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This is the 30th anniversary of the original *Havard’s Nursing Guide to Drugs*, then simply called *Nursing Guide to Drugs*, written by Margaret Havard. Margaret was a nurse educator and colleague who had worked for many years with hospital-trained nurses teaching pharmacology. Margaret's recognition of a need for an Australian book that would give nurses a guide to safe administration of medications to their patients gave her the impetus to write the first edition. Little did she imagine that 30 years later this book would still be in production and being used in all types of patient settings. This book is dedicated to Margaret.

As with the original aim of the book, *Havard’s Nursing Guide to Drugs* continues to be a guide only. This book is meant to be a companion guide to pharmacology texts, something smaller and easier to transport around and reference in the clinical situation, especially now that it is available in electronic form as well. As with previous editions, each drug has been reviewed to ensure it is still relevant to the healthcare setting, with old and obsolete drugs deleted and new drugs (or old drugs with new uses) added. New to this edition is an expanded ‘Patient teaching and advice’ section which highlights key points for teaching purposes.
THE NURSE’S ROLE IN DRUG THERAPY

The aims of administering medication are to do it safely and efficiently and to observe the patient for both desirable and undesirable effects. Therefore the nurse needs to:

- assess the patient, including medication history
- have an understanding of the legal requirements associated with the administration of drugs
- have pharmacological knowledge of the medication(s)
- be able to safely administer medications.

ASSESSING THE PATIENT

Patient assessment should be holistic, looking at the patient’s condition and personal circumstances as a whole, rather than simply as a disease to be treated. It should include:

- all current medical problems
- co-morbidities
- relevant past history
- physical assessment
- medication history (current medications, over-the-counter preparations, herbal preparations, vitamin and mineral supplements).

Medical history, co-morbidities and medication history are intertwined as a person with multiple co-morbidities often being prescribed multiple medications simultaneously (polypharmacy) increasing the risk of adverse effects and interactions. A person may see more than one medical practitioner (e.g. general practitioner (GP) plus a number of specialists) and they may not always review previous or current medications. Having prescriptions filled in multiple pharmacies may also be problematic as there is no on-going record of medications (and hence the possibility of the same prescription being filled multiple times using different brands).

People may become confused because medication can have more than one brand/trade name for the same generic drug and potentially end up taking the same drug twice (e.g. a patient taking Urex and Lasix (both trade names for frusemide) may become quickly dehydrated).

Unfortunately, people do not always complete courses of medications, especially antibiotics, and ‘keep the rest for next time’ with no understanding of the ramifications of doing this (e.g. bacteria becoming resistant to that antibiotic and the agent becoming ineffective in treating that same infection if it recurs).

Some people believe they are allergic to medications. It is important for the nurse to explore what form the supposed allergy takes (e.g. someone may mistakenly believe that he/she is allergic to morphine because he/she was nauseous and vomited after taking it (a common side-effect), whereas another patient may correctly describe an anaphylactic reaction with breathing difficulties after administration of an antibiotic).

Many people also take over-the-counter (OTC) preparations or alternative medicines, including herbal preparations, either concurrently or instead of traditional medication. OTC preparations are those that are non-prescription and are generally intended...
for short-term use only in self-limiting illnesses such as headache, heartburn and constipation. OTCs also include vitamins, minerals and herbal drugs and remedies (e.g. St John’s wort, ginseng) and unfortunately, many people consider them to be ‘safe’ because they are natural. However, many herbal drugs and remedies interact with prescription medications (e.g. St John’s wort interacts with warfarin increasing its metabolism and decreasing its effectiveness); antacids can interfere with some oral medications if not taken 2 hours apart; and non-prescription medications such as aspirin and ibuprofen can cause gastrointestinal bleeding and must only be taken at recommended doses. OTCs are readily available in pharmacies and supermarkets, with the buyer not needing to seek advice before purchasing these products.

It is essential for the nurse to establish if the patient is compliant/adherent/concordant with his or her medication regimen, and if not, why not. While these terms are sometimes used interchangeably, they do have some important differences. Compliance suggests that the patient has little input into his/her management strategy and follows doctor’s orders (power lies with the doctor), while concordance is at the other end of the spectrum, and is based on equality and respect between the patient and the health care practitioner. Adherence falls somewhere in between as there is negotiation between the patient and the health care professional which is based around the therapy (e.g. asthma management plan) (National Asthma Council, 2005). One Australian study looking at the use of antihypertensive medications found that 19% of people failed to have a second prescription filled. Furthermore, people persisted with their antihypertensive medications on average for only 20 months (Simons, Ortiz and Calcino, 2008).

Adherence is a very complex issue. Some of the factors that may lead to a patient not being adherent with a medication regimen may include:

- multiple medications
- complex dosing schedules (a person is more likely to remember a once-daily dosing schedule, compared to a 3–4 times daily regimen)
- medication difficult to take or administer (e.g. medications that have an unpleasant taste or are large in size; eye and ear drops that are difficult to instil)
- impairments including:
  - sight (e.g. unable to read directions)
  - dexterity (e.g. arthritis) may make it difficult to open containers with childproof lids or blister packs, or
  - memory (e.g. unable to remember instructions of how or when to take medication)
  - adverse effects (i.e. the person may decide that the side-effects of the medications are worse than the disease itself)
  - feeling ‘better’ and therefore not needing to take the medication any longer
  - not ‘seeing’ any effects from the medication (e.g. effects of lipid-lowering agents are not visible and these are commonly discontinued by patients)
  - cost and ease of filling prescriptions (e.g. decreased mobility or lack of transport to be able to go to the pharmacy)
— lack of knowledge/understanding of the disease process and the role of medication in disease management
— attitude towards medication, disease and/or health (e.g. a ‘devil may care’ attitude or thoughts such as ‘I have to die of something’)
— inconsistency in the messages that health providers are giving (e.g. one nurse advises the patient to take certain medications 30–60 minutes before food, while another nurse says that it doesn’t matter when the medication is taken). Not only are these inconsistent messages confusing for the patient but they also damage the trust the patient may have in the nurse(s), as well as potentially affecting the absorption and effectiveness of the medication.

Armed with all this information, the nurse is in an ideal position to support and educate the patient (see section on Patient teaching and advice).

CHILDREN AND THE ELDERLY

Children and the elderly require highly specialised nursing care and knowledge regarding administration of medications. Special care should be taken with dosages because overdose can occur easily due to smaller weights (and surface ratios), and differences in kidney and liver capacity. There are many specialised texts available that cover both these groups in detail and take into account the differences in drug administration. Specific paediatric and geriatric dosages are not generally included in this book. Doses are for the ‘average’ adult patient. The only exceptions are when a particular drug is mainly or specifically used in paediatrics (e.g. drugs used for attention deficit disorder, growth hormone).

Many older people require assistance with the administration of medications and the nurse may consider splitting or crushing tablets in order to make them easier to take. Before doing this, investigate whether the medication is available in a different oral form (e.g. liquid rather than solid) or a non-oral form (e.g. dermal, rectal, intranasal). Tablets with an enteric coating should not be crushed as these are formulated to ensure the medication passes through the stomach intact (e.g. enteric aspirin is formulated to prevent gastric irritation). Extended-release medications (often marked as CD, CR, SA, SR) are designed to release the active components over an extended period and therefore should not be crushed. There is further discussion on extended-release medication under Oral administration.

DRUGS IN SPORT

The World Anti-Doping Agency (WADA) was established in 1999 to foster a doping-free culture in sport by:
● conducting scientific research to develop new detection methods
● educating athletes and support personnel
● raising awareness and providing information about doping and its consequences
● conducting an unannounced out-of-competition testing program that complements the programs of the International Sports Federations (IFs)
● developing an independent observer program (which randomly monitors
and reports on all phases of doping control in an unbiased manner

● monitoring acceptance and compliance with the World Anti-Doping Code, which ensures all athletes in all sports are governed by the same anti-doping rules and regulations.

Groups of drugs or methods prohibited or restricted by WADA include: anabolic steroids (e.g. stanozolol, testosterone), peptide hormones (e.g. erythropoietin, insulin, tetracosactrin), growth factors and related substances (e.g. growth hormone), beta-2 adrenoceptor blocking agents (e.g. propranolol), beta-2 agonists (e.g. eformoterol, isoprenaline NOT salbutamol or salmeterol), hormone antagonists and modulators (e.g. clomiphene, aminoglutethimide, tamoxifen), diuretics (e.g. frusemide, acetazolamide, thiazide diuretics) and other masking agents (e.g. probenecid), substances enhancing oxygen transfer (e.g. haemoglobin products), blood doping (e.g. red blood cell product of any origin) and sample manipulation methods (e.g. tampering with samples or urine substitution), stimulants (e.g. amphetamines, adrenaline, pseudoephedrine), opioids (e.g. heroine, morphine), cannabinoids (e.g. marijuana), glucocorticosteroids (e.g. dexamethasone, prednisolone) and alcohol.

It is imperative that the athlete is aware of substances and methods that are prohibited at all times, substances that are prohibited in-competition and substances that are prohibited in particular sports (WADA, 2011).

PREGNANCY

Any medication (including OTCs, herbal preparations, alternative therapies or chemicals such as alcohol) has the potential to reach the developing fetus via the maternal circulation if taken during pregnancy. The risk to the fetus is dependent on a number of factors, including fetal gestational age on exposure (i.e. the fetus is most at risk during the first trimester when cells are rapidly proliferating and organs, muscles, CNS, arms, legs, toes and fingers are developing), duration of therapy (including dose, frequency and length of therapy), as well as any other medication taken concurrently (Bryant & Knights, 2011). Animal studies have shown considerable differences in species’ response with regard to the teratogenic effects of drugs and it may not be possible to extrapolate this data to humans. Fetal abnormalities include missing digits, excessive development or duplication of parts, splitting of parts abnormally, non-splitting of parts, fusion failure or over-fusion of some parts, openings failing to close or open adequately or abnormal placement of parts.

Generally, medications should be avoided during pregnancy if possible. However, this is not always practicable. The woman who is pregnant (or considering pregnancy) should work in partnership with her medical practitioner to develop a medication regimen that balances the benefits to the mother against the potential risks to the fetus. For example, a woman with epilepsy may need to consider the potentially life-threatening risks associated with uncontrolled epilepsy versus the benefits of controlling epilepsy with an agent that has an increased risk of causing fetal abnormalities.

LACTATION

Most drugs taken by a mother who is breastfeeding will be excreted to some
extent in the breast milk; however, the amount ingested by the infant will generally be extremely small but is dependent on the age of the infant and the amount of breast milk consumed.

However, some drugs are concentrated in breast milk relative to the maternal plasma concentration because of their chemical properties, including fat solubility and may be toxic to the infant because of immaturity of the liver and kidney detoxification systems (Bryant & Knights, 2011).

Administering the drug when or immediately after the infant feeds will result in the lowest amount of drug in the milk at subsequent feedings. If a drug is essential for the mother, but of uncertain effect on the infant, it may be necessary to temporarily discontinue breastfeeding and remove contaminated breast milk (via breast pump) which should be discarded. Medications that should be avoided during breastfeeding include amiodarone, chloramphenicol, cocaine, cyclosporin, diazepam, heroin, radioactive iodine, lithium, tetracyclines and theophylline (Bryant & Knights, 2011).

If medication is taken during breastfeeding, the infant should always be closely observed for any side-effects, including poor feeding, listlessness, withdrawal symptoms and other abnormal behaviours that should be reported if they occur.

**LEGAL REQUIREMENTS**

Before a drug can be administered safely, the nurse needs to be aware of the legal aspects of drug administrations. This includes knowledge of the laws governing the possession, use and dispensation of drugs and of the directives of the nurse’s registering body on the administration of medications to clients. It also means observing the employing health care facility’s occupational health and safety (OHS) regulations that are designed to promote safe storage, handling and use of drugs.

The Nursing and Midwifery Board of Australia (NMBA) is one of the national boards of the Australian Health Practitioner Regulation Agency (AHPRA). With the changes to registration of nurses by AHPRA from 2010, it was decided that enrolled nurses no longer required endorsement for medication administration. The NMBA’s goal is for all enrolled nurses to undertake relevant units of study that will enable them to administer medicines safely as part of their education program. However, for enrolled nurses who have not completed the required units, a notation reading ‘Does not hold Board-approved qualifications in administration of medicines’ will appear on the national nursing register against that nurse’s name (NMBA, 2010). Jurisdictional legislation and
policy specifies the routes and schedules of medicines that the enrolled nurse is able to administer and it is therefore of paramount importance that the nurse and employer understand and comply with the drugs and poisons legislation and policy. Furthermore, to administer intravenous medication, the enrolled nurse (Division 2) is required to have completed a separate NMBA-approved unit on the administration and monitoring of intravenous medications (NMBA, 2010).

Legal Acts concerning poisons and the poisons regulatory bodies in New Zealand and each state and territory in Australia deal with the control of all drugs, from prescription medication through to agricultural poisons and research drugs. The laws and regulations apply to sale, supply, storage, dispensing and labelling. The drugs and poisons schedules divide drugs into groups according to their mode of action, therapeutic use, potency, potential for abuse and addiction and safety. While there is currently no national medicines and poisons schedule in Australia, the recommendations of two expert advisory committees (Advisory Committee on Medicines Scheduling and Advisory Committee on Chemical Scheduling) in the form of the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP, Table 2) are usually incorporated into the legislation and regulations of each state and territory of Australia and New Zealand (Australian Government, TGA, 2010). Aims of this document include promoting uniform scheduling, labelling and controls on availability and use of medicines throughout Australia and New Zealand (Australian Government, TGA, 2010).

The recommendations of SUSMP apply for all medicines and poisons in Australia and medicines in Schedules 2, 3 and 4 in New Zealand. New Zealand specific legislation exists for medicines which fall outside these schedules.

Nurse practitioners, as defined by the Nurses Act 1993, are those whose registration has been endorsed as being qualified to obtain and have in her/his possession and to use, sell or supply Schedule 2, 3, 4 or 8 poisons, as described under the Drugs, Poisons and Controlled Substances Act 1981 (Version No. 065, 1/12/2003).

**STORAGE**

All medications in a ward or department should be kept in a locked cupboard, medication trolley or some other type of locked container, the key of which is kept by a nurse at all times. Victoria’s Drugs, Poisons and Controlled Substances Regulations 1995 are very specific about the storage requirements for Schedule 8 or Schedule 9 poisons (e.g. constructed of steel 10 millimetres thick; fitted with a 6-lever lock; able to resist attack by hand tools for 30 minutes or power tools for 5 minutes) with other states having similar requirements.

Drugs or preparations for external use should be stored apart from those intended for internal use, so that errors in administration do not occur. Suppositories, pessaries, insulins, antisera, vaccines, some blood products, some intravenous solutions and some antibiotics (particularly if reconstituted) should be stored in the refrigerator. Nothing else should be stored in the refrigerator (e.g. food) and it should also be kept locked.

The trend towards single-dose units being dispensed contributes to accuracy
in dosage, better economy and less risk of product contamination. Many institutions have policies that discourage the use of multi-dose vials because of the risk of cross-contamination between patients.

**DRUG ORDERS**

In 2004 the Australian health ministers advised that 'to reduce the harm to patients from medication errors, by June 2006, all public hospitals will be using a common medication chart. This means that the same chart will be used wherever a doctor or nurse works and wherever the patient is within a hospital' (ACSQHC, n.d.). The result was the National Inpatient Medication Chart (NIMC). Since then there have been additional national charts developed, which have included the National Aged Care Residential Medication Chart (NRMC), National Interim Residential Medication Administration Chart (NIRMAC), National Subcutaneous Insulin Chart, Paediatric Medication Chart and Private Hospital and Private Hospital Day Surgery NIMC (ACSQHC, 2012a).

A drug or preparation may be given only on written or verbal order from a medical officer, and must be clearly written and/or understood verbally. The law in all states requires that a legal drug order must be legibly written in ink, dated and signed by the prescriber and must include the patient’s name and identification number (if applicable), the name and strength of the drug, dose, route of administration, frequency of administration and duration of administration (if applicable). Any alteration to a drug order should be initialled. An unusual dose, drug strength or quantity should be underlined and initialled by the prescriber. If there is any doubt about the meaning of the order, the medical officer should be contacted immediately for clarification before administration.

The policy of the institution should be consulted before taking telephone orders for drugs. A telephone order should only be taken 'if in the opinion of the medical practitioner, dentist or nurse practitioner, an emergency exists' (Drugs, Poisons and Controlled Substances Regulations 2006, Reg. 47, 2 (C)). Errors may be eliminated if the nurse ensures that the drug has been ordered for the correct patient, writes it on the correct patient’s medication chart, then asks a second nurse to read the drug order back over the telephone to the medical officer. The order should be confirmed in writing by the prescriber as soon ‘as practicable’. However, institutions may have their own policies that require their medical officers to sign the order within 24 hours. If any doubt at all exists (e.g. the patient is unwell and requires reviewing, the nurse is unsure about the drug, dose etc.), the nurse should not take the telephone order and should ask the medical officer to review the patient or medication order as soon as practicable.

**LEGAL RESPONSIBILITY**

Following a medical officer’s order was once thought by many to absolve the nurse from all responsibility. However, legal judgements have shown that this is not always the case. The question that is often asked in situations of a drug error occurring is 'What would the reasonable nurse do in this situation?'

Given that administering drugs is an everyday part of the role of most nurses, it is therefore not an unfair expectation
that they will have some knowledge of
the drugs they are administering. This
includes the class of drug, why it is pre-
scribed (purpose), how it works (action),
recommended or usual dose range, how
it is administered, contraindications,
side-effects, potential for causing allergic
reactions, any interactions with foods or
other drugs and compatibility (especially
when multiple intravenous drugs are to
be administered).

It is not necessary for the nurse to
memorise all this information; however,
what is important is that the nurse has
ready access to information and knows
where or how to readily do so before ad-
ministration. Information on any drug
or preparation may be obtained from a
pharmacist, textbooks or reliable inter-
net sources. Once in possession of this
knowledge the nurse can question an un-
clear order, assess what skills are required
to carry out the order and will understand
what to observe in the patient in terms of
beneficial and adverse effects.

**DRUG INCIDENTS (ERRORS)**

Drug incidents (or errors) may occur at
the prescribing, dispensing or administ-
ering stage of the process. A study by Leape,
Bates and Cullen. (1995) found that doc-
tors and nurses were responsible for 39%
and 38% of errors respectively. They
found that the causes of errors included
lack of knowledge. A more recent study
by Nichols, Copeland, Craib et al. (2008)
found that added to this lack of knowl-
edge other causes of prescribing errors
included lack of supervision by senior
colleagues when prescribing unfamiliar
medications, dealing with unfamiliar pa-
tients, working on unfamiliar wards and
a lack of communication.

Administration incidents (errors) occur when:

- the wrong drug is administered, in-
  cluding the administration of the
  wrong intravenous fluid (e.g. drugs
  with similar names; use of abbrevia-
  tions for names)
- the wrong dose is given (e.g. misread-
  ing dosage or units; misinterpreting
  abbreviations used for units (e.g. mi-
  crograms))
- the drug is given via the wrong route
  (e.g. an oral drug given intravenous-
  ly)
- the drug is given to the wrong patient
- the drug is given at the wrong time or
  frequency, including omission
- an intravenous infusion is adminis-
  tered at the wrong rate.

Since 2008, standard prescribing termi-
nology, abbreviations and symbols have
been introduced in an attempt to reduce
the number of associated errors. Ab-
abbreviations are used when referring to
strength of medications such as grams
(g) and milligrams (mg). For example,
the abbreviation for micrograms using
the Greek letter μ (mu), that is, μg, is
not recommended, nor is mcg, as these
may lead to errors; microg is the pre-
ferred and recommended abbreviation,
or the whole word (microgram) should
be used. Other error prone abbreviations
and symbols that should be avoided in-
clude IU (international units – can be
mistaken for IV), IVI (intravenous injec-
tion – mistaken for IV 1) and qd (every
day – mistaken as qid (four times daily))
(Australian Commission on Safety and
Quality in Health Care, 2011).

The use of ‘dose administration aids’
commonly found in aged care facilities
may not necessarily reduce the number of
administration errors. A 2006 study
conducted in New South Wales (Aus-
tralia) found that ‘dose administration
aids’ contained a significant number of errors (incident rate 4.3% of packs and 12% of residents), which included missing medications, wrong medication or wrong strength of medication dispensed, incorrect dosage instructions supplied or medications being supplied that had been ceased by a doctor (Carruthers, Naughton & Mallarkey, 2008). Although on the surface this would appear to be a dispensing and pharmacy-related problem, it is also the responsibility of the nurse administering the medications to have some idea of what medication a patient has been prescribed (or no longer prescribed) and what the medication(s) actually looks like.

An administration error may or may not have an adverse effect. The seriousness of the outcome (e.g. the adverse effect or lack of) does not absolve the nurse from the mistake that was made. It is important to clearly document the error and outcome. Some institutions may also have policies regarding further documentation requirements when an error has occurred (e.g. a ‘drug incident’ form).

It is important for nurses to practise within their own limitations and within the policies and protocols of the institution. If this is not done and an error occurs (especially a serious one), the nurse may find that the institution (and its insurers) may abrogate any responsibility because the nurse did not follow its policies. The nurse may also be liable under common law.

**A LITTLE PHARMACOKINETICS**

For extensive pharmacokinetics, refer to pharmacology texts. Here are some basic concepts that nurses need to understand.

Pharmacology is the ‘study of drugs, including their actions and effects on living systems’ (Bryant & Knights, 2011, p. 2). **Pharmacokinetics** is the absorption, distribution, metabolism and excretion of these substances, and **pharmacodynamics** is concerned with the physiological effects that the substances have on the organism.

**Pharmacokinetics and the older person**

There are many age-related changes to the body that affect the way that a drug may be absorbed, distributed, metabolised and excreted. Because of these differences, all drug therapy should be given cautiously and monitored carefully in the older patient. Age-related changes that may affect the pharmacokinetics of a drug include:

- altered nutritional habits and ingestion of non-prescription drugs (e.g. antacids and laxatives) may affect drug absorption
- changes in the quantity and quality of digestive enzymes
- increase in gastric pH
- decrease in gastric motility
- decrease in intestinal blood flow
- delayed gastric emptying
- decreases in total body water, lean body mass and increase in body fat may all lead to an altered distribution of the drug
- decreases in plasma proteins, and therefore decreased protein binding of drugs, leading to higher levels of free drug (increasing the risk of adverse effects and/or toxicity)
- the greatest changes appear to be during Phase I metabolism in the liver, which involves microsomal enzymes
- the liver’s ability to recover from injury, such as hepatitis, is reduced with age
hepatic function may also be affected by severe nutritional deficiencies
- decreased cardiac output and reserve
- decreased blood flow to the liver and kidneys
- congestive heart failure reduces the capacity of the liver to metabolise drugs as well as reducing hepatic blood flow
- creatinine clearance decreases with age, resulting in a longer half-life of many drugs and the subsequent risk of accumulation (toxicity)
- decreased renal excretion.

**Drug dosage**

Dosage depends on the age, weight, sex, renal and liver function and general condition of the patient and can be based on age, body weight or body surface area. As children usually require smaller doses than adults, various rules are used to estimate the fraction of the adult dose (see inside front cover).

*Dose interval* is important (e.g. anti-infective agents are given at regular intervals, 4-, 6- or 8-hourly, to maintain adequate blood levels, while hormones are given at the same time each day for uniform effect). The time of day must be suitable to the individual's lifestyle. For example, diuretics may be ordered twice daily and normal convention would see them administered at a regular interval (e.g. 8–10 hourly during the day); however, for an older person it may be more practicable to administer the diuretic in the morning and at lunch time, so that sleep is not disturbed by frequent micturition, increasing the risk of falls.

**Drug half-life**

The half-life of a drug is a function of both distribution and elimination. In general terms, it is the time required for one-half of the amount of drug in the body to be eliminated. It is of practical use in calculating the frequency with which multiple doses of a drug can be administered to keep the blood level between the minimum effective concentration and the threshold for toxicity (e.g. a drug with a very short half-life may need to be administered intravenously to maintain levels, while another drug with a long half-life may be suitable for once-daily administration). Furthermore, a drug with a very long half-life may require patient monitoring for some time after the drug has been discontinued.

**Therapeutic drug monitoring**

Some drugs have a narrow therapeutic range (i.e. the difference between overdosing and underdosing). Serum drug levels are measured to determine that therapeutic levels are being achieved and/or to prevent toxicity. Information accompanying a request form should include the time the blood sample was taken, the time the last dose of the drug was given and its route of administration. The main aim of therapeutic drug monitoring is to optimise drug therapy by achieving adequate drug levels while minimising toxicity. It is especially important in those at the extremes of age (i.e. babies and the elderly).

**Why measure drug levels?**

Drug levels are measured for a number of reasons, which include:
- to individualise the dose (e.g. lithium, phenytoin, warfarin)
- to avoid toxicity (e.g. digoxin, vancomycin)
- to ensure effective blood levels (e.g. prophylactic antiepileptics, gentamicin)
to check adherence to regimen (e.g. antipsychotic agents)
- to check that co-morbidities that may alter drug metabolism and elimination (e.g. renal impairment, hepatic failure, shock, sepsis) are not affecting blood levels
- to ensure that concurrent drug administration is not affecting blood levels
- to change the route of administration or dosage (e.g. from IV or IM to oral administration) if necessary while maintaining adequate serum levels.

Drug route
The effectiveness of a drug often depends on the route of administration. A drug may have a systemic or local effect depending on whether it is taken orally, injected or applied topically (see Glossary for forms of preparations). Drugs are formulated to meet the requirements for rapid or slow absorption, metabolism or excretion in order to obtain the required therapeutic blood levels. The two most common routes of drug administration are oral and parenteral.

Oral administration
Many oral preparations are given on an empty stomach because food may decrease the absorption; however, if gastric irritation is a problem they may be given with or immediately after food.

It is recommended that a capsule is preceded by a small amount of water and then taken with half a glass of water to prevent it becoming lodged in the oesophagus. A number of medications known to cause oesophageal ulceration include aspirin, bisphosphonates (e.g. alendronate), doxycycline, iron tablets, potassium chloride and zidovudine (Gowan & Roller, 2010). Enteric-coated, slow-release, extended-release, modified-release, sustained-release and controlled-dosage tablets should be swallowed whole, not crushed or chewed, for a number of reasons, which may include:
- absorption will be altered (e.g. MS Contin, Keflor CD, Efexor XR, Dilantin)
- medication may become unstable (e.g. Augmentin Duo, Nimotop, Zoton)
- they may cause local irritation (e.g. Vibramycin, Fosamax, Cartia, Roaccutane)
- they will not reach the site of the intended action (e.g. Creon, Dipentum, Salazoprin)
- unacceptable taste (e.g. Neoral, Coloxyl)
- hazardous (e.g. Imuran, Myleran, Leukeran, Cycloblastin).

Care must be taken to select the correct formulation of tablets when several different formulations and/or dosages exist (e.g. Isoptin (verapamil) is available in 40 mg, 80 mg, 120 mg or 160 mg tablets; Isoptin SR is available as 180 mg or 240 mg), because the consequences may be very serious if the wrong formulation is administered (e.g. substituting Isoptin 80 mg (3 tablets), which will act quickly compared with Isoptin SR 240 mg, which is a sustained-release preparation and will act over 24 hours).

Parenteral administration
Parenteral medications are given either as injections or by infusion. The most common routes are intramuscular (IM), subcutaneous (SC) and intravenous (IV).

Intramuscular
The three main muscles used for intramuscular injections are:
● the lateral aspect of the thigh (middle third when the thigh is divided into three)
● the upper outer quadrant of the dorsogluteal
● the deltoid.

No more than 5 mL should be administered by intramuscular injection, and less into the deltoid muscle. If a volume > 5 mL is required, the dose should be divided and given into different sites. Furthermore, the deltoid muscle is not recommended for intramuscular injection in children.

Subcutaneous
Subcutaneous injection sites include:
● upper outer aspect (middle third) of the upper arm
● upper anterior thigh
● abdomen below the costal margins to the iliac crests (avoiding the area around the navel by about 5 cm).

When frequent administration is required (e.g. insulin administration in a patient with diabetes mellitus, daily heparin injections), administration sites should be rotated and documented on the medication chart to prevent atrophy of the subcutaneous tissue, increased risk of infection and pain.

Intravenous

A drug may be given by direct IV injection as a bolus in a volume of 20 mL or less in under 1 minute, or by slow IV injection over 5–15 minutes. It is important to check and adhere to the manufacturer’s information regarding the required administration time, because administering some drugs too quickly can cause pain, damage the blood vessel, as well as other adverse effects such as flushing, hyper- or hypotension, syncope, arrhythmias, feelings of warmth or anxiety, depending on the drug administered. This method is used when an immediate effect is required or the drug becomes unstable on reconstitution or dilution. The intermittent infusion method is used when a drug is diluted, when interval dosing is desired and when slow administration is required. The drug is diluted in 50–250 mL and infused over 15 minutes to 2 hours. This minimises stability and incompatibility problems and gives the ‘peak’ and ‘trough’ effect in antibiotic therapy. One of the advantages of intermittent IV administration is that the patient can have an intermittent venous access port, which increases client mobility, comfort and safety, there is a cost benefit from not having continuous IV therapy and the nurse does not have to continuously monitor flow rates.

When a drug must be highly diluted and a steady-state blood level is to be maintained, the continuous infusion method is used, in which the drug is diluted in 500–1000 mL and infused over 4–24 hours (e.g. potassium chloride requires high dilution and constant blood levels to prevent depression of cardiac function).

The IV flow rate may be controlled by using an infusion pump, a microdrip set or a burette. When a drug is added to the burette during intermittent infusion, details of the additive are indicated on a label that is stuck onto the burette. Any IV drug admixture must be prepared aseptically, mixed thoroughly and labelled with the name and amount of the additive, name of person adding the agent, name of person checking the addition and the time of starting the infusion. National recommendations for user-applied labelling of injectable medicines, fluids and lines now exist and it is
imperative that nurses understand and comply with these as consequences of non-labelling can result in a potentially life-threatening situation for the patient. These recommendations include colour coding the route of administration (e.g. red for intra-arterial, blue for intravenous, yellow for epidural or intrathecal and beige for subcutaneous), process for medicine and label preparation (including label placement), when to discard containers of injectable medicines and special circumstances (ACSQHC, 2012b). While these labelling recommendations do not apply to enteral, topical or inhalation routes, the general principles still apply as a way of improving practice and decreasing the risk of errors occurring.

An IV admixture should not be administered if there are signs of physical incompatibility such as a colour change, loss of clarity or precipitate formation. Chemical and physical compatibility and stability of admixtures should be checked before administration. If in any doubt, consult a pharmacist, textbooks, manufacturer’s information or a drug information centre.

Drugs generally should not be mixed with blood or blood products.

Other methods of administering medications include:
- transdermal patches, which deliver drugs through the skin at a steady concentration, avoiding first-pass metabolism in the liver and any gastric side-effects. Several types of drug, including glyceryl trinitrate, hormones and nicotine, are available as transdermal patches. Advantages include ease of application and frequency of application (once daily or longer), but the disadvantages include some skin reactions and the low number of drugs available via this route.
- intradermal implants, which are surgically implanted subcutaneously. Advantages include the frequency of administration (some may be implanted for 6-8 weeks or longer); however, they require surgical implanting and removal.

GUIDE FOR SAFE ADMINISTRATION

Check the order
- Check that the information on the drug name (preferably generic rather than trade name), dose, route, frequency, time due and when the drug was last given are all legible (if any doubt exists, withhold the drug and check with the medical officer) and that the order is signed by the medical officer.
- Check that patient details are correct, including any known allergies (it is important to discuss any allergy/sensitivity history with the patient as cross-sensitivity between products does occur).

Check the drug
- Check the container label against the medication order when selecting the preparation, before measuring out and when replacing the preparation.
- Check the expiry date of the drug.
- Check the drug calculation with another registered nurse, a pharmacist or medical officer (ask the second person to do the calculation independently, then compare answers, remembering that it is rare to give less than half a tablet or more than 2 tablets or 1 ampoule at a time).
Mix liquid contents thoroughly, but rotate protein preparations gently to prevent denaturation and frothing.

Note any discolouration, precipitate or foreign bodies (and do not administer if they are present).

**Check the patient**

- Check the patient’s identity carefully (check wrist identity band or verbally), taking extra care if there are patients with the same or similar names, or if the patient is unknown to the nurse.
- Check if the patient has any known allergies.
- Check that the patient knows the reason for the medication and discuss any query with the medical officer before giving it.
- Only give medications that you, the nurse, have prepared or seen a pharmacist prepare (i.e. do not administer an IV drug that was drawn up by someone else without you present).
- Give the correct drug and dose.
- Give to the correct patient.
- Give at the correct time.
- Give by the prescribed route.
- Do not handle tablets.
- Wait until oral medications are swallowed (never leave medications on bedside tables, lockers or dinner trays).

**Documentation**

- Ensure that the drug administration sheet is signed after administration.
- Document any discrepancies (e.g. patient unable or refuses to take medication, patient absent, medication not available).
- If Schedule 8 drugs are involved, ensure that the drug register is correctly filled in (date, time, patient, drug (form, strength, amount to be administered), persons administering drug, balance of drug remaining, any drug discarded).
- Observe the patient and document in the patient’s history.
- Note beneficial effects and/or report and chart any adverse effects (see brief discussion below).
- Correctly and safely dispose of equipment used (e.g. do not recap syringes – and dispose of them safely in a sharps container).
- A drug may produce more than one effect which may be beneficial or not:
  - The desired action is the physiological response the drug is expected to cause (e.g. antihypertensive medications are expected to lower blood pressure)
  - Side-effects (also called adverse effects or adverse reactions) are secondary effects caused by most drugs and are generally undesirable. Although the terms are sometimes used interchangeably, side-effects tend to be mild in nature, whereas adverse reactions are more serious (e.g. an adverse effect of acetylsalicylic acid (aspirin) is increased bleeding time; and a common side-effect of morphine is nausea)
  - Toxic effects develop after prolonged administration of high doses of medication, or when a drug accumulates in the blood because of impaired metabolism or excretion. Some drugs such as digoxin and lithium have a very narrow safety margin and toxicity can occur at recommended or therapeutic doses
  - Allergic reactions are unpredictable responses to a drug that
acts as an antigen, triggering the release of antibodies. Allergic reactions may be mild, such as urticaria (hives) and pruritus (itching), or they may be severe; for example, severe wheezing and respiratory distress, or life-threatening anaphylactic reaction. Some reactions occur within minutes of the drug being given, while other allergic reactions may be delayed for hours or days (Roach, 2005).

- **Idiosyncratic reactions** are those where the patient’s body either overreacts or underreacts to a drug, or when the reaction is unusual and there is no known cause (e.g. the antihistamine promethazine (Phenergan) is sometimes used for sedation, however, in some people (especially children) it can cause insomnia and agitation).

- **Pharmacogenetic reactions** occur because a person may have a genetic trait which leads to abnormal reactions to drugs (e.g. those with glucose-6-phosphate dehydrogenase (G6PD) deficiency may experience haemolysis if given aspirin, chloramphenicol or sulphonamides) (Roach, 2005).

- **Drug tolerance** may also occur where a person has a decreased response to a drug over time, necessitating an increase in dosage to achieve the required response (e.g. tolerance to opioids such as morphine may occur if given for more than 10 to 14 days) (Roach, 2005).

- **Drug interactions** occur when one drug modifies the action of another drug; for example, a drug may either increase or decrease the action of other drugs. A drug interaction may be synergistic (enhances the effects of another drug) (e.g. probenecid may be given orally before IM procaine penicillin to increase and prolong the serum level of penicillin), antagonistic (opposes the effects of another drug) (e.g. protamine sulphate can be given to neutralise the anticoagulant effects of heparin) or additive (where the two drug actions are added together (e.g. when alcohol is consumed by a person on heparin, the risk of bleeding is significantly increased)).

**SUMMARY**

Administering medication is one of the nurse’s most important responsibilities and should be treated with the due care it demands. It is not a task merely to be completed, but rather an opportunity for nurses to increase their own knowledge, to ensure that patients have been educated regarding their medications and to observe patients for both expected and unexpected responses – part of holistic nursing care. The right patient has a right to receive the right dose of the right medication in the right form at the right time by the right route for the right duration of therapy. If any doubt exists, the medication should be withheld; remember, WHEN IN DOUBT, DON’T!!
AT A GLANCE

AVAILABLE FORMS
This section outlines the various formulations for the medication.

ACTION
Because this is not a pharmacology text, only a brief description of the action of each agent is included. For more detailed information, a pharmacology text should be consulted.

USE
The most common uses of drugs (including both hospital and community uses).

DOSE
Dosages listed in this book are those for the average adult (unless otherwise stated). Occasionally a paediatric dose may be included if that particular agent is used predominantly in children (e.g. growth hormone, agents used to treat attention deficit disorder).

ADVERSE EFFECTS
Adverse effects are generally unwanted effects, some of which are predictable and often dose related. Other adverse effects may be unpredictable and occur less frequently (e.g. anaphylaxis, anaphylactoid reaction). Very common adverse effects are found in 1–10%, uncommon in 1–0.1% and rare adverse effects occur in less than 0.1%. The adverse effects listed in this book are generally those that are common or very common, and rare or less common adverse effects are listed when they require some action to be taken. For example, thrombocytopenia may be a rare adverse effect but there is a requirement for regular monitoring of blood counts.

INTERACTIONS
Interactions occur when one drug alters the action of the second drug or both agents affect each other. As with the adverse effects, the interactions listed are those that occur commonly or are the most dangerous. It should be noted, however, that interactions between any agents are always possible and caution should be taken when multiple agents are given. For detailed explanations of how and why interactions occur, a pharmacological text should be consulted.

NURSING POINTS/CAUTIONS
The points in this section are those most directly applicable to nurses and may include:
- IV administration rate
- monitoring advice
- reconstitution and storage recommendations
- incompatibilities

PATIENT TEACHING/ADVICE
Included in this section is important information that the patient should receive about his/her medication and includes:
- taking with food or fluids
- dividing of tablets
- grapefruit juice incompatibility
- driving warning
- when to seek medical advice (see following section for detailed patient teaching and advice information)

It is assumed that the nurse:
- will use an aseptic technique when reconstituting medication
will inspect the solution for any particulate matter or cloudiness
will not use the medication if either particulates or cloudiness is present
will administer the medication using a safe, aseptic and correct technique
will dispose of sharps in a safe and responsible manner.

These points are not made for every parenteral agent in the text:
• ‘cautions’ are the equivalent of amber traffic lights – go slow and take care. For example, a person with renal impairment may not excrete the medication at the same rate as someone with normal renal function, thus increasing the risk of adverse effects and toxicity. Therefore, a reduced dose may be required and/or close monitoring of renal function and drug excretion, as well as monitoring for adverse effects
• ‘contraindications’ are the equivalent of red traffic lights – no go!
• hypersensitivity to the agent itself is not listed for every agent as it is assumed that this will be checked routinely before administration (i.e. the patient will be asked ‘Have you had this medication before? Did you have any problems with it?’). Although cautions and contraindications are often more relevant to the person prescribing the medication, it is important that the nurse is also aware of these factors.

Patient teaching and advice regarding medications is an essential part of care which often involves the nurse, in addition to the pharmacist, doctor and/or other members of a multidisciplinary team. If possible, take time to build a rapport with the patient (and their significant other/carer/family member, if appropriate). It is easier to learn from and ask questions of someone with whom you are comfortable. Also, given the extent of this educational task, it should start on admission rather than a few days before (or on the day of) discharge.

There are a number of factors which may impact on a person’s ability to learn (Roach, 2005). Examples include:
• Environment and available time: It may be difficult to teach and/or learn in an area where there are constant distractions or interruptions. Consider using a small room where the door can be closed and at a time when the nurse knows that there will not be any interruptions (e.g. not during meal breaks or at other times of reduced staffing or during visiting hours). Although accessing a small room may not be possible, pulling the curtain around the person’s bed may alert others that something is taking place even if it doesn’t really afford privacy (curtains are not soundproof). The nurse should also consider how much time she/he has available to conduct the session. A short session crammed with too much information may cause confusion in the patient, as well as potentially overlooking important information.
• Pain and/or Discomfort: Are you able to concentrate if you are tired, in pain, need to go to the toilet, hungry or thirsty? All of these impact on a
person’s capacity to concentrate and should be eliminated or minimised before starting a teaching session

- **Sensory deficits:** Does the patient have a hearing impairment? Does he/she have a hearing aid? Does he/she have it in (and is it turned on)? Can the person read the label on the medication bottle or graduations on a syringe? Is the person dexterous enough to open medication bottles or operate an injector pen or glucometer? Does the person have sufficient coordination to use an inhaler or is a spacer device required?

- **Anxiety/stress/fear:** These are similar to pain and discomfort and should be minimised or alleviated before starting a teaching session

- **Learning styles:** Not everyone learns in the same manner. Some people learn by reading, others require demonstration while others may require both (e.g. demonstrate injection or puffer technique, get the patient to practise, as well as leaving literature for them to read). Consider your own learning style(s) – how do you prefer to learn about a new piece of equipment – play with it until you work out how it works, have it demonstrated to you, read the instruction manual from cover to cover or a combination of two or more methods? We often teach others in the manner we like to learn, therefore we should also consider teaching using the other, less comfortable, ways. In allowing the patient to practise the skills (e.g. injection technique, blood glucose monitoring, puffer technique), it gives the nurse an opportunity to observe and anticipate any problems (e.g. patient may require follow-up by a district nurse on discharge to ensure the technique is correct)

- **Literacy:** information should be presented at a level which takes into account the patient’s education and reading level

- **Language and culture:** Is an interpreter required? Does consideration need to be given of the nature of the material (e.g. contraception) and the genders of the teacher and patient? It is very difficult to give important information to someone who does not speak the same language as yourself, or may be able to understand but not able to ask questions. Further, it is important to use a professional interpreter if possible as using family members (especially children or adults of the opposite sex) can put them into situations where they are not comfortable (e.g. teenage son interpreting for his mother who is taking medication for gynaecological problems). There is also the issue of privacy and patient confidentiality to consider. It is also necessary to remember these issues of language and culture if giving the patient written information.

Before starting any teaching session, it is important to lay down the ‘ground rules’ (e.g. how long the session will last, what is going to be discussed, follow-up). Factors which can be alleviated or minimised should be attended to before starting the session. Other general considerations may include:

- **Use of appropriate language.** Nurses (and medical professionals in general) often use jargon (e.g. ‘obs’ or the ‘meds’) that can be confusing (and daunting) for non-medical people...
● previous knowledge and skills of the person. Even if the patient has been prescribed the medication before, assessing knowledge and any misunderstandings can be important as this may improve the patient’s motivation to take the medication, thereby improving adherence with the regimen. If the medication is new, it is important to determine if the information and/or skill (such as using an inhaler or administration of insulin) requires more than one session making discharge planning essential. This extra time gives the patient time not only to practise skills (supervised and/or unsupervised), but also ask questions and seek clarification of anything that he/she has not understood (Roach, 2005)
● importantly, returning at an agreed time to review information and follow up on any other questions the person may have.

Consideration should be given to including the following as part of patient teaching and advice:
● why the person is taking the medication (including the benefits). If the person has any concerns about taking the medication, he/she should be encouraged to discuss these with his/her doctor before starting
● a simplified explanation of how the medication works
● importance of telling other health professionals (e.g. dentist, specialist, surgeon, anaesthetist) that he/she is taking medications (e.g. it may be necessary to discontinue some medications before a procedure). This should also include the patient reminding the health professional of any allergies (including to food(s) or latex) or other medical conditions (past or present) (such as kidney impairment, asthma, tuberculosis, hepatitis B, heart failure, cancer, blood disorders, gastric ulcer or bleeding, diabetes, high blood pressure), whether he/she smokes or regularly drinks alcohol
● importance of telling doctor if the patient is pregnant, planning to become pregnant, breastfeeding or planning to breastfeed as many medications cross the placental barrier and/or are excreted in breast milk
● a recommendation that the patient carries a list of current medication (with exact names) in wallet/purse so that he/she can ensure that any other health professional knows what is being taken rather than a general description (e.g. ‘small blue pill for my heart’). This may also be important in the event of an emergency.

Dosage
● Name and strength of the medication (including information about differing strengths and trade names)
● What the medication looks like (e.g. capsules, tablets, liquid, injection)
● Dose – this may be straightforward (e.g. patient is ordered 10 mg and tablets are supplied as 10 mg) or not (e.g. patient is ordered 15 mg and tablets are supplied as 10 mg which means splitting one tablet. Depending on the dexterity of the person, this may not be a simple task)
● When to take (e.g. morning, evening, same time every day, in relation to food or other tablets, once per week, once per month)
● Not increasing, decreasing or stopping medication without seeking advice from doctor
How to take

- Swallow whole with glass of water (or other fluids as recommended). Some fluids may interfere with the medication and it is important to know which ones to avoid.
- Tablets/capsules should generally not be chewed (unless the tablets are chewable).
- Techniques (such as inhalation using a puffer or injection) will need to be demonstrated and taught. If the patient is unable to manage, consideration should be given to teaching a carer/family member/significant other, involving a community based service or discussion with the doctor regarding the appropriateness of the medication and the risk of non-adherence with the regimen.
- What to do if a dose is forgotten or omitted (e.g. seeking advice from a pharmacist or doctor; not taking a double dose to ‘catch up’).
- What to do if too much medication is taken (e.g. contacting doctor, pharmacist or Poisons Information Centre (131 126 in Australia or 0800 764 766 in New Zealand), going to the nearest Accident and Emergency Department).
- Length of time that the medication will be required (including emphasis on completing the course and not stopping the medication abruptly or without seeking medical advice).
- Whether there is anything that should be avoided while taking the medication (e.g. certain foods or fluids, shaking some medications, standing up quickly).

Adverse effects

- All medications cause some side/adverse effects. Some of these may be common, mild and transient in nature, while others are more serious (and may be life threatening). It is important for the patient to be made aware of any potential side/adverse effects which may require immediate medical attention. Caution should be taken with explaining side-effects. It may be safer and simpler to suggest seeing a doctor if anything unusual occurs. However, sometimes it is important to give specific directions such as ‘report to your doctor immediately if you develop any yellowing of the skin or whites of the eyes, your urine looks darker than usual, you develop nausea, vomiting or abdominal pain’.
- Life threatening side effects (such as allergic reaction including development of wheezing, shortness of breath, rash, difficulty swallowing) should be emphasised as requiring urgent medical attention.

Storage

- All medications should be kept out of reach of children.
- Medications should be correctly stored. If there are special storage requirements (such as refrigeration) these should be emphasised (e.g. not using if left out of the fridge for 12 hours or more).
- Medications should not be stored in a bathroom, near a sink, on a windowsill or in the car as heat and dampness may destroy them.
- Most medications should not be frozen.
- Medications should be kept in the original containers/packets with labels intact. Medication should not be taken if the packaging/container is...
torn or has signs of being tampered with

● If the medication changes colour, becomes cloudy, foreign particles are present or develops an odour, the medication should not be used and a pharmacist consulted immediately

● Medications have a ‘use by’ (or expiry) date and should not be used after this date. It is important to show the patient where this information is located (it can be difficult to see on some containers). Any unused medication should be safely disposed of (e.g. returned to the pharmacy). Some medications such as eye drops and ointments may have a very short life and deteriorate chemically after this time

**Other issues**

● Following all instructions on package/container (e.g. ‘shake well before use’, ‘keep refrigerated’, ‘take 1 hour before meals’)

● Seeking advice from doctor if symptoms do not improve or worsen

● Attending doctor’s appointments as requested, including the need for regular blood or other tests to monitor drug levels (e.g. some medications, such as warfarin, require regular monitoring of the therapeutic blood level and the dosage may be adjusted accordingly)

● Importance of having a current prescription and getting it filled/refilled before the medication runs out

● Medications should not be given to others with similar conditions, nor kept for the next time the condition recurs (e.g. antibiotics used to treat respiratory infection)

● Over-the-counter medications (such as simple analgesics, antacids, laxatives, cold and flu preparations) and herbal preparations or vitamins/minerals may interact with prescribed medications. It is important to consult with doctor or pharmacist before taking any of these preparations (including those bought from the supermarket or health food stores)

● Consideration should be given to wearing a Medic Alert pendant or bracelet or some other form of identification for some conditions/medications (e.g. diabetes, anticoagulants, corticosteroids, insulin) in case of an emergency

● Whether the patient is able to manage the medications alone (e.g. it may be appropriate to suggest using a Dosette box or involving a carer in any discussions or referring to a community-based agency (such as the district nursing service) for monitoring). This may also include the ability to open containers or split tablets if needed. Most pharmacies will provide a unit-dose packing service on request

● Warn patient against driving or operating machinery until he/she knows how the medication will affect them. This is particularly important if the medication has known side effects which affect vision, balance, co-ordination or reaction time or increases the effects of alcohol. If this is a known occurrence, extra labels will be attached to containers/packages (e.g. ‘this medication may cause drowsiness and may increase the effects of alcohol. If affected, do not drive a motor vehicle or operate machinery’)

● Other medication-specific considerations are discussed under patient teaching and advice in each section.
TECHNICAL REVIEWERS

Lynne M MacKinnon  
BPharm, MACP

Jerry Perkins  
BSc, BPharm

REVIEWERS

Karole Hogarth  
RN, BSc (Hons), PhD (Anatomy)  
Senior Lecturer, Otago Polytechnic, Dunedin, NZ

Nadim Rahman  
MBBS, AMC (Primary assessment), PGT (General Practice), RN, BN, GCHPE  
Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne

Angela Kucia  
BN, MA, PhD, Grad Cert Ed  
Senior Lecturer, School of Nursing and Midwifery, University of South Australia, Adelaide; Clinical Practice Consultant, Acute Cardiac Assessment, The Lyell McEwin Hospital, Adelaide, Australia

Sonia Reisenhofer  
RN, BN, PGDipEN, MCN  
School of Nursing & Midwifery, La Trobe University, Melbourne

Erica O’Donoghue RN  
Bachelor of Nursing, Grad Cert Emergency Nursing, Grad Cert in Nursing (Paediatric, Child and Youth Health Nursing), Cert IV Training and Assessment (TAE), MACN  
Lecturer in Acute Care, Bachelor of Nursing, Alfred Clinical School, La Trobe University, Melbourne
ANALGESICS AND NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) AND DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (DMARDS)

ANALGESICS AND NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs)

Action and use (not paracetamol)
During the inflammatory response, arachidonic acid is converted by the enzyme cyclo-oxygenase (COX) to prostaglandins and thromboxane A₂, and by the enzyme lipooxygenase to leukotrienes, which produce the pain, swelling, redness and heat associated with inflammation (Brenner & Stevens, 2010). Cyclo-oxygenase is present in two forms that have distinct properties. Cyclo-oxygenase-1 (COX-1) is found in the stomach, intestines, kidneys and platelets, and appears to be responsible for functions involving prostaglandins, such as renal function, platelet aggregation and cytoprotection of the stomach. NSAIDs inhibit COX-1 non-selectively, resulting in the common side-effects of gastric ulceration and, to a lesser extent, renal toxicity and increased risk of bleeding. Cyclo-oxygenase-2 (COX-2) is found in fewer tissues (including the brain, renal glomeruli and vasculature) at low levels; however, during inflammation, pro-inflammatory substances lead to an increase in COX-2 levels (Brenner & Stevens, 2010). Selectively inhibiting COX-2 decreases the signs and symptoms of inflammation and pain with less likelihood of causing gastric or renal problems. Recently, cyclo-oxygenase-3 (COX-3) has been discovered. It is thought that paracetamol inhibits COX-3, possibly explaining its lack of anti-inflammatory action (Brenner & Stevens, 2010).

The NSAIDs are a heterogeneous group of compounds, often chemically unrelated, that share some therapeutic actions and side-effects because of their non-selective inhibition of cyclo-oxygenase. Not all drugs in this class possess the anti-inflammatory, antipyretic and analgesic characteristics to the same degree (Brenner & Stevens, 2010). When used as analgesics, these drugs are usually effective against low to moderate intensity pain only. As anti-inflammatory agents, they are used in treating musculoskeletal disorders, providing symptomatic relief from pain and inflammation, but leaving the progression of the disease course unchanged. As antipyretics, they are thought to inhibit hypothalamic prostaglandins that act on the thermoregulatory centre in the hypothalamus. The
COX-2 inhibitors are a newer class of agents with similar properties to those of other NSAIDs without having the same side-effects (especially gastrointestinal), because of their selective inhibition.

Most NSAIDs are taken orally, while some are applied topically to relieve muscular and/or rheumatic pain, and others are used in ophthalmic preparations to reduce ocular inflammation.

**Adverse effects (not paracetamol)**
- epigastric pain, nausea, vomiting, diarrhoea, abdominal pain/cramps, heartburn, dyspepsia, flatulence, bloating, anorexia, constipation
- gastrointestinal bleeding and/or ulceration
- rash, pruritus
- tinnitus, temporary deafness
- headache, dizziness, vertigo, fatigue, drowsiness
- prolonged bleeding time
- fluid retention, oedema
- hypertension (new, or worsening of existing)
- increased risk of cardiovascular thrombotic events (COX-2 inhibitors)
- elevated liver enzymes (ALT, AST), jaundice, hepatitis
- blood dyscrasias, iron-deficiency anaemia
- may mask signs and symptoms of infection
- (prolonged therapy, high dose) visual disturbances, acute interstitial nephritis with haematuria, proteinuria, nephrotic syndrome, renal papillary necrosis, liver toxicity
- hypersensitivity reactions (especially in those with asthma or family history)
- (rare) anaphylactoid reactions, angioedema

**Interactions (not paracetamol)**
- may increase blood lithium or digoxin levels (except ketoprofen), thereby increasing the risk of toxicity; lithium or digoxin levels should be closely monitored, especially when starting or stopping therapy with NSAIDs
- use with aspirin or other NSAIDs is not recommended because of increased risk of gastrointestinal side-effects
- use caution and close monitoring if warfarin is given with NSAIDs because of increased risk of haemorrhage
- increased risk of nephrotoxicity if cyclosporin or tacrolimus are given with NSAIDs
- methotrexate toxicity may occur if NSAIDs are given within 24 hours of methotrexate therapy
- use of quinolone antibiotics and NSAIDs may lead to convulsions (not celecoxib)
- risk of gastric ulceration is increased if aspirin or NSAIDs are taken with alcohol and/or corticosteroids
- increased risk of bleeding if given with SSRIs, zidovudine or antiplatelet agents
- use of antacids may reduce absorption of aspirin or NSAIDs (except ketoprofen, ketorolac trometamol, sulindac and piroxicam)
- may decrease excretion of aminoglycoside antibiotics, increasing risk of toxicity
- avoid use with other nephrotoxic agents
- plasma levels may be increased if given with probenecid
- may increase serum potassium levels if given with potassium-sparing diuretics
may decrease diuretic, natriuretic and antihypertensive effects of loop, potassium-sparing and thiazide diuretics by inhibiting the synthesis of renal prostaglandin
may potentiate effects of sulfonyl-ureas
may reduce antihypertensive effects of beta-adrenergic blocking agents, ACE inhibitors and angiotensin II antagonists
risk of renal impairment is increased if NSAIDs, thiazide diuretics and ACE inhibitors/angiotensin II antagonists are given together, especially in the elderly or those with pre-existing renal impairment
increased risk of bleeding if given with Ginkgo biloba

Nursing points/Cautions (not paracetamol)

before starting therapy, the patient should be assessed for any allergic reactions after prior aspirin or other NSAID therapy, as cross-sensitivity occurs
any history of asthma (may induce asthma attack in susceptible individuals) or gastric ulceration/bleeding (due to increased risk of both) should be assessed before starting therapy
if administered preoperatively, patient should be carefully monitored for any signs of bleeding intra- or postoperatively
regular ophthalmological examination, haematological and liver enzyme monitoring should all be performed during prolonged therapy
in patients with concurrent hypertension and managed with antihypertensive agents (beta-adrenergic blocking agents, ACE inhibitors and angiotensin II antagonists) regular measurement of BP is recommended before starting therapy and then at regular intervals
cautions if used in those with hypertension, congestive cardiac failure or pre-existing oedema because of increased potential for fluid retention and oedema
cautions if given to those with pre-existing renal disease, uraemia or bleeding disorders
cautions if used in those with inflammatory bowel disease (IBD) as NSAIDs have been associated with exacerbation of IBD-associated spondyloarthropathies
contraindicated in those with a history of peptic or gastrointestinal ulceration or bleeding
contraindicated in those with salicylate hypersensitivity or with 'aspirin triad' (person with asthma who experiences rhinitis with/without nasal polyps, or experiences severe bronchospasm after taking aspirin or NSAIDs)

Patient teaching and advice for NSAIDs

recommend taking NSAIDs with food or milk (e.g. after meals) to reduce gastric irritation
patients should be warned to immediately report to their doctor any:
- changes in hearing or visual disturbances
- nausea, tiredness, lethargy, itching, yellowing of skin, eyes and urine, flu-like symptoms or abdominal tenderness (in upper outer right quadrant, as these are signs of impending liver toxicity)
patient should be advised to immediately seek medical attention if skin rash, hives, blistering or peeling skin, mouth ulcers or swelling of face, lips, mouth, tongue or throat, or wheezing/difficulty breathing occurs

cautions: patients not to drive or operate machinery if dizziness, drowsiness or visual disturbances occur

(gel) instruct patient to only apply gel to intact skin, avoiding any areas of broken or infected skin and wash hands after applying gel and avoid contact with eyes or mouth

counsel female patients not to take NSAIDs during pregnancy, especially during third trimester. If the patient becomes pregnant, she should be advised to tell doctor immediately

- not recommended during labour or delivery
- caution should also be used during breastfeeding because some NSAIDs and/or their metabolites are excreted in breast milk and their actions on the newborn may be unknown

**ASPIRIN** (Aspro preparations, Aspro Clear Extra Strength, Astrix 100, Astrix Tablets, Cardiprin 100, Cartia, Disprin preparations, Solprin)

**Available forms**
Capsules: 100 mg; Tablets: 100 mg, 300 mg, 320 mg, 500 mg; Tablets (enteric coated): 100 mg, Tablets (effervescent): 300 mg, 500 mg

**Action**
- see general Action for NSAIDs (p. 1)
- aspirin is converted to salicylate mainly in the GI tract
- absorption is dependent on formulation (e.g. soluble formulation increases rate of absorption)
- half-life of aspirin is about 30 minutes, half-life of salicylate is dose dependent

**Use**
- relief of mild to moderate non-visceral pain
- headache, migraine
- acute febrile illnesses (not for children or teenagers)
- dysmenorrhea
- rheumatic pain, including juvenile rheumatoid arthritis
- antiplatelet therapy (only on medical advice)
- cold and flu symptoms
- toothache

**Dose**
- (analgesic, antipyretic) 300–1000 mg orally with food 4–6 hourly as required (up to 4 g/day) OR
- (effervescent tablets) 300–1000 mg orally dissolved in ½ glass of water 4-hourly as required (up to 4 g/day) OR
- (antiplatelet) 100 mg daily

**Adverse effects**
- see general Adverse effects for NSAIDs (p. 2)

**Interactions**
- see general Interactions for NSAIDs
- may increase blood levels of sodium valproate, phenytoin, sulfonamides and methotrexate increasing risk of toxicity and/or adverse effects
- aspirin absorption is increased by metoclopramide during migraine attack
• action of probenecid may be reduced if given with aspirin
• hypoglycaemic action of sulfonylureas may be increased if given with high-dose aspirin and therefore blood glucose levels should be closely monitored
• excretion is increased if given with urinary alkalinisers
• may antagonise diuretic action of spironolactone
• rate and extent of absorption is increased by caffeine
• hydrocortisone may increase clearance. Further, when hydrocortisone is ceased, blood levels of aspirin may rise significantly, increasing risk of adverse effects and/or toxicity
• may interfere with a number of laboratory tests, including measurement of heparin activity, urinary glucose oxidase test in the presence of glycosuria, fluorometric assay of 5-hydroxyindole acetic acid, serum uric acid and phenylketonuria

Nursing points/Cautions
• see general points for NSAIDs
• soluble, effervescent, buffered and enteric-coated salicylate preparations reduce gastric irritation
• enteric-coated and sustained-action preparations have delayed absorption, which is useful for regular long-term therapy
• elderly patients are at greater risk of adverse effects, including tinnitus, nausea, anorexia and gastric irritation
• tinnitus (with normal hearing) is a reliable index of therapeutic plasma level, but may not be detected in patients with hearing loss
• symptoms of salicylism (chronic salicylate intoxication) are dizziness, tinnitus, deafness, sweating, nausea, vomiting, headache and mental confusion
• symptoms of acute salicylate poisoning include hyperventilation and disturbed acid–base balance. Other symptoms include fever, dehydration, gastrointestinal symptoms, hypoglycaemia, bleeding andencephalopathy. In severe poisoning, CNS symptoms such as delirium, tremor, hallucinations, restlessness and coma are common. Treatment involves determining salicylate levels, stomach emptying with/without forced alkaline diuresis (depending on blood salicylate level), treatment of hyperthermia and dehydration and correction of any disturbance in acid–base balance, as well as maintenance of renal function. If condition worsens, haemodialysis, peritoneal dialysis or exchange transfusion may be necessary
• aspirin should be avoided in infants, children and adolescents, including for the treatment of fever and/or muscle pain associated with febrile, viral illness because of the association with Reye’s syndrome (see Glossary)

Patient teaching and advice
• see general Patient teaching and advice (p. xxiii) and general Patient teaching and advice for NSAIDs
• stopping aspirin for any reason (e.g. donation of blood) should be discussed with doctor before discontinuing therapy
• effervescent and soluble preparations should be dissolved in ½–1 glass of water for more rapid absorption
• warn patients that sustained-release and enteric-coated preparations should be swallowed whole and not crushed or broken
• advise patient to avoid aspirin within 30 minutes of alcohol
• instruct patient to stop aspirin a week before any surgical procedure as the risk of bleeding is increased
• blood donors should not take aspirin in the week preceding the donation
● if patient is on a low sodium diet, he/she should be cautioned that effervescent preparations contain sodium

Note
● contained in Alka-Seltzer, Asasantin SR, Aspalgin, Clopidogrel Winthrop Plus Aspirin, Codis, CoPlavix, Disprin Forte, DuoCover

**BENZYMADINE (Difflam Solution, Anti-inflammatory Throat Spray and Gel)**

**Available forms**
- Throat spray: 1.5 mg/mL; Gel: 3%, 5%; Solution: 22.5 mg/15 mL

**Action**
● analgesic, anti-inflammatory

**Use**
● relief of inflammatory conditions of the mouth and throat (e.g. tonsillitis, radiation mucositis) (see Eye, ear, nose and throat agents)
● (topically) rheumatic disorders

**Dose**
● (rheumatic disorders) 3% or 5% gel massaged into affected area 3–6 times daily (maximum 6 times daily in severe conditions) for up to 14 days

**Adverse effects**
● (topical application) erythema, rash, photosensitivity

**Patient teaching and advice**
● patients should be advised to wash hands after applying gel and avoid contact with eyes or mouth
● see general Patient teaching and advice (p. xxiii)

**Note**
● contained in Difflam preparations (Lozenges, Mouth Gel and Solution), Logicin Rapid Relief Lozenges

**BUFEXAMAC (Paraderm Cream)**

**Available form**
- Cream: 50 mg/g

**Action/Use/Dose/Adverse effects/Nursing points/Cautions**
- topical anti-inflammatory (see Dermatological agents)

**Note**
● contained in Paraderm Plus, Resolve Balm

**CELECOXIB (Celebrex)**

**Available forms**
- Capsules: 100 mg, 200 mg

**Action**
● COX-2 inhibitor preventing prostaglandin synthesis with actions similar to other NSAIDs
● half-life 4–15 hours

**Use**
● osteoarthritis, rheumatoid arthritis, ankylosing spondylitis
● primary dysmenorrhoea
● (short-term) pain management postsurgery or musculoskeletal/soft tissue injury

**Dose**
● (osteoarthritis, ankylosing spondylitis)
  - 200 mg orally daily as single dose or 2 divided doses **OR**
  - (rheumatoid arthritis) 200 mg orally daily in 2 divided doses, increasing to 400 mg daily for short-term management of disease flares/exacerbations **OR**
  - (primary dysmenorrhoea) 400 mg orally daily as single dose or 2 divided doses (first day), then 200 mg daily on following days for up to 5 days maximum **OR**
  - (acute postsurgical pain, musculoskeletal and/or soft tissue injury) initially 400 mg orally daily, then 200 mg 1–2 times daily on following days for up to 5 days maximum
Adverse effects
- see general Adverse effects for NSAIDs, however, gastrointestinal adverse effects occur less frequently
- increased risk of cardiac and thrombotic events

Interactions
- increased plasma levels may occur if given with fluconazole
- increased risk of renal impairment if given with ACE inhibitor/angiotensin receptor antagonist and thiazide diuretic at same time
- may decrease antihypertensive effects of ACE inhibitor or angiotensin receptor antagonist
- may decrease natriuretic effect of frusemide and thiazide diuretics because of renal prostaglandin synthesis inhibition
- increased risk of gastrointestinal adverse effects if given with oral glucocorticoids, especially in the elderly
- increased risk of gastrointestinal adverse effects if given with aspirin
- may increase plasma levels of lithium and warfarin, thereby increasing risk of toxicity; lithium and warfarin levels should be closely monitored, especially when starting, stopping or altering doses of celecoxib
- decreased plasma levels may occur if given with aluminium- or magnesium-containing antacids
- not recommended with other NSAIDs

Nursing points/Cautions
- any dehydration should be corrected before starting therapy
- any skin reactions usually occur within 4 weeks of starting therapy
- to lessen the risk of cardiovascular events, the lowest effective dose should be used for the shortest possible duration
- (long-term treatment) haemoglobin or haematocrit levels should be monitored regularly for signs of anaemia
- contraindicated in those with sensitivity to sulfonamides
- contraindicated in the treatment of pain in those undergoing coronary artery bypass graft (CABG) surgery
- contraindicated in those with unstable or significant ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease; congestive heart failure; severe liver or kidney impairment or creatinine clearance < 30 mL/min
- see general Nursing points/Cautions for NSAIDs (p. 3)

Patient teaching and advice
- advise patient to take antacids 2 hours before or after celecoxib
- warn patient to seek medical advice immediately if fainting, collapse, shortness of breath, chest pain or irregular heart beat occurs
- see general Patient teaching and advice (p. xxiii) and general Patient teaching and advice for NSAIDs (p. 3)

CHOLINE SALICYLATE (Bonjela Mouth Ulcer Gel, Bonjela Teething Gel, Herron Baby Teething Gel)

Available form
Gel: 15 g

Action
- local analgesic

Use
- painful oral irritation (e.g. teething)
- lesions of the mouth

Dose
- (adult) massage 1 cm gel to painful area 3-hourly OR
- (infant > 4 months) massage 0.5 cm gel to painful area 3-hourly if required (up to 6 applications/24 hours)

Adverse effects
- transient stinging on application
### Nursing points/Cautions
- contraindicated in babies less than 4 months old or children under 12 in combination with aspirin-containing products (to avoid excessive salicylate levels)

### Patient teaching and advice
- gel should not be applied directly to dentures

### Note
- contained in Curash Family Oral Pain Relieving Gel, Ora-Sed Jel, Seda-Gel

### DICLOFENAC SODIUM (Clonac, Dencorub Anti-Inflammatory Gel, Dinac, Fenac, Imflac, Solaraze 3% Gel, Viclofen, Voltaren, Voltaren Ophtha)

### DICLOFENAC POTASSIUM (Voltaren Rapid, Voltfast)

### DICLOFENAC DIETHYLAMMONIUM (Voltaren Emulgel)

#### Available forms
- Gel: 1%, 3%; Tablets (enteric coated): 25 mg, 50 mg; Tablets (rapid release): 12.5 mg, 25 mg, 50 mg; Suppositories: 12.5 mg, 25 mg, 50 mg, 100 mg; Powder: 50 mg/sachet; Eye Drops: 1 mg/mL

#### Action
- see general Actions for NSAIDs

#### Use
- rheumatoid arthritis, osteoarthritis
- acute or chronic inflammatory conditions
- primary dysmenorrhea
- acute migraine, headache
- cold and flu symptoms
- dental pain, back ache, muscle pain
- postoperative pain management in children
- postoperative inflammation following eye surgery (see Eye, ear, nose and throat agents)

#### Dose
- (primary dysmenorrhea) initially 50–100 mg orally daily, starting with onset of symptoms, increasing gradually if necessary (daily maximum 200 mg) **OR**
- (arthritis, inflammatory conditions) initially 75–150 mg orally daily in 2–3 divided doses, reducing to 75–100 mg orally in divided doses for long-term therapy (enteric-coated tablets, rapid release tablets) **OR**
- (arthritis, inflammatory conditions) initially 25 mg orally, followed by 12.5–25 mg orally 4–6 hourly if needed (daily maximum 75 mg) (12.5 mg rapid release tablets) **OR**
- (acute migraine) 50 mg orally at first sign of migraine, followed by 50 mg 2 hours later if pain is not relieved. If needed, further 50 mg can be taken at 4–6 hourly intervals (daily maximum 200 mg) **OR**
- (postoperative pain management in children aged 12 months and above) initially 1–2 mg/kg, followed by 1 mg/kg 3 times daily for up to 3 days if needed (daily maximum 3 mg/kg) (suppositories) **OR**
- (local pain, soft tissue injury, soft tissue rheumatism) apply gel to affected area and rub gently 3–4 times daily for up to 14 days

#### Adverse effects/Interactions
- see general Adverse effects and Interactions for NSAIDs
- may impair female fertility
- (suppositories) worsening of haemorrhoids
- (gel, occasionally) itching, reddened or scaly skin, photosensitivity

#### Nursing points/Cautions
- care should be taken when selecting tablets as rapid release and slow-release forms are available
- 100 mg suppositories should not be used for children or teenagers
suppositories should not be used in infants under 12 months
- suppositories are contraindicated in proctitis
- tablets contain lactose and are therefore not recommended in galactose intolerance, severe lactase deficiency or glucose/galactose malabsorption
- see general points for NSAIDs

Patient teaching and advice
- instruct patient that tablets should be swallowed whole with fluids, preferably before food for better absorption and efficacy, but can be taken with food if stomach is upset
- advise patient that diclofenac should not be used to prevent migraine (prophylaxis), only for the management and should be taken at first sign of headache
- patients who experience night pain and/or morning stiffness should be advised to take oral treatment during the day and suppositories at bedtime for better control of symptoms (daily maximum 150 mg)
- patient should be instructed that powder should be dissolved in non-carbonated water and may be drunk even if solution appears cloudy
- instruct adult patient in correct technique for suppository insertion, including the need to empty bowel before insertion
- patients with lactose or galactose intolerance should be warned that tablets contain lactose
- see general Patient teaching and advice (p. xxiii) and general Patient teaching and advice for NSAIDs

Note
- contained in Anthrotec 50 with Misoprostol

ETORICOXIB (Arcoxia)

Available forms
Tablets: 30 mg, 60 mg, 120 mg

Action
- COX-2 inhibitor preventing prostaglandin synthesis with actions similar to other NSAIDs

Use
- osteoarthritis
- acute gouty arthritis
- primary dysmenorrhoea
- minor dental pain

Dose
- (osteoarthritis) initially 30 mg orally daily, increasing to 60 mg orally daily if needed OR
- (acute gouty arthritis, primary dysmenorrhoea, dental pain) 120 mg orally daily (maximum 8 days)

Adverse effects
- dizziness, headache, diarrhoea
- dyspepsia, upper abdominal pain, diarrhoea
- dyspnoea
- peripheral oedema
- hypertension
- increased risk of myocardial infarction and stroke
- (rare) jaundice

Interactions
- may increase levels of ethinyloestradiol resulting in an increased risk of adverse effects such as venous thromboembolic events in at-risk women
- may decrease antihypertensive effects of ACE inhibitor or angiotensin receptor antagonist
- may decrease natriuretic effect of frusemide and thiazide diuretics because of renal prostaglandin synthesis inhibition
- not recommended with aspirin or other NSAIDs
- increased risk of gastrointestinal adverse effects if given with aspirin
- may reduce clearance of lithium, increasing plasma levels and risk of toxicity
decreased levels (and therefore decreased analgesic effect) may occur if given with rifampicin

Nursing points/Cautions
- any dehydration should be corrected before starting therapy
- hypertension should be controlled before starting therapy. BP should be monitored every 2 weeks throughout therapy and stopped if there is a significant increase
- to lessen the risk of cardiovascular events, the lowest effective dose should be used for the shortest possible duration
- caution if used in those with increased risk factors for cerebrovascular events (diabetes, hypertension, hypercholesterolaemia, family history of ischaemic heart disease, cardiac failure and/or smokers)
- contraindicated in those who have recently undergone CABG surgery or angioplasty
- contraindicated in those with unstable or significant ischaemic heart disease, peripheral arterial disease and/or cerebrovascular disease; hypertension which is not adequately controlled, congestive heart failure; severe liver or kidney impairment or creatinine clearance < 30 mL/min, active peptic ulceration or GI bleeding
- see general Nursing points/Cautions for NSAIDs

Patient teaching and advice
- warn patient to seek medical advice immediately if any of the following occurs:
  - fainting, collapse, shortness of breath, chest pain or irregular heart beat
  - vomiting blood or material that looks like coffee grounds, bloody diarrhoea, black sticky bowel motions or bleeding from the back passage
- advise patient against driving or operating machinery if dizziness occurs
- see Patient teaching and advice for NSAIDs or general Patient teaching and advice (p. xxiii)

FLURBIPROFEN (Strepfen Intensive)

FLURBIPROFEN SODIUM (Ocufen Eye Drops)

Available forms
Eye drops: 300 microgram/mL (0.03%); Lozenges: 8.75 mg

Action
- analgesic, anti-inflammatory and antipyretic agent that blocks the prostaglandins that constrict the iris sphincter independently of the cholinergic system

Use
- intra-operative miosis (see Eye section of Eye, ear, nose and throat agents)
- severe sore throat (see Oropharynx section of Eye, ear, nose and throat agents)

IBUPROFEN (Advil, Brufen, Bugesic, Bugesic Oral Suspension, Dimetapp Children’s Pain and Fever Relief Ibuprofen Suspension, Dimetapp Infant’s Pain and Fever Relief Ibuprofen Colour Free Suspension, iProfen Suspension for Children, Nurofen, Nurofen for Children, Nurofen for Children Infant Drops, Nurofen Gel, Nurofen Liquid Capsules, Nurofen Meltlets Lemon, Nurofen Tension Headache, Panafen IB, ProVen, Rafen, Tri-Profen)
IBUPROFEN LYSINE (Nurofen Migraine Pain)

Available forms
Capsules: 200 mg; Tablets: 200 mg, 400 mg; Tablets (melt in mouth): 200 mg; Syrup/Suspension: 100 mg/5 mL, 200 mg/5 mL; Gel: 5%

Action
- see general Action for NSAIDs
- half-life approximately 2 hours

Use
- rheumatoid arthritis, including juvenile rheumatoid arthritis, osteoarthritis
- primary dysmenorrhoea
- migraine (see Antimigraine agents)
- acute/chronic pain with inflammatory component

Dose
- (rheumatoid arthritis, osteoarthritis (acute exacerbation)) initially 1200–2400 mg orally daily in 3–4 divided doses with food, reducing to 1600 mg when symptoms stabilise OR
- (primary dysmenorrhoea) 400–800 mg orally with food at the first sign of pain or menstrual bleeding, then 400 mg 4–6 hourly up to a maximum daily dose of 1600 mg OR
- (minor aches and pains, dental pain, headache) 200–400 mg orally 4–6 hourly as needed, up to a daily maximum of 1600 mg OR
- (topical) apply 4–10 cm of gel 4-hourly (as needed) to affected area and rub gently (maximum 4 applications daily)

Adverse effects/Interactions/Nursing points/Cautions/Patient teaching and advice
- see general points for NSAIDs
- see general Patient teaching and advice (p. xxiii)
- oral solution should be shaken well before use
- meltlet tablets should be placed on tongue, allowed to dissolve and then swallowed or may be taken with water

Note
- contained in Nurofen Cold and Flu, Nurofen Plus, Panafen Plus, ProVen Plus, Sudafed Sinus+ Anti-Inflammatory Pain Relief Caplets

INDOMETHACIN (Arthrexin, Indocid, Indocid PDA)

Available forms
Capsules: 25 mg; Vial: 1 mg; Suppositories: 100 mg

Action
- see general Action for NSAIDs
- half-life is about 4.5 hours

Use
- rheumatoid arthritis, osteoarthritis, ankylosing spondylitis
- degenerative hip disease
- gout
- bursitis, capsulitis, tenosynovitis
- sprains and strains
- low back pain (lumbago)
- inflammation, pain and oedema following orthopaedic surgery or reduction and immobilisation of fractures and dislocations
- primary dysmenorrhoea
- medical closure of patent ductus arteriosus in newborn infants

Dose
- 50–200 mg orally daily with food in divided doses (daily maximum 200 mg) OR
- 100 mg rectal suppository once or twice daily if oral therapy not tolerated OR
- in combination e.g. 25 mg orally 2–4 times daily and 100 mg rectal suppository at night (to a total of 200 mg) OR
- (acute gouty arthritis) 150–200 mg orally daily with food in divided doses until symptoms subside OR
- (primary dysmenorrhoea) 25 mg orally 3 times daily with food at the first sign of pain or menstrual bleeding and...
continuing for as long as the symptoms usually last OR
● (closure of patent ductus arteriosus in newborn) course of 3 IV doses at 12–24 hour intervals with dosage dependent on age of infant: initially 0.2 mg/kg, then 0.1–0.25 mg/kg for remaining 2 doses

Adverse effects
● see general Adverse effects for NSAIDs (p. 2)
● may aggravate pre-existing psychiatric disturbances, epilepsy or parkinsonism
● (IV, newborns) transient decreased urine output, elevated blood urea and creatinine, reduced creatinine clearance, intracranial bleeding, tissue irritation at IV site
● (suppository) burning, pain, discomfort, itching, proctitis, tenesmus

Interactions
● see general Interactions for NSAIDs

Nursing points/Cautions
● see general points for NSAIDs
● (rheumatic conditions) loading dose not required
● avoid extravasation as solution is irritating to tissue
● IV indomethacin should only be administered in specialised units with neonatologist supervision
● IV solution should be prepared with either 0.9% sodium chloride or water for injection (preservative free). The preservative benzyl alcohol may cause toxicity in newborns and should be avoided
● further dilution of IV solution is not recommended as there is a risk of precipitation occurring
● IV dose should be given over 5–10 seconds
● urine output of newborn must be closely monitored and IV indomethacin not administered if output is less than 0.6 mL/kg/hour. Serum electrolytes and renal function should be closely monitored during therapy
● infant should be closely monitored for any signs of bleeding
● if ductus closes after first dose and remains closed for 48 hours, no further doses are required
● second course of IV indomethacin (1–3 doses) may be given to newborn at 12–24 hour intervals if ductus reopens. Surgery may be necessary if newborn remains unresponsive after 2 courses (6 doses total) of IV indomethacin
● IV indomethacin is contraindicated in infants with untreated infections, bleeding or coagulation disorders, necrotising enterocolitis, impaired renal function, congenital heart disease where pulmonary or systemic blood flow is dependent on patency of ductus arteriosus
● (suppository) contraindicated in those with proctitis or recent rectal bleeding
● (IV) contraindicated if infection is present or active intracranial/gastrointestinal bleeding is present

Patient teaching and advice
● see general points for NSAIDs
● see general Patient teaching and advice (p. xxiii)
● patients who experience night pain and/or morning stiffness should be advised to take oral treatment during the day and suppositories at bedtime for better control of symptoms

KETOROLAC TROMETAMOL (Acular Eye Drops, Ketoral Injection, Toradol)

Available forms
Tablets: 10 mg; Ampoule: 10 mg/mL, 30 mg/mL; Eye drops: 5 mg/mL

Action
● inhibits prostaglandin synthesis by inhibiting COX
● potent peripherally-acting analgesic
● half-life 5–6 hours
ANALGESICS, NSAIDs AND DMADs

- platelet inhibition reverses 24–48 hours after stopping

Use
- pain after surgery (short term not exceeding 5 days)
- seasonal allergic conjunctivitis (short term); prophylaxis and reduction of inflammation after cataract surgery (see Eye section of Eye, ear, nose and throat agents)

Dose
- (under 65 years) initially 10–30 mg IM, followed by 10–30 mg 4–6 hourly (maximum 90 mg daily) OR
- (over 65 years, less than 50 kg or less severe pain) initially 10–15 mg IM, followed by 10–15 mg 4–6 hourly (maximum 60 mg daily) OR
- (under 65 years) 10 mg orally 4–6 hourly (maximum 40 mg daily) OR
- (over 65 years) 10 mg orally 6–8 hourly (maximum 30–40 mg daily)

Adverse effects
- (injection site) pain, tingling, ecchymosis, bruising
- may impair female fertility
- (rare, but fatal) haemorrhage
- see general Adverse effects for NSAIDs

Interactions
- increased risk of seizure activity if given with antiepileptic agents (e.g. phenytoin, carbamazepine)
- may be used with opioid analgesics to achieve optimal analgesia or when the sedative or anxiolytic effect of the opioid is wanted
- increased risk of hallucinations if given with fluoxetine or alprazolam
- contraindicated with aspirin, NSAIDs, pentoxifylline (oxpentifylline), lithium or probenecid
- see general interactions for NSAIDs

Nursing points/Cautions
- any hypovolaemia should be corrected before administration of ketorolac trometamol
- IM injection should be given deeply and slowly into large muscle
- pressure should be applied to injection site for 15–30 seconds to decrease local effects
- total duration of use should not exceed 5 days because the risk of adverse effects increases with prolonged use
- conversion from parenteral to oral route should occur as soon as practicable
- contraindicated via epidural or intrathecal route
- contraindicated in those with dehydration, hypovolaemia, moderate/severe kidney impairment, coagulation disorders or on anticoagulant therapy, surgical procedures with high risk of bleeding, history of bleeding (gastrointestinal or intracranial)
- not recommended for obstetric procedures
- see general points for NSAIDs

KETOPROFEN (Orudis Gel, Orudis SR, Oruvail SR)

Available forms
- Capsules (sustained release): 100 mg, 200 mg; Suppositories: 100 mg; Gel: 2.5%

Action
- see general actions for NSAIDs
- half-life less than 2 hours

Use
- rheumatoid arthritis, osteoarthritis
- musculoskeletal inflammation or injury

Dose
- 100 mg rectal suppository at night supplemented as required with 100 mg orally 1–2 times daily OR
- 100–200 mg orally daily with food OR
- massage sufficient gel into affected area 2–4 times daily for up to 7 days
**Adverse effects**
- see general Adverse effects for NSAIDs (p. 2)
- non-bacterial cystitis (bladder pain, dysuria, haematuria, increased micturition and frequency)
- (suppositories) pain, burning, itching, tenesmus
- (gel) allergic skin reactions, localised erythema (especially if skin is exposed to UV rays during therapy)

**Interactions**
- see general Interactions for NSAIDs
- may reduce efficacy of gemeprost and intrauterine contraceptive devices, increasing risk of pregnancy
- increased risk of bleeding if given with oxpentifylline (also known as pentoxifylline)

**Nursing points/Cautions**
- suppositories provide more consistent control of overnight symptoms than oral medication
- suppositories are not recommended in those with haemorrhoids or recent proctitis or rectal bleeding
- gel is contraindicated in open or infected wounds or skin conditions such as eczema
- see general points for NSAIDs

**Patient teaching and advice**
- patients who experience night pain and/or morning stiffness should be advised to take oral treatment during the day and suppositories at bedtime for better control of symptoms
- recommend that slow-release tablets should not be broken, crushed or chewed but swallowed whole
- warn patient about symptoms of non-bacterial UTI symptoms
- advise patient against using gel under an occlusive dressing
- (gel) warn patient to avoid exposure to ultraviolet light (including solarium) during treatment and for 2 weeks following therapy
- advise patient that if rash appears when using gel, therapy should be stopped
- patient should be advised to wash hands after applying gel and avoid contact with eyes or mouth
- see general Patient teaching and advice (p. xxiii)

**MEFENAMIC ACID (Ponstan)**

**Available form**
Capsules: 250 mg

**Action**
- see general Actions for NSAIDs
- half-life 2 hours

**Use**
- primary dysmenorrhoea
- primary menorrhagia
- mild to moderate pain (e.g. dental and soft tissue pain)

**Dose**
- (primary dysmenorrhoea) 500 mg orally 3 times daily with food from onset of pain for usual duration of pain **OR**
- (primary menorrhagia) 500 mg orally 3 times daily with food from onset of menses and continued according to doctor’s advice, not exceeding 7 days (except on doctor’s advice) **OR**
- (other indications) 500 mg orally 3 times daily with food

**Adverse effects**
- see general Adverse effects for NSAIDs, particularly diarrhoea

**Interactions/Nursing points/Cautions/Patient teaching and advice**
- see general points for NSAIDs
- advise patient that diarrhoea is dose dependent and disappears when medication is stopped
- contraindicated in those who have previously experienced mefenamic acid-induced diarrhoea
MELOXICAM (Meloxicibell, Meloxicam-GA, Mobic, Movalis, Movalis Capsules, Moxicam)

**Available forms**
Tablets: 7.5 mg, 15 mg; Capsules: 7.5 mg, 15 mg

**Action**
- selective COX-2 inhibitor
- half-life 20 hours
- see general Actions for NSAIDs

**Use**
- osteoarthritis, rheumatoid arthritis

**Dose**
- (osteoarthritis) 7.5 mg orally daily with food, increasing to 15 mg daily if needed (daily maximum dose 15 mg) **OR**
- (rheumatoid arthritis) 15 mg orally daily with food, decreasing to 7.5 mg daily if condition allows

**Adverse effects**
- diarrhoea, dyspepsia, abdominal pain
- headache
- oedema

**Interactions**
- caution if given with sulfamethoxazole as increased levels of either drug is possible, increasing risk of adverse effects
- caution if given with ketoconazole, itraconazole, erythromycin, cyclosporin and amiodarone
- increased elimination if given with cholestyramine
- see also general Interactions for NSAIDs

**Nursing points/Cautions**
- contains lactose, therefore contraindicated in those with hereditary galactose intolerance
- see general points for NSAIDs

METHYL SALICYLATE (Methyl Salicylate Liniment, Cream and Ointment)

**Available forms**
Cream, Liniment and Ointment

**Action**
- topical analgesic

**Use**
- relief of pain and inflammation associated with rheumatic conditions, lumbago and other musculoskeletal disorders

**Dose**
- massage into affected area 2–3 times daily

**Adverse effects**
- acute poisoning has occurred when taken orally
- mild skin irritation, erythema

**Interactions**
- excessive use may increase risk of bleeding in those taking warfarin or other anticoagulants

**Patient teaching and advice**
- patient should be advised to wash hands after applying gel and avoid contact with eyes or mouth
- warn patient to avoid vigorous rubbing
- caution patient to keep medication away from open flame

**Note**
- contained in Arthrirub, Biosal Arthritis Cream, Bosisto’s Eucalyptus Rub, Deep Heat, Dencorub Extra Strength Heat Gel, Dencorub Pain Relieving Cream, Goanna Heat Cream, Goanna Liniment, Goanna Salve, Metsal Heat Rub Cream and Gel

NAPROXEN (Inza, Naprosyn preparations, Proxen SR)
NAPROXEN SODIUM (Anaprox, Crysanal, Eazydayz Tablets, Naprofem, Naprogesic, Nurolasts)

Available forms
- Tablets: 220 mg, 250 mg, 275 mg, 500 mg, 550 mg; Tablets (sustained release): 750 mg, 1000 mg; Suspension: 25 mg/mL

Action
- see general Action for NSAIDs
- half-life 14 hours

Use
- rheumatoid arthritis, osteoarthritis, ankylosing spondylitis
- acute/chronic inflammatory pain
- migraine
- primary dysmenorrhoea

Dose
- (arthritis, spondylitis) 550–1100 mg orally daily in 2 divided doses with food OR
- (arthritis, spondylitis) 750–1000 mg orally once daily (SR) OR
- (primary dysmenorrhoea) 500–550 mg orally with food at the first sign of pain or bleeding, then 250–275 mg 6–8 hourly as required (daily maximum 1250–1375 mg) OR
- (primary dysmenorrhoea) 440 mg orally with food at the first sign of pain or bleeding, then 220 mg after 12 hours (daily maximum 660 mg) (220 mg tablets) OR
- (migraine) 825 mg orally at first sign of impending headache, then 275–550 mg throughout day, but not before 1 hour of initial dose (daily maximum 1375 mg) OR
- (acute inflammatory pain) initially 550 mg orally with food, then 275 mg 6–8 hourly (daily maximum 1375 mg) OR
- (acute inflammatory pain) initially 220–440 mg orally with food, then 220 mg after 12 hours (daily maximum 660 mg) (220 mg tablets)

Adverse effects/Interactions
- see general Adverse effects and Interactions for NSAIDs

Nursing points and Cautions/Patient teaching and advice
- instruct patient to discontinue medication 72 hours before adrenal function tests
- advise patients that sustained release tablets should be taken whole, not crushed or chewed
- caution patients on sodium restricted diet that tablets contain sodium (1 mEq) (Aleve)
- see general points for NSAIDs
- see general Patient teaching and advice (p. xxiii)

Note
- Contained in Vimovo with Esomeprazole

PARACETAMOL (Duatrol SR, Dymadon, Dymadon P, Febridol, Febridol Clear Effervescent Soluble Tablets, Febridol Infant Drops, Lemsip Max, Lemsip Original Lemon, Panadol preparations, Panamax, Paracetamol Soluble Tablets, Paralgin, Perfalgan)

Available forms
- Tablets: 500 mg; Tablets (modified release): 665 mg; Tablets (soluble): 250 mg, 500 mg; Tablets (chewable): 120 mg Caplets: 500 mg; Gel Caps: 500 mg; Suppositories: 125 mg, 250 mg, 500 mg; Sachets (powder): 500 mg, 1 g; Syrup/Suspension/Elixir: 24 mg/mL, 48 mg/mL, 120 mg/5 mL, 250 mg/5 mL; Drops: 50 mg/mL, 100 mg/mL; IV solution: 10 mg/mL

Action
- analgesic, antipyretic but has no useful anti-inflammatory properties
- action thought to be related to prostaglandin synthesis inhibition (via COX inhibition) in the CNS
• half-life 1–3 hours
• suitable alternative for those with aspirin allergy (including those with asthma), dyspepsia or peptic ulceration or children with fever caused by viral illness

Use
• mild to moderate pain
• headache, migraine, tension headache, sinus pain
• muscle ache
• arthritis
• toothache
• cold and flu symptoms
• fever

Dose
• 0.5–1 g orally 3–4 hourly as required (up to 4 g/day) OR
• 1330 mg orally 6–8 hourly as required (up to 4 g/day) (modified release tablets) OR
• 0.5–1 g rectal suppository 4–6 hourly as required (up to 4 g/day) OR
• (≥ 50 kg) 1 g IV up to 4 times daily (up to 4 g/day) OR
• (< 50 kg) 15 mg/kg IV up to 4 times daily (up to 4 g/day)

Adverse effects
• (rarely) nausea, dyspepsia, allergic or haematological reaction
• hepatic necrosis (10–15 g or more), renal dysfunction
• (IV) nausea, vomiting, diarrhoea, dyspepsia, increase in liver enzymes, injection site pain

Interactions
• absorption rate may be increased by metoclopramide
• prolonged dosage may require reduction in anticoagulant dose
• large or chronic doses of paracetamol increase the likelihood of hepatotoxicity if given with concurrent use of alcohol or antiepileptic drugs
• may decrease clearance of busulfan
• products containing paracetamol should not be given together (e.g. oral and IV) to avoid risk of overdose and hepatic damage
• (IV) probenecid reduces clearance
• (IV) metabolism may be increased (therefore increasing level of hepatotoxic metabolites) by barbiturates, anticoagulants, isoniazid, zidovudine, amoxycillin and clavulanic acid, carbamazepine and phenytoin

Nursing points/Cautions
• administer alone IV
• IV infusion given over 15 minutes
• IV solution has slight yellow colour
• IV administration should be changed to oral administration as soon as practicable
• overdose symptoms: anorexia, nausea, vomiting, abdominal pain, hypotension, lethargy, sweating, confusion, hepatic necrosis/failure (jaundice, hypoglycaemia, metabolic acidosis)
• symptoms of overdose in first 48 hours may not reflect potential seriousness, as symptoms of liver failure may not manifest for at least 72 hours
• caution if used in those with renal dysfunction or glucose-6-phosphate dehydrogenase deficiency as haemolytic anaemia may result
• safe to use during pregnancy and breastfeeding at analgesic doses
• (IV) caution if used in those with dehydration, hypovolaemia, chronic malnutrition (including anorexia, bulimia or cachexia) or chronic alcoholism (> 3 drinks/day)
• contraindicated in those with liver disease/failure

Patient teaching and advice
• instruct patient to dissolve effervescent and soluble preparations in ½–1 glass of water for more rapid absorption
• patient should be cautioned regarding risk of overdose
● caution if using paracetamol products containing sodium in those with a salt-restricted diet (e.g. Panadol Soluble, Panadol Rapid)

**Note**

● not recommended for infants under 1 month of age
● after taking blood for paracetamol assay, overdose should be treated promptly (within 10 hours) with activated charcoal and sorbitol or gastric lavage to reduce gastric absorption and with IV acetylcysteine (Parvolex) to protect against liver damage (see Chelating agents, antidotes and antagonists) if 10–15 g or more of paracetamol has been ingested. Liver tests are recommended at start of overdose management, then daily

**PARECOXIB SODIUM (Dynastat)**

*Available form*  
Vial: 40 mg

**Action**

● selective COX-2 inhibitor  
● rapidly converted to valdecoxib, which is the active component  
● see general Actions for NSAIDs  
● onset of analgesia 7–14 minutes, peak reached within 2 hours, duration of action 6–24 hours, half-life about 8 hours

**Use**

● postoperative pain (single dose)

**Dose**

● 40 mg IV or IM as once-only dose

**Adverse effects**

● hypotension, hypertension, dizziness
● peripheral oedema
● hypoaesthesia
● nausea, vomiting, abdominal pain, dyspepsia, constipation
● hypokalaemia
● insomnia
● pharyngitis, respiratory insufficiency
● pruritus, increased sweating
● oliguria

**Interactions**
● increased serum levels may occur if given with ketoconazole or fluconazole
● caution if given with warfarin, therefore international normalised ratio (INR) should be closely monitored
● may decrease clearance of lithium, therefore blood levels should be closely monitored
● caution if given with ACE inhibitors

**Nursing points/Cautions**
● reconstituted using sodium chloride 0.9% 2 mL (40 mg) or 1 mL (20 mg)
● administer alone
● incompatible with lactated Ringer’s or glucose 5% in lactated Ringer’s as precipitate will form and therefore should not be reconstituted with these fluids or added into IV lines with these fluids already running
● contraindicated in those with known allergy to sulfonamides
● see general points for NSAIDs

### PHENAZONE

**Action**
● topical analgesic

**Use**
● acute otitis media (see Ear section of Eye, ear, nose and throat agents)

**Note**
● contained in Auralgin Otic, Ear Clear for Ear Ache Relief

### PIROXICAM (Feldene, Feldene D, Feldene Gel, Mobilis, Mobilis D)

**Available forms**
Capsules: 10 mg, 20 mg; Capsules (dispersible): 10 mg, 20 mg; Tablets: Gel: 5 mg/g

**Action**
● see general Actions for NSAIDs
● half-life 36–45 hours

**Use**
● rheumatoid arthritis, osteoarthritis, ankylosing spondylitis
● acute soft tissue injuries

**Dose**
● 10–20 mg orally as a single daily dose
● OR
● 1 g (3 cm of gel) to affected area 3–4 times daily for up to 2 weeks

**Adverse effects**
● (gel) mild skin irritation, transient skin discolouration
● see general points for NSAIDs

**Interactions**
● see general points for NSAIDs

**Nursing points/Cautions**
● once-daily dose required because of long plasma half-life (capsules)
● see general points for NSAIDs

**Patient teaching and advice**
● patient should be advised to wash hands after applying gel and avoid contact with eyes or mouth
● instruct patient to dissolve dispersible tablets in not less than 50 mL of water
● caution patient to not cover gel with occlusive dressing
● warn patient that gel should not be applied to broken, irritated or infected skin
● advise patient that gel should be completely rubbed in to prevent skin discolouration or staining of clothes
SULINDAC (Aclin)

Available forms
Tablets: 100 mg, 200 mg

Action
- see general Action for NSAIDs
- prodrug that has a biologically active metabolite
- half-life 7–8 hours; half-life of active metabolite 16.4 hours

Use
- rheumatoid arthritis
- osteoarthritis
- ankylosing spondylitis
- acute gouty arthritis
- acute or chronic pain with an inflammatory component

Dose
- 400 mg orally daily or in 2 divided doses with food or milk

Adverse effects
- urine discolouration
- see general points for NSAIDs

Interactions
- see general points for NSAIDs
- if given as a single dose, patient should be advised to take in the evening
- if given for acute gouty arthritis, treatment is usually for 7 days
- see general points for NSAIDs
- see Patient teaching and advice for NSAIDs and general Patient teaching and advice (p. xxiii)

TIAPROFENIC ACID (Surgam)

Available form
Tablets: 300 mg

Action
- see general Actions for NSAIDs
- half-life 2–3 hours

Use
- rheumatoid arthritis, osteoarthritis

Dose
- 300–600 mg orally daily in divided doses

Adverse effects
- see general Adverse effects for NSAIDs (p. 2)
- non-bacterial cystitis (bladder pain, dysuria, haematuria, increased micturition and frequency)

Interactions/Nursing points/Cautions/Patient teaching and advice
- see general points for NSAIDs
- before starting therapy, patients should be assessed for any urinary symptoms
- patients should be advised to report any urinary symptoms promptly to their doctor
- urinary symptoms usually resolve quickly when medication is stopped
- advise patients to take tablets with plenty of fluids unless otherwise contraindicated
- not recommended in those with active bladder or prostate disease/symptoms, recurrent urinary tract disorders

DISEASE-MODIFYING ANTIRHEUMATIC DRUGS (DMARDs)

Arthritis is a term used to describe disease of the joints with common forms including rheumatoid arthritis (RA), osteoarthritis, juvenile idiopathic arthritis and spondylarthropathies (e.g. ankylosing spondylitis). RA is the most...
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common autoimmune disease in Australia, affecting about 1% of the population (AIHW, 2011a).

RA is characterised by inflammation and thickening of the synovial membrane (synovitis). This unrelenting inflammation leads to destruction of tissue, cartilage erosion and, at times, rupturing of tendon fibres (AIHW, 2011a). Most commonly, the small joints of the hands and feet are involved. RA is a rapidly progressing disease which often takes an erratic and unpredictable course (AIHW, 2011). Even with treatment, RA sometimes still progresses, with destruction of the affected joints, deformity, disability and possible reduction in life expectancy (RACGP, 2009). Early diagnosis and treatment with DMARDs is essential in slowing disease progression and achieving remission. There is some evidence to suggest that early use of DMARDs is associated with an improvement in long-term functional outcomes (RACGP, 2009).

The DMARDs are a heterogeneous group of drugs which are anti-inflammatory and immune-suppressing in nature (AIHW, 2011). Although mainly used to treat RA, they are also used to treat other autoimmune diseases such as Crohn's disease, psoriatic arthritis and systemic lupus erythematosus (SLE). DMARDs are broken up into two groups – the 'conventional' DMARDs (e.g. methotrexate, gold, sulfasalazine) and the biological DMARDs. These biological DMARDs (etanercept, infliximab, adalimumab, anakinra) are a newer group that target pro-inflammatory cytokines involved in joint destruction and although expensive, are being used more commonly in the treatment of RA (AIHW, 2011). Onset of action of the DMARDs is often slow, taking weeks to months before clinical improvement is apparent. They are used alone, or in combination with other DMARDs, NSAIDs and/or corticosteroids. Methotrexate is now considered to be first line treatment of RA, compared to earlier management which consisted of NSAIDs, with DMARDs only being added into the regimen when damage to the joint had occurred (RACGP, 2009).

Tumour necrosis factor alpha (TNF-α) is important for both immune responsibility and host defences and therefore TNF-α antagonist use predisposes the user to a range of infections (especially tuberculosis), particularly in the first 24 months of therapy. These biological agents should also be avoided in those with chronic hepatitis B and C if liver pathology is present, upper respiratory tract infections and fever, skin ulcers which have not healed, active herpes zoster infection or life-threatening fungal infection (Saag et al, 2008, cited in Bryant & Knights, 2011).

Adjunctive treatment for RA should also include physiotherapy, occupational therapy, exercises and, most importantly, patient education and access to support services (e.g. Arthritis Foundation).

**ABATACEPT (Orencia)**

**Available form**
Vial: 250 mg

**Action**
- modulates key co-stimulatory signal required for full activation of T-lymphocytes which are found in the synovium of those with RA
- half-life 8–25 days

**Use**
- moderate to severe rheumatoid arthritis (with methotrexate) (unresponsive to other DMARDs)
● moderate to severe active polyarticular juvenile idiopathic arthritis (unresponsive to other DMARDs) (alone or with methotrexate)

Dose
● (rheumatoid arthritis) (patient weight < 60 kg) 500 mg, (60–100 kg) 750 mg or (> 100 kg) 1 g IV over 30 minutes given 2 and 4 weeks after initial infusion, then monthly OR
● (polyarticular juvenile idiopathic arthritis) (patient weight < 75 kg) 10 mg/kg IV over 30 minutes given 2 and 4 weeks after initial infusion, then monthly (if patient weight is > 75 kg, regimen for rheumatoid arthritis is followed (maximum 1 g))

Adverse effects
● headache, dizziness, fatigue, asthenia
● nausea, abdominal pain, diarrhoea, dyspepsia
● infusion-related reaction (dizziness, hypertension, nausea, headache)
● infection (lower respiratory, urinary tract, upper respiratory), rhinitis, herpes simplex
● hypertension, flushing
● cough
● rash
● abnormal liver function
● (uncommon) hypersensitivity

Interactions
● not recommended with tumour necrosis factor (TNF) inhibitors, rituximab or anakinra
● not recommended with or within 3 months of live attenuated vaccine
● may cause a falsely elevated blood glucose reading on the day of infusion (if test strips contain glucose dehydrogenase pyrroloquinoline-quinone as this reacts with maltose in the solution)

Nursing points/Cautions
● patients should be screened for any signs of infection before starting therapy. This should include screening for hepatitis B and tuberculosis (clinical history, chest X-ray, skin tuberculin test). If latent tuberculosis is diagnosed, it should be treated with appropriate antimycobacterial agents before starting therapy
● (polyarticular juvenile idiopathic arthritis) vaccinations should be up-to-date before starting therapy
● dosage is dependent on body weight
● reconstitute by gently injecting Water for Injection into vial, avoiding vigorous agitation or shaking
● after reconstitution, vial should be vented with a needle to dispel any foam formed
● reconstituted solution should be clear and colourless to pale yellow
● reconstituted solution should then be added to a 100 mL bag of 0.9% sodium chloride, first removing the equivalent amount of sodium chloride (e.g. if 4 vials have been reconstituted equalling 40 mL, then 40 mL of sodium chloride should be removed before adding the reconstituted solution)
● administer alone
● contains 8.6 mg sodium per vial, which may need to be considered for those on a sodium-controlled diet
● patients should be monitored during and after infusion for any signs of infusion-related events
● patient should be monitored for any signs of infection and therapy discontinued if they develop a serious infection
● caution if used in those with chronic obstructive pulmonary disease as respiratory symptoms (cough, dyspnoea, rhonchi) may be exacerbated
● contraindicated in those with severe infections, including sepsis and tuberculosis

Patient teaching and advice
● tell patient that IV infusion will take 30 minutes
patients requiring blood glucose monitoring should be warned that falsely elevated levels may occur post-infusion
- advise patients not to drive or operate machinery if they experience dizziness
- see general Patient teaching and advice (p. xxiii)

not recommended during pregnancy or breastfeeding

**ADALIMUMAB (Humira)**

**Available forms**
Prefilled syringe: 20 mg/0.4 mL, 40 mg/0.8 mL; Prefilled pen: 40 mg/0.8 mL

**Action**
- recombinant monoclonal antibody (IgG1) that neutralises activity of tumour necrosis factor (TNF). (TNF is involved in inflammatory and immune responses and found in high levels in the synovial fluid of those with RA. It is thought to be involved in both joint inflammation and erosion. Raised TNF levels are also found in those with psoriatic arthritis, psoriatic plaques and ankylosing spondylitis)
- long half-life 10–20 days

**Use**
- rheumatoid arthritis
- psoriatic arthritis (unresponsive to other DMARDs)
- ankylosing spondylitis
- polyarticular juvenile idiopathic arthritis (over 4 years)
- psoriasis
- Crohn’s disease (inadequate response to conventional therapies or intolerant/unresponsive to infliximab) (see Gastrointestinal agents (Miscellaneous))

**Dose**
- (rheumatoid arthritis) 40 mg SC fortnightly (or weekly if not given concurrently with methotrexate) OR
- (psoriatic arthritis, ankylosing spondylitis) 40 mg SC fortnightly OR
- (psoriasis) initially 80 mg SC, then 1 week later 40 mg SC, repeated fortnightly OR
- (polyarticular juvenile idiopathic arthritis) 20 mg SC fortnightly (weight 15 kg to less than 30 kg) or 40 mg SC fortnightly (weight 30 kg or more)

**Adverse effects**
- injection site reaction (erythema, itching, swelling)
- rash, pruritus, urticaria, dermatitis herpes simplex, bruising, dermatitis
- cough, sinusitis, dyspnoea, asthma
- visual impairment
- musculoskeletal pain, muscle spasm
- headache, migraine, vertigo
- paraesthesia, sciatica
- tachycardia, hypertension
- depression, anxiety, insomnia
- nausea, vomiting, abdominal pain, dyspepsia, elevated liver enzymes
- haematuria, renal impairment
- benign neoplasm, skin cancer
- leucopenia, thrombocytopenia, leukocytosis
- hyperlipidaemia, hyperkalaemia, hypercalcaemia, hyperglycaemia
- impaired healing
- infection (upper and lower respiratory, urinary tract, soft tissue, reproductive tract, ear and oral, fungal)
- (uncommonly) reactivation of tuberculosis, development of autoantibodies, lupus-like syndrome, serious allergic reaction

**Interactions**
- not recommended with live attenuated vaccines
- contraindicated with anakinra
- not recommended with abatacept
Nursing points/Cautions

- before starting therapy, patients should be:
  - screened for any signs of infection. This should include screening for hepatitis B and tuberculosis (TB) (clinical history, chest X-ray, skin tuberculin test) as these can become reactivated. If latent TB is diagnosed, it should be treated with appropriate antimycobacterial agents before starting therapy. If active TB is found, therapy should not be started; and
  - examined for non-melanoma skin cancer
- rotate injection sites (thigh or abdomen), avoiding skin that is reddened, bruised, tender or hard
- do not mix with other agents in the syringe
- patients may be taught to self-administer medication SC. They should be educated about rotation of sites, injection technique, storage requirements and safe disposal of used needles
- (polyarticular juvenile idiopathic arthritis) all immunisations should be up-to-date before starting therapy
- therapy should be stopped if any new serious infection or lupus-like symptoms develop
- needle covers of prefilled syringes contain latex and should not be handled by or administered to anyone with a latex sensitivity
- if undergoing surgery, patient should be closely monitored for any signs of infection
- caution if used in those who have recently been diagnosed with CNS demyelinating disease, on concurrent immunosuppressive therapy (as there is an increased risk of infection) or heart failure (as it may be worsened)
- contraindicated in those with severe infections (including active tuberculosis) or moderate to severe heart failure

Patient teaching and advice

- patients should be counselled to immediately seek medical advice if they develop persistent cough, loss of weight or low-grade fever (signs of TB)
- ask patient if he/she has a latex sensitivity as needle covers of prefilled syringes contain latex
- women of childbearing age should be advised to use adequate contraception during therapy
- patients may be taught to self-administer medication SC. Information should include:
  - checking expiry date before using and not giving injection if syringe has been out of the refrigerator for more than 12 hours
  - allowing syringe to come to room temperature before administration
  - gently inverting, not shaking, syringe before administration. If solution looks frothy, it should be allowed to rest until it clears before using
  - giving SC injection under the skin using the technique demonstrated by the doctor/nurse. Sites should be rotated between abdomen and thigh to prevent discomfort
  - giving SC injection at the same time every day
  - protecting prefilled syringes from light before use and storing them at 2–8°C, but not frozen
  - safe disposal of used syringe

ANAKINRA (Kineret)

Available form
Prefilled syringe: 100 mg/0.67 mL

Action

- recombinant, non-glycosylated human interleukin-1 receptor antagonist
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(interleukin-1 is thought to play a part in both inflammatory and immunological responses, including the degradation of cartilage and stimulation of bone resorption)

- half-life 4–6 hours

**Use**
- active rheumatoid arthritis (with methotrexate) that is unresponsive to other DMARDs

**Dose**
- 100 mg daily SC

**Adverse effects**
- increased incidence of infections (including cellulitis, pneumonia, bone/joint)
- mild injection site reaction (erythema, ecchymosis, inflammation, pain)
- headache, dizziness, insomnia
- nausea, diarrhoea, abdominal pain, dyspepsia
- hypertension
- limb pain, back pain, myalgia
- increased risk of lymphoma

**Interactions**
- contraindicated with TNF-alpha antagonist drugs (e.g. etanercept, infliximab)
- should not be given with live attenuated vaccines

**Nursing points/Cautions**
- baseline blood counts (WBC, platelets, absolute neutrophil count) should be measured before starting and monitored regularly throughout therapy
- needle covers of prefilled syringes contain latex and should not be handled by or administered to anyone with a latex sensitivity
- caution if used in those with a known history of recurring infections or conditions that may predispose them to infection
- not recommended in those with severe renal impairment
- contraindicated in those with known hypersensitivity to *E. coli*-derived products

**Patient teaching and advice**
- patients may be taught to self-administer ankakirna SC. They should be educated about rotation of sites, injection technique, storage requirements and safe disposal of used needles
- patients can be instructed to self-administer anakinra subcutaneously. See patient teaching and advice for adalimumab for specific subcutaneous injection advice
- see also general Patient teaching and advice (p. xxiii)

**AURANOFIN (Ridaura)**

**Available form**
- Tablets: 3 mg

**Action**
- synthetic gold complex that decreases inflammation, levels of rheumatoid factor and elevated immunoglobulin levels
- may slow progression of joint erosion
- anti-inflammatory action
- clinical improvement seen in 3–4 months after initiation of therapy
- elimination half-life increased from about 17 days to 26 days after 6 months of therapy

**Use**
- rheumatoid arthritis that is unresponsive or intolerant to NSAIDs

**Dose**
- initially 6 mg orally daily with food, increasing to 9 mg in 3 divided doses if needed
Adverse effects
- diarrhoea, constipation, flatulence
- anorexia, nausea, vomiting, abdominal pain/cramps, dyspepsia, distorted taste, stomatitis, glossitis
- conjunctivitis
- rash, pruritus, hair loss
- phototoxicity
- blood dyscrasia
- haematuria, proteinuria, blood urea and serum creatinine, nephrotoxicity
- increased liver enzymes

Interactions
- not recommended with other agents causing blood dyscrasias or bone marrow depression
- caution if used with warfarin, clonidine or dextropropoxyphene

Nursing points/Cautions
- diabetes, heart failure or hypertension should be controlled/corrected before starting therapy
- GI symptoms are dose-related and those with low body weight are at greatest risk
- auranofin-induced diarrhoea can be controlled by decreasing dose
- renal and liver function tests, blood count (with differential white cell count), haemoglobin, complete urinalysis (with urinary protein levels) should be performed before starting therapy
- monthly blood counts (with differential white cell count), platelet count and urinary protein levels are recommended
- ophthalmological examination is recommended periodically throughout therapy
- overlap or washout period not required if transferring from injectable gold preparations
- caution if used in those with inflammatory bowel disease or history of atopy
- contraindicated in those with previous toxicity or sensitivity to gold or heavy metals, liver/kidney disease, severe chronic dermatitis, bone marrow depression or haematological disorders or gold-induced pulmonary fibrosis or necrotising enterocolitis

Patient teaching and advice
- instruct patient to avoid exposure to strong direct sunlight
- patient should be advised to immediately report any metallic taste (sign of impending toxicity) or pruritus (early sign of intolerance) to doctor
- tablets should be protected from sunlight
- caution women of childbearing age to use adequate contraception during and for at least 6 months after stopping therapy because gold is slowly excreted from the body, which may have negative effects on a developing fetus
- see also general Patient teaching and advice (p. xxiii)

Not recommended during pregnancy

Secrected in breast milk, therefore not recommended during breastfeeding; because gold is slowly excreted from the body after stopping therapy, this should be taken into account if a woman wants to breastfeed

CYCLOSPORIN (Neoral, Sandimmun)

Available forms
Capsules: 10 mg, 25 mg, 50 mg, 100 mg; Oral solution: 100 mg/mL; Ampoule: 50 mg/mL, 250 mg/5 mL

Action
- potent immunosuppressive agent
- thought to act by blocking both lymphocytes and antigen-triggered lymphokine release by activated T cells
- half-life 6.3 hours, increasing to 20.4 hours in those with severe liver disease

**Use**
- prevention of graft versus host disease in organ transplantation (see Immunomodifiers)
- induction and/or maintenance of remission in nephrotic syndrome (when other therapies have been ineffective or inappropriate and renal function is still intact)
- severe, active rheumatoid arthritis (when other therapies have been ineffective or inappropriate)
- severe psoriasis (when other therapies have been ineffective or inappropriate)
- severe atopic dermatitis (when other therapies have been ineffective or inappropriate)

**Dose**
- (rheumatoid arthritis) 3 mg/kg daily orally in 2 divided doses for first 6 weeks of therapy (which may be continued to 12 weeks for full effectiveness). If no clinical response in 4–8 weeks, dose may be increased by 0.5–1.0 mg/kg/day at 1–2-month intervals to 5 mg/kg/day maximum. If the patient has been stable for at least 3 months, the dose may be decreased by 0.5 mg/kg/day at 1–2-month intervals to achieve the lowest effective dose OR
- (psoriasis) 2.5 mg/kg orally daily in 2 divided doses, increasing to 5 mg/kg if there is no clinical response in 4 weeks OR
- (nephrotic syndrome) 2.5–5 mg/kg/day, decreasing to lowest effective dose (maintenance) OR
- (atopic dermatitis) initially 2.5–5 mg/kg orally daily in 2 divided doses, reducing dose gradually when satisfactory response has been achieved

**Adverse effects**
- hypertension
- fluid retention and oedema
- hyperkalaemia, hyperuricaemia, hypomagnesaemia, hyperlipidaemia
- weight increase
- tremor, fatigue, burning sensation in hands and feet (initially)
- muscle cramps, myalgia
- headache, paraesthesia, convulsions
- hirsutism, rash
- dysmenorrhoea/amenorrhoea (reversible)
- gingival hypertrophy
- anorexia, nausea, vomiting, diarrhoea, abdominal pain
- anaemia, increased susceptibility to or aggravation of infection
- impaired renal function, hepatic dysfunction, acute pancreatitis
- increased risk of malignancy
- (IV) anaphylactoid reactions

**Interactions**
- increased risk of nephrotoxicity when low dose cyclosporin is given with NSAIDs requiring regular monitoring of kidney function
- may increase serum levels of sirolimus and everolimus
- increased serum creatinine may occur if given with sirolimus or everolimus
- increased risk of nephrotoxicity if given with tacrolimus
- may increase bioavailability of diclofenac
- caution if given with lercanidipine as serum level of both agents may be increased
- increased risk of hyperkalaemia if given with potassium containing or potassium sparing medications
- caution if given with ACE inhibitors or angiotensin II receptor antagonists
- not recommended with UVB irradiation or PUVA chemotherapy because of increased risk of skin cancer development
reversible renal impairment may occur if given with fenofibrate or other fibric acid derivatives

not recommended with other known nephrotoxic drugs such as aminoglycosides, amphotericin, ciprofloxacins, colchicine, histamine H₂ antagonists, melphalan, methotrexate, NSAIDs, trimethoprim and vancomycin

blood levels (and associated toxicity) may be increased if given with allopurinol, amiodarone, azole antifungal agents, cholic acid, colchicine, danazol, diltiazem, doxycycline, grapefruit juice, imatinib, macrolide antibiotics, metoclopramide, methylprednisolone (high dose), oral contraceptives, protease inhibitors, verapamil and voriconazole

increased risk of muscle toxicity (muscle pain, weakness, myositis, rhabdomyolysis) if given with atorvastatin, colchicine, pravastatin or simvastatin because of decreased clearance

blood levels may be decreased if given with barbiturates, carbamazepine, ciprofloxacins, isoniazid, octreotide, orlistat, phenytoin, rifampicin, St John’s wort, sulfamethoxazole/trimethoprim (IV)

not recommended with thiazide or loop diuretics because of increased risk of pre-renal azotaemia, worsening hyperuricaemia, glucose intolerance or hyperlipidaemia

not recommended with live attenuated vaccines

not recommended with alcohol

increased risk of gingival hyperplasia if given with nifedipine or amlodipine

may decrease clearance (and therefore increase blood levels) of colchicine, digoxin, etoposide, prednisolone and statins, and increasing risk of toxicity

**Nursing points/Cautions**

- capsules and oral solution are bioequivalent
- any infections should be identified and treated before starting therapy
- adverse effects are more common when cyclosporin is used for transplant patients than when used for other conditions because the dose is higher
- (nephrotic syndrome) dose is dependent on renal function. If improvement is not seen in 12 weeks, therapy should be stopped
- (nephrotic syndrome) renal biopsy is recommended if therapy continues for 12 months
- (psoriasis) any unusual lesions should be biopsied before starting therapy to decrease risk of cancer occurring
- (psoriasis) if there is no improvement within 6 weeks of therapy at 5 mg/kg/day, therapy should be stopped
- (atopic dermatitis) lymphadenopathy should be monitored during therapy. If lymphadenopathy is present after skin improves with therapy, a biopsy is recommended to rule out lymphoma
- blood pressure should be monitored regularly throughout therapy and hypertension treated with appropriate antihypertensive medication if it occurs. However, diuretic therapy should be avoided. If hypertension cannot be controlled, cyclosporin therapy should be stopped
- blood lipids should be measured before starting therapy and after 4 weeks of therapy. If lipids increase, dose should be decreased and a fat-reduced diet started
- blood concentration levels need not be measured in non-transplant patients unless indicated by risk of adverse reactions or potential drug interaction
- discontinue therapy if there is no improvement in 6 months where
maximum tolerable dose has been achieved for 3 months

- creatinine levels should be measured twice before and every 2 weeks during the first 3 months and then monthly. Doses should then be adjusted accordingly. Therapy should stop if reducing the dose does not reduce creatinine levels within 1 month

- creatinine levels should be measured more frequently when the dose of cyclosporin is increased or if the patient is taking NSAIDs concurrently

- serum potassium levels should be monitored regularly, as should serum uric acid levels in high-risk patients (e.g. gout) and serum magnesium (as hypomagnesaemia increases risk of neurotoxicity)

- changes between brands should be done carefully. Cyclosporin blood level, serum creatinine level and blood pressure should be measured at 2, 4 and 8 weeks (or within 4–7 days if used for transplant) after changeover. If blood pressure or creatinine levels are greater than the pre-changeover levels, decreasing the dose is recommended

- (oral solution) 0.1 mL solution = 10 mg cyclosporin

- (non-transplant use) contraindicated in those with uncontrolled hypertension or infection, primary or secondary immunodeficiency, impaired baseline renal function with serum creatinine greater than 200 micromol/L (nephrotic syndrome use), any renal impairment (other uses), or any existing malignant or premalignant conditions

Patient teaching and advice

- advise patients to avoid drinking alcohol while taking cyclosporin, especially red wine

- instruct patients to take doses 12 hours apart at the same time each day

- caution patients to swallow capsules whole, with or without food

- tell patients that oral solution comes with two syringes (1 mL and 4 mL). The 1 mL syringe should be used for doses less than or equal to 1 mL, while the 4 mL syringe is used for doses between 1 mL and 4 mL

- instruct patients to dilute oral solution of cyclosporin with apple or orange juice (not grapefruit) or soft drink and stir well before drinking immediately. Glass should be rinsed with more juice or soft drink to ensure whole dose is taken

- warn patient to avoid grapefruit juice during therapy

- instruct patient that the dose-dispensing syringe should not come into contact with juice or soft drink and should be wiped clean, not rinsed with water or other fluids

- patients should be advised to avoid foods high in potassium, and potassium-containing or potassium-sparing medications to avoid an increase in potassium levels

- counsel patients to avoid excessive unprotected sun exposure due to increased risk of skin cancer and wear a hat, 30+ sunscreen and protective clothing if sun exposure cannot be avoided

- educate patient regarding care of teeth and gums during therapy

- instruct patient to discard solution after 2 months of opening

- advise patients that oral solution should be stored in a cool dark place (20–25°C), but not refrigerated. Oily components of cyclosporin may solidify below 20°C and a jelly-like substance may also occur. This is reversible at warmer temperatures and it does not affect the safety or efficacy of cyclosporin

- cyclosporin is generally not recommended during pregnancy or breastfeeding
ETANERCEPT (Enbrel)

Available forms
- Vial: 25 mg
- Prefilled syringe: 50 mg/1 mL
- Autoinjector: 25 mg/0.5 mL

Action
- Neutralises activity of tumour necrosis factor (TNF) (TNF is involved in inflammatory and immune responses and is found in high levels in synovial fluid of those with rheumatoid arthritis. It is thought to be involved in both joint inflammation and erosion. Raised TNF levels are also found in those with psoriatic arthritis, psoriatic plaques and ankylosing spondylitis).
- Reaches maximum concentration in 24–96 hours
- Half-life approximately 80 hours

Use
- Rheumatoid arthritis that is unresponsive to other DMARDs
- Active polyarticular-course juvenile chronic arthritis that is unresponsive to other DMARDs
- Psoriatic arthritis that is unresponsive to other DMARDs
- Active ankylosing spondylitis
- Moderate to severe chronic plaque psoriasis

Dose
- 50 mg SC weekly or 25 mg SC twice weekly 3–4 days apart OR
- (plaque psoriasis) 50 mg SC weekly or 25 mg SC twice weekly 3–4 days apart. Dose may be increased to 50 mg SC twice weekly for up to 12 weeks if necessary, then reduced

Adverse effects
- Injection site reaction (erythema, itching, pain, swelling)
- Upper respiratory infection, non-upper respiratory infection, rhinitis, pharyngitis, cough, sinusitis, bronchitis
- Other infection (cystitis, cellulitis, septicaemia)
- Headache, dizziness, asthenia
- Fever
- Abdominal pain, dyspepsia
- Rash, pruritus
- Antinuclear antibody development, allergic reactions
- (Rare) worsening congestive heart failure, pancytopenia

Interactions
- Contraindicated with interleukin-1 antagonists (e.g. anakinra)
- Not recommended with abatacept
- Not recommended with live attenuated vaccines

Nursing points/Cautions
- All patients should be assessed before, during and after treatment for any signs of infection, which may include active or latent tuberculosis or hepatitis B or C
- Reconstitute by gently injecting Water for Injection into vial, avoiding vigorous agitation or shaking
- Clear and colourless solution should result within 10 minutes of reconstitution
- Solution should not be filtered, nor used if discoloured, cloudy or containing particulate matter
- Use within 6 hours of reconstitution
- Rotate injection sites, avoiding skin that is reddened, bruised, tender or hard or within 3 cm of previous injection sites
- Administer alone
- Solution in prefilled syringe or autoinjector should be clear, colourless or pale yellow with no visible particles
- Prefilled syringes (with needle cover intact) or autoinjector should be allowed to reach room temperature before being administered
- Needle covers of prefilled syringes contain latex and should not be handled by or administered to anyone with a latex sensitivity
- Therapy should be stopped if new, serious infection develops
- vials should be refrigerated
- caution if used in those with diabetes as there is an increased risk of hypoglycaemia, necessitating a decreased dose in antidiabetic medication
- caution if used in those with a history of blood dyscrasias, infection or congestive heart failure or with a recent diagnosis of CNS demyelinating disease
- not recommended in those with alcoholic hepatitis
- contraindicated in those with or at risk of serious active infection

**Patient teaching and advice**
- inform patient that injection site reaction reduces after initial 4 weeks
- patients may be taught to self-administer medication SC. They should be educated about rotation of sites, injection technique, storage requirements and safe disposal of used needles
- needle covers of prefilled syringes contain latex and should not be handled by or administered to anyone with a latex sensitivity
- patients should be advised to immediately report any persistent fever, sore throat, bruising or bleeding
- if patient has diabetes, he/she should be instructed to monitor blood glucose levels closely as etanercept may cause hypoglycaemia. Dose of antidiabetic medications may need to be adjusted accordingly
- see general Patient teaching and advice (p. xxiii)

**Use during pregnancy or breastfeeding**
- use during pregnancy or breastfeeding only if benefits clearly outweigh potential risks to fetus

**GOLIMUMAB (Simponi)**

**Available form**
- Prefilled syringe/injector pen: 50 mg/0.5 mL

**Action**
- IgG1 monoclonal antibody
- binds to tumour necrosis factor (TNF), which mediates chronic inflammation
- half-life 9–15 days

**Use**
- moderate to severe active rheumatoid arthritis (with methotrexate)
- active, progressive psoriatic arthritis (with methotrexate)
- active ankylosing spondylitis

**Dose**
- 50 mg SC monthly

**Adverse effects**
- upper respiratory tract infections, viral infections, bronchitis, sinusitis, fungal infection
- injection site reaction (erythema, urticaria, induration, pain, pruritus, bruising)
- dizziness, paraesthesia, asthenia
- rash
- hypertension
- constipation
- elevation liver enzymes
- autoantibody formation, increased risk of malignancy
- allergic reaction

**Interactions**
- contraindicated with anakinra or abatacept
- not recommended with live attenuated vaccines

**Nursing points/Cautions**
- patient should be screened for any signs of infection and/or abscesses before starting therapy. This should include screening for tuberculosis (clinical history, chest X-ray, skin tuberculin test) and hepatitis B. If latent tuberculosis is diagnosed, it should be treated with appropriate antimycobacterial agents before starting therapy. Patient should also be asked about recent travel or residence in areas where fungal infections are common
- SC injections should be given on same date each month
- rotate injection sites, avoiding skin that is reddened, bruised, tender or hard or within 3 cm of previous injection sites
- do not administer if solution is discoloured, cloudy or if foreign particles are present
- long half-life should be taken into consideration if patient is undergoing surgery; post-surgery, patient should be closely monitored for any signs of infection (due to increased risk)
- patients should be closely monitored during and after therapy for any signs of infection for at least 5 months
- needle covers of prefilled syringes contain latex and should not be handled by or administered to anyone with a latex sensitivity
- protect from light by storing prefilled pen/syringe in outer carton in fridge (2–8° C); do not shake prefilled pen/syringe
- patients with active rheumatoid arthritis (especially if treated previously with immunosuppressant agents) are at increased risk of leukaemia and lymphoma and should be carefully monitored during and after therapy
- therapy is not recommended in those an active infection
- caution if used in those with a history of malignancy, congestive heart failure, demyelinating diseases, chronic obstructive pulmonary disease or heavy smokers
- contraindicated in those with active tuberculosis or severe infection, or moderate to severe heart failure

**Patient teaching and advice**

- instruct patients to seek medical advice immediately if they develop persistent fever, bruising, bleeding or paleness (signs of blood dyscrasias), upset stomach, loss of appetite, vomiting, tiredness, urine becomes yellow or brown, skin or eyes yellow (signs of hepatitis B), persistent cough, weight loss, fever or lethargy (signs of tuberculosis)
- patients may be taught to self-administer medication SC. They should be educated about rotation of sites, injection technique (including not shaking solution), storage requirements and safe disposal of used needles, as well as what to do if they forget to administer a dose
- needle covers on prefilled syringe and injector pen contains latex and should not be handled by or administered to anyone with a latex sensitivity
- counsel women of childbearing potential to use reliable contraception during therapy and for 6 months post-therapy, and also the importance of telling their doctor if menstruation is delayed. Breastfeeding should not be commenced within 6 months of stopping therapy
- see general Patient teaching and advice (p. xxiii)

**Hydroxychloroquine Sulfate** *(Plaquenil)*

**Available form**
Tablets: 200 mg

**Action**
- aminoquinoline antimalarial
- onset of action: may take 2–6 months before benefits are apparent

**Use**
- rheumatoid arthritis
- systemic and discoid lupus erythematosus (mild)
- treatment and suppression of malaria (see Antimalarial agents)
Dose

- (lupus erythematosus) initially 400–800 mg orally daily for several weeks reducing to maintenance dose of 200–400 mg daily OR
- (rheumatoid arthritis) 400–600 mg orally daily with food, increasing dose slowly after 5–10 days until optimal dose is achieved without adverse effects for 4–12 weeks, reducing to a maintenance dose of 200–400 mg daily when clinical improvement is established

Adverse effects

- nausea, abdominal pain, diarrhoea
- skin eruptions, alopecia
- (rare) corneal/retinal changes, blurred vision, photophobia, halos, retinopathy, bone marrow depression, muscle weakness, decreased/absent deep tendon reflexes, anorexia, vomiting

Interactions

- incompatible with MAOIs
- use with digoxin may increase plasma digoxin levels leading to toxicity
- may enhance hypoglycaemic action of insulin or oral hypoglycaemic agents

Nursing points/Cautions

- because the effect of hydroxychloroquine accumulates, maximum clinical effects may take several months to be achieved; however, side-effects may appear much earlier
- ophthalmological examination (colour vision, fundoscopy, visual fields) should be done before starting therapy and continued every 6 months during treatment or more often in those at high risk (e.g. dose > 6 mg/kg, elderly, kidney/liver impairment, visual problems in previous 8 years). Visual disturbances/retinal changes can continue to occur after therapy has stopped
- patients on long-term therapy should have regular full blood counts and testing of knee and ankle reflexes to monitor muscle strength. If any weakness occurs, medication should be stopped
- if rash appears, the drug should be withdrawn and recommenced at a lower dose
- therapy should be stopped if there is no clinical improvement in 6 months
- caution if used in those with kidney or liver impairment, quinine sensitivity or G-6-PD deficiency
- not recommended in those with porphyria or psoriasis as symptoms may become exacerbated, or in those with severe GI, neurological or blood disorders
- contraindicated in those with pre-existing maculopathy
- contraindicated in those with hypersensitivity to 4-aminoquinolone compounds
- contraindicated as long term therapy in children

Patient teaching and advice

- patients concurrently taking digoxin should have digoxin levels monitored regularly
- patient should be advised to report any visual disturbances (e.g. blurred vision, changes to night vision, light flashes or streaks) or rash immediately to doctor
- warn patients about dangers of driving or operating machinery if blurred vision or impaired coordination occurs
- patient should be advised to wear sunglasses in strong sunlight
- inform patients that clinical effect may take months to be noticeable, however, adverse effects may occur sooner
- if patient has diabetes, he/she should be instructed to monitor blood glucose levels closely as etanercept may cause hypoglycaemia. Dose of antidiabetic medications may need to be adjusted accordingly
INFLIXIMAB (Remicade)

Available form
Vial: 100 mg

Action
- IgG1 monoclonal antibody
- binds to tumour necrosis factor (TNF), which mediates chronic inflammation
- half-life 8–9.5 days

Use
- moderate to severe Crohn’s disease (in patients over 6 years) who do not respond to conventional treatment), moderately severe to severe active ulcerative colitis, treatment of refractory fistulising Crohn’s disease (see Gastrointestinal agents (Miscellaneous))
- rheumatoid arthritis (with methotrexate)
- ankylosing spondylitis
- psoriatic arthritis (not responsive to other DMARDS)
- severe plaque psoriasis (not responsive to other conventional treatment)

Dose
- (rheumatoid arthritis) initially 3 mg/kg IV over 2 hours, then 3 mg/kg IV given at 2 and 6 weeks after the first infusion, then 3 mg/kg IV 8-weekly (with methotrexate) OR
- (ankylosing spondylitis) 5 mg/kg IV over 2 hours, then 5 mg/kg IV given at 2 and 6 weeks after the first infusion, followed by 5 mg/kg IV 6-weekly OR
- (psoriatic arthritis, plaque psoriasis) 5 mg/kg IV over 2 hours, then 5 mg/kg at 2 and 6 weeks after initial dose, then 8-weekly (maintenance)

Adverse effects
- infusion-related reaction (dyspnoea, urticaria, hypertension, flushing, headache)
- headache, fatigue, fever, dizziness, vertigo
- nausea, abdominal pain, diarrhoea, dyspepsia
- upper and lower respiratory tract infection, dyspnoea, sinusitis, reactivation of tuberculosis (rare)
- viral infection
- chest pain
- rash, pruritus, urticaria, dry skin, increased sweating
- abnormal liver function
- flushing, serum sickness-like reaction
- autoantibody development
- (long-term) development of malignancy

Interactions
- contraindicated with anakinra (interleukin-1 receptor antagonist)
- should not be given with live attenuated vaccines

Nursing points/Cautions
- patient should be screened for any signs of infection and/or abscesses before starting therapy. This should include screening for tuberculosis (clinical history, chest X-ray, skin tuberculin test). If latent tuberculosis is diagnosed, it should be treated with appropriate antimycobacterial agents before starting therapy
- gently add 10 mL Water for Injection down the inside of the vial, swirl gently and avoid shaking to dissolve. Foaming may occur
- allow solution to stand for 5 minutes before administering
- solution may be colourless to light yellow and clear
- should be diluted to 250 mL with sodium chloride 0.9%, gently mixed and then given as an IV infusion (rate not...
greater than 2 mL/min) over at least 2 hours
● a filter (micron size 1.2 or less) should be added to the infusion set
● administer alone
● patient should be carefully observed for at least 2 hours post-infusion (especially after the first and second dose), because infusion reactions are most likely to occur during this time
● if infusion reaction occurs, infusion should be slowed or stopped until symptoms subside, then started at a lower rate
● paracetamol, antihistamines, corticosteroids, adrenaline and artificial airway should be readily available for infusion reaction
● premedication with paracetamol, hydrocortisone and/or antihistamine may prevent mild and transient effects of infusion reaction
● re-administration after a 16-week drug-free interval is not recommended because of increased risk of hypersensitivity reaction
● caution if given to those with CNS demyelinating disease or history of malignancy
● contraindicated in those with severe infections (including active tuberculosis) or congestive heart failure

**Patient teaching and advice**

● patient should be advised to immediately report any persistent cough, weight loss or low-grade fever
● see also general Patient teaching and advice (p. xxiii)

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**LEFLUNOMIDE (Arabloc, Arava, Lunava)**

**Available forms**

Tablets: 10 mg, 20 mg, 100 mg

**Action**

● immunomodulating and immunosuppressant actions
● weak anti-inflammatory properties
● converted to active metabolite by first-pass metabolism in the gut wall and liver
● active metabolite has a half-life of approximately 2 weeks
● clinical improvement may occur in 4 weeks, and usually occurs in 4–6 months

**Use**

● active rheumatoid arthritis
● active psoriatic arthritis

**Dose**

● 100 mg orally daily for 3 days (loading dose), then 10–20 mg daily (maintenance)

**Adverse effects**

● rash, hair loss (reversible), pruritus, dry skin, hair and skin discolouration
● allergic reaction
● diarrhoea, abdominal pain, dyspepsia, nausea, anorexia, vomiting, mouth ulceration, weight loss
● elevated liver enzymes
● cystitis
● hypertension, chest pain
● respiratory infection, bronchitis, cough, pharyngitis, sinusitis, rhinitis, pneumonia
● dizziness, headache
● paraesthesia, asthenia
● blurred vision
● hypokalaemia
● arthralgia, leg cramps, synovitis, tenosynovitis, tendon rupture
● (rare) haematological disorder, hepatitis, jaundice, severe infection
● (very rare) severe skin reaction
Interactions
- cholestyramine and activated charcoal rapidly decrease plasma levels
- may increase plasma levels of rifampicin and phenytoin
- excessive alcohol intake should be avoided
- vaccination with live vaccines should be avoided during and for at least 6 months after finishing therapy
- not recommended with other agents that are hepatotoxic or haemotoxic/myelotoxic (e.g. methotrexate). If used together, increased monitoring of adverse effects is recommended
- caution if given with NSAIDs because of increased risk of hepatotoxicity

Nursing points/Cautions
- before starting, every 4 weeks for 6 months and then 6–8 weekly during therapy patients should have a full blood count (including differential white cell count), platelet count and liver function tests
- patients with previous tuberculosis should be closely monitored for any reactivation and should be advised to report any persistent cough or weight loss immediately
- blood pressure should be monitored before starting and throughout therapy
- treatment should be immediately ceased if ulcerative stomatitis is evident
- because of the long half-life (1–4 weeks) of the active metabolite, recovery from any adverse effects may take some time
- risk of adverse effects when given with methotrexate may be lessened by avoiding giving a loading dose of methotrexate
- (washout procedure before conception) leflunomide is stopped, then cholestyramine 8 g orally three times daily or 50 g orally activated charcoal 4 times daily for 11 days total.

Cholestyramine and activated charcoal may both interfere with oral contraceptives, and therefore barrier forms of contraception should also be used. Plasma levels should be measured twice, 2 weeks apart
- contraindicated in those with severe immunodeficiency states, impaired bone marrow function, blood dyscrasias, severe uncontrolled infection, liver impairment, severe hypoproteinemia or who have (or had) severe skin reactions (e.g. Stevens–Johnson syndrome)

Patient teaching and advice
- patients should be advised to swallow the tablet whole with water, at the same time every day
- warn patients to avoid excessive alcohol intake
- instruct patient to immediately report any sore throat, rash, excessive tiredness or flu-like symptoms
- caution patients against driving or operating machinery if dizziness or blurred vision occur
- if female patient is undergoing washout procedure prior to conception (see above), advise her to use a barrier method of contraception in addition to oral contraceptive, as failure may occur due to the cholestyramine or activated charcoal
- counsel women of childbearing potential to use reliable contraception during therapy and the importance of telling their doctor if menstruation is delayed
- men and women are advised that levels of active metabolite should be below 0.02 mg/L on two separate tests taken 14 days apart before considering pregnancy after washout procedure (above)
- see general Patient teaching and advice (p. xxiii)
before starting treatment, pregnancy must be excluded and women of childbearing potential should be advised to use reliable contraception during therapy and must advise their doctor if menstruation is delayed

very high risk of causing permanent damage to the fetus and therefore contraindicated during pregnancy or breast-feeding

METHOTREXATE (Methaccord, Methoblastin, Methotrexate Injection and Tablets)

Available forms
- Tablets: 2.5 mg, 10 mg; Vials: 5 mg/2 mL, 50 mg/2 mL, 100 mg/4 mL, 500 mg/5 mL, 500 mg/20 mL, 1000 mg/10 mL, 5000 mg/50 mL

Action
- inhibits metabolism of folic acid, thereby interfering with cell replication (especially in rapidly dividing cells such as dermal epithelial cells, buccal and intestinal cells)
- decreases swelling, pain and stiffness in rheumatoid arthritis, but does not induce remission or affect bone erosion
- onset of action may take 6–8 weeks

Use
- antineoplastic agent (see Antineoplastic agents)
- severe psoriasis that is unresponsive to other treatments
- severe rheumatoid arthritis that is unresponsive to other treatments

Dose
- (rheumatoid arthritis) 7.5 mg orally once weekly (or 2.5 mg orally for 3 doses at 12-hourly intervals weekly). May be increased by 15 mg/week after 6 weeks if no response (weekly maximum 20 mg). Once a response is established, dose should be decreased to the lowest that produces a clinical effect OR
- (psoriasis) 10–25 mg orally once weekly, gradually increasing to achieve optimal response but not exceeding 50 mg/week. Once a response is established, dose should be decreased to the lowest that produces a clinical effect OR
- (psoriasis) 2.5 mg orally for 3 doses at 12-hourly intervals weekly, gradually increasing to achieve optimal response, but not exceeding 30 mg/week. Once a response is established, dose should be decreased to the lowest that produces a clinical effect OR
- (psoriasis) 2.5 mg orally daily for 5 days, followed by 2-day rest period, gradually increasing to achieve optimal response, but not exceeding 6.25 mg/day. Once a response is established, dose should be decreased to the lowest that produces a clinical effect

Adverse effects
- nausea, abdominal pain, diarrhoea, anorexia, vomiting
- ulcerative stomatitis, mucositis
- decreased serum albumin, acute or chronic liver toxicity
- skin reaction, hair loss (reversible), dermatitis, photosensitivity
- cystitis, haematuria, dysuria, renal failure
- pneumonitis, pulmonary fibrosis
- bone marrow depression
- hypotension, pericarditis
- malaise, fatigue, chills and fever, headache, dizziness, drowsiness, tinnitus, blurred vision, eye discomfort, decreased resistance to infection
- increased risk of secondary tumour formation, increased risk of infection
- (high and prolonged therapy) hepatotoxicity
Interactions

- Serum levels (and associated risk of toxicity) may be increased by salicylates, sulfonamides, sulfonylureas, phenytoin, penicillins, chloramphenicol, probenecid and are therefore not recommended together
- (High dose) not recommended with NSAIDs due to increase risk of myelosuppression and GI toxicity because half-life of methotrexate is prolonged. Caution should also be used with lower doses of methotrexate
- Increased risk of soft tissue necrosis and osteonecrosis if given with radiotherapy
- Toxicity may be increased by folate deficiency
- Serum levels may be decreased by cholestyramine
- Risk of toxicity increased if given with other antineoplastic agents
- (Antineoplastic agent) not recommended with vitamin supplements containing folic or folinic acid
- Contraindicated with acitretin or other retinoids
- Contraindicated with alcohol and other hepatotoxic agents (e.g. retinoids, azathioprine, leflunamide)
- Not recommended with live, attenuated vaccines
- Increased risk of bone marrow depression if given with allopurinol, trimethoprim/sulfamethoxazole, pyrimethamine and triamterene
- Increased risk of myelosuppression and stomatitis if given with nitrous oxide
- (Use in psoriasis) increased risk of skin ulceration if given with amiodarone
- May decrease clearance of theophylline, thereby increasing risk of toxicity. Theophylline levels should be closely monitored during concurrent therapy
- May be antagonised by asparaginase
- Increased risk of toxicity if given with transfusion of packed red blood cells
- Incompatible with cytarabine, fluorouracil and prednisolone
- Absorption and metabolism may be decreased by chloramphenicol, tetracycline and non-absorbable broad spectrum antibiotics
- May increase plasma levels of mercaptopurine
- Increased risk of pancytopenia if given with leflunomide
- Increased risk of skin cancer if given with PUVA therapy

Nursing points/Cautions

- Pregnancy should be excluded before starting therapy
- Adverse effects are generally dose related
- Full blood count, haematocrit, renal function test, liver function test (including serum albumin and prothrombin time), urinalysis (urine should be alkaline) and chest X-ray should all be completed before, during (4–8 weekly) and after therapy. Liver biopsy may be recommended if patient has history of excessive alcohol use, chronic hepatitis B or C infection or persistently abnormal liver function test
- (Psoriasis) liver biopsy is recommended before, during (2–4 monthly), after a cumulative dose of 1.5 g and then after each additional 1–1.5 g
- It is important to ensure the patient has a good understanding of the dosing regimen as accidental daily dosing (instead of weekly) may be fatal
- Pregnant staff should be cautioned not to handle methotrexate
- Tablets contain lactose and are therefore not recommended in those with galactose intolerance, Lapp lactase deficiency or glucose galactose malabsorption
- Contraindicated in those with poor nutrition, bone marrow depression, blood dyscrasias, liver/renal disorders (including alcoholism or alcoholic liver disease), immunodeficiency
syndromes, blood dyscrasias, peptic ulcer disease, ulcerative colitis, active or serious infection

**Patient teaching and advice**

- caution patients not to crush or chew tablets, and swallow tablets with a full glass of water. Hands should be washed immediately after taking tablets
- warn patients with psoriasis that burning and redness is common in psoriatic area for 1–2 days post-therapy
- advise patients to maintain good hydration throughout therapy and immediately report any vomiting, diarrhoea or stomatitis that might lead to dehydration
- instruct patients to immediately report any fever, non-productive cough, chest pain or shortness of breath (dyspnoea) or vomiting, diarrhoea and/or ulcerative stomatitis
- warn patient with rheumatoid arthritis that it may worsen within 3–6 weeks of therapy being withdrawn
- caution patient to avoid excessive sun exposure or sunlamps, as photosensitivity reaction may occur, or to wear a hat and long-sleeved shirt/garment and 30+ sunscreen to protect skin if sun exposure cannot be avoided
- it is important to ensure the patient has a good understanding of the dosing regimen as accidental daily dosing (instead of weekly) may be fatal
- caution patients not to drive or operate machinery if dizziness, drowsiness, blurred vision or fatigue occur
- advise patients that tablets contain lactose and are therefore not recommended in those with galactose intolerance, Lapp lactase deficiency or glucose galactose malabsorption
- before treatment begins, all patients (male and female) should be counselled regarding potential benefits and risks of therapy, including effects on reproduction, and the importance of using effective contraception throughout therapy and for a further 3 months after therapy has stopped. Female patients should be instructed to seek medical advice immediately if menstruation does not occur and pregnancy is suspected
- see also general Patient teaching and advice (p. xxiii)

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**PENICILLAMINE (D-Penamine)**

**Available forms**

Tablets: 125 mg, 250 mg

**Action**

- exact mode of action in rheumatoid arthritis is unknown (possibly interferes with immune response), although it does chelate metals and decrease cystine excretion
- half-life about 90 hours

**Use**

- chelating agent (see Antidotes, antagonists and chelating agents)
- management of cysturia
- severe active rheumatoid arthritis

**Dose**

- (rheumatoid arthritis) up to 250 mg orally daily in divided doses 1 hour before or 2 hours after food for 1 month, then increasing by the same amount monthly to a maximum of 1500 mg daily. The dose is then
lowered to achieve the lowest effective dose (maintenance dose)

**Adverse effects/Interactions/Nursing points/Cautions**
- if no response occurs in 6 months at full maintenance dose, therapy should be discontinued
- contraindicated with current gold salt therapy
- contraindicated with antimalarial drugs
- see Adverse effects, Interactions, Nursing points/Cautions for Antidotes, antagonists and chelating agents

**Patient teaching and advice**
- warn patient that it may take 6 to 8 weeks for a response to be seen
- see general Patient teaching and advice (p. xxiii)

**SODIUM AUROTHIOMALATE (Gold Salt) (Myocrisin)**

**Available forms**
Ampoules: 10 mg/0.5 mL, 20 mg/0.5 mL, 50 mg/0.5 mL

**Action**
- penetrates joint cavity affecting lysosomal membrane
- binds to plasma proteins (including rheumatoid factor). When ingested by lysosomes the gold is absorbed, inactivating the enzymes

**Use**
- rheumatoid arthritis that is not controlled adequately by other DMARDs (adjunctive treatment)
- Still’s disease

**Dose**

**Rheumatoid arthritis**
- 1 mg, 5 mg, then 10 mg IM at weekly intervals to test tolerance, then 50 mg/week to a total of 1 g **OR**
- 50 mg/week IM for 20 weeks to a total of 1 g

For both dosages, continue therapy at 50 mg/month until a total of 3 g has been given (maintenance) or continued for 2 years after remission

**Still’s disease**
- under 25 kg: 10 mg
- 25–50 kg: 20 mg
- over 50 kg: 50 mg

Give IM weekly for 6 months. If no improvement, cease therapy. If responsive, maintenance therapy is continued every 2–4 weeks for 1–5 years

**Adverse effects**
- rash, pruritus (early sign of intolerance), erythema, transient eczema
- flushing, fainting, dizziness, sweating
- proteinuria, haematuria
- stomatitis, mouth ulcers
- gold deposits on cornea or lens (clear within 3–6 months of stopping therapy)
- (uncommon) anorexia, nausea, vomiting, abdominal cramps, diarrhoea
- (rare but may be fatal) agranulocytosis, thrombocytopenia, aplastic anaemia
- (rare) anaphylactoid reactions, peripheral neuropathy, nephritic syndrome, encephalopathy

**Interactions**
- not recommended with penicillamine as risk of rashes and bone marrow depression is increased
- gold may exacerbate aspirin-induced hepatic dysfunction
- increased risk of anaphylactoid reactions if given with ACE inhibitors

**Nursing points/Cautions**
- before injection, inspect for rashes and test urine for protein (30 mg/100 mL or more) and blood; discontinue treatment if proteinuria/haematuria, eosinophilia or rash is present. Full blood count (including platelet count) should also be performed before administration
patient should be observed for at least 10 minutes after administration for any sign of reaction

- shake vial thoroughly while holding horizontal before withdrawing the dose

- syringe and needle must be dry

- warm vial to body temperature (by immersion in warm water) to facilitate drawing suspension into syringe

- give by deep IM injection, then massage the site; the patient must remain recumbent for 30 minutes after injection because of the possibility of vasomotor reactions/anaphylactic reaction, which can occur after any course of the therapy

- ampoules of gold salts are stored in a cool place, protected from light and not used if darkened in colour

- ophthalmological examination is recommended if any ocular adverse effect occurs

- severe blood dyscrasias may occur with little warning

- caution if used in those with marked hypertension, compromised cerebral or cardiovascular circulation

- contraindicated in those with kidney or liver disease, diabetes, marked toxaemia, or history of exfoliative dermatitis or blood dyscrasia

### Patient teaching and advice

- advise patients to report sore throat, mouth or tongue, mouth ulcers, metallic taste, and any bruising or unusual bleeding or skin reactions to the doctor as blood test (full blood count including platelet count) is required immediately

- women of childbearing potential should be counselled against becoming pregnant during therapy and the importance of using effective contraception during therapy and for up to 6 months after finishing therapy, as gold is very slowly excreted and may persist in the tissues for some time

- see also general Patient teaching and advice (p. xxiii)

### gold preparations are contraindicated during pregnancy or breastfeeding

### SULFASALAZINE (Pyralin EN, Salazopyrin, Salazopyrin EN-Tabs)

#### Available forms

- Tablets: 500 mg; Tablets (enteric coated): 500 mg

#### Action

- broken down in the colon by bacteria to 5-aminosalicylic acid and sulfapyridine producing an anti-inflammatory effect by its action on prostaglandin synthesis, leukotrienes and arachidonic acid metabolites

- onset of action may take 6–12 weeks

#### Use

- ulcerative colitis and Crohn’s disease (see Gastrointestinal agents (Miscellaneous agents))

- rheumatoid arthritis that is unresponsive to other drug therapy

#### Dose

- (rheumatoid arthritis) initially 500 mg orally at night for 1 week, 500 mg twice daily for 1 week, 500 mg in the morning and 1 g at night for 1 week, then 1 g twice daily for 1 week (to daily maximum of 3 g)

#### Adverse effects

- anorexia, nausea, vomiting, diarrhoea

- fever, headache

- erythema, pruritus, rash

- reversible oligospermia

- (rare) hypersensitivity reaction, agranulocytosis, aplastic anaemia

#### Interactions

- may potentiate oral anticoagulants, methotrexate and sulfonyleureas

- reduces absorption and metabolism of folic acid, resulting in folic acid
deficiency, macrocytosis and pancytopenia
● reduces absorption of digoxin, therefore blood levels should be monitored
● increased blood levels may occur in patients taking oral anticoagulants, indomethacin, sulfinpyrazone, urinary acidifiers or salicylates
● decreased absorption may occur if given with antacids or ferrous sulfate
● increased risk of bone marrow depression and leucopenia if given with azathioprine
● activity may be decreased if given with para-aminobenzoic acid-type local anaesthetics

Nursing points/Cautions
● enteric-coated tablets are available if GI intolerance is experienced
● monitor blood counts (including differential white cell count), liver function tests and renal function analysis (including urinalysis) before starting therapy, second weekly for 3 months and then every 3 months
● adverse effects are mainly dose dependent
● encourage adequate fluid intake to reduce risk of crystalluria and stone formation
● caution if given to those with glucose-6-phosphate dehydrogenase deficiency (as risk of haemolytic anaemia is increased) or severe allergy, bronchial asthma or atopic disease
● not recommended in those with blood dyscrasia or impaired liver or kidney function
● contraindicated in those with any allergy/hypersensitivity to sulfonamide or salicylate derivatives, intestinal/urinary obstruction, porphyria or blood dyscrasias

Patient teaching and advice
● instruct patients that enteric-coated tablets should not be crushed or broken but swallowed whole with plenty of water
● warn patient to report sore throat, fever, pallor, purpura, jaundice, yellow-orange discolouration of skin, urine and other body fluids to doctor immediately
● instruct patient to drink plenty of water during therapy
● counsel male patients about reversible male infertility and female patients regarding potential harm to developing fetus
● see also general Patient teaching and advice (p. xxiii)

Sample chapter