium concentration should therefore be monitored in severe asthma. The potential for paradoxical bronchospasm (calling for discontinuation and alternative therapy) should be borne in mind.

Side-effects

See notes above; also palpitation; fine tremor (particularly in the hands), nervous tension, headache; less commonly nausea, tachycardia, arrhythmias, dizziness, muscle cramps; very rarely QT-interval prolongation; taste disturbances, hypotension; peripheral vasodilatation, myocardial ischaemia and collapse also reported; high doses of $beta_2$ agonists are associated with hypokalaemia.

Drug: budesonide with formoterol fumarate (Symbicort®)

Indications: asthma, maintenance and reliever therapy

Cautions: see notes above

Contra-indications: none noted

Available forms: Symbicort 100/6 Turbohaler® (dry powder inhaler), budesonide 100 micrograms, formoterol fumarate 6 micrograms/metered inhalation (120-dose unit)

Dose: as follows:

- by inhalation of powder: asthma maintenance therapy, 1–2 puffs twice daily increased if necessary to maximum 4 puffs twice daily, reduced to 1 puff once daily if control maintained
- asthma, maintenance and reliever therapy, 2 puffs daily in 1–2 divided doses; for relief of symptoms, 1 puff as needed up to maximum 6 puffs at a time; maximum 8 puffs daily; up to 12 puffs daily can be used for a limited time but medical assessment should be considered

Side-effects: see notes above

Status: permitted

Drug: fluticasone propionate with salmeterol (Seretide®)

Indications: prophylaxis of asthma

Cautions: see notes above

Contra-indications: none noted

Available forms: Seretide 125 Evohaler® (aerosol inhalation), fluticasone propionate 125 micrograms, salmeterol (as xinafoate) 25 micrograms/metered inhalation (120-dose unit)

Dose: prophylaxis of asthma, adult and child over 12 years: 2 puffs twice daily (although patient may require a different strength preparation)

Side-effects: see notes above

Status: permitted

3.3 Drug delivery devices

Spacer devices remove the need for coordination between actuation of a pressurised metered-dose inhaler and inhalation. The spacer device reduces the velocity of the aerosol and subsequent impaction on the oropharynx and allows more time for evaporation of the propellant so that a larger proportion of the particles can be inhaled and deposited in the lungs. Spacer devices are particularly useful for patients with poor inhalation technique and for patients requiring high doses of inhaled corticosteroids, for nocturnal asthma and for patients prone to candidiasis with inhaled corticosteroids. The size of the spacer is important, the larger spacers with a one-way valve (Volumatic®) being most effective

Device: AeroChamber® Plus

A medium-volume device. For use with all pressurised (aerosol) inhalers.

Device: Volumatic

A large-volume device. For use with Clenil Modulite®, Flixotide®, Seretide®, Serevent® and Ventolin® inhalers.

3.4 Antihistamines

All antihistamines are of potential value in the treatment of nasal allergies, particularly seasonal allergic rhinitis (hay fever), and they may be of some value in vasomotor rhinitis. They reduce rhinorrhoea and sneezing but are usually less effective for nasal congestion. Oral antihistamines are also of some value in preventing urticaria and are used to treat urticarial rashes, pruritus, and insect bites and stings; they are also used in drug allergies.

All older antihistamines cause sedation but promethazine may be more sedating whereas chlorphenamine may be less so. This sedating activity is sometimes used to manage the pruritus associated with some allergies. Non-sedating antihistamines such as cetirizine and loratadine cause less sedation and psychomotor impairment than the older antihistamines because they penetrate the blood brain barrier only to a slight extent.

Cautions and contra-indications

Sedating antihistamines have significant antimuscarinic activity and should therefore be used with caution in prostatic hypertrophy, urinary retention, susceptibility to angle-closure glaucoma and pyloroduodenal obstruction. Caution may be required in epilepsy. Many antihistamines should be avoided in acute porphyria, but some are thought to be safe.

Side-effects

Drowsiness is a significant side-effect with most of the older antihistamines although paradoxical stimulation may occur rarely, especially with high doses or in children and the elderly. Drowsiness may diminish after a few days of treatment and is considerably less of a problem with the newer antihistamines (see also notes above). Side-effects that are more common with the older antihistamines include headache, psychomotor impairment and antimuscarinic effects such as urinary retention, dry mouth, blurred vision and gastro-intestinal disturbances.

Other rare side-effects of antihistamines include hypotension, palpitation, arrhythmias, extrapyramidal effects, dizziness, confusion, depression, sleep disturbances, tremor, convulsions, hypersensitivity reactions (including bronchospasm, angioedema and anaphylaxis, rashes and photosensitivity reactions), blood disorders, liver dysfunction and angle-closure glaucoma.

3.4.1 Non-sedating antihistamines

Although drowsiness is rare, patients should be advised that it can occur and may affect performance of skilled tasks (for example, driving); excess alcohol should be avoided.

Drug: cetirizine

Indications: symptomatic relief of allergy such as hay fever, chronic idiopathic urticaria

Cautions: see notes above

Contra-indications: see notes above

Available forms: tablets, cetirizine hydrochloride 10mg (7-tablet and 30-tablet packs)

Dose: adult and child over 12 years: 10mg once daily

Side-effects: see notes above

Status: permitted

Drug: loratidine

Indications: symptomatic relief of allergy such as hay fever, chronic idiopathic urticaria

Cautions: see notes above

Contra-indications: see notes above

Available forms: tablets, loratidine 10mg (30-tablet pack)

Dose: adult and child over 12 years: 10mg once daily

Side-effects: see notes above

Status: permitted

3.4.2 Sedating antihistamines

Drowsiness may affect performance of skilled tasks (for example, driving); sedating effects are enhanced by alcohol.

Drug: chlorphenamine

Indications: symptomatic relief of allergy such as hay fever, urticaria; emergency treatment of anaphylactic reactions

Cautions: see notes above

Contra-indications: see notes above

Available forms: tablets, chlorphenamine maleate 4mg (28-tablet pack); oral solution, chlorphenamine maleate 2mg/5mL (150mL bottle); injection, chlorphenamine maleate 10mg/mL (1mL ampoule)

Dose: as follows:
- by mouth: 4mg every 4–6 hours, maximum 24mg daily
- by intramuscular injection or by intravenous injection over 1 minute, 10mg, repeated if required up to maximum 4 doses in 24 hours

Side-effects: see notes above; also exfoliative dermatitis and tinnitus reported; injections may cause transient hypotension or CNS stimulation and may be irritant

Status: permitted

Drug: promethazine hydrochloride

Indications: symptomatic relief of allergy such as hay fever and urticaria

Cautions: see notes above

Contra-indications: see notes above

Available forms: tablets, promethazine hydrochloride 10mg (56-tablet pack)

Dose: by mouth, 10–20mg 2–3 times daily

Side-effects: see notes above, also restlessness

Status: permitted

3.5 Allergic emergencies

Adrenaline (epinephrine) provides physiological reversal of the immediate symptoms associated with hypersensitivity reactions such as anaphylaxis and angioedema. The intramuscular route is the first choice route for the administration of adrenaline (epinephrine) in the management of anaphylaxis.

Drug: adrenaline/epinephrine

Indications: emergency treatment of acute anaphylaxis; angioedema

Cautions: in non-life threatening situations: elderly; ischaemic heart disease, severe angina, obstructive cardiomyopathy, hypertension, arrhythmias, cerebrovascular disease, occlusive vascular disease, arteriosclerosis, monitor blood pressure and ECG; cor pulmonale; organic brain damage, psychoneurosis; diabetes mellitus, hyperthyroidism, phaeochromocytoma; prostate disorders; hypokalaemia, hypercalcaemia; susceptibility to angle-closure glaucoma

Contra-indications: none noted

Available forms: EpiPen® Auto-injector 0.3mg (delivering a single dose of adrenaline 300 micrograms)

Dose: by intramuscular injection, adult and child body-weight over 30kg: 300 micrograms repeated after 5–15 minutes as necessary

Side-effects: nausea, vomiting, dry mouth, hypersalavation; arrhythmias, syncope, angina, pallor, palpitation, cold extremities, hypertension (risk of cerebral haemorrhage); dyspnoea, pulmonary oedema (on excessive dosage or extreme sensitivity); anxiety, tremor, restlessness, headache, weakness, dizziness, hallucinations; hyperglycaemia; urinary retention, difficulty in micturition; metabolic acidosis; hypokalaemia; tissue necrosis at injection site and of extremities, liver and kidneys; mydriasis, angle-closure glaucoma, sweating

Status: prohibited

3.6 Cough preparations:

Cough may be a symptom of an underlying disorder, such as asthma, gastro-oesophageal reflux disease or rhinitis, which should be addressed before prescribing cough suppressants (for example, pholcodine).

Demulcent cough preparations contain soothing substances such as syrup or glycerol and some patients believe that such preparations relieve a dry irritating cough. Preparations such as simple linctus have the advantage of being harmless and inexpensive.

Drug: pholcodine

Indications: dry cough

Cautions: asthma; chronic, persistent, or productive cough

Contra-indications: chronic bronchitis, chronic obstructive pulmonary disease, bronchiectasis, patients at risk of respiratory failure

Available forms: linctus (oral solution), pholcodine 5mg/5mL in a suitable flavoured vehicle, containing citric acid monohydrate 1% (200mL bottle)

Dose: 5–10mL 3–4 times daily

Side-effects: nausea, vomiting, constipation, sputum retention, drowsiness, dizziness, excitation, confusion, rash

Status: permitted

Drug: simple linctus BP

Indications: cough

Cautions: none noted

Contra-indications: none noted

Available forms: linctus (oral solution), citric acid monohydrate 2.5% in a suitable vehicle with an anise flavour (200mL bottle)

Dose: 5mL 3–4 times daily

Side-effects: none noted

Status: permitted

4.0 Central nervous system

4.1 Hypnotics and anxiolytics

Most anxiolytics ('sedatives') will induce sleep when given at night and most hypnotics will sedate when given during the day. Prescribing of these drugs is widespread but dependence (both physical and psychological) and tolerance occur. This may lead to difficulty in withdrawing the drug after the patient has been taking it regularly for more than a few weeks. Hypnotics and anxiolytics should therefore be reserved for short courses to alleviate acute conditions after causal factors have been established.

Hypnotics should not be prescribed indiscriminately and routine prescribing is undesirable. They should be reserved for short courses in the acutely distressed. Tolerance to their effects develops within three to 14 days of continuous use and long-term efficacy cannot be assured. A major drawback of long-term use is that withdrawal can cause rebound insomnia and a withdrawal syndrome.

Temazepam acts for a short time and has little or no hangover effect. However, withdrawal phenomena are more common with short-acting benzodiazepines such as temazepam. If insomnia is associated with daytime anxiety, then the use of a long-acting benzodiazepine anxiolytic such as diazepam given as a single dose at night may effectively treat both symptoms.

Zopiclone is a non-benzodiazepine hypnotic, but it acts at the benzodiazepine receptor. It is not licensed for long-term use; dependence has been reported in a small number of patients. Zopiclone has a short duration of action.

Some antihistamines such as promethazine are used to treat occasional insomnia; their prolonged duration of action can often cause drowsiness the following day. The sedative effect of antihistamines may diminish after a few days of continued treatment; antihistamines are associated with headache, psychomotor impairment and antimuscarinic effects.

4.1.1 Hypnotics

Drug: promethazine hydrochloride

Indications: sedation (short-term use)

Cautions: sedating antihistamines have significant antimuscarinic activity and they should therefore be used with caution in prostatic hypertrophy, urinary retention, susceptibility to angle-closure glaucoma, pyloroduodenal obstruction; caution may be required in epilepsy; children and the elderly are more susceptible to side-effects

Contra-indications: many antihistamines should be avoided in acute porphyria but some are thought to be safe

Available forms: tablets, promethazine hydrochloride 10mg (56-tablet pack)

Dose: 25–50mg at bedtime

Side-effects: drowsiness is a significant side-effect with most of the older antihistamines, although paradoxical stimulation may occur rarely, especially with high doses or in children and the elderly. Side-effects that are more common with the older antihistamines include headache, psychomotor impairment, antimuscarinic effects such as urinary retention, dry mouth, blurred vision, gastro-intestinal disturbances. Other rare side-effects of antihistamines include hypotension, palpitation, arrhythmias, extrapyramidal effects, dizziness, confusion, depression, sleep disturbances, tremor, convulsions, hypersensitivity reactions (including bronchospasm, angioedema, anaphylaxis, rashes, photosensitivity reactions), blood disorders, liver dysfunction, angle-closure glaucoma

Status: permitted

Drug: temazepam

Indications: insomnia (short-term use)

Cautions: respiratory disease, muscle weakness and myasthenia gravis, history of drug or alcohol abuse, marked personality disorder; reduce dose in elderly and debilitated; avoid prolonged use (and abrupt withdrawal thereafter); acute porphyria

Contra-indications: respiratory depression; marked neuromuscular respiratory weakness including unstable myasthenia gravis; acute pulmonary insufficiency; sleep apnoea syndrome; not for use alone to treat depression (or anxiety associated with depression) or chronic psychosis

Available forms: tablets, temazepam 10mg (28-tablet pack)

Dose: as follows:
– 10–20mg at bedtime, exceptional circumstances 30–40mg
– elderly (or debilitated): 10mg at bedtime, exceptional circumstances 20mg

Side-effects: potentially drowsiness and lightheadedness the next day; confusion and ataxia (especially in the elderly); amnesia may occur; dependence

Status: permitted

Drug: zopiclone

Indications: insomnia (short-term use: up to 4 weeks)

Cautions: elderly; muscle weakness and myasthenia gravis, history of drug abuse, psychiatric illness; avoid prolonged use (risk of tolerance and withdrawal symptoms); drowsiness may persist the next day and affect performance of skilled tasks (for example, driving); effects of alcohol enhanced

Contra-indications: marked neuromuscular respiratory weakness including unstable myasthenia gravis, respiratory failure, severe sleep apnoea syndrome

Available forms: tablets, zopiclone 7.5mg (28-tablet pack)

Dose: adult over 18 years: 7.5mg at bedtime

Side-effects: taste disturbance; less commonly nausea, vomiting; dizziness, drowsiness, dry mouth, headache; rarely amnesia, confusion, depression, hallucinations, nightmares; very rarely light-headedness, incoordination; paradoxical effects and sleep-walking also reported

Status: permitted

4.1.2 Anxiolytics

Benzodiazepine anxiolytics can be effective in alleviating anxiety states. Although these drugs are sometimes prescribed for stress-related symptoms, unhappiness or minor physical disease, their use in such conditions is inappropriate. Benzodiazepine anxiolytics should not be used as sole treatment for chronic anxiety and are not appropriate for treating depression or chronic psychosis. Diazepam has a sustained action, whereas lorazepam is a shorter-acting compound. Anxiolytic benzodiazepine treatment should be limited to the lowest possible dose for the shortest possible time.

Drug: diazepam

Indications: short-term use in anxiety or insomnia

Cautions: respiratory disease, muscle weakness and myasthenia gravis, history of drug or alcohol abuse, marked personality disorder; reduce dose in elderly and debilitated; avoid prolonged use (and abrupt withdrawal thereafter); special precautions for intravenous injection; acute porphyria); when given parenterally, close observation required until full recovery from sedation

Contra-indications: respiratory depression; marked neuromuscular respiratory weakness including unstable myasthenia gravis; acute pulmonary insufficiency; sleep apnoea syndrome; not for chronic psychosis; should not be used alone in depression or in anxiety with depression

Available forms: tablets, diazepam 2mg (28-tablet pack); tablets, diazepam 5mg (28-tablet pack); injection, diazepam 5mg/mL (2mL ampoule); rectal tubes (rectal solution), diazepam 2mg/mL (2.5mL (5mg) tube); rectal tubes (rectal solution), diazepam 4mg/mL (2.5mL (10mg) tube)

Dose: as follows:

- by mouth: anxiety, 2mg 3 times daily increased if necessary to 15–30mg daily in divided doses; elderly (or debilitated) half adult dose; insomnia associated with anxiety, 5–15mg at bedtime
- by intramuscular injection or slow intravenous injection (into a large vein, at a rate of not more than 5mg/minute): for severe acute anxiety, control of acute panic attacks, 10mg, repeated if necessary after not less than 4 hours; only use intramuscular route when oral and intravenous routes not possible; emulsion formulation preferred for intravenous injection
- by rectum as rectal solution: acute anxiety and agitation, 500 micrograms/kg repeated after 12 hours as required; elderly 250 micrograms/kg

Side-effects: drowsiness and lightheadedness the next day; confusion and ataxia (especially in the elderly); amnesia; dependence; paradoxical increase in aggression; muscle weakness; occasionally headache, vertigo, hypotension, salivation changes, gastro-intestinal disturbances, visual disturbances, dysarthria, tremor, changes in libido, incontinence, urinary retention; blood disorders and jaundice reported; skin reactions; on intravenous injection, pain, thrombophlebitis, rarely apnoea

Status: permitted

Drug: lorazepam

Indications: short-term use in anxiety or insomnia

Cautions: see diazepam notes on p45

Contra-indications: see diazepam notes on p45

Available forms: tablets, lorazepam 1mg (28-tablet pack)

Dose: as follows:
- by mouth, anxiety, 1–4mg daily in divided doses
- elderly or debilitated, half adult dose
- insomnia associated with anxiety, 1–2mg at bedtime

Side-effects: see diazepam notes on p45

Status: permitted

4.2 Antipsychotic drugs

Antipsychotic drugs generally tranquillise without impairing consciousness and without causing paradoxical excitement, but should not be regarded merely as tranquillisers. In the short term, they are used to calm disturbed patients whatever the underlying psychopathology, which may be schizophrenia, brain damage, mania, toxic delirium or agitated depression. Antipsychotic drugs are used to alleviate severe anxiety, but this, too, should be a short-term measure.

Drug: chlorpromazine hydrochloride

Indications: schizophrenia and other psychoses, mania, short-term adjunctive management of severe anxiety, psychomotor agitation, excitement, violent or dangerously impulsive behaviour

Cautions: antipsychotic drugs should be used with caution in patients with cardiovascular disease, Parkinson's disease (may be exacerbated by antipsychotics), epilepsy (and conditions predisposing to epilepsy), depression, myasthenia gravis, prostatic hypertrophy or a susceptibility to angle-closure glaucoma. Caution is also required in severe respiratory disease and in patients with a history of jaundice or who have blood dyscrasias (perform blood counts if unexplained infection or fever develops). As photosensitisation may occur with higher dosages, patients should avoid direct sunlight. Also diabetes

Contra-indications: antipsychotic drugs may be contra-indicated in comatose states, CNS depression, phaeochromocytoma; also hypothyroidism

Available forms: tablets, chlorpromazine hydrochloride 25mg (28-tablet pack)

Dose: initially 25mg 3 times daily (or 75mg at night), adjusted according to response, to usual maintenance dose of 75–300mg daily; elderly or debilitated patients should be treated with a third to half adult dose

Side-effects: potential side-effects include extrapyramidal symptoms and hypotension and interference with temperature regulation. Neuroleptic malignant syndrome (hyperthermia, fluctuating level of consciousness, muscle rigidity, autonomic dysfunction with pallor, tachycardia, labile blood pressure, sweating, urinary incontinence) is a rare but potentially fatal side-effect of some drugs. Other side-effects include drowsiness; apathy; agitation, excitement and insomnia; convulsions; dizziness; headache; confusion; gastro-intestinal disturbances; nasal congestion; antimuscarinic symptoms (such as dry mouth, constipation, difficulty with micturition, blurred vision; very rarely, precipitation of angle-closure glaucoma); cardiovascular symptoms (such as hypotension, tachycardia, arrhythmias); ECG changes (cases of sudden death have occurred); venous thromboembolism; endocrine effects such as menstrual disturbances, galactorrhoea, gynaecomastia, impotence, weight gain; blood dyscrasias (such as agranulocytosis and leucopenia), photosensitisation, contact sensitisation and rashes, and jaundice (including cholestatic); corneal and lens opacities, and purplish pigmentation of the skin, cornea, conjunctiva, retina. Also hyperglycaemia

Status: permitted

4.3 Antidepressant drugs

Antidepressant drugs are effective for treating moderate to severe depression associated with psychomotor and physiological changes such as loss of appetite and sleep disturbance; improvement in sleep is usually the first benefit of therapy. Antidepressant drugs should not be used routinely in mild depression and psychological therapy should be considered initially.

Drug: amitriptyline hydrochloride

Indications: depressive illness, neuropathic pain (unlicensed indication), migraine prophylaxis (unlicensed indication)

Cautions: amitriptyline should be used with caution in patients with cardiovascular disease because of the risk of arrhythmias; patients with concomitant conditions such as hyperthyroidism and phaeochromocytoma should be treated with care. Care is also needed in patients with epilepsy and diabetes. Tricyclic antidepressant drugs have antimuscarinic activity, and therefore caution is needed in patients with prostatic hypertrophy, chronic constipation, increased intra-ocular pressure, urinary retention, or those with a susceptibility to angle-closure glaucoma. Tricyclic and related antidepressant drugs should be used with caution in patients with a significant risk of suicide, or a history of psychosis or bipolar disorder, because antidepressant therapy may aggravate these conditions; treatment should be stopped if the patient enters a manic phase

Contra-indications: tricyclic and related antidepressants are contra-indicated in the immediate recovery period after myocardial infarction, in arrhythmias (particularly heart block) and in the manic phase of bipolar disorder; avoid treatment with tricyclic antidepressant drugs in acute porphyria

Available forms: tablets, amitriptyline hydrochloride 10mg (28-tablet pack), 25mg (28-tablet pack)

Dose: according to indications as outlined below:

- depression: adult and child over 16 years: initially 75mg (elderly and adolescents 30–75mg) daily in divided doses or as a single dose at bedtime, increased gradually as necessary to 150–200mg
- neuropathic pain (unlicensed indication): initially 10mg daily at night, gradually increased if necessary to 75mg daily; higher doses under specialist supervision
- migraine prophylaxis (unlicensed indication):, initially 10mg at night, increased if necessary to maintenance of 50–75mg at night; maximum 150mg at night

Side-effects: arrhythmias and heart block occasionally follow the use of tricyclic antidepressants, particularly amitriptyline. Other cardiovascular side-effects include postural hypotension, tachycardia and ECG changes. Central nervous system side-effects are common, particularly in the elderly, and include anxiety, dizziness, agitation, confusion, sleep disturbances, irritability, paraesthesia; drowsiness is associated with some of the tricyclic antidepressants. Convulsions, hallucinations, delusions, mania and hypomania may occur, and, rarely, extrapyramidal symptoms including tremor and dysarthria. Antimuscarinic side-effects include dry mouth, blurred vision (very rarely precipitation of angle-closure glaucoma), constipation (rarely leading to paralytic ileus, particularly in the elderly), urinary retention. Endocrine effects include breast enlargement, galactorrhoea, gynaecomastia. Sexual dysfunction may occur. Changes in blood sugar, increased appetite and weight gain can accompany treatment with tricyclic antidepressant drugs, but anorexia and weight loss are also seen. Another side-effect to which the elderly are particularly susceptible is hyponatraemia. Other class side-effects include nausea, vomiting, taste disturbance, tinnitus, rash, urticaria, pruritus, photosensitivity, alopecia, sweating. Also abdominal pain, stomatitis, palpitation, oedema, hypertension, restlessness, fatigue, mydriasis, increased intra-ocular pressure

Status: permitted

4.4 Drugs used in nausea and vertigo

Antiemetics should be prescribed only when the cause of vomiting is known, because otherwise they may delay diagnosis. If antiemetic drug treatment is indicated, the drug is chosen according to the aetiology of vomiting.

Antihistamines (for example, promethazine or cyclizine) are effective against nausea and vomiting resulting from many underlying conditions.

Phenothiazines (for example, prochorperazine) are dopamine antagonists and act centrally by blocking the chemoreceptor trigger zone. Phenothiazines should be used with caution in patients with cardiovascular disease. They should also be used with caution in Parkinson's disease (which may be exacerbated by antipsychotics), epilepsy (and conditions predisposing to epilepsy), depression, myasthenia gravis, prostatic hypertrophy or a susceptibility to angle-closure glaucoma. Caution is also required in severe respiratory disease and in patients with a history of jaundice or who have blood dyscrasias (perform blood counts if unexplained infection or fever develops). As photosensitisation may occur with higher dosages, patients should avoid direct sunlight.

Antipsychotic drugs may be contra-indicated in comatose states, CNS depression and phaeochromocytoma. Potential side-effects include extrapyramidal symptoms, and hypotension and interference with temperature regulation. Neuroleptic malignant syndrome (hyperthermia, fluctuating level of consciousness, muscle rigidity and autonomic dysfunction with pallor, tachycardia, labile blood pressure, sweating and urinary incontinence) is a rare but potentially fatal side-effect of some drugs. Other side-effects include: drowsiness; apathy; agitation, excitement and insomnia; convulsions; dizziness; headache; confusion; gastro-intestinal disturbances; nasal congestion; antimuscarinic symptoms (such as dry mouth, constipation, difficulty with micturition and blurred vision; very rarely, precipitation of angle-closure glaucoma); cardiovascular symptoms (such as hypotension, tachycardia and arrhythmias); ECG changes (cases of sudden death have occurred); venous thromboembolism; endocrine effects such as menstrual disturbances, galactorrhoea, gynaecomastia, impotence and weight gain; blood dyscrasias (such as agranulocytosis and leucopenia), photosensitisation, contact sensitisation and rashes, and jaundice (including cholestatic); corneal and lens opacities, and purplish pigmentation of the skin, cornea, conjunctiva and retina.

Prochlorperazine can also be administered as a buccal tablet, placed between the upper lip and the gum.

Metoclopramide is an effective antiemetic and its activity closely resembles that of the phenothiazines. It also acts directly on the gastro-intestinal tract and may be superior to the phenothiazines for emesis associated with gastroduodenal, hepatic and biliary disease. As with the phenothiazines, metoclopramide can induce acute dystonic reactions involving facial and skeletal muscle spasms and oculogyric crises. These dystonic effects are more common in the young (especially girls and young women) and the very old; they usually occur shortly after starting treatment with metoclopramide and subside within 24 hours of stopping it.

Domperidone acts at the chemoreceptor trigger zone; it is used for the relief of nausea and vomiting. It has the advantage over metoclopramide and the phenothiazines of being less likely to cause central effects such as sedation and dystonic reactions because it does not readily cross the blood-brain barrier. Domperidone is also used to treat vomiting due to emergency hormonal contraception.

Ondansetron is a specific 5HT3-receptor antagonist that blocks 5HT3 receptors in the gastro-intestinal tract and in the CNS.

Drug: cyclizine

Indications: nausea, vomiting, vertigo, motion sickness, labyrinthine disorders

Cautions: see promethazine hydrochloride notes on p51

Contra-indications: see promethazine hydrochloride notes on p51

Available forms: injection, cyclizine lactate 50mg/mL (1mL ampoule)

Dose: by intramuscular or intravenous injection, cyclizine lactate 50mg 3 times daily

Side-effects: see notes above; also hypertension, paraesthesia and twitching

Status: permitted

Drug: domperidone

Indications: nausea and vomiting, dyspepsia, gastro-oesophageal reflux

Cautions: children

Contra-indications: prolactinoma; if increased gastro-intestinal motility harmful

Available forms: tablets, 10mg (as maleate) (30-tablet pack)

Dose: by mouth, adult and child bodyweight over 35kg: 10–20mg 3–4 times daily; maximum 80mg daily

Side-effects: rarely gastro-intestinal disturbances (including cramps) and hyperprolactinaemia; very rarely ventricular arrhythmias, agitation, drowsiness, nervousness, seizures, extrapyramidal effects, headache, rashes; also reported QT-interval prolongation

Status: permitted

Drug: metoclopramide

Indications: adults, nausea and vomiting, particularly in gastro-intestinal disorders; migraine

Cautions: elderly, young adults (15–19 years) and children; atopic allergy (including asthma); may mask underlying disorders such as cerebral irritation; acute porphyria; epilepsy

Contra-indications: gastro-intestinal obstruction, perforation or haemorrhage; 3–4 days after gastro-intestinal surgery; phaeochromocytoma

Available forms: tablets, metoclopramide hydrochloride 10mg (28-tablet pack); injection, metoclopramide hydrochloride 5mg/mL (2mL ampoule)

Dose: by mouth or by intramuscular injection or by intravenous injection over 1–2 minutes, nausea and vomiting, 10mg (5mg in young adults 15–19 years, bodyweight under 60kg) 3 times daily

Side-effects: extrapyramidal effects (especially in children and young adults (15–19 years), hyperprolactinaemia, occasionally tardive dyskinesia on prolonged administration; also reported, anxiety, confusion, drowsiness, restlessness, diarrhoea, depression, neuroleptic malignant syndrome, rashes, pruritus, oedema; cardiac conduction abnormalities reported following intravenous administration; rarely methaemoglobinaemia (more severe in G6PD deficiency)

Status: permitted

Drug: ondansetron

Indications: various forms of nausea and vomiting

Cautions: QT-interval prolongation (avoid concomitant use of drugs that prolong QT interval); subacute intestinal obstruction; adenotonsillar surgery

Contra-indications: none noted

Available forms: injection, ondansetron (as hydrochloride) 2mg/mL (2mL ampoule)

Dose: by intramuscular or slow intravenous injection, 4–8mg

Side-effects: constipation; headache; flushing; injection site-reactions; less commonly hiccups, hypotension, bradycardia, chest pain, arrhythmias, movement disorders, seizures; on intravenous administration, rarely dizziness, transient visual disturbances (very rarely transient blindness)

Status: permitted

Drug: prochlorperazine

Indications: severe nausea, vomiting, vertigo, labyrinthine disorders

Cautions: see notes above

Contra-indications: see notes above

Available forms: tablets (buccal), prochlorperazine maleate 3mg (10-tablet pack)

Dose: 1–2 tablets twice daily; tablets are placed high between upper lip and gum and left to dissolve

Side-effects: see notes above

Status: permitted

Drug: promethazine hydrochloride

Indications: nausea, vomiting, vertigo, labyrinthine disorders, motion sickness; allergy and urticaria

Cautions: promethazine has significant antimuscarinic activity and should therefore be used with caution in prostatic hypertrophy, urinary retention, susceptibility to angle-closure glaucoma and pyloroduodenal obstruction; caution may be required in epilepsy

Contra-indications: many antihistamines should be avoided in acute porphyria but some are thought to be safe

Available forms: tablets, promethazine hydrochloride 10mg (56-tablet pack)

Dose: by mouth, 20–25mg at bedtime on night before travel, repeat following morning if necessary

Side-effects: see notes above; also restlessness

Status: permitted

4.4.1 Other drugs for Ménière's disease

Betahistine has been promoted as a specific treatment for Ménière's disease.

Drug: betahistine hydrochloride

Indications: vertigo, tinnitus and hearing loss associated with Ménière's disease

Cautions: asthma, history of peptic ulcer

Contra-indications: phaeochromocytoma

Available forms: tablets, betahistine dihydrochloride 8mg (84-tablet pack)

Dose: initially 16mg 3 times daily, preferably with food; maintenance 24–48mg daily

Side-effects: gastro-intestinal disturbances; headache, rashes and pruritus reported

Status: permitted

4.5 Analgesics

The non-opioid drugs, paracetamol and aspirin (and other non-steroidal anti-inflammatory drugs, or NSAIDs; see section 9.1, p89), are particularly suitable for pain in musculoskeletal conditions, whereas the opioid analgesics are more suitable for moderate to severe pain, particularly of visceral origin.

The pain of mild sickle-cell crises is managed with paracetamol, an NSAID or dihydrocodeine. Severe crises may require the use of morphine; concomitant use of a NSAID may potentiate analgesia and allow lower doses of the opioid to be used.

The choice of an analgesic for dental purposes should be based on its suitability for the patient. Most dental pain is relieved effectively by NSAIDs. NSAIDs that are used for dental pain include ibuprofen, diclofenac and aspirin. Paracetamol has analgesic and antipyretic effects but no anti-inflammatory effect.

Non-steroidal anti-inflammatory analgesics are particularly useful for the treatment of patients with chronic disease accompanied by pain and inflammation. Some of them are also used in the short-term treatment of mild to moderate pain, including transient musculoskeletal pain, but paracetamol is now often preferred, particularly in the elderly. They are also suitable for the relief of pain in dysmenorrhoea.

4.5.1 Non-opioid analgesics

Aspirin is indicated for headache, transient musculoskeletal pain, dysmenorrhoea and pyrexia. In inflammatory conditions, most physicians prefer anti-inflammatory treatment with another NSAID, which may be better tolerated and more convenient for the patient (see section 9.1, p89). Gastric irritation may be a problem; it is minimised by taking the dose after food. Paracetamol is similar in efficacy to aspirin but has no demonstrable anti-inflammatory activity; it is less irritant to the stomach and for that reason is now generally preferred to aspirin, particularly in the elderly.

Drug: aspirin (acetylsalicylic acid)

Indications: mild to moderate pain, pyrexia

Cautions: asthma, allergic disease, dehydration; preferably avoid during fever or viral infection in children (risk of Reye's syndrome), elderly; G6PD-deficiency; concomitant use of drugs that increase risk of bleeding

Contra-indications: children under 16 years (Reye's syndrome); previous or active peptic ulceration, haemophilia; not for treatment of gout. Hypersensitivity: aspirin and other NSAIDs are contra-indicated in patients with a history of hypersensitivity to aspirin or any other NSAID, which includes those in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by aspirin or any other NSAID

Available forms: dispersible tablets, aspirin 300mg (28-tablet pack)

Dose: by mouth, 300–900mg every 4–6 hours when necessary; maximum 4g daily; child under 16 years not recommended

Side-effects: generally mild and infrequent but high incidence of gastro-intestinal irritation with slight asymptomatic blood loss, increased bleeding time, bronchospasm and skin reactions in hypersensitive patients

Status: permitted

Drug: paracetamol (acetaminophen)

Indications: mild to moderate pain, pyrexia

Cautions: alcohol dependence

Contra-indications: none noted

Available forms: tablets, paracetamol 500mg (32-tablet and 100-tablet packs); soluble tablets (dispersible tablets), paracetamol 500mg (24-tablet and 60-tablet packs); oral suspension (paediatric mixture), paracetamol 120mg/5mL (100mL pack), 250mg/5mL (300mL pack), sachets 120mg/5mL (20-sachet pack); suppositories, paracetamol 500mg (10-suppository pack)

Dose: as follows:
- by mouth, 0.5–1g every 4–6 hours to a maximum of 4g daily; child: 3 months–1 year 60–120mg, 1–6 years 120–250mg, 6–12 years 250–500mg; doses may be repeated every 4–6 hours when necessary (maximum of 4 doses in 24 hours)
- by rectum, adult and child over 12 years: 0.5–1g every 4–6 hours to a maximum of 4g daily

Side-effects: rare, but rashes, blood disorders (including thrombocytopenia, leucopenia, neutropenia) reported; important: liver damage (and less frequently renal damage) following overdosage

Status: permitted

Drug: paracetamol and phenylephrine (Benylin Cold & Flu®)

Indications: relief of symptoms of cold and influenza, including the relief of headaches, aches, pains, sore throat, nasal congestion and lowering of temperature

Cautions: see paracetamol notes on p53

Contra-indications: should not be used within 2 weeks of stopping treatment with a mono-amine oxidase inhibitor; avoid use in patients with hypertension or cardiovascular disease

Available forms: sachets containing paracetamol 1000mg and phenylephrine hydrochloride 12.2mg (10 sachets)

Dose: contents of 1 sachet dissolved in hot water, may be repeated after 4–6 hours; maximum of 4 sachets in 24 hours

Side-effects: none noted

Status: permitted

4.5.2 Compound analgesic preparations

Compound analgesic preparations that contain a simple analgesic (such as paracetamol) with an opioid component reduce the scope for effective titration of the individual components in the management of pain of varying intensity.

Compound analgesic preparations containing paracetamol with a low dose of an opioid analgesic (for example, 8mg of codeine phosphate per compound tablet) are commonly used, but the advantages have not been substantiated. The low dose of the opioid may be enough to cause opioid side-effects (in particular, constipation) and can complicate the treatment of overdosage yet may not provide significant additional relief of pain.

A full dose of the opioid component (for example, 60mg codeine phosphate) in compound analgesic preparations effectively augments the analgesic activity but is associated with the full range of opioid side-effects (including nausea, vomiting, severe constipation, drowsiness, respiratory depression, risk of dependence on long-term administration).

In general, when assessing pain, it is necessary to weigh up carefully whether there is a need for a non-opioid and an opioid analgesic to be taken simultaneously.

Drug: co-codamol

Indications: mild to moderate pain

Cautions: hypotension, asthma (avoid during attack) and impaired respiratory function (avoid in chronic obstructive pulmonary disease), prostatic hypertrophy; shock; myasthenia gravis; obstructive or inflammatory bowel disorders; diseases of the biliary tract; reduced dose recommended in elderly and debilitated patients, in hypothyroidism and in adrenocortical insufficiency; convulsive disorders; cardiac arrhythmias; acute abdomen; gallstones; alcohol dependence; avoid abrupt withdrawal after long-term treatment

Contra-indications: avoid in acute respiratory depression, in comatose patients, and where risk of paralytic ileus; also avoid in raised intracranial pressure or head injury (affects pupillary responses vital for neurological assessment)

Available forms: tablets, co-codamol 8/500 (codeine phosphate 8mg, paracetamol 500mg) (30-tablet pack); tablets, co-codamol 30/500 (codeine phosphate 30mg, paracetamol 500mg) (30-tablet pack)

Dose: 1–2 tablets every 4 hours; maximum 8 tablets daily

Side-effects: nausea and vomiting (particularly in initial stages), constipation, dry mouth, biliary spasm; larger doses produce respiratory depression, hypotension, muscle rigidity; other side-effects include abdominal pain, anorexia, bradycardia, tachycardia, palpitation, oedema, postural hypotension, seizures, malaise, hypothermia; hallucinations, vertigo, euphoria, dysphoria, mood changes, dependence, dizziness, confusion, drowsiness, sleep disturbances, headache; sexual dysfunction, difficulty with micturition, urinary retention, ureteric spasm, muscle fasciculation; blood disorders (including thrombocytopenia, leucopenia, neutropenia), miosis, visual disturbances, flushing, sweating, rashes, urticaria, pruritus; pancreatitis also reported; important: liver damage (and less frequently renal damage) following overdosage with paracetamol

Status: permitted

Drug: co-dydramol

Indications: mild to moderate pain

Cautions: see co-codamol notes above

Contra-indications: see co-codamol notes above

Available forms: tablets, scored, co-dydramol 10/500 (dihydrocodeine tartrate 10mg, paracetamol 500mg) (30-tablet pack)

Dose: 1–2 tablets every 4 hours; maximum 8 tablets daily

Side-effects: see co-codamol notes above

Status: permitted

4.5.3 Opioid analgesics

Opioid analgesics are usually used to relieve moderate to severe pain, particularly of visceral origin.

Cautions

Opioids should be used with caution in patients with impaired respiratory function (avoid in chronic obstructive pulmonary disease) and asthma (avoid during an acute attack), hypotension, shock, myasthenia gravis, prostatic hypertrophy, obstructive or inflammatory bowel disorders, diseases of the biliary tract and convulsive disorders. A reduced dose is recommended in elderly or debilitated patients, in hypothyroidism and in adrenocortical insufficiency. Repeated use of opioid analgesics is associated with the development of psychological and physical dependence; although this is rarely a problem with therapeutic use, caution is advised if prescribing for patients with a history of drug dependence. Avoid abrupt withdrawal after long-term treatment.

Contra-indications

Opioid analgesics should be avoided in patients with acute respiratory depression and when there is a risk of paralytic ileus. They are also contra-indicated in conditions associated with raised intracranial pressure and in head injury (opioid analgesics interfere with pupillary responses vital for neurological assessment). Comatose patients should not be treated with opioid analgesics.

Side-effects

The most common side-effects include nausea and vomiting (particularly in initial stages), constipation, dry mouth and biliary spasm; larger doses produce muscle rigidity, hypotension and respiratory depression. Other common side-effects of opioid analgesics include bradycardia, tachycardia, palpitation, oedema, postural hypotension, hallucinations, vertigo, euphoria, dysphoria, mood changes, dependence, dizziness, confusion, drowsiness, sleep disturbances, headache, sexual dysfunction, difficulty with micturition, urinary retention, ureteric spasm, miosis, visual disturbances, sweating, flushing, rash, urticaria and pruritus.

Morphine remains the most valuable opioid analgesic for severe pain, although it frequently causes nausea and vomiting. In addition to relief of pain, morphine also confers a state of euphoria and mental detachment. Tramadol produces analgesia by two mechanisms: an opioid effect and an enhancement of serotonergic and adrenergic pathways. It has fewer of the typical opioid side-effects (notably, less respiratory depression, less constipation and less addiction potential); psychiatric reactions have been reported. Tramadol is not as effective in severe pain as other opioid analgesics. Dihydrocodeine is used for the treatment of mild to moderate pain. The dose of dihydrocodeine by mouth is usually 30mg every four hours; doubling the dose to 60mg may provide some additional pain relief, but this may be at the cost of more nausea and vomiting. Like other opioids, dihydrocodeine often causes nausea and vomiting that limits its value in dental pain; if taken for more than a few doses, it is also liable to cause constipation.

Drug: codeine

Indications: mild to moderate pain

Cautions: see notes above; also cardiac arrhythmias; acute abdomen; gallstones

Contra-indications: see notes above

Available forms: tablets, codeine phosphate 30mg (28-tablet pack)

Dose: by mouth, 30–60mg every 4 hours when necessary, to a maximum of 240mg daily

Side-effects: see notes above; also abdominal pain, anorexia, seizures, malaise, hypothermia, muscle fasciculation; pancreatitis also reported

Status: permitted

Drug: dihydrocodeine

Indications: moderate to severe pain

Cautions: see notes above; also pancreatitis; severe cor pulmonale

Contra-indications: see notes above

Available forms: tablets, dihydrocodeine tartrate 30mg (28-tablet pack)

Dose: by mouth, 30mg every 4–6 hours when necessary

Side-effects: see notes above

Status: permitted

Drug: morphine sulphate

Indications: acute pain, myocardial infarction, acute pulmonary oedema

Cautions: see notes above; also pancreatitis; cardiac arrhythmias, severe cor pulmonale

Contra-indications: see notes above; also delayed gastric emptying, acute abdomen; heart failure secondary to chronic lung disease; phaeochromocytoma

Available forms: injection, morphine sulphate 10,mg/mL (1mL ampoule)

Dose: as follows:
- acute pain: by subcutaneous injection or by intramuscular injection, initially 10mg (elderly or frail 5mg) every 4 hours (or more frequently during titration), adjusted according to response
- myocardial infarction: by slow intravenous injection (1–2mg/minute), 5–10mg followed by a further 5–10mg if necessary; elderly or frail patients, reduce dose by half
- acute pulmonary oedema: by slow intravenous injection (2mg/minute) 5–10mg; elderly or frail patients, reduce dose by half

Side-effects: see notes above; also paralytic ileus, abdominal pain, anorexia, dyspepsia, exacerbation of pancreatitis, taste disturbance; hypertension, hypothermia, syncope; bronchospasm, inhibition of cough reflex; restlessness, seizures, paraesthesia, asthenia, malaise, disorientation, excitation, agitation, delirium, raised intracranial pressure; amenorrhoea; myoclonus, muscle fasciculation, rhabdomyolysis, nystagmus

Status: prohibited

Drug: tramadol

Indications: moderate to severe pain

Cautions: see notes above; also impaired consciousness; excessive bronchial secretions; not suitable as a substitute in opioid-dependent patients

Contra-indications: see notes above; also uncontrolled epilepsy

Available forms: capsules, tramadol hydrochloride 50mg (30-capsule pack); injection, tramadol hydrochloride 50mg/mL (2mL ampoule)

Dose: as follows:
- adult and child over 12 years: by mouth, 50–100mg not more often than every 4 hours; total of more than 400mg daily not usually required
- adult and child over 12 years: by intramuscular injection or by intravenous injection (over 2–3 minutes)

Side-effects: see notes above; also diarrhoea; fatigue; less commonly retching, gastritis, flatulence; rarely anorexia, syncope, hypertension, bronchospasm, dyspnoea, wheezing, seizures, paraesthesia, muscle weakness; blood disorders also reported

Status: permitted

4.6 Antimigraine drugs

Treatment of a migraine attack should be guided by response to previous treatment and the severity of the attacks. A simple analgesic such as aspirin, paracetamol (preferably in a soluble or dispersible form) or a NSAID is often effective; concomitant antiemetic treatment may be required. If treatment with an analgesic is inadequate, an attack may be treated with a specific antimigraine compound such as a 5HT1-receptor agonist ('triptan').

Drug: naratriptan

Indications: treatment of acute migraine

Cautions: 5HT1-receptor agonists should be used with caution in the elderly (unlicensed), and in conditions which predispose to coronary artery disease (pre-existing cardiac disease); also sensitivity to sulfonamides

Contra-indications: 5HT1-receptor agonists are contra-indicated in ischaemic heart disease, previous myocardial infarction, coronary vasospasm (including Prinzmetal's angina), uncontrolled or severe hypertension. Also previous cerebrovascular accident or transient ischaemic attack; peripheral vascular disease

Available forms: tablets, naratriptan (as hydrochloride) 2.5mg (6-tablet pack)

Dose: 2.5mg, repeated after at least 4 hours if migraine recurs (patient not responding should not take second dose for same attack); maximum 5mg in 24 hours

Side-effects: side-effects of the 5HT1-receptor agonists include sensations of tingling, heat, heaviness, pressure, or tightness of any part of the body (including throat and chest; discontinue if intense, may be due to coronary vasoconstriction or to anaphylaxis), flushing, dizziness, feeling of weakness; fatigue; nausea and vomiting also reported. Also less commonly bradycardia, tachycardia, palpitation, visual disturbance; rarely ischaemic colitis, rash, pruritus

Status: permitted

Drug: sumatriptan

Indications: treatment of acute migraine; cluster headache

Cautions: see naratriptan notes on p58; sensitivity to sulfonamides

Contra-indications: see naratriptan notes on p58; previous cerebrovascular accident or transient ischaemic attack; peripheral vascular disease; moderate and severe hypertension

Available forms: sumatriptan (as succinate) 50mg (6-tablet pack); injection, sumatriptan (as succinate) 12mg/mL (6mg/0.5mL syringe); treatment pack (2 × 0.5mL prefilled syringes and auto-injector); nasal spray, sumatriptan 10mg/0.1mL actuation (2 unit-dose spray device)

Dose: as follows:

- by mouth, migraine, 50mg (some patients may require 100mg); dose may be repeated after at least 2 hours if migraine recurs; maximum 300mg in 24 hours
- by subcutaneous injection, cluster headache or migraine, using auto-injector, 6mg; dose may be repeated once after at least 1 hour if headache recurs; maximum 12mg in 24 hours
- intranasally, cluster headache (unlicensed) or migraine, 10–20mg into one nostril; dose may be repeated once after at least 2 hours if headache recurs; maximum 40mg in 24 hours.

note: patient not responding to initial dose should not take second dose for same attack

Side-effects: see 5HT1-receptor agonists notes above; also dyspnoea, drowsiness, transient increase in blood pressure, myalgia; also reported diarrhoea, ischaemic colitis, hypotension, bradycardia or tachycardia, palpitation, arrhythmias, myocardial infarction, Raynaud's syndrome, anxiety, seizures, tremor, dystonia, nystagmus, arthralgia, visual disturbances, sweating; epistaxis with nasal spray

Status: permitted

Drug: zolmitriptan

Indications: treatment of acute migraine; cluster headache

Cautions: see naratriptan notes on p58; should not be taken within 12 hours of any other 5HT1-receptor agonist

Contra-indications: see naratriptan notes on p58; Wolff-Parkinson-White syndrome or arrhythmias associated with accessory cardiac conduction pathways; previous cerebrovascular accident or transient ischaemic attack

Available forms: tablets, zolmitriptan 2.5mg (6-tablet pack)

Dose: by mouth, migraine, adult over 18 years: 2.5mg repeated after not less than 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

Side-effects: see naratriptan notes on p58; also abdominal pain, dry mouth; palpitation; drowsiness, paraesthesia, headache; myalgia, muscle weakness; less commonly tachycardia, transient increase in blood pressure, polyuria; rarely urticaria; very rarely gastro-intestinal and splenic infarction, ischaemic colitis, angina, myocardial infarction

Status: permitted

4.7 Drugs used in status epilepticus

Where facilities for resuscitation are not immediately available, diazepam can be administered as a rectal solution, or midazolam can be given into the buccal cavity.

Drug: diazepam

Indications: status epilepticus; febrile convulsions; convulsions due to poisoning

Cautions: respiratory disease, muscle weakness and myasthenia gravis, history of drug or alcohol abuse, marked personality disorder; reduce dose in elderly and debilitated; special precautions for intravenous injection; acute porphyria; when given parenterally, close observation required until full recovery from sedation

Contra-indications: respiratory depression; marked neuromuscular respiratory weakness including unstable myasthenia gravis; acute pulmonary insufficiency; sleep apnoea syndrome

Available forms: injection, diazepam 5mg/mL (0.5%) (2mL ampoule); rectal tubes (rectal solution), diazepam 2mg/mL (2.5mL (5mg) tube), 4mg/mL (2.5mL (10mg) tube)

Dose: as follows:

– status epilepticus, febrile convulsions and convulsions due to poisoning, by intravenous injection: 10mg at a rate of 1mL (5mg) per minute, repeated once after 10 minutes if necessary
– by rectum as rectal solution, adult and child over 12 years: 10–20mg, repeated once after 10–15 minutes if necessary

Side-effects: drowsiness and lightheadedness the next day; confusion and ataxia (especially in the elderly); amnesia; dependence; paradoxical increase in aggression; muscle weakness; occasionally: headache, vertigo, hypotension, salivation changes, gastro-intestinal disturbances, visual disturbances, dysarthria, tremor, changes in libido, incontinence, urinary retention; blood disorders and jaundice reported; skin reactions; on intravenous injection, pain, thrombophlebitis, rarely apnoea

Status: permitted

Drug: midazolam

Indications: status epilepticus; febrile convulsions

Cautions: cardiac disease; respiratory disease; myasthenia gravis; history of drug or alcohol abuse; reduce dose in elderly and debilitated; risk of severe hypotension in hypovolaemia, vasoconstriction, hypothermia

Contra-indications: marked neuromuscular respiratory weakness including unstable myasthenia gravis; severe respiratory depression; acute pulmonary insufficiency

Available forms: midazolam, 10mg (2mL pre-filled syringe)

Dose: by buccal administration, adult and child over 10 years: 10mg, repeated once after 10 minutes if necessary

Side-effects: gastro-intestinal disturbances, increased appetite, jaundice; hypotension, cardiac arrest, heart rate changes, anaphylaxis, thrombosis; laryngospasm, bronchospasm, respiratory depression and respiratory arrest (particularly with high doses); drowsiness, confusion, ataxia, amnesia, headache, euphoria, hallucinations, convulsions (more common in neonates), dizziness, vertigo, involuntary movements, paradoxical excitement and aggression (especially in children and elderly), dysarthria; urinary retention, incontinence, changes in libido; blood disorders; muscle weakness; visual disturbances; salivation changes; skin reactions; injection-site reactions

Status: permitted

5.0 Infections

5.1 Antibacterial drugs

Before selecting an antibacterial drug, the clinician must first consider two factors: the patient and the known or likely causative organism. Factors related to the patient that must be considered include history of allergy, renal and hepatic function, susceptibility to infection (that is, whether immunocompromised), ability to tolerate drugs by mouth, severity of illness, ethnic origin, age, whether taking other medication and, if female, whether pregnant, breastfeeding or taking an oral contraceptive.

The known or likely organism and its antibacterial sensitivity, in association with the above factors, will suggest one or more antibacterials, the final choice depending on the microbiological, pharmacological and toxicological properties.

5.1.1 Pencillins

The penicillins are bactericidal and act by interfering with bacterial cell wall synthesis.

The most important side-effect of the penicillins is hypersensitivity, which causes rashes and anaphylaxis and can be fatal. Allergic reactions to penicillins occur in 1–10% of exposed individuals; anaphylactic reactions occur in fewer than 0.05% of treated patients. Patients with a history of atopic allergy (for example, asthma, eczema, hay fever) are at a higher risk of anaphylactic reactions to penicillins. Individuals with a history of anaphylaxis, urticaria or rash immediately after penicillin administration are at risk of immediate hypersensitivity to a penicillin; these individuals should not receive a penicillin. Patients who are allergic to one penicillin will be allergic to all because the hypersensitivity is related to the basic penicillin structure. As patients with a history of immediate hypersensitivity to penicillins may also react to the cephalosporins and other beta-lactam antibiotics, they should not receive these antibiotics. Individuals with a history of a minor rash (that is, non-confluent, non-pruritic rash restricted to a small area of the body) or a rash that occurs more than 72 hours after penicillin administration are probably not allergic to penicillin and in these individuals a penicillin should not be withheld unnecessarily for serious infections; the possibility of an allergic reaction should, however, be borne in mind. Other beta-lactam antibiotics (including cephalosporins) can be used in these patients.

Other side-effects: a rare but serious toxic effect of the penicillins is encephalopathy due to cerebral irritation. This may result from excessively high doses or in patients with severe renal failure. Diarrhoea frequently occurs during oral penicillin therapy. It is most common with broad-spectrum penicillins, which can also cause antibiotic-associated colitis.

Most staphylococci are now resistant to benzylpenicillin because they produce penicillinases. Flucloxacillin, however, is not inactivated by these enzymes and is thus effective in infections caused by penicillin-resistant staphylococci, which is the sole indication for its use.

Amoxicillin is active against certain Gram-positive and Gram-negative organisms but is inactivated by penicillinases including those produced by Staphylococcus aureus and by common Gram-negative bacilli such as Escherichia coli. Almost all staphylococci, approximately 60% of E. coli strains and approximately 20% of Haemophilus influenzae strains are now resistant. The likelihood of resistance should therefore be considered before using amoxicillin for the 'blind' treatment of infections. It is principally indicated for the treatment of exacerbations of chronic bronchitis and middle ear infections, both of which may be due to Streptococcus pneumoniae and H. influenzae, and for urinary-tract infections. Maculopapular rashes commonly occur with amoxicillin but are not usually related to true penicillin allergy. They almost always occur in patients with glandular fever; broad-spectrum penicillins should not therefore be used for 'blind' treatment of a sore throat.

Co-amoxiclav consists of amoxicillin with the beta-lactamase inhibitor clavulanic acid. Clavulanic acid itself has no significant antibacterial activity but, by inactivating beta-lactamases, it makes the combination active against beta-lactamase-producing bacteria that are resistant to amoxicillin. These include resistant strains of Staph. aureus, E. coli, and H. influenzae, as well as many Bacteroides and Klebsiella spp.

Drug: amoxicillin

Indications: urinary-tract infections, otitis media, sinusitis, oral infections, bronchitis, low or moderate-severity community-acquired pneumonia, also Lyme disease

Cautions: history of allergy; erythematous rashes common in glandular fever; increased risk of erythematous rashes in cytomegalovirus infection, acute or chronic lymphocytic leukaemia

Contra-indications: penicillin hypersensitivity

Available forms: capsules, amoxicillin (as trihydrate) 250mg (21-cap pack), 500mg (21-cap pack); oral suspension, amoxicillin (as trihydrate) for reconstitution with water, 250mg/5mL (100mL); sachets, sugar-free, amoxicillin (as trihydrate) 3g/sachet (2-sachet pack)

Dose: as follows:
- by mouth, adult and child over 5 years: 250mg every 8 hours, dose doubled in severe infection
- short-course oral therapy: dental abscess, adult over 18 years: 3g repeated after 8 hours
- urinary-tract infections, adult over 18 years: 3g repeated after 10–12 hours

Side-effects: see phenoxymethylpenicillin (penicillin V) notes on p64. Also nausea, vomiting, diarrhoea; rashes (discontinue treatment); rarely, antibiotic-associated colitis

Status: permitted

Drug: benzylpenicillin sodium

Indications: throat infections, otitis media, endocarditis, meningococcal disease, pneumonia, cellulitis

Cautions: history of allergy; false-positive urinary glucose (if tested for reducing substances)

Contra-indications: penicillin hypersensitivity

Available forms: injection, powder for reconstitution, benzylpenicillin sodium (unbuffered) (600mg vial)

Dose: as follows:
- by intramuscular or by slow intravenous injection or by infusion, 0.6–1.2g every 6 hours, increased if necessary in more serious infections
- meningitis, meningococcal disease: by slow intravenous injection or by infusion, 2.4g every 4 hours.

note: if meningococcal disease (meningitis with non-blanching rash or meningococcal septicaemia) is suspected, a single dose of benzylpenicillin should be given before transferring the patient to hospital urgently, so long as this does not delay the transfer. If a patient with suspected bacterial meningitis without non-blanching rash cannot be transferred to hospital urgently, a single dose of benzylpenicillin should be given before the transfer. Suitable doses of benzylpenicillin by intravenous injection (or by intramuscular injection) are: adult 1.2g; infant under 1 year 300mg; child 1–9 years 600mg; 10 years and over as for adult

Side-effects: hypersensitivity reactions including urticaria, fever, joint pains, rashes, angioedema, anaphylaxis, serum sickness-like reaction; rarely CNS toxicity including convulsions (especially with high doses or in severe renal impairment), interstitial nephritis, haemolytic anaemia, leucopenia, thrombocytopenia, coagulation disorders; also reported diarrhoea (including antibiotic-associated colitis)

Status: permitted

Drug: co-amoxiclav

Indications: infections due to beta-lactamase-producing strains (where amoxicillin alone not appropriate) including respiratory-tract infections, bone and joint infections, genito-urinary and abdominal infections, cellulitis, animal bites, severe dental infection with spreading cellulitis or dental infection not responding to first-line antibacterial

Cautions: see amoxicillin notes on p62

Contra-indications: penicillin hypersensitivity, history of co-amoxiclav-associated or penicillin-associated jaundice or hepatic dysfunction

Available forms: tablets, co-amoxiclav 250/125 (amoxicillin 250mg as trihydrate, clavulanic acid 125mg as potassium salt) (21-tablet pack); tablets, co-amoxiclav 500/125 (amoxicillin 500mg as trihydrate, clavulanic acid 125mg as potassium salt) (21-tablet pack)

Dose: by mouth, expressed as co-amoxiclav, one 250/125 strength tablet every 8 hours; increased in severe infection to one 500/125 strength tablet every 8 hours

Side-effects: see amoxicillin notes on p62; also hepatitis, cholestatic jaundice, Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis, vasculitis reported; rarely prolongation of bleeding time, dizziness, headache, convulsions (particularly with high doses or in renal impairment)

Status: permitted

Drug: flucloxacillin

Indications: infections due to beta-lactamase-producing staphylococci including otitis externa, adjunct in pneumonia, impetigo, cellulitis, osteomyelitis and in staphylococcal endocarditis

Cautions: see phenoxymethylpenicillin (penicillin V) notes on p64; also flucloxacillin should be used with caution in patients with hepatic impairment

Contra-indications: see phenoxymethylpenicillin (penicillin V) notes on p64

Available forms: capsules, flucloxacillin (as sodium salt) 250mg (28-capsule pack)

Dose: by mouth, 250–500mg every 6 hours, at least 30 minutes before food

Side-effects: see phenoxymethylpenicillin (penicillin V) notes on p64; also gastro-intestinal disturbances; very rarely hepatitis and cholestatic jaundice

Status: permitted

Drug: phenoxymethylpenicillin (penicillin V)

Indications: oral infections (dentoalveolar abscess); tonsillitis, otitis media, erysipelas, cellulitis; group A streptococcal infection, rheumatic fever and pneumococcal infection prophylaxis

Cautions: history of allergy; false-positive urinary glucose (if tested for reducing substances)

Contra-indications: penicillin hypersensitivity

Available forms: tablets, phenoxymethylpenicillin (as potassium salt) 250mg (28-tablet pack)

Dose: 500mg every 6 hours, increased up to 1g every 6 hours in severe infections

Side-effects: hypersensitivity reactions including urticaria, fever, joint pains, rashes, angioedema, anaphylaxis, serum sickness-like reaction; rarely CNS toxicity including convulsions (especially with high doses or in severe renal impairment), interstitial nephritis, haemolytic anaemia, leucopenia, thrombocytopenia, coagulation disorders; also reported diarrhoea (including antibiotic-associated colitis)

Status: permitted

5.1.2 Cephalosporins

The cephalosporins are broad-spectrum antibiotics that are used for the treatment of septicaemia, pneumonia, meningitis, biliary-tract infections, peritonitis and urinary-tract infections. The principal side-effect of the cephalosporins is hypersensitivity, and about 0.5–6.5% of penicillin-sensitive patients will also be allergic to the cephalosporins. Patients with a history of immediate hypersensitivity to penicillin should not receive a cephalosporin. If a cephalosporin is essential in these patients because a suitable alternative antibacterial is not available, then ceftriaxone can be used with caution.

Drug: ceftriaxone

Indications: infections due to sensitive Gram-positive and Gram-negative bacteria. Also prophylaxis of meningococcal meningitis (unlicensed indication)

Cautions: sensitivity to beta-lactam antibacterials (avoid if history of immediate hypersensitivity reaction, false positive urinary glucose (if tested for reducing substances) and false positive Coombs' test

Contra-indications: cephalosporin hypersensitivity

Available forms: injection, powder for reconstitution, ceftriaxone (as sodium salt) (2g vial)

Dose: by deep intramuscular injection, or by intravenous injection over at least 2–4 minutes, or by intravenous infusion, 1g daily; 2–4g daily in severe infections; intramuscular doses over 1g divided between more than one site; single intravenous doses above 1g by intravenous infusion only

Side-effects: diarrhoea (rarely antibiotic-associated colitis), nausea and vomiting, abdominal discomfort, headache; allergic reactions including rashes, pruritus, urticaria, serum sickness-like reactions with rashes, fever and arthralgia, anaphylaxis; Stevens-Johnson syndrome, toxic epidermal necrolysis reported; disturbances in liver enzymes, transient hepatitis, cholestatic jaundice; other side-effects reported include eosinophilia and blood disorders (including thrombocytopenia, leucopenia, agranulocytosis, aplastic anaemia, haemolytic anaemia); reversible interstitial nephritis, hyperactivity, nervousness, sleep disturbances, hallucinations, confusion, hypertonia, dizziness. Also rarely prolongation of prothrombin time, pancreatitis

Status: permitted

5.1.3 Tetracyclines

The tetracyclines are broad-spectrum antibiotics whose value has decreased owing to increasing bacterial resistance. However, they remain the treatment of choice for infections caused by chlamydia (trachoma, psittacosis, salpingitis, urethritis and lymphogranuloma venereum), rickettsia (including Q-fever), brucella (doxycycline with either streptomycin or rifampicin) and the spirochaete, Borrelia burgdorferi (Lyme disease). They are also used in respiratory and genital mycoplasma infections, in acne, in destructive (refractory) periodontal disease, in exacerbations of chronic bronchitis (because of their activity against Haemophilus influenzae) and for leptospirosis in penicillin hypersensitivity (as an alternative to erythromycin).

Drug: doxycycline

Indications: see notes above; chronic prostatitis; sinusitis, syphilis, pelvic inflammatory disease; treatment and prophylaxis of anthrax (unlicensed indication); malaria treatment and prophylaxis; recurrent aphthous ulceration; oral herpes simplex; rosacea, acne vulgaris

Cautions: tetracyclines may increase muscle weakness in patients with myasthenia gravis, and exacerbate systemic lupus erythematosus. Antacids and aluminium, calcium, iron, magnesium and zinc salts decrease the absorption of tetracyclines. Also alcohol dependence; photosensitivity reported (avoid exposure to sunlight or sun lamps)

Contra-indications: deposition of tetracyclines in growing bone and teeth (by binding to calcium) causes staining and occasionally dental hypoplasia, and they should not be given to children under 12 years, or to pregnant or breastfeeding women

Available forms: capsules, doxycycline (as hyclate) 100mg (8-capsule pack)

Dose: 200mg on first day, then 100mg daily; severe infections (including refractory urinary-tract infections), 200mg daily (for other indications, see the full edition of the British National Formulary; www.bnf.org)

Side-effects: include nausea, vomiting, diarrhoea (antibiotic-associated colitis reported occasionally), dysphagia, oesophageal irritation. Other rare side-effects include hepatotoxicity, pancreatitis, blood disorders, photosensitivity (particularly with demeclocycline), hypersensitivity reactions (including rash, exfoliative dermatitis, Stevens-Johnson syndrome, urticaria, angioedema, anaphylaxis, pericarditis). Headache and visual disturbances may indicate benign intracranial hypertension (discontinue treatment). Also anorexia, dry mouth, flushing, anxiety, tinnitus

Status: permitted

5.1.4 Macrolides

The macrolides have an antibacterial spectrum that is similar but not identical to that of penicillin; they are thus an alternative in penicillin-allergic patients. They are active against many-penicillin-resistant staphylococci, but some are now also resistant to the macrolides. Indications for the macrolides include campylobacter enteritis, respiratory infections (including pneumonia, whooping cough, Legionella, chlamydia and mycoplasma infection) and skin infections. Macrolides should be used with caution in patients with a predisposition to QT interval prolongation (including electrolyte disturbances and concomitant use of drugs that prolong the QT interval). Nausea, vomiting, abdominal discomfort and diarrhoea are the most common side-effects of the macrolides, but they are mild and less frequent with azithromycin and clarithromycin than with erythromycin. Hepatotoxicity (including cholestatic jaundice) and rash occur less frequently. Other side-effects reported rarely or very rarely include pancreatitis, antibiotic-associated colitis, QT interval prolongation, arrhythmias, generally reversible hearing loss (sometimes with tinnitus) after large doses, Stevens-Johnson syndrome and toxic epidermal necrolysis.

Drug: azithromycin

Indications: respiratory-tract infections; otitis media; skin and soft-tissue infections; uncomplicated gonorrhoea (unlicensed indication), uncomplicated genital chlamydial infections and non-gonococcal urethritis; prophylaxis of group A streptococcal infection

Cautions: see notes above

Contra-indications: none noted

Available forms: capsules, azithromycin (as dihydrate) 250mg (6-capsule pack)

Dose: 500mg once daily for 3 days, or 500mg on first day then 250mg once daily for 4 days; for genital infections, see the full edition of the British National Formulary (www.bnf.org)

Side-effects: see notes above; also anorexia, dyspepsia, flatulence, dizziness, headache, drowsiness, convulsions, arthralgia, disturbances in taste and smell; rarely constipation, syncope, insomnia, agitation, anxiety, asthenia, paraesthesia, hyperactivity, thrombocytopenia, haemolytic anaemia, interstitial nephritis, acute renal failure, photosensitivity, tooth and tongue discoloration

Status: permitted

Drug: clarithromycin

Indications: respiratory-tract infections, mild to moderate skin and soft-tissue infections, otitis media; Lyme disease

Cautions: see notes above

Contra-indications: none noted

Available forms: tablets, clarithromycin 250mg (14-tablet pack)

Dose: by mouth, adult and child over 12 years: 250mg every 12 hours for 7 days, increased in pneumonia or severe infections to 500mg every 12 hours for up to 14 days

Side-effects: see notes above; also dyspepsia, tooth and tongue discoloration, smell and taste disturbances, stomatitis, glossitis, headache; less commonly arthralgia and myalgia; rarely tinnitus; very rarely dizziness, insomnia, nightmares, anxiety, confusion, psychosis, paraesthesia, convulsions, hypoglycaemia, renal failure, interstitial nephritis, leucopenia, thrombocytopenia

Status: permitted

Drug: erythromycin

Indications: susceptible infections in patients with penicillin hypersensitivity; oral infections; campylobacter enteritis, syphilis, non-gonococcal urethritis, respiratory-tract infections (including Legionella infection), skin infections; chronic prostatitis; prophylaxis of diphtheria, group A streptococcal infection, pneumococcal infection, pertussis; acne vulgaris and rosacea

Cautions: see notes above; avoid in acute porphyria

Contra-indications: none noted

Available forms: tablets, e/c, erythromycin 250mg (28-tablet pack)

Side-effects: see notes above; also myasthenia-like syndrome

Status: permitted

5.1.5 Clindamycin

Clindamycin is active against Gram-positive cocci, including streptococci and penicillin-resistant staphylococci, and also against many anaerobes, especially Bacteroides fragilis. Clindamycin is recommended for staphylococcal joint and bone infections such as osteomyelitis and intra-abdominal sepsis; it is an alternative to macrolides for erysipelas or cellulitis in penicillin-allergic patients. Clindamycin can also be used for infections associated with meticillin-resistant Staphylococcus aureus (MRSA) in bronchiectasis, bone and joint infections, and skin and soft-tissue infections.

Clindamycin has been associated with antibiotic-associated colitis, which may be fatal; it is most common in middle-aged and elderly women, especially following an operation. Although antibiotic-associated colitis can occur with most antibacterials, it occurs more frequently with clindamycin. Patients should therefore discontinue treatment immediately if diarrhoea develops.

Clindamycin should not be used routinely for the treatment of oral infections because it may be no more effective than penicillins against anaerobes and there may be cross-resistance with erythromycin-resistant bacteria. Clindamycin can be used for the treatment of dentoalveolar abscess that has not responded to penicillin or to metronidazole.

Drug: clindamycin

Indications: see notes above; staphylococcal bone and joint infections, peritonitis; falciparum malaria

Cautions: discontinue immediately if diarrhoea or colitis develops; monitor liver and renal function if treatment exceeds 10 days, avoid in acute porphyria

Contra-indications: diarrhoeal states

Available forms: capsules, clindamycin (as hydrochloride) 150mg (24-capsule pack)

Dose: by mouth, 150–300mg every 6 hours; up to 450mg every 6 hours in severe infections

Side-effects: diarrhoea (discontinue treatment), abdominal discomfort, oesophagitis, oesophageal ulcers, taste disturbances, nausea, vomiting, antibiotic-associated colitis; jaundice; leucopenia, eosinophilia, thrombocytopenia reported; polyarthritis reported; rash, pruritus, urticaria, anaphylactoid reactions, Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative and vesiculobullous dermatitis reported; pain, induration, abscess after intramuscular injection; thrombophlebitis after intravenous injection

Status: permitted

5.1.6 Trimethoprim

Trimethoprim can be used alone for urinary- and respiratory-tract infections, and for prostatitis, shigellosis and invasive salmonella infections.

Drug: trimethoprim

Indications: urinary-tract infections, acute and chronic bronchitis; pneumocystis pneumonia

Cautions: predisposition to folate deficiency; elderly; acute porphyria. Blood disorders. On long-term treatment, patients and their carers should be told how to recognise signs of blood disorders and advised to seek immediate medical attention if symptoms such as fever, sore throat, rash, mouth ulcers, purpura, bruising or bleeding develop

Contra-indications: blood dyscrasias

Available forms: tablets, trimethoprim, 200mg (14-tablet pack)

Dose: acute infections, 200mg every 12 hours; prophylaxis, 100mg at night

Side-effects: gastro-intestinal disturbances including nausea and vomiting, pruritus, rashes, hyperkalaemia, depression of haematopoiesis; rarely erythema multiforme, toxic epidermal necrolysis, photosensitivity and other allergic reactions including angioedema and anaphylaxis; aseptic meningitis and uveitis reported

Status: permitted

5.1.7 Metronidazole

Metronidazole is an antimicrobial drug with high activity against anaerobic bacteria and protozoa; indications include trichomonal vaginitis, bacterial vaginosis (notably Gardnerella vaginalis infections) and Entamoeba histolytica and Giardia lamblia infections. Metronidazole by mouth is effective for the treatment of Clostridium difficile infection. Metronidazole is an alternative to penicillin for the treatment of many oral infections where the patient is allergic to penicillin or the infection is due to beta-lactamase-producing anaerobes.

Drug: metronidazole

Indications: anaerobic infections (including dental), protozoal infections

Cautions: disulfiram-like reaction with alcohol; avoid in acute porphyria

Contra-indications: none noted

Available forms: tablets, metronidazole 200mg (21-tablet pack), 400mg (21-tablet pack)

Dose: as follows:

- anaerobic infections (usually treated for 7 days and for 10–14 days in Clostridium difficile infection), by mouth, either 400mg every 8 hours or 500mg every 8 hours
- bacterial vaginosis, by mouth, 400–500mg twice daily for 5–7 days or 2g as a single dose
- pelvic inflammatory disease, by mouth, 400mg twice daily for 14 days
- acute ulcerative gingivitis, by mouth, 200–250mg every 8 hours for 3 days
- acute oral infections, by mouth, 200mg every 8 hours for 3–7 days

Side-effects: gastro-intestinal disturbances (including nausea and vomiting), taste disturbances, furred tongue, oral mucositis, anorexia; very rarely hepatitis, jaundice, pancreatitis, drowsiness, dizziness, headache, ataxia, psychotic disorders, darkening of urine, thrombocytopenia, pancytopenia, myalgia, arthralgia, visual disturbances, rash, pruritus, erythema multiforme; on prolonged or intensive therapy peripheral neuropathy, transient epileptiform seizures, leucopenia; also reported aseptic meningitis, optic neuropathy

Status: permitted

5.1.8 Quinolones

Norfloxacin is effective in uncomplicated urinary-tract infections.

Ciprofloxacin is active against both Gram-positive and Gram-negative bacteria. It is particularly active against Gram-negative bacteria, including salmonella, shigella, campylobacter, neisseria and pseudomonas. Ciprofloxacin has only moderate activity against Gram-positive bacteria such as Streptococcus pneumoniae and Enterococcus faecalis; it should not be used for pneumococcal pneumonia. It is active against chlamydia and some mycobacteria. Most anaerobic organisms are not susceptible. Ciprofloxacin can be used for respiratory tract infections (but not for pneumococcal pneumonia), urinary-tract infections, infections of the gastro-intestinal system (including typhoid fever), bone and joint infections, gonorrhoea and septicaemia caused by sensitive organisms.

Cautions

Quinolones should be used with caution in patients with a history of epilepsy or conditions that predispose to seizures, in G6PD deficiency, myasthenia gravis (risk of exacerbation), and in children or adolescents (arthropathy has developed in weight-bearing joints in young animal; see below). Exposure to excessive sunlight should be avoided (discontinue if photosensitivity occurs). Quinolones can prolong the QT interval. They should be used in caution in patients with risk factors for QT interval prolongation. The CSM has warned that quinolones may induce convulsions in patients with or without a history of convulsions; taking NSAIDs at the same time may also induce them.

Side-effects

Side-effects of the quinolones include nausea, vomiting, dyspepsia, abdominal pain, diarrhoea (rarely antibiotic-associated colitis), headache, dizziness and rash (very rarely Stevens-Johnson syndrome and toxic epidermal necrolysis). Less frequent side-effects include anorexia, sleep disturbances, asthenia, confusion, anxiety, depression, hallucinations, tremor, blood disorders (including eosinophilia, leucopenia and thrombocytopenia), arthralgia, myalgia, disturbances in vision and taste. Other side-effects reported rarely or very rarely include hepatic dysfunction (including jaundice and hepatitis), hypotension, vasculitis, dyspnoea (more frequent with moxifloxacin), convulsions, psychoses, paraesthesia, renal failure, interstitial nephritis, tendon inflammation and damage (see also tendon damage above), photosensitivity, and disturbances in hearing and smell. The drug should be discontinued if psychiatric, neurological or hypersensitivity reactions (including severe rash) occur.

Drug: ciprofloxacin

Indications: see notes above

Cautions: see notes above; avoid excessive alkalinity of urine and ensure adequate fluid intake (risk of crystalluria); may impair performance of skilled tasks (for example, driving); effects enhanced by alcohol

Contra-indications: quinolone hypersensitivity

Available forms: tablets, ciprofloxacin (as hydrochloride) 250mg (10-tablet pack), 500mg (10-tablet pack)

Dose: as follows:
- by mouth, respiratory-tract infections, 500–750mg twice daily (750mg twice daily in pseudomonal lower respiratory-tract infection in cystic fibrosis)
- urinary-tract infections, 250–750mg twice daily (250mg twice daily for 3 days usually adequate for acute uncomplicated cystitis in women)
- acute or chronic prostatitis, 500mg twice daily for 28 days; gonorrhoea, 500mg as a single dose
- most other infections, 500mg twice daily (increased to 750mg twice daily in severe or deep-seated infection)

Side-effects: see notes above; also flatulence, pain and phlebitis at injection site; rarely dysphagia, pancreatitis, chest pain, tachycardia, syncope, oedema, hot flushes, abnormal dreams, sweating, hyperglycaemia, erythema nodosum; very rarely movement disorders, tinnitus, tenosynovitis

Status: permitted

Drug: norfloxacin

Indications: 'lower' urinary-tract infections, chronic relapsing 'lower' urinary-tract infections, chronic prostatitis

Cautions: see notes above; may impair performance of skilled tasks (for example, driving)

Contra-indications: quinolone hypersensitivity

Available forms: tablets, norfloxacin 400mg (6-tablet pack)

Dose: as follows:
- 'lower' urinary-tract infections, 400mg twice daily for 7–10 days (3 days for uncomplicated infections in women)
- chronic relapsing 'lower' urinary-tract infections, 400mg twice daily for up to 12 weeks, may be reduced to 400mg once daily if adequate suppression within first 4 weeks
- chronic prostatitis, 400mg twice daily for 28 days

Side-effects: see notes above; also tinnitus, epiphora; rarely pancreatitis; very rarely arrhythmias; also reported, polyneuropathy and exfoliative dermatitis

Status: permitted

5.2 Antifungal drugs

Candidiasis: many superficial candidal infections including infections of the skin are treated locally (see appropriate section); widespread or intractable infection requires systemic antifungal treatment. Vaginal candidiasis may be treated with locally acting antifungals (see appropriate section) or with fluconazole given by mouth.

Oropharyngeal candidiasis generally responds to topical therapy (see appropriate section). Fluconazole is given by mouth for unresponsive infections; it is effective and is reliably absorbed.

Drug: fluconazole

Indications: vaginal candidiasis, candidal balanitis, mucosal candidiasis (except genital), Tinea pedis, corporis, cruris, pityriasis versicolor, dermal candidiasis

Cautions: concomitant use with hepatotoxic drugs, monitor liver function with high doses or extended courses: discontinue if signs or symptoms of hepatic disease (risk of hepatic necrosis); susceptibility to QT interval prolongation

Contra-indications: acute porphyria

Available forms: capsules, fluconazole 50mg (7-capsule pack), 150mg (single-capsule pack)

Dose: as follows:

- vaginal candidiasis and candidal balanitis, adult and child over 16 years: by mouth, a single dose of 150mg
- mucosal candidiasis (except genital), by mouth, 50mg daily (100mg daily in unusually difficult infections) given for 7–14 days in oropharyngeal candidiasis (maximum 14 days except in severely immunocompromised patients); for 14 days in atrophic oral candidiasis associated with dentures; for 14–30 days in other mucosal infections (for example, oesophagitis, candiduria, non-invasive bronchopulmonary infections)
- Tinea pedis, corporis, cruris, pityriasis versicolor, dermal candidiasis, by mouth, 50mg daily for 2–4 weeks (for up to 6 weeks in tinea pedis); maximum duration of treatment 6 weeks

Side-effects: nausea, abdominal discomfort, diarrhoea, flatulence, headache, rash (discontinue treatment or monitor closely if infection invasive or systemic); less frequently dyspepsia, vomiting, taste disturbance, hepatic disorders, hypersensitivity reactions, anaphylaxis, dizziness, seizures, alopecia, pruritus, toxic epidermal necrolysis, Stevens-Johnson syndrome (severe cutaneous reactions more likely in HIV-positive patients), hyperlipidaemia, leucopenia, thrombocytopenia, hypokalaemia reported

Status: permitted

5.3 Antiviral drugs

5.3.1 Herpesvirus infections

Aciclovir is active against herpesviruses but does not eradicate them. Uses of aciclovir include systemic treatment of varicella-zoster and the systemic and topical treatment of herpes simplex infections of the skin (see section 12.7.3, p120). It is used by mouth for severe herpetic stomatitis. Aciclovir eye ointment (see section 10.1.2, p100) is used for herpes simplex infections of the eye; it is combined with systemic treatment for ophthalmic zoster.

Drug: aciclovir (acyclovir)

Indications: herpes simplex and varicella-zoster

Cautions: maintain adequate hydration (especially with high doses, or during renal impairment); elderly (risk of neurological reactions)

Contra-indications: none noted

Available forms: tablets, aciclovir 200mg (25-tablet pack)

Dose: as follows:

- by mouth, non-genital herpes simplex, treatment, 200mg (400mg in the immunocompromised or if absorption impaired) 5 times daily, usually for 5 days (longer if new lesions appear during treatment or if healing incomplete)
- genital herpes simplex, treatment of first episode, 200mg 5 times daily or 400mg 3 times daily usually for 5 days, longer if new lesions appear during treatment or if healing is incomplete (400mg 5 times daily for 7–10 days in immunocompromised or HIV-positive patients); treatment of recurrent infection, 800mg 3 times daily for 2 days or 200mg 5 times daily for 5 days or 400mg 3 times daily for 3–5 days (400mg 3 times daily for 5–10 days in immunocompromised or HIV-positive patients)
- herpes simplex, suppression, 400mg twice daily or 200mg 4 times daily; increased to 400mg 3 times daily if recurrences occur on standard suppressive therapy
- herpes simplex, prophylaxis in the immunocompromised, 200–400mg 4 times daily

Side-effects: nausea, vomiting, abdominal pain, diarrhoea, headache, fatigue, rash, urticaria, pruritus, photosensitivity; very rarely hepatitis, jaundice, dyspnoea, neurological reactions (including dizziness, confusion, hallucinations, convulsions, ataxia, dysarthria, drowsiness), acute renal failure, anaemia, thrombocytopenia and leucopenia; on intravenous infusion, severe local inflammation (sometimes leading to ulceration), very rarely agitation, tremors, psychosis and fever

Status: permitted

5.3.2 Influenza

Oseltamivir reduces replication of influenza A and B viruses by inhibiting viral neuraminidase. It is most effective for the treatment of influenza if started within a few hours of the onset of symptoms; it is licensed for use within 48 hours of the first symptoms. In otherwise healthy individuals, it reduces the duration of symptoms by about 1–1.5 days. Oseltamivir can reduce the risk of complications from influenza in the elderly and in patients with chronic disease. Oseltamivir is licensed for post-exposure prophylaxis of influenza when influenza is circulating in the community. Oseltamivir should be given within 48 hours of exposure to influenza.

Drug: oseltamivir

Indications: see notes above

Cautions: none noted

Contra-indications: none noted

Available forms: capsules, oseltamivir (as phosphate) 75mg (10-capsule pack)

Dose: as follows:
- prevention of influenza, adult and child over 13 years: 75mg once daily for 10 days for post-exposure prophylaxis; for up to 6 weeks during an epidemic
- treatment of influenza, adult and child over 13 years: 75mg every 12 hours for 5 days

Side-effects: nausea, vomiting, abdominal pain, diarrhoea; headache; conjunctivitis; less commonly eczema; also reported hepatitis, gastro-intestinal bleeding, arrhythmias, neuropsychiatric disorders (more frequent in children and adolescents), thrombocytopenia, visual disturbances, Stevens-Johnson syndrome, toxic epidermal necrolysis

Status: permitted

5.4 Drugs for threadworms

Anthelmintics are effective in threadworm infections, but their use needs to be combined with hygienic measures to break the cycle of auto-infection. All members of the family require treatment.

Adult threadworms do not live for longer than six weeks, and for development of fresh worms, ova must be swallowed and exposed to the action of digestive juices in the upper intestinal tract. Direct multiplication of worms does not take place in the large bowel. Adult female worms lay ova on the perianal skin, which causes pruritus; scratching the area then leads to ova being transmitted on fingers to the mouth, often via food eaten with unwashed hands. Washing hands and scrubbing nails before each meal and after each visit to the toilet is essential. A bath taken immediately after rising will remove ova laid during the night.

Mebendazole is the drug of choice for treating threadworm infection in patients of all ages over two years. It is given as a single dose; as reinfection is very common, a second dose may be given after two weeks.

Drug: mebendazole

Indications: threadworm, roundworm, whipworm and hookworm infections

Cautions: none noted

Contra-indications: none noted

Available forms: tablets, chewable, mebendazole 100mg (6-tablet pack)

Dose: as follows:
- threadworms, adult and child over 2 years: 100mg as a single dose; if reinfection occurs second dose may be needed after 2 weeks
- whipworms, adult and child over 2 years: 100mg twice daily for 3 days
- roundworms: usual dose is 100mg twice daily for 3 days or 500mg as a single dose (unlicensed single dose)
- hookworms: usual dose is 100mg twice daily for 3 days

Side-effects: abdominal pain; less commonly diarrhoea, flatulence; rarely hepatitis, convulsions, dizziness, neutropenia, urticaria, alopecia, rash (including Stevens-Johnson syndrome and toxic epidermal necrolysis)

Status: permitted

6.0 Endocrine system

6.1 Drugs used in diabetes

6.1.1 Short-acting insulins

Soluble insulin is a short-acting form of insulin. For maintenance regimens, it is usual to inject it 15–30 minutes before meals. Soluble insulin is the most appropriate form of insulin for use in diabetic emergencies (for example, diabetic ketoacidosis). When injected subcutaneously, soluble insulin has a rapid onset of action (30–60 minutes), a peak action between two and four hours, and a duration of action of up to eight hours. The rapid-acting human insulin analogues, insulin aspart and insulin lispro have a faster onset and shorter duration of action than soluble insulin; as a result, compared to soluble insulin, fasting and preprandial blood-glucose concentrations are a little higher, postprandial blood-glucose concentration is a little lower and hypoglycaemia occurs slightly less frequently. Subcutaneous injection of insulin analogues may be convenient for those who wish to inject shortly before or, when necessary, shortly after a meal. They can also help those susceptible to hypoglycaemia before lunch and those who eat late in the evening and are prone to nocturnal hypoglycaemia.

Drug: insulin (insulin injection; neutral insulin; soluble insulin)

Indications: diabetes mellitus; diabetic ketoacidosis

Cautions: see notes above

Contra-indications: none noted

Available forms: soluble insulin (human, pyr), 100 units/mL (10mL vial)

Dose: by subcutaneous, intramuscular or intravenous injection or intravenous infusion, according to requirements

Side-effects: see notes above; transient oedema; local reactions and fat hypertrophy at injection site; rarely hypersensitivity reactions including urticaria, rash; overdose causes hypoglycaemia

Status: prohibited

Drug: insulin aspart (recombinant human insulin analogue)

Indications: diabetes mellitus

Cautions: see notes above

Contra-indications: none noted

Available forms: injection, insulin aspart (recombinant human insulin analogue) 100 units/mL (10mL vial)

Dose: by subcutaneous injection, adult and child over 2 years: immediately before meals or when necessary shortly after meals, according to requirements; by subcutaneous infusion, or intravenous injection, or intravenous infusion, adult and child over 2 years: according to requirements

Side-effects: see insulin notes above

Status: prohibited

Drug: insulin lispro (recombinant human insulin analogue)

Indications: diabetes mellitus

Cautions: see notes above

Contra-indications: none noted

Available forms: injection, insulin lispro (recombinant human insulin analogue) 100 units/mL (10mL vial)

Dose: by subcutaneous injection shortly before meals or when necessary shortly after meals, according to requirements; by subcutaneous infusion, or intravenous injection, or intravenous infusion, according to requirements

Side-effects: see insulin notes on p75

Status: prohibited

6.1.2 Intermediate and long-acting insulins

When given by subcutaneous injection, intermediate- and long-acting insulins have an onset of action of approximately 1–2 hours, a maximal effect at 4–12 hours, and a duration of 16–35 hours. Some are given twice daily in conjunction with short-acting (soluble) insulin, and others are given once daily, particularly in elderly patients. Isophane insulin is a suspension of insulin with protamine; it is of particular value for initiation of twice-daily insulin regimens. Patients usually mix isophane with soluble insulin but ready-mixed preparations may be appropriate (biphasic isophane insulin or biphasic insulin aspart).

Insulin glargine is a long-acting human insulin analogues with a prolonged duration of action; insulin glargine is given once daily.

Drug: biphasic insulin aspart (Novomix 30®)

Indications: diabetes mellitus

Cautions: see notes above

Contra-indications: none noted

Available forms: injection, biphasic insulin aspart (recombinant human insulin analogue), 30% insulin aspart, 70% insulin aspart protamine, 100 units/mL, 5 × 3mL FlexPen® prefilled disposable injection devices (range 1–60 units, allowing 1-unit dosage adjustment)

Dose: by subcutaneous injection, up to 10 minutes before or soon after a meal, according to requirements

Side-effects: see insulin notes on p75; also, protamine may cause allergic reactions

Status: prohibited

Drug: insulin glargine (recombinant human insulin analogue – long-acting)

Indications: diabetes mellitus

Cautions: see notes above

Contra-indications: none noted

Available forms: insulin glargine (recombinant human insulin analogue), 100 units/mL (10mL vial)

Dose: by subcutaneous injection, adult and child over 6 years: according to requirements

Side-effects: see insulin notes on p75

Status: prohibited

Drug: isophane insulin

Indications: diabetes mellitus

Cautions: see notes above

Contra-indications: none noted

Available forms: injection, isophane insulin (human, pyr) 100 units/mL, 10mL vial

Dose: by subcutaneous injection, according to requirements

Side-effects: see insulin notes on p75; also, protamine may cause allergic reactions

Status: prohibited

6.1.3 Treatment of hypoglycaemia

Initially, glucose 10–20g is given by mouth either in liquid form (Glucogel®) or as granulated sugar or sugar lumps. If necessary, this may be repeated in 10–15 minutes. After initial treatment, a snack providing sustained availability of carbohydrate (for example, a sandwich, fruit, milk or biscuits) or the next meal, if it is due, can prevent blood-glucose concentration from falling again.

Hypoglycaemia that causes unconsciousness is an emergency. Glucagon®, a polypeptide hormone produced by the alpha cells of the islets of Langerhans, increases plasma-glucose concentration by mobilising glycogen stored in the liver. In hypoglycaemia, if sugar cannot be given by mouth, Glucagon® can be given by injection. Carbohydrates should be given as soon as possible to restore liver glycogen; Glucagon® is not appropriate for chronic hypoglycaemia.

Drug: Glucagon®

Indications: see notes above and under Dose below

Cautions: see notes above, insulinoma, glucagonoma; ineffective in chronic hypoglycaemia, starvation, adrenal insufficiency

Contra-indications: phaeochromocytoma

Available forms: injection, powder for reconstitution, Glucagon® (rys) as hydrochloride with lactose (1mg vial with prefilled syringe containing water for injection)

Dose: insulin-induced hypoglycaemia, by subcutaneous, intramuscular or intravenous injection, adult and child over 8 years (or body-weight over 25kg): 1mg

Side-effects: nausea, vomiting, abdominal pain, hypokalaemia, hypotension, rarely hypersensitivity reactions

Status: permitted

Drug: Glucogel®

Indications: to supplement glucose levels

Cautions: oral use only for conscious patients

Contra-indications: none noted

Available forms: 25g tube containing 10g glucose

Dose: see notes above

Side-effects: none noted

Status: permitted

6.2 Glucocorticoid therapy

Whenever possible, local treatment with creams, intra-articular injections, inhalations, eye-drops or enemas should be used in preference to systemic treatment.

Prolonged courses of corticosteroids increase susceptibility to infections and severity of infections; clinical presentation of infections may also be atypical. Serious infections (for example, septicaemia and tuberculosis) may reach an advanced stage before being recognised, and amoebiasis or strongyloidiasis may be activated or exacerbated (exclude before initiating a corticosteroid in those at risk or with suggestive symptoms). Fungal or viral ocular infections may also be exacerbated.

Unless they have had chickenpox, patients receiving oral or parenteral corticosteroids for purposes other than replacement should be regarded as being at risk of severe chickenpox. Manifestations of fulminant illness include pneumonia, hepatitis and disseminated intravascular coagulation; rash is not necessarily a prominent feature.

Systemic corticosteroids, particularly in high doses, are linked to psychiatric reactions including euphoria, nightmares, insomnia, irritability, mood lability, suicidal thoughts, psychotic reactions and behavioural disturbances. A serious paranoid state or depression with risk of suicide can be induced, particularly in patients with a history of mental disorder. These reactions frequently subside on reducing the dose or discontinuing the corticosteroid but they may also require specific management. Patients should be advised to seek medical advice if psychiatric symptoms (especially depression and suicidal thoughts) occur and they should also be alert to the rare possibility of such reactions during withdrawal of corticosteroid treatment.

Other cautions include: children and adolescents (growth restriction possibly irreversible), elderly (close supervision required particularly on long-term treatment); frequent monitoring required if history of tuberculosis (or X-ray changes), hypertension, recent myocardial infarction (rupture reported), congestive heart failure, diabetes mellitus including family history, osteoporosis (post-menopausal women at special risk), glaucoma (including family history), ocular herpes simplex – risk of corneal perforation, severe affective disorders (particularly if history of steroid-induced psychosis – see also psychiatric reactions), epilepsy, peptic ulcer, hypothyroidism, history of steroid myopathy, ulcerative colitis, diverticulitis, recent intestinal anastomoses, thromboembolic disorders; myasthenia gravis. Other contra-indications include: systemic infection (unless specific therapy given); avoid live virus vaccines in those receiving immunosuppressive doses (serum antibody response diminished).

Overdosage or prolonged use can exaggerate some of the normal physiological actions of corticosteroids leading to mineralocorticoid and glucocorticoid side-effects. Mineralocorticoid side-effects include hypertension, sodium and water retention, and potassium and calcium loss. Mineralocorticoid actions occur only slightly with methylprednisolone, prednisolone and triamcinolone. Glucocorticoid side-effects include diabetes and osteoporosis. In addition, high doses are associated with avascular necrosis of the femoral head. Muscle wasting (proximal myopathy) can also occur. Corticosteroid therapy is also weakly linked with peptic ulceration and perforation; there is no conclusive evidence that the use of enteric-coated preparations of prednisolone reduces the risk of peptic ulceration.

Side-effects can be minimised by using the lowest effective dose for the minimum period possible. Other side-effects include:

- gastro-intestinal effects: dyspepsia, abdominal distension, acute pancreatitis, oesophageal ulceration and candidiasis
- musculoskeletal effects: muscle weakness, vertebral and long bone fractures, tendon rupture
- endocrine effects: menstrual irregularities and amenorrhoea, hirsutism, weight gain, hypercholesterolaemia, hyperlipidaemia, negative nitrogen and calcium balance, increased appetite
- increased susceptibility to and severity of infection, reactivation of dormant tuberculosis
- neuropsychiatric effects: psychological dependence, insomnia, increased intracranial pressure with papilloedema in children (usually after withdrawal), aggravation of schizophrenia, aggravation of epilepsy
- ophthalmic effects: glaucoma, papilloedema, posterior subcapsular cataracts, corneal or scleral thinning and exacerbation of ophthalmic viral or fungal disease, increased intra-ocular pressure, exophthalmos
- also impaired healing, petechiae, ecchymoses, facial erythema, suppression of skin test reactions, urticaria, hyperhidrosis, skin atrophy, bruising, telangiectasia, myocardial rupture following recent myocardial infarction, congestive heart failure, leucocytosis, hyperglycaemia, thromboembolism, nausea, malaise, hiccups, headache, vertigo

Drug: hydrocortisone

Indications: hypersensitivity reactions (for example, anaphylaxis and angioedema); asthma; rheumatic disease

Cautions: see notes above

Contra-indications: see notes above

Available forms: injection, powder for reconstitution, hydrocortisone (as sodium succinate) (100mg vial)

Dose: by intramuscular injection or slow intravenous injection or infusion, 100–500mg, 3–4 times in 24 hours or as required

Side-effects: see notes above; also phosphate ester associated with paraesthesia and pain (particularly in the perineal region)

Status: intramuscular and intravenous use prohibited

Drug: methylprednisolone

Indications: suppression of inflammatory and allergic disorders; see also notes above; rheumatic disease

Cautions: see notes above; also rapid intravenous administration of large doses associated with cardiovascular collapse

Contra-indications: see notes above

Available forms: injection, powder for reconstitution, methylprednisolone (as sodium succinate) (all with solvent) (125mg vial)

Dose: by intramuscular injection or slow intravenous injection or infusion, initially 10–500mg

Side-effects: see notes above

Status: prohibited

Drug: prednisolone

Indications: suppression of inflammatory and allergic disorders; rheumatic disease

Cautions: see notes above; also Duchenne's muscular dystrophy (possible transient rhabdomyolysis and myoglobinuria following strenuous physical activity)

Contra-indications: see notes above

Available forms: soluble tablets, prednisolone 5mg (as sodium phosphate) (30-tablet pack)

Dose: by mouth, initially, up to 10–20mg daily (severe disease, up to 60mg daily), preferably taken in the morning after breakfast; can often be reduced within a few days but may need to be continued for several weeks or months. Maintenance, usual range, 2.5–15mg daily, but higher doses may be needed; cushingoid side-effects increasingly likely with doses above 7.5mg daily

Side-effects: see notes above

Status: prohibited

Drug: triamcinolone

Indications: suppression of inflammatory and allergic disorders; rheumatic disease

Cautions: see notes above; also high dosage may cause proximal myopathy, avoid in chronic therapy

Contra-indications: see notes above

Available forms: injection (aqueous suspension), triamcinolone acetonide 40mg/mL (1mL vial)

Dose: by deep intramuscular injection, into gluteal muscle, 40mg of acetonide for depot effect, repeated at intervals according to the patient's response; maximum single dose 100mg

Side-effects: see notes above

Status: intramuscular and intravenous use prohibited

6.3 Female sex hormones

6.3.1 Progestogens

Where endometriosis requires drug treatment, it may respond to a progestogen (for example, norethisterone) administered on a continuous basis. Although oral progestogens have been used widely for menorrhagia, they are relatively ineffective compared with tranexamic acid (see section 2.9, p32) or, particularly where dysmenorrhoea is also a factor, mefenamic acid (see section 9.1, p92). Oral progestogens have also been used for severe dysmenorrhoea, but where contraception is also required in younger women, the best choice is a combined oral contraceptive.

Progestogens have also been advocated for the alleviation of premenstrual symptoms, but no convincing physiological basis for such treatment has been shown.

Cautions

Progestogens should be used with caution in conditions that may worsen with fluid retention (for example, epilepsy, hypertension, migraine, asthma or cardiac dysfunction) and in those susceptible to thromboembolism (particular caution with high dose). Care is also required in those with a history of depression. Progestogens can decrease glucose tolerance and patients with diabetes should be monitored closely.

Contra-indications

Progestogens should be avoided in patients with a history of liver tumours. They are also contra-indicated in those with genital or breast cancer (unless progestogens are being used in the management of these conditions), severe arterial disease, undiagnosed vaginal bleeding and acute porphyria. Progestogens should not be used if there is a history during pregnancy of idiopathic jaundice, severe pruritus or pemphigoid gestationis.

Side-effects

Side-effects of progestogens include menstrual disturbances, premenstrual-like syndrome (including bloating, fluid retention, breast tenderness), weight change, nausea, headache, dizziness, insomnia, drowsiness, depression, change in libido; also skin reactions (including urticaria, pruritus, rash, acne), hirsutism and alopecia. Jaundice and anaphylactoid reactions have also been reported.

Drug: norethisterone

Indications: endometriosis, dysfunctional uterine bleeding, menorrhagia, dysmenorrhoea, premenstrual syndrome, postponement of menstruation

Cautions: see notes above

Contra-indications: see notes above

Available forms: tablets, norethisterone 5mg (30-tablet pack)

Dose: as follows:

- endometriosis, by mouth, 10–15mg daily for 4–6 months or longer, starting on day 5 of cycle (if spotting occurs increase dose to 20–25mg daily, reduced once bleeding has stopped)
- dysfunctional uterine bleeding, menorrhagia (but see notes above), by mouth, 5mg 3 times daily for 10 days to arrest bleeding; to prevent bleeding 5mg twice daily from day 19 to 26
- dysmenorrhoea (but see notes above), by mouth, 5mg 3 times daily from day 5 to 24 for 3–4 cycles
- premenstrual syndrome (but not recommended, see notes above), by mouth, 5mg 2–3 times daily from day 19 to 26 for several cycles
- postponement of menstruation, by mouth, 5mg 3 times daily starting 3 days before expected onset (menstruation occurs 2–3 days after stopping)

Side-effects: see notes above

Status: permitted

7.0 Gynaecology and urinary-tract disorders

7.1 Vaginal and vulval infections

7.1.1 Fungal infections

Candidal vulvitis can be treated locally with cream but is almost invariably associated with vaginal infection, which should also be treated. Vaginal candidiasis is treated primarily with antifungal pessaries or cream inserted high into the vagina (including during menstruation). Single-dose preparations offer an advantage when compliance is a problem. Local irritation may occur on application of vaginal antifungal products.

Imidazole drugs (for example, clotrimazole) are effective against candida in short courses of 1–14 days according to the preparation used; treatment can be repeated if initial course fails to control symptoms or if symptoms recur. Vaginal applications may be supplemented with antifungal cream for vulvitis and to treat other superficial sites of infection.

Oral treatment of vaginal infection with fluconazole (see section 5.2, p71) is also effective.

Drug: clotrimazole

Indications: candidal vulvitis

Cautions: cream may damage latex condoms and diaphragms

Contra-indications: none noted

Available forms: Canestan Combi®, clotrimazole 500mg pessary and cream (topical) 2% (1 pessary and 10g cream); clotrimazole cream 2%, clotrimazole (500mg pessary)

Dose: apply cream to anogenital area 2–3 times daily; insert 1 pessary at night as a single dose; can be repeated once if necessary

Side-effects: occasional local irritation

Status: permitted

7.2 Contraceptives

7.2.1 Emergency contraception

Hormonal emergency contraceptives include levonorgestrel and ulipristal; either drug should be taken as soon as possible after unprotected intercourse to increase efficacy.

Levonorgestrel is effective if taken within 72 hours (three days) of unprotected intercourse and may also be used between 72 and 120 hours (three and five days) after unprotected intercourse (unlicensed use), but efficacy decreases with time. Ulipristal is effective if taken within 120 hours (five days) of unprotected intercourse. If vomiting occurs within two hours of taking levonorgestrel or within three hours of taking ulipristal, a replacement dose should be given. If an antiemetic is required, domperidone (see section 4.4, p50) is preferred.

Drug: levonorgestrel

Indications: emergency contraception

Cautions: see notes above; past ectopic pregnancy; severe malabsorption syndromes; active trophoblastic disease (until return to normal of urine- and plasma-gonadotrophin concentration) – seek specialist advice

Contra-indications: acute porphyria

Available forms: tablets, levonorgestrel 1.5mg (1-tablet pack)

Dose: 1.5mg as a single dose as soon as possible after coitus (preferably within 12 hours but no later than after 72 hours)

Side-effects: menstrual irregularities, nausea, low abdominal pain, fatigue, headache, dizziness, breast tenderness, vomiting

Status: permitted

Drug: ulipristal

Indications: emergency contraception

Cautions: see notes above; uncontrolled severe asthma; effectiveness of combined hormonal and progestogen-only contraceptives may be reduced – additional precautions (barrier methods) required; repeated use within a menstrual cycle

Contra-indications: none noted

Available forms: tablets, ulipristal acetate 30mg (1-tablet pack)

Dose: 30mg as a single dose as soon as possible after coitus, but no later than after 120 hours

Side-effects: gastro-intestinal disturbances (including nausea, vomiting, diarrhoea, abdominal pain); dizziness, fatigue, headache; menstrual irregularities (see notes above); back pain, muscle spasms; less commonly tremor, hot flushes, uterine spasm, breast tenderness, dry mouth, blurred vision, pruritus, rash

Status: permitted

7.3 Drugs used in urological pain

Alkalinisation of urine can be undertaken with potassium citrate. The alkalinising action may relieve the discomfort of cystitis caused by lower urinary tract infections.

Drug: potassium citrate

Indications: relief of discomfort in mild urinary-tract infections; alkalinisation of urine

Cautions: cardiac disease; elderly

Contra-indications: none noted

Available forms: Effercitrate® tablets containing potassium citrate 1.5g, citric acid 0.25g (12 tablets); Cystopurin® sachets containing 3g potassium citrate (6 sachets)

Dose: as follows:
– Effercitrate®: 2 tablets in water up to 3 times daily with meals
– Cystopurin®: 1 sachet dissolved in 200mL cold water taken 3 times daily for 2 days

Side-effects: hyperkalaemia on prolonged high dosage

Status: permitted

Drug: sodium citrate (Canestan Oasis®)

Indications: relief of symptoms of cystitis in women

Cautions: cardiac disease, elderly, may need to be avoided in patients on a low salt diet

Contra-indications: not recommended for men or children

Available forms: sachet containing 4g sodium citrate (6-sachet pack)

Dose: contents of 1 sachet dissolved in a glass of cold water 3 times a day for 2 days

Side-effects: none noted

Status: permitted

8.0 Nutrition and blood

8.1 Anaemias

8.1.1 Iron deficiency anaemias

Before initiating treatment for anaemia, it is essential to determine which type is present. Iron salts may be harmful and result in iron overload if given alone to patients with anaemias other than those due to iron deficiency. Treatment with an iron preparation is justified only in the presence of a demonstrable iron-deficiency state. Before starting treatment, it is important to exclude any serious underlying cause of the anaemia (for example, gastric erosion). Prophylaxis with an iron preparation may be appropriate in malabsorption, menorrhagia, pregnancy, after subtotal or total gastrectomy.

The oral dose of elemental iron for iron-deficiency anaemia should be 100–200mg daily. It is customary to give this as dried ferrous sulphate, 200mg (≡ 65mg elemental iron) three times daily; for prophylaxis of iron-deficiency anaemia, a dose of ferrous sulphate 200mg once or twice daily may be effective. Gastro-intestinal irritation can occur with iron salts. Nausea and epigastric pain are dose-related, but the relationship between dose and altered bowel habit (constipation or diarrhoea) is less clear. Oral iron can exacerbate diarrhoea in patients with inflammatory bowel disease; care is also needed in patients with intestinal strictures and diverticular disease.

Iron preparations taken orally can be constipating, particularly in older patients, and occasionally lead to faecal impaction.

Drug: ferrous sulphate

Indications: iron-deficiency anaemia

Cautions: see notes above

Contra-indications: none noted

Available forms: tablets, coated, dried ferrous sulphate 200mg (65mg iron) (28-tablet pack)

Dose: prophylactic, 1 tablet daily; therapeutic, 1 tablet 2–3 times daily

Side-effects: see notes above

Status: permitted

8.1.2 Drugs used in megaloblastic anaemias

Most megaloblastic anaemias result from a lack of either vitamin B12 or folate, and it is essential to establish in every case which deficiency is present and the underlying cause. Folic acid has few indications for long-term therapy, as most causes of folate deficiency are self-limiting or will yield to a short course of treatment. In folate-deficient megaloblastic anaemia (for example, because of poor nutrition, pregnancy or antiepileptic drugs), daily folic acid supplementation for four months brings about haematological remission and replenishes body stores. For prophylaxis in chronic haemolytic states, malabsorption or in renal dialysis, folic acid is given daily or sometimes weekly, depending on the diet and the rate of haemolysis. Folic acid supplements taken before and during pregnancy can reduce the occurrence of neural tube defects. Women at low risk of conceiving a child with a neural tube defect should be advised to take folic acid 400 micrograms daily before conception and until week 12 of pregnancy.

Drug: folic acid

Indications: see notes above

Cautions: should never be given alone for pernicious anaemia and other vitamin B12 deficiency states (may precipitate subacute combined degeneration of the spinal cord)

Contra-indications: none noted

Available forms: tablets, folic acid 400 micrograms (90-tablet pack)

Dose: see notes above; for other indications seek specialist opinion

Side-effects: rarely gastro-intestinal disturbances

Status: permitted

8.2 Oral rehydration therapy (ORT)

Replacement of fluid and electrolytes lost through diarrhoea can be achieved by giving solutions containing sodium, potassium and glucose. Once rehydration is complete, further dehydration is prevented by encouraging the patient to drink normal volumes of an appropriate fluid and by replacing continuing losses with an oral rehydration solution.

Drug: Dioralyte®

Indications: fluid and electrolyte loss in diarrhoea, see notes above

Cautions: none noted

Contra-indications: none noted

Available forms: oral powder, sodium chloride 470mg, potassium chloride 300mg, disodium hydrogen citrate 530mg, glucose 3.56g/sachet (20-sachet pack)

Dose: according to fluid loss, usually 200–400mL solution after every loose motion

Side-effects: none noted

Status: permitted

8.3 Oral potassium supplements

If potassium salts are used for the prevention of hypokalaemia, then doses of potassium chloride of 2–4g (approximately 25–50mmol) daily (in divided doses) by mouth are suitable in patients taking a normal diet. Smaller doses must be used if there is renal insufficiency (common in the elderly) to reduce the risk of hyperkalaemia. Potassium salts cause nausea and vomiting and poor compliance is a major limitation to their effectiveness. Regular monitoring of plasma-potassium concentration is essential in those taking potassium supplements. When there is established potassium depletion, larger doses may be necessary, the quantity depending on the severity of any continuing potassium loss (monitoring of plasma-potassium concentration and specialist advice would be required). Potassium depletion is frequently associated with chloride depletion and with metabolic alkalosis, and these disorders require correction.

Drug: potassium chloride

Indications: potassium depletion (see notes above)

Cautions: see notes above; cardiac disease; elderly

Contra-indications: plasma-potassium concentration above 5mmol/litre

Available forms: tablets, effervescent, potassium bicarbonate and chloride equivalent to potassium 470mg (12mmol of K+) and chloride 285mg (8mmol of Cl-) (20-tablet pack)

Dose: see notes above

Side-effects: nausea, vomiting, abdominal pain, diarrhoea, flatulence; with modified-release preparations, gastro-intestinal obstruction, ulceration and bleeding also reported

Status: permitted

8.4 Oral calcium supplements

Calcium supplements are usually only required where dietary calcium intake is deficient. This dietary requirement varies with age and is relatively greater in childhood, pregnancy and lactation, due to an increased demand, and in old age, due to impaired absorption. If the actual dietary intake is less than the recommended amount, a supplement of as much as 40mmol is appropriate.

Drug: calcium salts

Indications: see notes above; calcium deficiency

Cautions: sarcoidosis; history of nephrolithiasis

Contra-indications: conditions associated with hypercalcaemia and hypercalciuria (for example, some forms of malignant disease)

Available forms: Sandocal 400 tablets®, effervescent, orange flavour, calcium lactate gluconate 930mg, calcium carbonate 700mg, providing calcium 400mg (Ca2+ 10mmol) (20-tablet pack)

Dose: see notes above

Side-effects: gastro-intestinal disturbances; bradycardia, arrhythmias

Status: permitted

8.5 Vitamin C

Vitamin C therapy is essential in scurvy, but less florid manifestations of vitamin C deficiency are commonly found, especially in the elderly. It is rarely necessary to prescribe more than 100mg daily except early in the treatment of scurvy. Claims that vitamin C ameliorates colds or promotes wound healing have not been proved.

Drug: ascorbic acid

Indications: prevention and treatment of scurvy

Cautions: none noted

Contra-indications: none noted

Available forms: tablets, ascorbic acid 50mg (28-tablet pack)

Dose: prophylactic, 25–75mg daily; therapeutic, not less than 250mg daily in divided doses

Side-effects: none noted

Status: permitted

9.0 Musculoskeletal and joint diseases

A non-steroidal anti-inflammatory drug (NSAID) is indicated for pain and stiffness resulting from inflammatory rheumatic disease; analgesics such as paracetamol or codeine can also be used. For pain relief in osteoarthritis and soft-tissue disorders, paracetamol (see section 4.5.1, p53) should be used first and may need to be taken regularly. A topical NSAID should also be considered, particularly for knee or hand osteoarthritis. An oral NSAID can be substituted for, or used in addition to, paracetamol. If further pain relief is required in osteoarthritis, then the addition of an opioid analgesic (see section 4.5.3, p56) may be considered, but with a substantial risk of adverse effects. Intra-articular corticosteroid injections may produce temporary benefit in osteoarthritis, especially if associated with soft-tissue inflammation.

9.1 Non-steroidal anti-inflammatory drugs (NSAIDs)

In single doses, NSAIDs have analgesic activity comparable to that of paracetamol, but paracetamol is preferred, particularly in the elderly. In regular full dosage, NSAIDs have both a lasting analgesic and an anti-inflammatory effect that makes them particularly useful for the treatment of continuous or regular pain associated with inflammation. NSAIDs can also be of benefit in the less well-defined conditions of back pain and soft-tissue disorders.

Pain relief starts soon after taking the first dose. A full analgesic effect should normally be obtained within a week, whereas an anti-inflammatory effect may not be achieved (or may not be clinically assessable) for up to three weeks.

Ibuprofen is a propionic acid derivative with anti-inflammatory, analgesic and antipyretic properties. It has fewer side-effects than other non-selective NSAIDs, but its anti-inflammatory properties are weaker. Naproxen is one of the first choices because it combines good efficacy with a low incidence of side-effects (but more than ibuprofen). Diclofenac has actions and side-effects similar to those of naproxen.

The selective inhibitor of cyclo-oxygenase-2, celecoxib, is as effective as non-selective NSAIDs such as diclofenac and naproxen. Short-term data indicate that the risk of serious upper gastro-intestinal events is lower with selective inhibitors compared to non-selective NSAIDs.

Most mild to moderate dental pain and inflammation is effectively relieved by NSAIDs. Those used for dental pain include ibuprofen and diclofenac.

Cautions and contra-indications

NSAIDs should be used with caution in the elderly (risk of serious side-effects and fatalities), in allergic disorders (they are contra-indicated in patients with a history of hypersensitivity to aspirin or any other NSAID, which includes those in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by aspirin or any other NSAID) and in coagulation defects.

In patients with cardiac impairment, caution is required as NSAIDs may impair renal function. All NSAIDs are contra-indicated in severe heart failure. Non-selective NSAIDs should be used with caution in uncontrolled hypertension, heart failure, ischaemic heart disease, peripheral artery disease and cerebrovascular disease, and when used long-term in patients with risk factors for cardiovascular events. The selective inhibitors of cyclo-oxygenase-2 (celecoxib) is contra-indicated in ischaemic heart disease, cerebrovascular disease, peripheral arterial disease and mild to severe heart failure. The selective inhibitors of cyclo-oxygenase-2 should be used with caution in patients with a history of cardiac failure, left ventricular dysfunction, hypertension, in patients with oedema for any other reason, and in patients with risk factors for cardiovascular events.

Non-selective NSAIDs are contra-indicated in patients with previous or active peptic ulceration and that selective inhibitors of cyclo-oxygenase-2 are contra-indicated in active peptic ulceration. Patients at risk of gastro-intestinal ulceration (including the elderly) who need NSAID treatment should receive gastroprotective treatment.

NSAIDs should be avoided if possible, or should be used with caution in patients with renal impairment; the lowest effective dose should be used for the shortest possible duration, and renal function should be monitored. Sodium and water retention may occur and renal function may deteriorate, possibly leading to renal failure.

Side-effects
Gastro-intestinal disturbances including discomfort, nausea and diarrhoea, and occasionally bleeding and ulceration, occur. Other side-effects include hypersensitivity reactions (particularly rashes, angioedema and bronchospasm), headache, dizziness, nervousness, depression, drowsiness, insomnia, vertigo, hearing disturbances such as tinnitus, photosensitivity and haematuria. Blood disorders have also occurred. Fluid retention may occur (rarely precipitating congestive heart failure); blood pressure may be raised.

Any degree of worsening of asthma may be related to the ingestion of NSAIDs, either prescribed or (in the case of ibuprofen and others) purchased over the counter. Renal failure may be provoked by NSAIDs, especially in patients with pre-existing renal impairment. Rarely, papillary necrosis or interstitial fibrosis associated with NSAIDs can lead to renal failure. Hepatic damage, alveolitis, pulmonary eosinophilia, pancreatitis, visual disturbances, Stevens-Johnson syndrome and toxic epidermal necrolysis are other rare side-effects. Induction of or exacerbation of colitis or Crohn's disease has been reported. Aseptic meningitis has been reported rarely with NSAID; patients with connective-tissue disorders such as systemic lupus erythematosus may be especially susceptible.

Mefenamic acid has minor anti-inflammatory properties. It has occasionally been associated with diarrhoea and haemolytic anaemia that require discontinuation of treatment.

Drug: celecoxib

Indications: pain and inflammation in osteoarthritis, rheumatoid arthritis, ankylosing spondylitis

Cautions: see notes above; monitor blood pressure before and during treatment

Contra-indications: see notes above; sulphonamide sensitivity; inflammatory bowel disease

Available forms: capsules, celecoxib 100mg (60-capsule pack), 200mg (30-capsule pack)

Dose: as follows:
- osteoarthritis, 200mg daily in 1–2 divided doses, increased if necessary to maximum 200mg twice daily
- rheumatoid arthritis, 100mg twice daily, increased if necessary to 200mg twice daily
- ankylosing spondylitis, 200mg daily in 1–2 divided doses, increased if necessary to maximum 400mg daily in 1–2 divided doses

Side-effects: see notes above; dyspnoea, influenza-like symptoms; less commonly stomatitis, palpitation, cerebral infarction, fatigue, paraesthesia, muscle cramps; rarely taste disturbance, alopecia; very rarely seizures; also reported chest pain

Status: permitted

Drug: diclofenac

Indications: pain and inflammation in rheumatic disease (including juvenile idiopathic arthritis) and other musculoskeletal disorders; acute gout

Cautions: see notes above; avoid in acute porphyria

Contra-indications: see notes above

Available forms: tablets, e/c, diclofenac sodium 25mg (84-tablet pack), 50mg (84-tablet pack); tablets, modified release, diclofenac sodium 75mg (28-tablet pack); tablets, modified release, diclofenac sodium 100mg (28-tablet pack); suppositories, diclofenac sodium 50mg (10-pack)

Dose: as follows:
- by mouth, 75–150mg daily in 2–3 divided doses
- by rectum in suppositories, 75–150mg daily in divided doses

Side-effects: see notes above; suppositories may cause rectal irritation

Status: permitted

Drug: ibuprofen

Indications: pain and inflammation in rheumatic disease (including juvenile idiopathic arthritis) and other musculoskeletal disorders; mild to moderate pain including dysmenorrhoea; postoperative analgesia; migraine; dental pain; fever with discomfort and pain in children

Cautions: see notes above

Contra-indications: see notes above

Available forms: tablets, ibuprofen 200mg (48-tablet and 84-tablet packs), 400mg (84-tablet pack); oral suspension, ibuprofen 100mg/5mL (100mL)

Dose: as follows:
- adult and child over 12 years: initially 300–400mg 3–4 times daily; increased if necessary to maximum 2.4g daily; maintenance dose of 0.6–1.2g daily may be adequate
- for dose in children under 12 years, see the full edition of the British National Formulary or the British National Formulary for Children (www.bnf.org)

Side-effects: see notes above

Status: permitted

Drug: ketorolac

Indications: short-term management of moderate to severe acute postoperative pain only

Cautions: see notes above, avoid in acute porphyria

Contra-indications: see notes above; also complete or partial syndrome of nasal polyps; haemorrhagic diatheses (including coagulation disorders) and following operations with high risk of haemorrhage or incomplete haemostasis; confirmed or suspected cerebrovascular bleeding; hypovolaemia or dehydration

Available forms: injection, ketorolac trometamol 30mg/mL (1mL ampoule)

Dose: adult and child over 16 years: by intramuscular injection or by intravenous injection over at least 15 seconds, initially 10mg, then 10–30mg every 4–6 hours as required (up to every 2 hours during initial postoperative period); maximum 90mg daily (elderly and patients weighing less than 50kg maximum 60mg daily); maximum duration of treatment 2 days

Side-effects: see notes above; also gastro-intestinal disturbances, taste disturbances, dry mouth; flushing, bradycardia, palpitation, chest pain, hypertension, pallor; dyspnoea, asthma; malaise, euphoria, psychosis, paraesthesia, convulsions, abnormal dreams, hyperkinesia, confusion, hallucinations; urinary frequency, thirst, sweating; hyponatraemia, hyperkalaemia, myalgia; visual disturbances (including optic neuritis); purpura, pain at injection site

Status: permitted

Drug: mefenamic acid

Indications: pain and inflammation in rheumatoid arthritis and osteoarthritis; postoperative pain; mild to moderate pain; dysmenorrhoea, menorrhagia

Cautions: see notes above; epilepsy; acute porphyria

Contra-indications: see notes above; inflammatory bowel disease

Available forms: tablets, mefenamic acid 500mg (28-tablet pack)

Dose: adult over 18 years: 500mg 3 times daily

Side-effects: see notes above; also diarrhoea or rashes (withdraw treatment), stomatitis; less commonly paraesthesia and fatigue; rarely hypotension, palpitation, glucose intolerance, thrombocytopenia, haemolytic anaemia (positive Coombs' test), aplastic anaemia

Status: permitted

Drug: naproxen

Indications: pain and inflammation in rheumatic disease (including juvenile idiopathic arthritis) and other musculoskeletal disorders; dysmenorrhoea; acute gout

Cautions: see notes above

Contra-indications: see notes above

Available forms: tablets, naproxen 250mg (28-tablet pack)

Dose: as follows:
- rheumatic disease, 0.5–1g daily in 1–2 divided doses
- acute musculoskeletal disorders and dysmenorrhoea, 500mg initially, then 250mg every 6–8 hours as required; maximum dose after first day 1.25g daily
- acute gout, 750mg initially, then 250mg every 8 hours until attack has passed

Side-effects: see notes above

Status: permitted

9.2 Acute attacks of gout

Acute attacks of gout are usually treated with high doses of NSAIDs such as diclofenac (see section 9.1, p91) or naproxen (see section 9.1, p93). Colchicine is an alternative in patients in whom NSAIDs are contra-indicated. The use of colchicine is limited by the development of toxicity at higher doses, but it is often of value in patients with heart failure because, unlike NSAIDs, it does not induce fluid retention. Oral or parenteral corticosteroids are an effective alternative in those who cannot tolerate NSAIDs or who are resistant to other treatments. Intra-articular injection of a corticosteroid can be used in acute monoarticular gout (unlicensed indication).

Drug: colchicine

Indications: acute gout

Cautions: see notes above; also elderly; gastro-intestinal disease; cardiac disease

Contra-indications: blood disorders

Available forms: tablets, colchicine 500 micrograms (100-tablet pack)

Dose: acute gout: 500 micrograms 2–4 times daily until symptoms relieved, maximum 6mg per course; course not to be repeated within 3 days

Side-effects: nausea, vomiting, abdominal pain; excessive doses may cause profuse diarrhoea, gastrointestinal haemorrhage, rash, renal and hepatic damage; rarely peripheral neuritis, inhibition of spermatogenesis, myopathy, alopecia, and with prolonged treatment blood disorders

Status: permitted

9.3 Hyaluronic acid

Hyaluronic acid and its derivatives are available for osteoarthritis of the knee, but are not recommended. Sodium hyaluronate (Ostenil®) is injected intra-articularly to supplement natural hyaluronic acid in the synovial fluid. These injections may reduce pain over one to six months, but are associated with a short-term increase in knee inflammation.

Drug: hyaluronate

Indications: pain and restricted mobility in degenerative and traumatic changes of the knee and other synovial joints

Cautions: venous or lymphatic stasis of the leg

Contra-indications: infection, skin disease or severe inflammation at injection site

Available forms: sodium hyaluronate 20mg per 2mL (2mL pre-filled syringe (Ostenil®)); sodium hyaluronate 40mg per 2mL (2mL pre-filled syringe (Ostenil Plus®)); sodium hyaluronate 10mg per 1mL (1mL pre-filled syringe (Ostenil Mini®))

Dose: as follows:

- Ostenil®: up to 2mL is administered as an intra-articular injection once weekly for 3–5 consecutive weeks
- Ostenil Plus®: up to 2mL is administered as an intra-articular injection once weekly for a course of 1–3 injections
- Ostenil Mini®: used in small synovial joints, and up to 1mL is administered as an intra-articular injection once weekly for a course of 1–3 injections

Side-effects: pain, swelling, heat and redness at injection site. Very rarely, allergic-type reactions

Status: permitted

9.4 Corticosteroids

The general actions, uses, cautions and availability of systemic corticosteroids are described in the section on corticosteroid therapy.

Corticosteroids are injected locally for an anti-inflammatory effect. In inflammatory conditions of the joints, particularly in rheumatoid arthritis, they are given by intra-articular injection to relieve pain, increase mobility and reduce deformity in one or a few joints. Full aseptic precautions are essential; infected areas should be avoided. Occasionally, an acute inflammatory reaction develops after an intra-articular or soft-tissue injection of a corticosteroid. This may be a reaction to the microcrystalline suspension of the corticosteroid used, but must be distinguished from sepsis introduced into the injection site.

Smaller amounts of corticosteroids may also be injected directly into soft tissues for the relief of inflammation in conditions such as tennis or golfer's elbow or compression neuropathies. In tendinitis, injections should be made into the tendon sheath and not directly into the tendon (due to the absence of a true tendon sheath and a high risk of rupture, the Achilles tendon should not be injected).

Hydrocortisone acetate or one of the synthetic analogues is generally used for local injection. Intra-articular corticosteroid injections can cause flushing and may affect the hyaline cartilage. Each joint should not usually be treated more than four times in one year.

Drug: betamethasone

Indications: local inflammation of joints and soft tissues

Cautions: see notes above

Contra-indications: see notes above

Available forms: injection, betamethasone (as sodium phosphate) 4mg/mL (1mL ampoule)

Dose: local injections of 4–8mg betamethasone may be used when treating soft tissue lesions in adults

Side-effects: see notes above

Status: intra-articular and other local (but not intravenous or intramuscular) injections are permitted

Drug: hydrocortisone acetate

Indications: local inflammation of joints and soft tissues

Cautions: see notes above

Contra-indications: see notes above

Available forms: injection (aqueous suspension), hydrocortisone acetate 25mg/mL (1mL ampoule)

Dose: by intra-articular injection (for details consult product literature), 5–50mg according to size; where appropriate, may be repeated at intervals of 21 days; not more than 3 joints should be treated on any 1 day

Side-effects: see notes above

Status: intra-articular and other local (but not intravenous or intramuscular) injections are permitted

9.5 Skeletal muscle relaxants

Skeletal muscle relaxants are effective in most forms of spasticity except the rare alpha variety. Diazepam can be used, but sedation and occasionally extensor hypotonus are disadvantages. Muscle-relaxant doses of benzodiazepines are similar to anxiolytic doses.

Drug: diazepam

Indications: muscle spasm of varied aetiology

Cautions: respiratory disease, muscle weakness and myasthenia gravis, history of drug or alcohol abuse, marked personality disorder; reduce dose in elderly and debilitated; avoid prolonged use (and abrupt withdrawal thereafter); special precautions for intravenous injection; acute porphyria); when given parenterally, close observation required until full recovery from sedation

Contra-indications: respiratory depression; marked neuromuscular respiratory weakness including unstable myasthenia gravis; acute pulmonary insufficiency; sleep apnoea syndrome; not for chronic psychosis; should not be used alone in depression or in anxiety with depression

Available forms: tablets, diazepam, 2mg (28-tablet pack), 5mg (28-tablet pack)

Dose: muscle spasm, by mouth, 2–15mg daily in divided doses

Side-effects: drowsiness and lightheadedness the next day; confusion and ataxia (especially in the elderly); amnesia; dependence; paradoxical increase in aggression; muscle weakness; occasionally: headache, vertigo, hypotension, salivation changes, gastro-intestinal disturbances, visual disturbances, dysarthria, tremor, changes in libido, incontinence, urinary retention; blood disorders and jaundice reported; skin reactions; on intravenous injection, pain, thrombophlebitis, rarely apnoea. Also hypotonia

Status: permitted

9.6 Nocturnal leg cramps

Quinine salts, such as quinine sulphate 200–300mg at bedtime, are effective in reducing the frequency of nocturnal leg cramps by about 25 per cent in ambulatory patients. However, because of potential toxicity, quinine is not recommended for routine treatment and should not be used unless cramps cause regular disruption to sleep. Quinine should only be considered when cramps are very painful or frequent; when other treatable causes of cramp have been excluded; and when non-pharmacological treatments have not worked (for example, passive stretching exercises).

Drug: quinine

Indications: nocturnal leg cramps

Cautions: cardiac disease (including atrial fibrillation, conduction defects, heart block)

Contra-indications: haemoglobinuria, myasthenia gravis, optic neuritis, tinnitus

Available forms: tablets, coated, quinine sulphate 200mg (28-tablet pack)

Dose: see notes above

Side-effects: cinchonism, including tinnitus, hearing impairment, vertigo, headache, nausea, vomiting, abdominal pain, diarrhoea, visual disturbances (including temporary blindness), confusion; cardiovascular effects (see Cautions above); dyspnoea; hypersensitivity reactions including angioedema, rashes, hot and flushed skin; hypoglycaemia (especially after parenteral administration); blood disorders (including thrombocytopenia and intravascular coagulation); acute renal failure; muscle weakness; photosensitivity

Status: permitted

9.7 Rubifacients and topical NSAIDs

Rubefacients act by counter-irritation. Pain, whether superficial or deep-seated, is relieved by any method that itself produces irritation of the skin. Topical rubefacient preparations may contain nicotinate and salicylate compounds, essential oils, capsicum and camphor. The evidence available does not support the use of topical rubefacients in acute or chronic musculoskeletal pain.

The use of a NSAID by mouth is effective for relieving musculoskeletal pain. Topical NSAIDs (for example, ibuprofen or ketoprofen) may provide some relief of pain in musculoskeletal conditions. Apply with gentle massage only; avoid contact with eyes, mucous membranes and inflamed or broken skin, and discontinue if rash develops. Hands should be washed immediately after use. Topical application of large amounts can result in systemic effects, including hypersensitivity and asthma (renal disease has also been reported).

Patients should be advised against excessive exposure to sunlight of the area treated, in order to avoid possibility of the photosensitivity. Patients using preparations containing ketoprofen should be advised not to expose the area treated to sunbeds or sunlight (even on a bright but cloudy day) during and for two weeks after stopping treatment; treated areas should be protected with clothing.

Drug: diclofenac

Indications: see notes above

Cautions: see notes above. Counselling, photosensitivity

Contra-indications: contra-indicated in patients with a history of hypersensitivity to aspirin or any other NSAID, which includes those in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by aspirin or any other NSAID, and in coagulation defects

Available forms: gel, diclofenac diethylammonium salt 1.16% (equivalent to diclofenac sodium 1%) (100g tube)

Dose: apply 3–4 times daily; therapy should be reviewed after 14 days

Side-effects: see notes above

Status: permitted

Drug: diclofenac (Voltarol Gel patch®)

Indications: ankle sprain, epicondylitis

Cautions: see notes above

Contra-indications: contra-indicated in patients with a history of hypersensitivity to aspirin or any other NSAID, which includes those in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by aspirin or any other NSAID, and in coagulation defects

Available forms: gel patch, diclofenac epolamine (equivalent to 140mg diclofenac sodium per patch) (10-patch pack)

Dose: as follows:
- ankle sprain, apply 1 patch daily for up to 3 days
- epicondylitis, apply 1 patch twice daily for up to 14 days

Side-effects: see notes above

Status: permitted

Drug: ibuprofen

Indications: see notes above

Cautions: see notes above

Contra-indications: contra-indicated in patients with a history of hypersensitivity to aspirin or any other NSAID, which includes those in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by aspirin or any other NSAID, and in coagulation defects

Available forms: gel, ibuprofen 5% (50g pack)

Dose: apply up to 3 times daily

Side-effects: see notes above

Status: permitted

Drug: ketoprofen

Indications: see notes above

Cautions: see notes above

Contra-indications: contra-indicated in patients with a history of hypersensitivity to aspirin or any other NSAID, which includes those in whom attacks of asthma, angioedema, urticaria or rhinitis have been precipitated by aspirin or any other NSAID, and in coagulation defects

Available forms: gel, ketoprofen 2.5% (50g pack)

Dose: apply 2–4 times daily for up to 7 days (usual maximum 15g daily)

Side-effects: see notes above

Status: permitted

Drug: menthol and methylsalicylate cream (Ralgex cream®)

Indications: symptomatic relief of muscular pain and stiffness

Cautions: none noted

Contra-indications: none noted

Available forms: cream containing glycol monosalicylate 10%, methyl nicotinate 1%, capsicum oleoresin 0.12% (100g pack)

Dose: apply as required up to 4 times a day

Side-effects: none noted

Status: permitted

10.0 Eye

10.1 Anti-infective eye preparations

10.1.1 Antibacterials

Most acute superficial eye infections can be treated topically. Blepharitis and conjunctivitis are often caused by staphylococci; keratitis and endophthalmitis may be bacterial, viral, or fungal. Bacterial blepharitis is treated by application of an antibacterial eye ointment to the conjunctival sac or to the lid margins. Most cases of acute bacterial conjunctivitis are self-limiting; where treatment is appropriate, antibacterial eye drops or an eye ointment are used. A poor response might indicate viral or allergic conjunctivitis.

Chloramphenicol has a broad spectrum of activity and is the drug of choice for superficial eye infections. Chloramphenicol eye drops are well tolerated and the recommendation that chloramphenicol eye drops should be avoided because of an increased risk of aplastic anaemia is not well founded. Fusidic acid is useful for staphylococcal infections.

Administration

Frequency of application depends on the severity of the infection and the potential for irreversible ocular damage; antibacterial eye preparations are usually administered as follows:

- Eye drops: apply one drop at least every two hours then reduce frequency as infection is controlled and continue for 48 hours after healing.
- Eye ointment: Apply either at night (if eye drops used during the day) or three to four times daily (if eye ointment used alone).

Drug: chloramphenicol

Cautions: see notes above

Contra-indications: none noted

Available forms: eye drops, chloramphenicol 0.5% (10mL pack); eye ointment, chloramphenicol 1% (4g pack)

Dose: see notes above

Side-effects: see notes above; also transient stinging

Status: permitted

Drug: fusidic acid

Cautions: see notes above

Contra-indications: none noted

Available forms: eye drops, m/r, fusidic acid 1% in gel basis (liquifies on contact with eye) (5g pack)

Dose: apply twice daily

Side-effects: none noted

Status: permitted

10.1.2 Antivirals

Herpes simplex infections producing, for example, dendritic corneal ulcers can be treated with aciclovir. Aciclovir eye ointment is used in combination with systemic treatment for ophthalmic zoster.

Drug: aciclovir (acyclovir)

Indications: local treatment of herpes simplex infections

Cautions: none noted

Contra-indications: none noted

Available forms: eye ointment, aciclovir 3% (4.5g pack)

Dose: apply 5 times daily; continue for at least 3 days after complete healing

Side-effects: local irritation and inflammation, superficial punctate keratopathy; rarely blepharitis; very rarely hypersensitivity reactions including angioedema

Status: permitted

10.2 Corticosteroids

Corticosteroids administered locally to the eye or given by mouth are effective for treating anterior segment inflammation, including that which results from surgery.

Topical corticosteroids are applied frequently for the first 24–48 hours; once inflammation is controlled, the frequency of application is reduced. They should normally only be used under expert supervision. The three main dangers associated with their use are as follows:

– A 'red eye', when the diagnosis is unconfirmed, may be due to herpes simplex virus, and a corticosteroid may aggravate the condition, leading to corneal ulceration, with possible damage to vision and even loss of the eye. Bacterial, fungal and amoebic infections pose a similar hazard.
– 'Steroid glaucoma' can follow the use of corticosteroid eye preparations in susceptible individuals.
– A 'steroid cataract' can follow prolonged use.

Other side-effects of ocular corticosteroids include thinning of the cornea and sclera.

Drug: betamethasone

Indications: local treatment of inflammation (short-term)

Cautions: see notes above

Contra-indications: none noted

Available forms: drops (for ear, eye, or nose), betamethasone sodium phosphate 0.1% (10mL pack)

Dose: apply eye drops every 1–2 hours until controlled, then reduce frequency

Side-effects: see notes above

Status: permitted

Drug: dexamethasone

Indications: local treatment of inflammation (short-term)

Cautions: see notes above

Contra-indications: none noted

Available forms: eye drops, dexamethasone 0.1%, hypromellose 0.5% (10mL pack)

Dose: apply eye drops every 30–60 minutes until controlled, then reduce frequency to 4–6 times daily

Side-effects: see notes above

Status: permitted

Drug: fluorometholone

Indications: local treatment of inflammation (short-term)

Cautions: see notes above

Contra-indications: none noted

Available forms: ophthalmic suspension (eye drops), fluorometholone 0.1%, polyvinyl alcohol (Liquifilm®) 1.4% (10mL pack)

Dose: apply every hour for 24–48 hours, then reduce frequency to 2–4 times daily

Side-effects: see notes above

Status: permitted

10.3 Other anti-inflammatory preparations

Other preparations used for the topical treatment of inflammation and allergic conjunctivitis include antihistamines and sodium cromoglicate. Eye drops containing antihistamines, such as olopatadine, can be used for allergic conjunctivitis. Sodium cromoglicate (sodium cromoglycate) eye drops can be useful for vernal keratoconjunctivitis and other allergic forms of conjunctivitis.

Drug: olopatadine

Indications: seasonal allergic conjunctivitis

Cautions: none noted

Contra-indications: none noted

Available forms: eye drops, olopatadine (as hydrochloride) 1mg/mL (5mL pack)

Dose: adult and child over 3 years: apply twice daily; maximum duration of treatment 4 months

Side-effects: local irritation; less commonly keratitis, dry eye, local oedema, photophobia; headache, asthenia, dizziness; dry nose also reported

Status: permitted

Drug: sodium cromoglicate (sodium cromoglycate)

Indications: allergic conjunctivitis; seasonal keratoconjunctivitis

Cautions: none noted

Contra-indications: none noted

Available forms: eye drops, sodium cromoglicate 2% (13.5mL pack)

Dose: adult and child: apply eye drops 4 times daily

Side-effects: burning and stinging

Status: permitted

10.4 Local anaesthetics

Tetracaine is a widely used topical local anaesthetic that produces a profound anaesthesia and is suitable for use before minor surgical procedures, such as the removal of corneal sutures. It has a temporary disruptive effect on the corneal epithelium. Local anaesthetics should never be used for the management of ocular symptoms.

Drug: tetracaine

Indications: local anaesthetic

Cautions: see notes above

Contra-indications: none noted

Available forms: eye drops, tetracaine hydrochloride 0.5% and 1% (20 × 0.5mL minims)

Dose: to be used as needed for procedure

Side-effects: none noted

Status: permitted

10.5 Tear deficiency

Chronic soreness of the eyes associated with reduced or abnormal tear secretion often responds to tear replacement therapy. The severity of the condition and patient preference will often guide the choice of preparation. Hypromellose is the traditional choice of treatment for tear deficiency. It may need to be instilled frequently (for example, hourly) for adequate relief. The ability of carbomers to cling to the eye surface may help reduce frequency of application to four times daily.

Drug: hypromellose

Indications: tear deficiency

Cautions: none noted

Contra-indications: none noted

Available forms: eye drops, hypromellose 0.3% (10mL pack); single-use eye drops, hypromellose 0.3% (30 × 0.4mL)

Dose: see notes above

Side-effects: none noted

Status: permitted

11.0 Ear, nose and oropharynx

11.1 Drugs acting on the ear

Otitis externa

Otitis externa is an inflammatory reaction of the meatal skin. It is important to exclude an underlying chronic otitis media before treatment. Many cases recover after thorough cleansing of the external ear canal by suction or dry mopping. A frequent problem in resistant cases is the difficulty in applying lotions and ointments satisfactorily to the relatively inaccessible affected skin. The most effective method is to introduce a ribbon gauze dressing or a sponge wick soaked with corticosteroid ear drops. When this is not practical, the ear should be gently cleansed with a probe covered in cotton wool and the patient should be encouraged to lie with the affected ear uppermost for 10 minutes after the canal has been filled with a liberal quantity of the appropriate solution.

If infection is present, a topical anti-infective that is not used systemically (such as neomycin or clioquinol) may be used, but for only about a week as excessive use may result in fungal infections; these may be difficult to treat and require expert advice. Solutions containing an anti-infective and a corticosteroid (such as Locorten-Vioform®) are used for treating cases where infection is present with inflammation and eczema.

For severe pain associated with otitis externa, a simple analgesic, such as paracetamol or ibuprofen, can be used. A systemic antibacterial can be used if there is spreading cellulitis or if the patient is systemically unwell. When a resistant staphylococcal infection (a boil) is present in the external auditory meatus, flucloxacillin is the drug of choice; ciprofloxacin may be needed in pseudomonal infections, which may occur if the patient has diabetes or is immunocompromised.

11.1.1 Anti-inflammatory preparations

Drug: acetic acid

Indications: treatment of superficial infections of the external auditory canal

Cautions: none noted

Contra-indications: none noted

Available forms: pump-action spray containing glacial acetic acid 2%

Dose: 1 metered dose (60mg) sprayed into the affected ear at least 3 times daily, with a maximum dosage of 1 spray every 2–3 hours; continue treatment until 2 days after symptoms have disappeared but for no longer than 7 days

Side-effects: none noted

Status: permitted

Drug: betamethasone

Indications: eczematous inflammation in otitis externa

Cautions: prolonged use of topical corticosteroid ear preparations should be avoided

Contra-indications: corticosteroid ear preparations should be avoided in the presence of an untreated ear infection; if infection is present, the corticosteroid should be used in combination with a suitable anti-infective

Available forms: drops (for ear, eye, or nose), betamethasone sodium phosphate 0.1% (10mL pack)

Dose: ear, apply 2–3 drops every 2–3 hours; reduce frequency when relief obtained

Side-effects: local sensitivity reactions may occur

Status: permitted

11.1.2 Anti-infective preparations

Drug: dexamethasone (with antibacterial – Otomize®)

Indications: eczematous inflammation in otitis externa

Cautions: prolonged use of topical corticosteroid ear preparations should be avoided

Contra-indications: none noted

Available forms: ear spray, dexamethasone 0.1%, neomycin sulphate 3250 units/mL, glacial acetic acid 2% (5mL pump-action aerosol unit)

Dose: ear, adult and child over 2 years: apply 1 metered spray 3 times daily

Side-effects: local sensitivity reactions may occur

Status: permitted

Drug: flumetasone and clioquinol (Locorten-Vioform®)

Indications: mild bacterial or fungal infections in otitis externa

Cautions: prolonged use of topical corticosteroid ear preparations should be avoided; manufacturer advises avoid in perforated tympanic membrane (but used by specialists for short periods)

Contra-indications: corticosteroid ear preparations should be avoided in the presence of an untreated ear infection. If infection is present, the corticosteroid should be used in combination with a suitable anti-infective. Also iodine sensitivity

Available forms: ear drops, flumetasone pivalate 0.02%, clioquinol 1% (7.5mL pack)

Dose: adult and child over 2 years: apply 2–3 drops into the ear twice daily for 7–10 days

Side-effects: local sensitivity reactions may occur; stains skin and clothing

Status: permitted

Drug: framycetin sulphate (Sofradex®)

Indications: bacterial infection in otitis externa

Cautions: see notes above and avoid prolonged use

Contra-indications: perforated tympanic membrane

Available forms: drops (for ear or eye), dexamethasone (as sodium metasulphobenzoate) 0.05%, framycetin sulphate 0.5%, gramicidin 0.005% (10mL pack)

Dose: ear, apply 2–3 drops 3–4 times daily

Side-effects: local sensitivity

Status: permitted

11.1.3 Removal of ear wax

Wax is a normal bodily secretion that provides a protective film on the meatal skin and only needs to be removed if it causes hearing loss or interferes with a proper view of the ear drum. Wax can be softened using simple remedies such as olive oil ear drops; sodium bicarbonate ear drops are also effective, but may cause dryness of the ear canal. If the wax is hard and impacted, the drops can be used twice daily for several days and this may reduce the need for mechanical removal of the wax. The patient should lie with the affected ear uppermost for five to 10 minutes after a generous amount of the softening remedy has been introduced into the ear.

Drug: sodium bicarbonate

Indications: removal of ear wax

Cautions: none noted

Contra-indications: none noted

Available forms: ear drops, sodium bicarbonate 5% (10mL pack)

Dose: see notes above

Side-effects: see notes above

Status: permitted

11.2 Drugs acting on the nose

11.2.1 Drugs used in nasal allergy

Mild allergic rhinitis is controlled by antihistamines (see section 3.4, p39) or topical nasal corticosteroids. Topical nasal decongestants can be used for a short period to relieve congestion and allow penetration of a topical nasal corticosteroid.

More persistent symptoms and nasal congestion can be relieved by topical nasal corticosteroids; sodium cromoglicate is an alternative, but may be less effective. Topical antihistamines are considered less effective than topical corticosteroids but probably more effective than cromoglicate. In seasonal allergic rhinitis (for example, hay fever), treatment should begin two to three weeks before the season commences and may have to be continued for several months; continuous treatment may be required for years in perennial rhinitis.

Very disabling symptoms occasionally justify the use of systemic corticosteroids for short periods (see section 3.2, p36). They may also be used at the beginning of a course of treatment with a corticosteroid spray to relieve severe mucosal oedema and allow the spray to penetrate the nasal cavity.

Nasal preparations containing corticosteroids (betamethasone, fluticasone) have a useful role in the prophylaxis and treatment of allergic rhinitis (see notes above).

Cautions

Corticosteroid nasal preparations should be avoided in the presence of untreated nasal infections. Patients transferred from systemic corticosteroids may experience exacerbation of some symptoms. Systemic absorption may follow nasal administration, particularly if high doses are used or if treatment is prolonged; for cautions and side-effects of systemic corticosteroids, see section 3.2 (p36).

Side-effects

Local side-effects include dryness, irritation of nose and throat and epistaxis. Nasal ulceration has been reported. Nasal septal perforation (usually following nasal surgery) occurs very rarely. Nasal ulceration has been reported, but occurs commonly with nasal preparations containing fluticasone furoate. Raised intra-ocular pressure or glaucoma may occur rarely. Headache, smell and taste disturbances may also occur. Hypersensitivity reactions, including bronchospasm, have been reported.

Drug: beclometasone dipropionate

Indications: prophylaxis and treatment of allergic and vasomotor rhinitis

Cautions: see notes above

Contra-indications: none noted

Available forms: nasal spray, beclometasone dipropionate 50 micrograms/metered spray (100-spray unit with applicator)

Dose: adult and child over 6 years: 100 micrograms (2 sprays) into each nostril twice daily; maximum total 400 micrograms (8 sprays) daily; when symptoms controlled, reduce dose to 50 micrograms (1 spray) into each nostril twice daily

Side-effects: see noted above

Status: permitted

Drug: betamethasone sodium phosphate

Indications: non-infected inflammatory conditions of nose

Cautions: see notes above

Contra-indications: see notes above

Available forms: drops (for ear, eye, or nose), betamethasone sodium phosphate 0.1% (10mL pack)

Dose: nose, 2–3 drops into each nostril 2–3 times daily

Side-effects: see notes above

Status: permitted

Drug: fluticasone propionate

Indications: prophylaxis and treatment of allergic rhinitis and perennial rhinitis

Cautions: see notes above

Contra-indications: none noted

Available forms: aqueous nasal spray, fluticasone propionate 50 micrograms/metered spray (60-spray unit and 150-spray unit with applicator)

Dose: rhinitis, 100 micrograms (2 sprays) into each nostril once daily, preferably in the morning, increased to maximum twice daily if required; when control achieved, reduce to 50 micrograms (1 spray) into each nostril once daily

Side-effects: see notes above

Status: permitted

11.2.2 Cromoglicate

Drug: sodium cromoglicate (sodium cromoglycate)

Indications: prophylaxis of allergic rhinitis

Cautions: none noted

Contra-indications: none noted

Available forms: 4% aqueous nasal spray, sodium cromoglicate 4% (5.2mg/spray) (150-spray unit with pump)

Dose: adult and child: 1 spray into each nostril 2–4 times daily

Side-effects: local irritation; rarely transient bronchospasm

Status: permitted

11.2.3 Topical nasal decongestants

Symptoms of nasal congestion associated with vasomotor rhinitis and the common cold can be relieved by the short-term use (usually not longer than seven days) of decongestant nasal drops and sprays. These all contain sympathomimetic drugs that exert their effect by vasoconstriction of the mucosal blood vessels, which in turn reduces oedema of the nasal mucosa. They are of limited value because they can give rise to a rebound congestion (rhinitis medicamentosa) on withdrawal, due to a secondary vasodilatation with a subsequent temporary increase in nasal congestion. This in turn tempts the further use of the decongestant, leading to a vicious cycle of events. Sodium chloride 0.9% given as nasal drops or spray may relieve nasal congestion by helping to liquefy mucous secretions.

Drug: sodium chloride

Indications: nasal congestion

Cautions: none noted

Contra-indications: none noted

Available forms: nasal drops, 0.9% sodium chloride (10mL pack); Sterimar Isotonic Nasal Spray® (100mL pack)

Dose: as follows:
- nasal drops: 2–3 drops into each nostril as required
- nasal spray: 1 spray into each nostril as required

Status: permitted

Drug: xylometazoline hydrochloride

Indications: nasal congestion

Cautions: hyperthyroidism; diabetes mellitus; ischaemic heart disease; hypertension; elderly; prostatic hypertrophy (risk of acute retention); also, avoid excessive or prolonged use

Contra-indications: none noted

Available forms: nasal drops, xylometazoline hydrochloride 0.1% (10mL pack); nasal spray, xylometazoline hydrochloride 0.1% (10mL pack)

Dose: as follows:
- nasal drops: 2–3 drops into each nostril 2–3 times daily when required; maximum duration 7 days; not recommended for children under 12 years
- nasal spray: 1 spray into each nostril 1–3 times daily when required; maximum duration 7 days; not recommended for children under 12 years

Side-effects: local irritation, nausea, headache; after excessive use tolerance with diminished effect, rebound congestion; cardiovascular effects also reported

Status: permitted

11.3 Drugs acting on the oropharynx

11.3.1 Drugs for oral ulceration, inflammation and sore throat

Ulceration of the oral mucosa may be caused by trauma (physical or chemical), recurrent aphthae, infections, carcinoma, dermatological disorders, nutritional deficiencies, gastro-intestinal disease, haematopoietic disorders and drug therapy. It is important to establish the diagnosis in each case as the majority of these lesions require specific management in addition to local treatment. Local treatment aims to protect the ulcerated area, to relieve pain, to reduce inflammation or to control secondary infection. Patients with an unexplained mouth ulcer of more than three weeks' duration require an urgent referral to hospital to exclude oral cancer.

Antiseptic mouthwashes

Secondary bacterial infection may be a feature of any mucosal ulceration; it can increase discomfort and delay healing. Use of chlorhexidine mouthwash is often beneficial and may accelerate healing of recurrent aphthae.

Local analgesics

Local analgesics have a limited role in the management of oral ulceration. When applied topically, their action is of a relatively short duration so that analgesia cannot be maintained continuously throughout the day. The main indication for a topical local analgesic is to relieve the pain of otherwise intractable oral ulceration, particularly when due to major aphthae. For this purpose, lidocaine 5% ointment is applied to the ulcer. When local anaesthetics are used in the mouth, care must be taken not to produce anaesthesia of the pharynx before meals as this might lead to choking.

Benzydamine mouthwash or spray may be useful in reducing the discomfort associated with a variety of ulcerative conditions. Some patients find the full-strength mouthwash causes some stinging; for them, it should be diluted with an equal volume of water.

Choline salicylate dental gel has some analgesic action and may provide relief for recurrent aphthae, but excessive application or confinement under a denture irritates the mucosa and can itself cause ulceration.

Mechanical protection

Carmellose gelatine paste may relieve some discomfort arising from ulceration by protecting the ulcer site. As the paste adheres to dry musosa, it is difficult to apply to the tongue and oropharynx.

Drug: benzydamine hydrochloride

Indications: painful inflammatory conditions of oropharynx

Cautions: none noted

Contra-indications: none noted

Available forms: oral rinse, green, benzydamine hydrochloride 0.15% (300mL pack); spray, benzydamine hydrochloride 0.15% (30mL unit)

Dose: as follows:
- oral rinse, adult and adolescent over 12 years: rinse or gargle, using 15mL (dilute with an equal volume of water if stinging occurs) every 1.5–3 hours as required, usually for not more than 7 days
- spray, adult: 4–8 sprays on to affected area every 1.5–3 hours

Side-effects: occasional numbness or stinging; rarely hypersensitivity reactions

Status: permitted

Drug: carmellose sodium

Indications: mechanical protection of oral and perioral lesions

Cautions: none noted

Contra-indications: none noted

Available forms: protective paste (oral paste), carmellose sodium 16.7%, gelatine 16.7%, in Plastibase® (30g tube)

Dose: apply a thin layer after meals

Side-effects: none noted

Status: permitted

Drug: cetylpyridinium chloride (Merocets Lozenges®)

Indications: symptomatic relief of sore throat

Cautions: none noted

Contra-indications: none noted

Available forms: lozenges containing cetylpyridinium chloride 1.4mg (24-lozenge pack)

Dose: dissolve 1 lozenge slowly in the mouth every 3 hours

Side-effects: none noted

Status: permitted

Drug: choline salicylate dental gel

Indications: mild oral and perioral lesions

Cautions: not to be applied to not to be applied to dentures: leave at least 30 minutes before re-insertion of dentures; frequent application, especially in children, may give rise to salicylate poisoning

Contra-indications: children under 16 years

Available forms: oral gel, choline salicylate 8.7% in a flavoured gel basis (15g pack)

Dose: adult and child over 16 years: apply 0.5-inch of gel with gentle massage not more often than every 3 hours

Side-effects: none noted

Status: permitted

Drug: lidocaine

Indications: relief of pain in oral lesions

Cautions: avoid prolonged use; hypersensitivity; avoid anaesthesia of the pharynx before meals – risk of choking

Contra-indications: none noted

Available forms: ointment, lidocaine 5% in a water-miscible basis (15g pack)

Dose: rub sparingly and gently on affected areas

Side-effects: none noted

Status: permitted

Drug: Strepsils Extra Strength Lozenge®

Indications: symptomatic relief of sore throat

Cautions: none noted

Contra-indications: none noted

Available forms: lozenges containing hexylresorcinol 2.4mg (36-lozenge pack)

Dose: dissolve 1 lozenge slowly in the mouth every 3 hours as required

Side-effects: none noted

Status: permitted

Drug: Strepsils Honey and Lemon Lozenge®

Indications: Symptomatic relief of mouth and throat infections

Cautions: none noted

Contra-indications: none noted

Available forms: lozenges containing 2,4- Dichlorobenzyl alcohol 1.2mg (36-lozenge pack)

Dose: dissolve 1 lozenge slowly in the mouth every 2–3 hours as required

Side-effects: none noted

Status: permitted

11.3.2 Oropharyngeal anti-infective drugs

The most common cause of a sore throat is a viral infection that does not benefit from anti-infective treatment. Streptococcal sore throats require systemic penicillin therapy (see section 5.1.1, p61). Acute ulcerative gingivitis (Vincent's infection) responds to systemic metronidazole (see section 5.1.7, p68).

Oropharyngeal fungal infections

Fungal infections of the mouth are usually caused by Candida spp. (candidiasis or candidosis). Different types of oropharyngeal candidiasis are managed as follows:

Thrush

Acute pseudomembranous candidiasis (thrush) is usually an acute infection but it may persist for months in patients receiving inhaled corticosteroids, cytotoxics or broad-spectrum antibacterials. When thrush is associated with corticosteroid inhalers, rinsing the mouth with water immediately after using the inhaler may avoid the problem. Treatment with nystatin or miconazole may be needed. Fluconazole (see section 5.2, p71) is effective for unresponsive infections, or if a topical antifungal drug cannot be used, or if the patient has dry mouth.

Acute erythematous candidiasis

Acute erythematous (atrophic) candidiasis is a relatively uncommon condition associated with corticosteroid and broad-spectrum antibacterial use and with HIV disease. It is usually treated with fluconazole (see section 5.2, p71).

Drugs used in oropharyngeal candidiasis

Nystatin is not absorbed from the gastro-intestinal tract and is applied locally (as a suspension) to the mouth for treating local fungal infections. Miconazole is applied locally (as an oral gel) in the mouth but it is absorbed to the extent that potential interactions need to be considered. Fluconazole (see section 5.2, p71) is given by mouth for infections that do not respond to topical therapy or when topical therapy cannot be used. It is reliably absorbed and effective.

Drug: miconazole

Indications: prevention and treatment of oral and intestinal fungal infections, treatment of localised lesions

Cautions: avoid in acute porphyria

Contra-indications: none stated

Available forms: oral gel, sugar-free, orange-flavoured, miconazole 24mg/mL (20mg/g) (80g tube)

Dose: prevention and treatment of oral and intestinal fungal infections, 5–10mL in the mouth after food 4 times daily, retained near oral lesions before swallowing; treatment should be continued for 48 hours after lesions have healed; for treatment of localised lesions for adult and child over 2 years, smear small amount on affected area with clean finger 4 times daily for 5–7 days (dental prostheses should be removed at night and brushed with gel), treatment should be continued for 48 hours after lesions have healed

Side-effects: nausea, vomiting; rash; with buccal tablets, abdominal pain, taste disturbance, burning sensation at application site, pruritus, oedema; with oral gel, very rarely diarrhoea (usually on long-term treatment), hepatitis, toxic epidermal necrolysis, Stevens-Johnson syndrome

Status: permitted

Drug: nystatin

Indications: oral and perioral fungal infections

Cautions: none noted

Contra-indications: none noted

Available forms: oral suspension, nystatin 100,000 units/mL (30mL pack)

Dose: treatment, adult and child: 100,000 units 4 times daily after food, usually for 7 days (continued for 48 hours after lesions have resolved)

Side-effects: oral irritation and sensitisation, nausea reported

Status: permitted

11.3.3 Mouthwashes and gargles

Superficial infections of the mouth are often helped by warm mouthwashes, which have a mechanical cleansing effect and cause some local hyperaemia. However, to be effective, they must be used frequently and vigorously. A warm saline mouthwash is ideal and can be prepared by dissolving half a teaspoonful of salt in a glassful of warm water.

Chlorhexidine is an effective antiseptic, which has the advantage of inhibiting plaque formation on the teeth. However, it does not completely control plaque deposition and is not a substitute for effective toothbrushing. Moreover, chlorhexidine preparations do not penetrate significantly into stagnation areas and are therefore of little value in the control of dental caries or of periodontal disease once pocketing has developed. Chlorhexidine mouthwash is used in the treatment of denture stomatitis. It is also used in the prevention of oral candidiasis in immunocompromised patients. Chlorhexidine mouthwash reduces the incidence of alveolar osteitis following tooth extraction. Chlorhexidine mouthwash should not be used for the prevention of endocarditis in patients undergoing dental procedures. Chlorhexidine can be used as a mouthwash, for secondary infection in mucosal ulceration and for controlling gingivitis, as an adjunct to other oral hygiene measures. Chlorhexidine preparations are of little value in the control of acute necrotising ulcerative gingivitis.

Drug: chlorhexidine gluconate

Indications: oral hygiene and plaque inhibition, oral candidiasis, gingivitis and management of aphthous ulcers, denture stomatitis

Cautions: none noted

Contra-indications: none noted

Available forms: mouthwash, chlorhexidine gluconate 0.2% (300mL pack)

Dose: rinse mouth with 10mL for about 1 minute twice daily; for denture stomatitis, cleanse and soak dentures in mouthwash solution for 15 minutes twice daily

Side-effects: mucosal irritation (if desquamation occurs, discontinue treatment or dilute mouthwash with an equal volume of water); taste disturbance; reversible brown staining of teeth and of silicate or composite restorations; tongue discoloration; parotid gland swelling reported; note: chlorhexidine gluconate may be incompatible with some ingredients in toothpaste, so leave an interval of at least 30 minutes between using mouthwash and toothpaste

Status: permitted

12.0 Skin

12.1 Emollients

Emollients soothe, smooth and hydrate the skin and are indicated for all dry or scaling disorders. Their effects are short-lived and they should be applied frequently even after improvement occurs. They are useful in dry and eczematous disorders, and to a lesser extent in psoriasis. The choice of an appropriate emollient will depend on the severity of the condition, patient preference and the site of application. Emollients should be applied in the direction of hair growth. Ointments may exacerbate acne and folliculitis. Some ingredients rarely cause sensitisation and this should be suspected if an eczematous reaction occurs. The use of aqueous cream as a leave-on emollient may increase the risk of skin reactions, particularly in eczema.

Emulsifying ointment in contact with dressings and clothing is easily ignited by a naked flame. The risk is greater when these preparations are applied to large areas of the body, and clothing or dressings become soaked with the ointment. Patients should be told to keep away from fire or flames, and not to smoke when using these preparations. The risk of fire should be considered when using large quantities of any paraffin-based emollient. Preparations such as aqueous cream and emulsifying ointment can be used as soap substitutes for hand washing and in the bath; the preparation is rubbed on the skin before rinsing off completely.

Drug: aqueous cream

Indications: see notes above

Cautions: none noted

Contra-indications: none noted

Available forms: cream (100g pack)

Dose: see notes above

Side-effects: see notes above

Status: permitted

Drug: emulsifying ointment

Indications: see notes above

Cautions: none noted

Contra-indications: none noted

Available forms: ointment (500g pack)

Dose: see notes above

Side-effects: see notes above

Status: permitted

Drug: white soft paraffin

Indications: see notes above

Cautions: none noted

Contra-indications: none noted

Available forms: ointment (100g pack)

Dose: see notes above

Side-effects: see notes above

Status: permitted

12.1.1 Preparations for sore lips

Drug: Blistex Relief Cream®

Indications: relief of occasional cold sores, cracked, chapped and sore lips

Cautions: none noted

Contra-indications: none noted

Available forms: cream containing ammonia solution aromatic 6.04%, ammonia solution strong 0.1%, liquefied phenol 0.494% (5g tube)

Dose: apply every hour at appearance of first symptoms

Side-effects: none noted

Status: permitted

12.2 Barrier preparations

Barrier preparations often contain water-repellent substances such as dimeticone or other silicones. They are used on the skin around stomas, bedsores and pressure areas in the elderly where the skin is intact. Where the skin has broken down, barrier preparations have a limited role in protecting adjacent skin.

Drug: Sudocrem®

Indications: see notes above

Cautions: none noted

Contra-indications: none noted

Available forms: cream (100g pack)

Dose: see notes above

Side-effects: see notes above

Status: permitted

12.3 Topical corticosteroids

Topical corticosteroids are used for the treatment of inflammatory conditions of the skin (other than those arising from an infection), and in particular eczema, contact dermatitis, insect stings and eczema of scabies. Corticosteroids suppress the inflammatory reaction during use; they are not curative and on discontinuation a rebound exacerbation of the condition may occur. They are generally used to relieve symptoms and suppress signs of the disorder when other measures such as emollients are ineffective.

Topical corticosteroids are of no value in the treatment of urticaria and they are contra-indicated in rosacea; they may worsen ulcerated or secondarily infected lesions. They should not be used indiscriminately in pruritus (where they will only benefit if inflammation is causing the itch) and are not recommended for acne vulgaris.

Hydrocortisone cream 1% can be used for up to seven days to treat uninfected inflammatory lesions on the lips. Hydrocortisone and miconazole cream is useful where infection by susceptible organisms and inflammation co-exist, particularly for initial treatment (up to seven days): for example, in angular cheilitis. Organisms susceptible to miconazole include candida spp. and many gram-positive bacteria including streptococci and staphylococci.

Cautions
Avoid prolonged use of a topical corticosteroid on the face (and keep away from eyes).

Contra-indications
Topical corticosteroids are contra-indicated in untreated bacterial, fungal or viral skin lesions, in acne, in rosacea and in perioral dermatitis; potent corticosteroids are contra-indicated in widespread plaque psoriasis.

Side-effects
Mild and moderately potent topical corticosteroids are associated with few side-effects but care is required in the use of potent and very potent corticosteroids. Absorption through the skin can rarely cause adrenal suppression and even Cushing's syndrome, depending on the area of the body being treated and the duration of treatment. Absorption is greatest where the skin is thin or raw and from intertriginous areas; it is increased by occlusion. Local side-effects include:

- spread and worsening of untreated infection
- thinning of the skin, which may be restored over a period after stopping treatment but the original structure may never return
- irreversible striae atrophicae and telangiectasia
- contact dermatitis
- perioral dermatitis
- acne, or worsening of acne or rosacea
- mild depigmentation, which may be reversible
- hypertrichosis also reported

Drug: betamethasone valerate

Indications: severe inflammatory skin disorders such as eczemas unresponsive to less potent corticosteroids; psoriasis (potency – potent)

Cautions: see notes above

Contra-indications: see notes above

Available forms: cream, betamethasone (as valerate) 0.1% (30g pack)

Dose: apply thinly 1–2 times daily

Side-effects: see notes above

Status: permitted

Drug: clobetasone butyrate (Eumovate®)

Indications: eczemas and dermatitis of all types; maintenance between courses of more potent corticosteroids (potency – moderate)

Cautions: see notes above

Contra-indications: see notes above

Available forms: cream, clobetasone butyrate 0.05% (15g pack)

Dose: apply thinly 1–2 times daily

Side-effects: see notes above

Status: permitted

Drug: hydrocortisone

Indications: mild inflammatory skin disorders such as eczemas (potency – mild)

Cautions: see notes above

Contra-indications: see notes above

Available forms: cream, hydrocortisone 1% (15g and 30g packs)

Dose: apply thinly 1–2 times daily

Side-effects: see notes above

Status: permitted

12.4 Topical local anaesthetics and antipruritics

12.4.1 Topical antihistamines

Topical antihistamines can cause skin sensitivity.

Drug: mepyramine maleate

Indications: symptomatic relief of skin irritation caused by insect stings, insect bites and nettle stings

Cautions: see notes above

Contra-indications: none noted

Available forms: cream containing mepyramine maleate 2% (20g pack)

Dose: apply to the affected area 2–3 times daily

Status: permitted

12.4.2 Local anaesthetics

These agents can cause skin irritation.

Drug: benzocaine

Indications: symptomatic relief of pain from minor, superficial burns and scalds

Cautions: do not spray near eyes or mouth

Contra-indications: none noted

Available forms: aerosol spray containing benzocaine 1% (60mL pack)

Dose: spray the affected area once for 2–3 seconds; the application may be repeated once only after 15 minutes

Side-effects: see notes above

Status: permitted

Drug: benzocaine and mepyramine (Wasp-eze®)

Indications: for treatment of insect bites and stings, nettle stings and jellyfish stings

Cautions: do not spray near eyes or mouth

Contra-indications: none noted

Available forms: aerosol spray containing benzocaine 1% (60mL pack)

Dose: spray the affected area once for 2–3 seconds; the application may be repeated once only after 15 minutes

Side-effects: see notes above

Status: permitted

12.5 Topical preparations for acne

In mild to moderate acne, comedones and inflamed lesions respond well to benzoyl peroxide. It is usual to start with a lower strength and to increase the concentration of benzoyl peroxide gradually. Adverse effects include local skin irritation, particularly when therapy is initiated, but the scaling and redness often subside with treatment continued at a reduced frequency of application. If the acne does not respond after two months, then use of a topical antibacterial should be considered.

Drug: benzoyl peroxide

Indications: acne vulgaris

Cautions: avoid contact with eyes, mouth and mucous membranes; may bleach fabrics and hair; avoid excessive exposure to sunlight

Contra-indications: none noted

Available forms: cream, benzoyl peroxide 5% in a non-greasy basis (40g pack)

Dose: apply 1–2 times daily, preferably after washing with soap and water; start treatment with lower-strength preparations

Side-effects: skin irritation (reduce frequency or suspend use until irritation subsides and reintroduce at reduced frequency)

Status: permitted

12.6 Preparations for warts and calluses

Warts (verrucas) are caused by a human papillomavirus that most frequently affects the hands, the feet (plantar warts) and the anogenital region (see below); treatment usually relies on local tissue destruction. Warts may regress on their own and treatment is required only if the warts are painful, unsightly or persistent, or cause distress.

Salicylic acid is a useful keratolytic, which may be considered first; it is also suitable for the removal of corns and calluses. Preparations of salicylic acid in a collodion basis are available, but some patients may develop an allergy to colophony in the formulation. Cryotherapy causes pain, swelling and blistering, and may be no more effective than topical salicylic acid in the treatment of warts.

Drug: salicylic acid

Indications: warts, particularly plantar warts, verrucas, corns and calluses

Cautions: significant peripheral neuropathy, patients with diabetes at risk of neuropathic ulcers; impaired peripheral circulation; protect surrounding skin and avoid broken skin; not suitable for application to face, anogenital region or large areas

Contra-indications: none noted

Available forms: Salatac® Paint, salicylic acid 16.7%, lactic acid 16.7%, in flexible collodion, 10mL (with applicator); Bazuka Treatment Gel®, salicylic acid 12%, lactic acid 4%

Dose: apply daily, advise patient to apply carefully to wart and to protect surrounding skin (for example, with soft paraffin or specially designed plaster); rub wart surface gently with file or pumice stone once weekly; treatment may need to be continued for up to 3 months

Side-effects: skin irritation, skin ulceration (with high concentrations)

Status: permitted

12.7 Anti-infective skin preparations

12.7.1 Antibacterial preparations

Although many antibacterial drugs are available in topical preparations, some are potentially hazardous, and frequently their use is not necessary if adequate hygienic measures can be taken. Moreover, not all skin conditions that are oozing, crusted or characterised by pustules are actually infected. To minimise the development of resistant organisms, it is advisable to limit the choice of antibacterials applied topically to those not used systemically. Sodium fusidate is a narrow-spectrum antibacterial used for staphylococcal infections. Mupirocin is not related to any other antibacterial in use; it is effective for skin infections, particularly those due to Gram-positive organisms, but it is not indicated for pseudomonal infection. Although Staphylococcus aureus strains with low-level resistance to mupirocin are emerging, it is generally useful in infections resistant to other antibacterials. To avoid the development of resistance, mupirocin or fusidic acid should not be used for longer than 10 days.

Drug: fusidic acid

Indications: staphylococcal skin infections

Cautions: see notes above; avoid contact with eyes

Contra-indications: none noted

Available forms: cream, fusidic acid 2% (15g tube)

Dose: apply 3–4 times daily

Side-effects: rarely hypersensitivity reactions

Status: permitted

Drug: mupirocin

Indications: bacterial skin infections (see also notes above)

Cautions: none noted

Contra-indications: none noted

Available forms: cream, mupirocin (as mupirocin calcium) 2% (15g tube)

Dose: adult and child over 1 year: apply up to 3 times daily for up to 10 days

Side-effects: local reactions including urticaria, pruritus, burning sensation, rash

Status: permitted

Drug: silver sulfadiazine

Indications: prophylaxis and treatment of infection in burn wounds; as an adjunct to prophylaxis of infection in extensive abrasions; for conservative management of fingertip injuries

Cautions: G6PD deficiency; may inactivate enzymatic debriding agents: concomitant use may be inappropriate

Contra-indications: sensitivity to sulfonamides

Available forms: cream, silver sulfadiazine 1% (20g pack)

Dose: burns: apply daily or more frequently if very exudative; finger-tip injuries: apply every 2–3 days

Side-effects: allergic reactions including burning, itching and rashes; argyria reported following prolonged use; leucopenia reported (monitor blood levels)

Status: permitted

12.7.2 Antifungal preparations

Most localised fungal infections are treated with topical preparations. To prevent relapse, local antifungal treatment should be continued for one to two weeks after the disappearance of all signs of infection.

Ringworm infection can affect the scalp (tinea capitis), body (tinea corporis), groin (tinea cruris), hand (tinea manuum), foot (tinea pedis, athlete's foot) or nail (tinea unguium). Most local ringworm infections can be treated adequately with topical antifungal preparations. The imidazole antifungals clotrimazole and miconazole are all effective. Terbinafine cream is also effective but it is more expensive. Antifungal dusting powders are of little therapeutic value in the treatment of fungal skin infections and may cause skin irritation; they may have some role in preventing re-infection.

Candidal skin infections can be treated with a topical imidazole antifungal, such as clotrimazole, or miconazole; topical terbinafine is an alternative. Refractory candidiasis requires systemic treatment (see section 5.2, p71) generally with a triazole such as fluconazole.

Miconazole cream is used in the fissures of angular cheilitis when associated with Candida.

Cautions

Contact with eyes and mucous membranes should be avoided.

Side-effects

Occasional local irritation and hypersensitivity reactions include mild burning sensation, erythema and itching. Treatment should be discontinued if these are severe.

Drug: clotrimazole

Indications: fungal skin infections

Cautions: see notes above

Available forms: cream, clotrimazole 1% (20g pack)

Dose: apply 2–3 times daily

Side-effects: see notes above

Status: permitted

Drug: miconazole nitrate

Indications: fungal skin infections

Cautions: see notes above

Available forms: cream, miconazole nitrate 2% (15g pack, 20g pack); powder, miconazole nitrate 2% (30g pack)

Dose: apply twice daily, continuing for 10 days after lesions have healed; for nail infections, apply 1–2 times daily

Side-effects: see notes above

Status: permitted

Drug: terbinafine

Indications: fungal skin infections

Cautions: avoid contact with eyes

Contra-indications: none noted

Available forms: cream, terbinafine hydrochloride 1% (15g pack)

Dose: apply thinly 1–2 times daily for up to 1 week in tinea pedis, 1–2 weeks in tinea corporis and tinea cruris, 2 weeks in cutaneous candidiasis and pityriasis versicolor; review after 2 weeks

Side-effects: see notes above

Status: permitted

12.7.3 Antiviral preparations

Aciclovir cream is licensed for the treatment of initial and recurrent labial and genital herpes simplex infections; treatment should begin as early as possible. Systemic treatment is necessary for buccal or vaginal infections and for herpes zoster (shingles). Herpes labialis: aciclovir cream can be used for the treatment of initial and recurrent labial herpes simplex infections (cold sores). It is best applied at the earliest possible stage, usually when prodromal changes of sensation are felt in the lip and before vesicles appear.

Drug: aciclovir (acyclovir)

Indications: see notes above

Cautions: avoid contact with eyes and mucous membranes

Contra-indications: none noted

Available forms: cream, aciclovir 5% (2g pack)

Dose: apply to lesions every 4 hours (5 times daily) for 5–10 days, starting at first sign of attack

Side-effects: transient stinging or burning; occasionally erythema, itching or drying of the skin

Status: permitted

12.7.4 Parasiticidal preparations

Scabies

Permethrin is used for the treatment of scabies (Sarcoptes scabiei); malathion can be used if permethrin is inappropriate. All members of the affected household should be treated simultaneously. Treatment should be applied to the whole body including the scalp, neck, face and ears. Particular attention should be paid to the webs of the fingers and toes, and lotion brushed under the ends of nails. It is now recommended that malathion and permethrin should be applied twice, one week apart. It is important to warn users to reapply treatment to the hands if they are washed. Patients with hyperkeratotic scabies may require two or three applications of acaricide on consecutive days to ensure that enough penetrates the skin crusts to kill all the mites.

Head lice

Dimeticone is effective against head lice (Pediculus humanus capitis) and acts on the surface of the organism. Malathion, an organophosphorus insecticide, is an alternative, but resistance has been reported. Head lice infestation (pediculosis) should be treated using lotion or liquid formulations only if live lice are present. Shampoos are diluted too much in use to be effective. In general, a course of treatment for head lice should consist of two applications of the product seven days apart to kill lice emerging from any eggs that survive the first application. All affected household members should be treated simultaneously.

Crab lice

Permethrin and malathion are used to eliminate crab lice (Pthirus pubis). An aqueous preparation should be applied, allowed to dry naturally and washed off after 12 hours; a second treatment is needed after seven days to kill lice emerging from surviving eggs. All surfaces of the body should be treated, including the scalp, neck and face (paying particular attention to the eyebrows and other facial hair). A different insecticide should be used if a course of treatment fails.

Malathion is recommended for scabies, head lice and crab lice (for details, see notes above). The risk of systemic effects associated with one or two applications of malathion is considered to be very low. Dimeticone coats head lice and interferes with water balance in lice by preventing the excretion of water; it is less active against eggs and treatment should be repeated after seven days. Permethrin is effective for scabies and crab lice (for details, see notes above). Permethrin is active against head lice, but the formulation and licensed methods of application of the current products make them unsuitable for the treatment of head lice.

Drug: cyclometicone and isopropyl myristicate (Full Marks Solution®)

Indications: head lice

Cautions: avoid contact with eyes

Available forms: lotion (200mL pack)

Dose: rub into dry hair and scalp, leave on for 10 minutes then comb through using the provided comb to remove the dead lice and eggs; repeat application after 7 days

Side-effects: skin irritation

Status: permitted

Drug: dimeticone

Indications: head lice

Cautions: avoid contact with eyes

Available forms: lotion, dimeticone 4% (150mL pack)

Dose: rub into dry hair and scalp, allow to dry naturally, shampoo after minimum 8 hours (or overnight); repeat application after 7 days

Side-effects: skin irritation

Status: permitted

Drug: malathion

Indications: see notes above

Cautions: avoid contact with eyes; do not use on broken or secondarily infected skin

Contra-indications: none noted

Available forms: liquid, malathion 0.5% in an aqueous basis (50mL pack)

Dose: as follows:

- head lice: rub 0.5% preparation into dry hair and scalp, allow to dry naturally, remove by washing after 12 hours (see also notes above); repeat application after 7 days
- crab lice: apply 0.5% aqueous preparation over whole body, allow to dry naturally, wash off after 12 hours or overnight; repeat application after 7 days
- scabies: apply 0.5% preparation over whole body and wash off after 24 hours; if hands are washed with soap within 24 hours, they should be retreated; see also notes above; repeat application after 7 days. For scabies, manufacturer recommends application to the body but not necessarily to the head and neck; however, application should be extended to the scalp, neck, face and ears

Side-effects: skin irritation and hypersensitivity reactions; chemical burns also reported

Status: permitted

Drug: permethrin

Indications: see notes above and under Dose below

Cautions: avoid contact with eyes; do not use on broken or secondarily infected skin; medical supervision required for dermal cream (scabies)

Contra-indications: none noted

Available forms: cream, permethrin 5% (30g pack)

Dose: as follows:
- crab lice: adult over 18 years: apply 5% cream over whole body, allow to dry naturally and wash off after 12 hours or after leaving on overnight; repeat application after 7 days
- scabies: apply 5% preparation over whole body and wash off after 8–12 hours; manufacturer recommends application to the body but not head and neck; however, application should be extended to the scalp, neck, face and ears; larger patients may require up to two 30g packs for adequate treatment

Side-effects: pruritus, erythema and stinging; rarely rashes and oedema

Status: permitted

12.8 Topical circulatory preparations

These preparations are used to improve circulation in conditions such as bruising and superficial thrombophlebitis, but are of little value.

Drug: Hirudoid®

Indications: bruising and superficial soft tissue injuries

Cautions: none noted

Contra-indications: none noted

Available forms: cream, heparinoid 0.3% in a vanishing-cream basis (50g pack)

Dose: apply up to 4 times daily in superficial soft-tissue injuries and superficial thrombophlebitis

Side-effects: none noted

Status: permitted

13.0 Local anaesthesia

Local anaesthetic drugs act by causing a reversible block to conduction along nerve fibres. They vary widely in potency, toxicity, duration of action, stability, solubility in water and ability to penetrate mucous membranes. These factors determine their application: for example, topical (surface), infiltration or peripheral nerve block. The dose of local anaesthetic depends on the injection site and the procedure used. In determining the safe dosage, it is important to take account of the rate of absorption and excretion and of the potency. The patient's age, weight, physique and clinical condition, and the vascularity of the administration site and the duration of administration, must also be considered. Uptake of local anaesthetics into the systemic circulation determines their duration of action and produces toxicity.

Great care must be taken to avoid accidental intravascular injection; local anaesthetic injections should be given slowly in order to detect inadvertent intravascular administration. Local anaesthesia around the oral cavity may impair swallowing and therefore increases the risk of aspiration.

Use of vasoconstrictors
Local anaesthetics cause dilation of blood vessels. The addition of a vasoconstrictor such as adrenaline (epinephrine) to the local anaesthetic preparation diminishes local blood flow, slowing the rate of absorption and thereby prolonging the anaesthetic effect. Great care should be taken to avoid inadvertent intravenous administration of a preparation containing adrenaline, and it is not advisable to give adrenaline with a local anaesthetic injection in digits or appendages because of the risk of ischaemic necrosis. For patients with severe hypertension or unstable cardiac rhythm, the use of adrenaline with a local anaesthetic may be hazardous. For these patients, an anaesthetic without adrenaline should be used.

Cautions
Local anaesthetics should be administered with caution in elderly or debilitated patients (consider dose reduction), or in patients with impaired cardiac conduction, cardiovascular disease, hypovolaemia, shock, impaired respiratory function, epilepsy or myasthenia gravis.

Contra-indications
Local anaesthetics should not be injected into inflamed or infected tissues, nor should they be applied to damaged skin. In such circumstances, increased absorption into the blood increases the possibility of systemic side-effects, and the local anaesthetic effect may also be reduced by altered local pH.

Toxicity and side-effects
A single application of a topical lidocaine preparation does not generally cause systemic side-effects. Toxic effects after administration of local anaesthetics are a result of excessively high plasma concentrations; severe toxicity usually results from inadvertent intravascular injection or too rapid injection.

The systemic toxicity of local anaesthetics mainly involves the central nervous and cardiovascular systems. CNS effects include a feeling of inebriation and lightheadedness followed by drowsiness, numbness of the tongue and perioral region, restlessness, paraesthesia (including sensations of hot and cold), dizziness, blurred vision, nausea and vomiting, muscle twitching, tremors and convulsions. Transient excitation may also occur, followed by depression with drowsiness, respiratory failure, unconsciousness and coma. Effects on the cardiovascular system include myocardial depression and peripheral vasodilatation resulting in hypotension and bradycardia; arrhythmias and cardiac arrest can occur.

Hypersensitivity reactions occur mainly with the ester-type local anaesthetics, such as tetracaine; reactions are less frequent with the amide types, such as bupivacaine, lidocaine and ropivacaine. Cross-sensitivity reactions may be avoided by using the alternative chemical type.

Bupivacaine has a longer duration of action than other local anaesthetics. It has a slow onset of action, taking up to 30 minutes for full effect.

Drug: bupivacaine hydrochloride

Indications: peripheral nerve block; for other indications, see the full edition of the British National Formulary (www.bnf.org)

Cautions: see notes above; myocardial depression may be more severe and more resistant to treatment; cardiovascular disease; hypertension; hypotension; cerebral atheroma

Contra-indications: see notes above

Available forms: injection, anhydrous bupivacaine hydrochloride 5mg/mL (0.5%) (10mL ampoule)

Dose: peripheral nerve block, maximum 30mL, using a 5mg/mL (0.5%) solution; for other indications, see the full edition of the British National Formulary (www.bnf.org)

Side-effects: see notes above

Status: permitted

Drug: lidocaine

Indications: intravenous regional anaesthesia and nerve blocks; for other indications, see the full edition of the British National Formulary (www.bnf.org)

Cautions: see notes above; also hypertension

Contra-indications: see notes above

Available forms: injection, lidocaine hydrochloride 10mg/mL (1%) (5mL ampoule)

Dose: seek expert advice

Side-effects: see notes above

Status: permitted

Drug: lidocaine with adrenaline

Indications: intravenous regional anaesthesia and nerve blocks; for other indications, see the full edition of the British National Formulary (www.bnf.org)

Cautions: see notes above on cautions and use of vasoconstrictors; also hypertension

Contra-indications: see notes above

Available forms: injection, anhydrous lidocaine hydrochloride 10mg/mL (1%), adrenaline 1 in 200,000 (5 micrograms/mL) (20mL ampoule)

Dose: seek expert advice

Side-effects: see notes above

Status: permitted

Drug: lidocaine with prilocaine cream (EMLA®)

Indications: anaesthesia before minor skin procedures including venepuncture

Cautions: none noted

Contra-indications: none noted

Available forms: cream, lidocaine 2.5%, prilocaine 2.5% (5g tube)

Dose: as follows:
- adult and child over 1 year: anaesthesia before minor skin procedures including venepuncture, apply thick layer under occlusive dressing 1–5 hours before procedure anaesthesia on genital skin before injection of local anaesthetics in adult men: apply under occlusive dressing for 15 minutes
- anaesthesia before surgical treatment of lesions on genital mucosa in adults: apply up to 10g 5–10 minutes before procedure

Side-effects: a single application of a topical lidocaine preparation does not generally cause systemic side-effects

Status: permitted

Drug: ropivacaine hydrochloride

Indications: see the full edition of the British National Formulary (www.bnf.org)

Cautions: see notes above; also acute porphyria

Contra-indications: see notes above

Available forms: injection, ropivacaine hydrochloride 2mg/mL (10mL ampoule)

Dose: seek expert advice

Side-effects: see notes above

Status: permitted

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