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BRITISH NATIONAL FORMULARY

British Medical Association

Royal Pharmaceutical Society of Great Britain

Emergency supply of medicines

Pharmacists are sometimes called upon by members of the public to supply medicines in emergencies. For details of emergency supply at the request of a doctor, see *Medicines, Ethics and Practice*, No. 25, London, Pharmaceutical Press, 2001 (and subsequent editions).

The Medicines (Products Other Than Veterinary Drugs) (Prescription Only) Order 1983, as amended, allows exemptions from the Prescription Only requirements for emergency supply to be made by a person lawfully conducting a retail pharmacy business provided:

(a) that the pharmacist has interviewed the person requesting the prescription-only medicine and is satisfied:
  (i) that there is immediate need for the prescription-only medicine and that it is impracticable in the circumstances to obtain a prescription without undue delay;
  (ii) that treatment with the prescription-only medicine has on a previous occasion been prescribed by a doctor[1] for the person requesting it;
  (iii) as to the dose which it would be appropriate for the person to take;
(b) that no greater quantity shall be supplied than will provide 5 days' treatment except when the prescription-only medicine is:
  (i) insulin, an ointment, cream, or preparation for the relief of asthma in an aerosol dispenser when the smallest pack can be supplied;
  (ii) an oral contraceptive when a full cycle may be supplied;
  (iii) an antibiotic in liquid form for oral administration when the smallest quantity that will provide a full course of treatment can be supplied;
(c) that an entry shall be made in the prescription book stating:
  (i) the date of supply;
  (ii) the name, quantity and, where appropriate, the pharmaceutical form and strength;
  (iii) the name and address of the patient;
  (iv) the nature of the emergency;
(d) that the container or package must be labelled to show:
  (i) the date of supply;
  (ii) the name, quantity and, where appropriate, the pharmaceutical form and strength;
  (iii) the name of the patient;
  (iv) the name and address of the pharmacy;
  (v) the words 'Emergency supply'.
(e) that the prescription-only medicine is not a substance specifically excluded from the emergency supply provision, and does not contain a Controlled Drug specified in schedules 1, 2, or 3 to the Misuse of Drugs Regulations 1985 except for phenobarbital or phenobarbital sodium for the treatment of epilepsy: for details see *Medicines, Ethics and Practice*, No. 25, London, Pharmaceutical Press, 2001 (and subsequent editions as available).

1 The doctor must be a UK-registered doctor.

Royal Pharmaceutical Society's Guidelines

(1) The pharmacist should consider the medical consequences of *not* supplying.
(2) If the patient is not known to the pharmacist, the patient's identity should be established by way of appropriate documentation.
(3) It may occasionally be desirable to contact the prescriber, e.g. when the medicine requested has a potential for misuse or the prescriber is not known to the pharmacist.
(4) Care should be taken to ask whether the patient's doctor has stopped the treatment, or whether the patient is taking any other medication.
(5) Except for conditions which may occur infrequently (e.g. hay fever, asthma attack or migraine), a supply should not be made if the item requested was last prescribed more than 6 months ago.
(6) Consideration should be given to supplying less than 5 days' quantity if this is justified.
(7) Where a prescription is to be provided later, a record of emergency supply as required by law must still be made. It is good practice to add to the record the date on which the prescription is received. Payment for the medicine supplied is not a legal requirement, but may help to minimise the abuse of the emergency supply exemption. If an NHS prescription is to be provided, a refundable charge may be made.

Controlled drugs and drug dependence

PRESCRIPTIONS. Preparations which are subject to the prescription requirements of the Misuse of Drugs Regulations 1985, i.e. preparations specified in schedules 2 and 3, are distinguished throughout the BNF by the symbol CD (Controlled Drugs). The principal legal requirements relating to medical prescriptions are listed below.

Prescriptions ordering Controlled Drugs subject to prescription requirements must be *signed* and *dated*[1] by the prescriber and specify the prescriber's *address*. The prescription must always state *in the prescriber's own handwriting*[2] in ink or otherwise so as to be indelible:

1. The name and address of the patient;
2. In the case of a preparation, the form[3] and where appropriate the strength[4] of the preparation;
3. The total quantity of the preparation, or the number of dose units, *in both words and figures*;[5]
4. The dose;[6]
5. The words 'for dental treatment only' if issued by a dentist.

A prescription may order a Controlled Drug to be dispensed by instalments; the amount of the instalments and the intervals to be observed must be specified.[7,8] Prescriptions ordering 'repeats' on the same form are **not** permitted. A prescription is valid for 13 weeks from the date stated thereon.

It is an offence for a prescriber to issue an incomplete prescription and a pharmacist is **not** allowed to dispense a Controlled Drug unless all the information required by law is given on the prescription. Failure to comply with the regulations concerning the writing of prescriptions will result in inconvenience to patients and delay in supplying the necessary medicine.

DEPENDENCE AND MISUSE. The most serious drugs of addiction are **cocaine**, **diamorphine** (heroin), **morphine**, and the **synthetic opioids**. For arrangements for prescribing of diamorphine, dipipanone or cocaine for addicts, see p. 9.

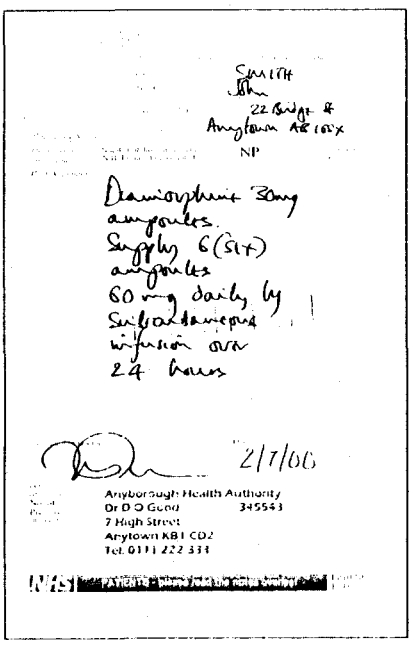
Despite marked reduction in the prescribing of **amphetamines** there is concern that abuse of illicit amfetamine and related compounds is widespread.

Owing to problems of abuse, **flunitrazepam** and **temazepam** are subject to additional controlled drug requirements (but temazepam remains exempt from the additional prescribing requirements).

The principal **barbiturates** are now Controlled Drugs, but phenobarbital (phenobarbitone) and phenobarbital sodium (phenobarbitone sodium) or a preparation containing either of these are exempt from the handwriting requirement but must fulfil all other controlled drug prescription requirements (**important:** the own handwriting exemption does **not** apply to the date; a computer-generated date need not be deleted but the date must also be added by the prescriber). Moreover, for the treatment of epilepsy phenobarbital and phenobarbital sodium are available under the emergency supply regulations (p. 6).

Cannabis (Indian hemp) has no approved medicinal use and cannot be prescribed by doctors. Its use is illegal but has become widespread. Cannabis is a mild hallucinogen seldom accompanied by a desire to increase the dose; withdrawal symptoms are unusual. **Lysergide** (lysergic acid diethylamide, LSD) is a much more potent hallucinogen; its use can lead to severe psychotic states in which life may be at risk.

1. A computer-generated date is **not** acceptable; however, the prescriber may use a date stamp.
2. Does not apply to prescriptions for temazepam. Otherwise applies unless the prescriber has been specifically exempted from this requirement or unless the prescription contains no controlled drug other than phenobarbital or phenobarbital sodium or a preparation containing either of these; the exemption does **not** apply to the date: a computer-generated date need not be deleted but the date must also be added by the prescriber.
3. The dosage form (e.g. tablets) must be included on a Controlled Drugs prescription irrespective of whether it is implicit in the proprietary name (e.g. *MST Continus*) or of whether only one form is available.
4. When more than one strength of a preparation exists the strength required must be specified.
5. Does not apply to prescriptions for temazepam.
6. The instruction 'one as directed' constitutes a dose but 'as directed' does not.
7. A total of 14 days' treatment by instalment of any drug listed in Schedule 2 of the Misuse of Drugs Regulations may be prescribed. In *England and Wales*, form FP10HP(AD)1000 (pink: mainly used by hospital-based treatment units) or form FP10MDA1000 (blue: mainly used by general practitioners) should be used; in *Scotland* forms HBP(A) (hospital-based prescribers) or GP10 (general practitioners) should be used.
8. Buprenorphine (Schedule 3) may be prescribed by instalment in England and Wales on form FP10HP(AD)1000 and in England, general practitioners may also prescribe it by instalment on form FP10MDA1000.



PRESCRIBING DRUGS LIKELY TO CAUSE DEPENDENCE OR MISUSE. The prescriber has three main responsibilities:

1. To avoid creating dependence by introducing drugs to patients without sufficient reason. In this context, the proper use of the morphine-like drugs is well understood. The dangers of other controlled drugs are less clear because recognition of dependence is not easy and its effects, and those of withdrawal, are less obvious. Perhaps the most notable result of uninhibited prescribing is that a very large number of patients in the country take tablets which do them neither much good nor much harm, but are committed to them indefinitely because they cannot readily be stopped.
2. To see that the patient does not gradually increase the dose of a drug, given for good medical reasons, to the point where dependence becomes more likely. This tendency is seen especially with hypnotics and anxiolytics (for CSM advice see section 4.1). The prescriber should keep a close eye on the amount prescribed to prevent patients from accumulating stocks that would enable them to arrange their own dosage or even that of their families and friends. A minimal amount should be prescribed in the first instance, or when seeing a new patient for the first time.
3. To avoid being used as an unwitting source of supply for addicts. Methods include visiting more than one doctor, fabricating stories, and forging prescriptions.

Patients under temporary care should be given only small supplies of drugs unless they present an unequivocal letter from their own doctors. Doctors should also remember that their own patients may be doing a collecting round with other doctors, especially in hospitals. It is sensible to decrease dosages steadily or to issue weekly or even daily prescriptions for small amounts if it is apparent that dependence is occurring.

The stealing and misuse of prescription forms could be minimised by the following precautions:

(a) do not leave unattended if called away from the consulting room or at reception desks; do not leave in a car where they may be visible; when not in use, keep in a locked drawer within the surgery and at home;

(b) draw a diagonal line across the blank part of the form under the prescription;

(c) write the quantity in words and figures when prescribing drugs prone to abuse; this is obligatory for controlled drugs (see Prescriptions, above);

(d) alterations are best avoided but if any are made they should be clear and unambiguous; add initials against altered items;

(e) if prescriptions are left for collection they should be left in a safe place in a sealed envelope.

TRAVELLING ABROAD. Prescribed drugs listed in schedules 4 and 5 to the Misuse of Drugs Regulations 1985 are not subject to import or export licensing but doctors are advised that patients intending to carry Schedule 2 and 3 drugs abroad may require an export licence. This is dependent upon the amount of drug to be exported and further details may be obtained from the Home Office by telephoning (020) 7273 3806. Applications for licences should be sent to the Home Office, Drugs Branch, Queen Anne's Gate, London SW1H 9AT.

There is no standard application form but applications must be supported by a letter from a doctor giving details of:

- the patient's name and current address;
- the quantities of drugs to be carried;
- the strength and form in which the drugs will be dispensed;
- the dates of travel to and from the United Kingdom.

Ten days should be allowed for processing the application.

Individual doctors who wish to take Controlled Drugs abroad while accompanying patients, may similarly be issued with licences. Licences are not normally issued to doctors who wish to take Controlled Drugs abroad solely in case a family emergency should arise.

These import/export licences for named individuals do not have any legal status outside the UK and are only issued to comply with the Misuse of Drugs Act and facilitate passage through UK Customs and Excise control. For clearance in the country to be visited it would be necessary to approach that country's consulate in the UK.

Misuse of Drugs Act

The Misuse of Drugs Act, 1971 prohibits certain activities in relation to 'Controlled Drugs', in particular their manufacture, supply, and possession. The penalties applicable to offences involving the different drugs are graded broadly according to the *harmfulness attributable to a drug when it is misused* and for this purpose the drugs are defined in the following three classes:

Class A includes: alfentanil, cocaine, dextromoramide, diamorphine (heroin), dipipanone, lysergide (LSD), methadone, methylenedioxymethamfetamine (MDMA, 'ecstasy'), morphine, opium, pethidine, phencyclidine, and class B substances when prepared for injection

Class B includes: oral amphetamines, barbiturates, cannabis, cannabis resin, codeine, ethylmorphine, glutethimide, pentazocine, phenmetrazine, and pholcodine

Class C includes: certain drugs related to the amphetamines such as benzfetamine and chlorphentermine, buprenorphine, diethylpropion, mazindol, meprobamate, pemoline, pipradrol, most benzodiazepines, androgenic and anabolic steroids, clenbuterol, chorionic gonadotrophin (HCG), non-human chorionic gonadotrophin, somatotropin, somatrem, and somatropin

The Misuse of Drugs Regulations 2001 define the classes of person who are authorised to supply and possess controlled drugs while acting in their professional capacities and lay down the conditions under which these activities may be carried out. In the regulations drugs are divided into five schedules each specifying the requirements governing such activities as import, export, production, supply, possession, prescribing, and record keeping which apply to them.

Schedule 1 includes drugs such as cannabis and lysergide which are not used medicinally. Possession and supply are prohibited except in accordance with Home Office authority.

Schedule 2 includes drugs such as diamorphine (heroin), morphine, pethidine, secobarbital, glutethimide, amfetamine, and cocaine and are subject to the full controlled drug requirements relating to prescriptions, safe custody (except for secobarbital), the need to keep registers, etc. (unless exempted in schedule 5).

Schedule 3 includes the barbiturates (except secobarbital now schedule 2), buprenorphine, diethylpropion, flunitrazepam, mazindol, meprobamate, pentazocine, phentermine, and temazepam. They are subject to the special prescription requirements (except for phenobarbital and temazepam, see p. 7) but not to the safe custody requirements (except for buprenorphine, diethylpropion, flunitrazepam, and temazepam) nor to the need to keep registers (although there are requirements for the retention of invoices for 2 years).

Schedule 4 includes in Part I benzodiazepines (except flunitrazepam and temazepam which are in schedule 3) that are subject to minimal control. Part II includes androgenic and anabolic steroids, clenbuterol, chorionic gonadotrophin (HCG), non-human chorionic gonadotrophin, somatotropin, somatrem, and somatropin. Controlled drug prescription requirements do not apply and Schedule 4 Controlled Drugs are not subject to safe custody requirements.

Schedule 5 includes those preparations which, because of their strength, are exempt from virtually all Controlled Drug requirements other than retention of invoices for two years.

Notification of drug misusers

Doctors are expected to report on a standard form cases of drug misuse to their regional or national drug misuse database or centre—see below for contact telephone numbers. The National Drugs Treatment Monitoring System was introduced in England in April 2001; regional centres replace the Regional Drug Misuse Databases. A similar system has been introduced in Wales.

A report (notification) to their regional or national drug misuse database or centre should be made when a patient starts treatment for drug misuse. In England and Wales further information is collected in Spring, including whether or not patients are continuing to receive treatment. All types of problem drug misuse should be reported including opioid, benzodiazepine, and CNS stimulant.

The regional or national drug misuse database or centres are now the only national and local source of epidemiological data on people presenting with problem drug misuse; they provide valuable information to those working with drug misusers and those planning services for them. The databases cannot, however, be used as a check on multiple prescribing for drug addicts because the data are anonymised.

Enquiries about the regional or national drug misuse database or centres (including requests for supplies of notification forms) can be made by contacting one of the centres listed below:

ENGLAND

North West

Merseyside and Cheshire: telephone (0151) 231 4319; fax (0151) 231 4320

North Western: telephone (0161) 772 3782; fax (0161) 772 3445

Northern and Yorkshire

Telephone (0113) 295 1337; fax (0113) 295 1310

South East (West) and Eastern

Telephone (01865) 226734; fax (01865) 226652

South West

Telephone (0117) 918 6880; fax (0117) 918 6883

Thames and South East (East)

Telephone (020) 7594 0811; fax (020) 7594 0866

Trent

Telephone (0116) 225 6360; fax (0116) 225 6370

West Midlands

Telephone (0121) 580 4331; fax (0121) 525 7980

SCOTLAND

Telephone (0131) 551 8715; fax (0131) 551 1392

WALES

Telephone (029) 2082 6260; fax (029) 2082 5473

In **Northern Ireland**, the Misuse of Drugs (Notification of and Supply to Addicts) (Northern Ireland) Regulations 1973 require doctors to send particulars of persons whom they consider to be addicted to certain controlled drugs to Chief Medical Officer of the Department of Health and Social Services. The Northern Ireland contacts are:

Medical contact:
Dr Ian McMaster
C3 Castle Buildings
Belfast BT4 3PP
Telephone (028) 9052 2421
Fax (028) 9052 0781

Administrative contact:
Health Promotion Branch
C4.22 Castle Buildings
Belfast BT4 3PP
Telephone (028) 9052 0532

Prescribing of diamorphine (heroin), dipipanone, and cocaine for addicts

The Misuse of Drugs (Supply to Addicts) Regulations 1997 require that only medical practitioners who hold a special licence issued by the Home Secretary may prescribe, administer or supply diamorphine, dipipanone[1] (*Diconal*®) or cocaine in the treatment of drug addiction; other practitioners must refer any addict who requires these drugs to a treatment centre. Whenever possible the addict will be introduced by a member of staff from the treatment centre to a pharmacist whose agreement has been obtained and whose pharmacy is conveniently sited for the patient. Prescriptions for weekly supplies will be sent to the pharmacy by post and will be dispensed on a daily basis as indicated by the doctor. If any alterations of the arrangements are requested by the addict, the portion of the prescription affected must be represcribed and not merely altered. *General practitioners and other doctors may still prescribe diamorphine, dipipanone, and cocaine for patients (including addicts) for relief of pain due to organic disease or injury without a special licence.*

For guidance on prescription writing, see p. 7

1 Dipipanone in *Diconal*® tablets has been much misused by opioid addicts in recent years. Doctors and others should be suspicious of people who ask for the tablets, especially if temporary residents.

Adverse reactions to drugs

Any drug may produce unwanted or unexpected adverse reactions. Detection and recording of these is of vital importance. Doctors and pharmacists are urged to help by reporting adverse reactions to:

Medicines Control Agency
CSM Freepost
London SW8 5BR
(0800 731 6789)

Prepaid Yellow Cards for reporting are available from the above address and are also bound in this book (inside back cover).

A 24-hour Freefone service is available to all parts of the UK for advice and information on suspected adverse drug reactions; contact the National Yellow Card Information Service at the MCA on 0800 731 6789. Outside office hours a telephone-answering machine will take messages.

The following regional centres also collect data:

CSM Mersey
Freepost
Liverpool L3 3AB.
(0151) 794 8206

CSM Wales
Freepost
Cardiff CF4 1ZZ
(029) 2074 4181
(Direct Line)

CSM Northern
Freepost 1085
Newcastle upon Tyne
NE1 1BR
(0191) 232 1525 (Direct Line)

CSM West Midlands
Freepost SW2991
Birmingham B18 7BR
(0121) 507 5672

The MCA's Adverse Drug Reactions On-line Information Tracking (ADROIT) facilitates the monitoring of adverse drug reactions.

Suspected adverse reactions to *any* therapeutic agent should be reported, including drugs (*self-medication* as well as *prescribed* ones), blood products, vaccines, X-ray contrast media, dental or surgical materials, intra-uterine devices, herbal products, and contact lens fluids.

More detailed information on reporting and a list of drugs/products currently under intensive monitoring can be found on the CSM homepage: www.mca.gov.uk/aboutagency/regframework/csm/csmhome.htm.

NEWER DRUGS AND VACCINES. Only limited information is available from clinical trials on the safety of new medicines. Further understanding about the safety of medicines depends on the availability of information from routine clinical practice.

The black triangle symbol (▼) identifies newly licensed medicines that are monitored intensively by the MCA/CSM. Such medicines include those that have been licensed for administration by a new route or drug delivery system, or for significant new indications which may alter the established risks and benefits of that drug. There is no standard time for which products retain a black triangle; safety data are usually reviewed after 2 years.

Spontaneous reporting is particularly valuable for recognising possible new hazards rapidly. For medicines showing the black triangle symbol, the MCA/CSM asks that **all** suspected reactions (including those considered not to be serious) are reported through the Yellow Card scheme. An adverse reaction should be reported even if it is not certain that the drug has caused it, or if the reaction is well recognised, or if other drugs have been given at the same time.

ESTABLISHED DRUGS AND VACCINES. Doctors and pharmacists are asked to report *all* serious suspected reactions, including those that are fatal, life-threatening, disabling, incapacitating, or which result in or prolong hospitalisation; they should be reported even if the effect is well recognised. Examples include anaphylaxis, blood disorders, endocrine disturbances, effects on fertility, haemorrhage from any site, renal impairment, jaundice, ophthalmic disorders, severe CNS effects, severe skin reactions, reactions in pregnant women, and any drug interactions. Reports of serious adverse reactions are required to enable comparision with other drugs of a similar class. Information obtained from overdoses (deliberate or accidental) can complicate the assessment of adverse drug reactions, but provides important information on the potential toxicity of drugs.

For established drugs doctors and pharmacists are asked not to report well-known, relatively minor side-effects, such as dry mouth with tricyclic antidepressants or constipation with opioids.

Special problems

Delayed drug effects. Some reactions (e.g. cancers, chloroquine retinopathy, and retroperitoneal fibrosis) may become manifest months or years after exposure. Any suspicion of such an association should be reported.

The elderly. Particular vigilance is required to identify adverse reactions in the elderly.

Congenital abnormalities. When an infant is born with a congenital abnormality or there is a malformed aborted fetus doctors are asked to consider whether this might be an adverse reaction to a drug and to report all drugs (including self-medication) taken during pregnancy.

Children. Particular vigilance is required to identify and report adverse reactions in children, including those resulting from the unlicensed use of medicines; **all** suspected reactions should be reported (see p. 11).

Prevention of adverse reactions

Adverse reactions may be prevented as follows:

1. Never use any drug unless there is a good indication. If the patient is pregnant do not use a drug unless the need for it is imperative.
2. Allergy and idiosyncrasy are important causes of adverse drug reactions. Ask if the patient had previous reactions.
3. Ask if the patient is already taking other drugs *including self-medication drugs*; interactions may occur.
4. Age and hepatic or renal disease may alter the metabolism or excretion of drugs, so that much smaller doses may be needed. Genetic factors may also be responsible for variations in metabolism, notably of isoniazid and the tricyclic antidepressants.
5. Prescribe as few drugs as possible and give very clear instructions to the elderly or any patient likely to misunderstand complicated instructions.
6. When possible use a familiar drug. With a new drug be particularly alert for adverse reactions or unexpected events.
7. If serious adverse reactions are liable to occur warn the patient.

Defective Medicines

During the manufacture or distribution of a medicine an error or accident may occur whereby the finished product does not conform to its specification. While such a defect may impair the therapeutic effect of the product and could adversely affect the health of a patient, it should not be confused with an Adverse Drug Reaction where the product conforms to its specification.

The Defective Medicines Report Centre assists with the investigation of problems arising from licensed medicinal products thought to be defective and co-ordinates any necessary protective action. Reports on suspect defective medicinal products should include the brand or the non-proprietary name, the name of the manufacturer or supplier, the strength and dosage form of the product, the product licence number, the batch number or numbers of the product, the nature of the defect, and an account of any action already taken in consequence. The Centre can be contacted at:

The Defective Medicines Report Centre
Medicines Control Agency
Room 1801, Market Towers
1 Nine Elms Lane
London SW8 5NQ
(020) 7273 0574 (weekdays 9.00 am–5.00 pm)
or (020) 7210 3000 or 5371 (any other time)

Prescribing for children

Children, and particularly neonates, differ from adults in their response to drugs. Special care is needed in the neonatal period (first 30 days of life) and doses should always be calculated with care. At this age, the risk of toxicity is increased by inefficient renal filtration, relative enzyme deficiencies, differing target organ sensitivity, and inadequate detoxifying systems causing delayed excretion.

Whenever possible painful intramuscular injections should be **avoided** in children.

Where possible, medicines for children should be prescribed within the terms of the product licence (marketing authorisation). However, many children may require medicines not specifically licensed for paediatric use.

Although medicines cannot be promoted outside the limits of the licence, the Medicines Act does not prohibit the use of unlicensed medicines. It is recognised that the informed use of unlicensed medicines or of licensed medicines for unlicensed applications ('off-label' use) is often necessary in paediatric practice.

ADVERSE DRUG REACTIONS IN CHILDREN. The reporting of all suspected adverse drug reactions in children is **strongly encouraged** through the Yellow Card scheme (see p. 10) even if the intensive monitoring symbol (▼) has been removed, because experience in children may still be limited.

The identification and reporting of adverse reactions to drugs in children is particularly important because:

- the action of the drug and its pharmacokinetics in children (especially in the very young) may be different from that in adults
- drugs are not extensively tested in children
- many drugs are not specifically licensed for use in children and are used 'off-label'
- suitable formulations may not be available to allow precise dosing in children
- the nature and course of illnesses and adverse drug reactions may differ between adults and children

PRESCRIPTION WRITING. Prescriptions should be written according to the guidelines in Prescription Writing (p. 4). Inclusion of age is a legal requirement in the case of prescription-only medicines for children under 12 years of age, but it is preferable to state the age for **all** prescriptions for children.

It is particularly important to state the strengths of capsules or tablets. Although liquid preparations are particularly suitable for children, they may contain sugar which encourages dental decay. Sugar-free medicines are preferred for long term treatment.

Many children are able to swallow tablets or capsules and may prefer a solid dose form; involving the child and parents in choosing the formulation is helpful.

When a prescription for a liquid oral preparation is written and the dose ordered is smaller than 5 ml, an **oral syringe** will be supplied (for details, see p. 1). Parents should be advised not to add any med-

Prescribing in palliative care

Palliative care is the active total care of patients whose disease is not responsive to curative treatment. Control of pain, of other symptoms, and of psychological, social and spiritual problems, is paramount to provide the best quality of life for patients and their families. Careful assessment of symptoms and needs of the patient should be undertaken by a multidisciplinary team.

Specialist palliative care is available in most areas as day hospice care, home care teams (often known as Macmillan teams), in-patient hospice care, and hospital teams. Many acute hospitals and teaching centres now have consultative, hospital-based teams.

Hospice care of terminally ill patients has shown the importance of symptom control and psychosocial support of the patient and family. Families should be included in the care of the patient if they wish.

Many patients wish to remain at home with their families. Although some families may at first be afraid of caring for the patient at home, support can be provided by community nursing services, social services, voluntary agencies and hospices together with the general practitioner. The family may be reassured by the knowledge that the patient will be admitted to a hospital or hospice if the family cannot cope.

DRUG TREATMENT. The number of drugs should be as few as possible, for even the taking of medicine may be an effort. Oral medication is usually satisfactory unless there is severe nausea and vomiting, dysphagia, weakness, or coma, in which case parenteral medication may be necessary.

Pain

Analgesics are more effective in preventing pain than in the relief of established pain; it is important that they are given regularly.

The non-opioid analgesics **aspirin** or **paracetamol** given regularly will often make the use of opioids unnecessary. Aspirin (or other NSAIDs, if preferred) may also control the pain of *bone secondaries*; naproxen, flurbiprofen, and indometacin (section 10.1.1) are valuable and if necessary can be given rectally. Radiotherapy, bisphosphonates (section 6.6.2) and radioactive isotopes of **strontium** (*Metastron*® available from Amersham) may also be useful for pain due to bone metastases.

An opioid such as **codeine** or **dextropropoxyphene**, alone or in combination with a non-opioid analgesic at adequate dosage, may be helpful in the control of moderate pain if non-opioids alone are not sufficient. If these preparations are not controlling the pain, **morphine** is the most useful opioid analgesic. Alternatives to morphine are **hydromorphone**, **oxycodone** (section 4.7.2) and transdermal **fentanyl** (see below and section 4.7.2). Initiation of an opioid analgesic should not be delayed by concern over a theoretical likelihood of psychological dependence (addiction).

Equivalent single doses of strong analgesics

These equivalences are intended **only** as an approximate guide; patients should be carefully monitored after **any** change in medication and dose titration may be required

Analgesic	Dose
Morphine salts (oral)	10 mg
Diamorphine hydrochloride (intramuscular)	3 mg
Hydromorphone hydrochloride	1.3 mg
Oxycodone	5 mg

ORAL ROUTE. Morphine is given *by mouth* as an oral solution or as standard ('immediate release') tablets regularly every 4 hours, the initial dose depending largely on the patient's previous treatment. A dose of 5–10 mg is enough to replace a weaker analgesic (such as paracetamol or co-proxamol), but 10–20 mg or more is required to replace a strong one (comparable to morphine itself). If the first dose of morphine is no more effective than the previous analgesic, the next dose should be increased by 50%, the aim being to choose the lowest dose which prevents pain. The dose should be adjusted with careful assessment of the pain and the use of adjuvant analgesics (such as NSAIDs) should also be considered. Although morphine in a dose of 5–20 mg is usually adequate there should be no hesitation in increasing it stepwise according to response to 100 mg or occasionally up to 500 mg or higher if necessary. It may be possible to omit the overnight dose if double the usual dose is given at bedtime.

If pain occurs between regular doses ('breakthrough pain'), an additional dose ('rescue dose') should be given. An additional dose should also be given 30 minutes before an activity that causes pain (e.g. wound dressing). Fentanyl lozenges are also licensed for breakthrough pain.

When the pain is controlled and the patient's 24-hour morphine requirement is established, the daily dose can be given as a single dose or in 2 divided doses as a *modified-release preparation*.

Preparations suitable for twice daily administration include *MST Continus*® tablets or suspension, and *Zomorph*® capsules. Preparations that allow administration of the total daily morphine requirement as a single dose include *MXL*® capsules. *Morcap SR*® capsules may be given either twice daily or as a single daily dose.

The starting dose of modified-release preparations designed for twice daily administration is usually 10–20 mg every 12 hours if no other analgesic (or only paracetamol) has been taken previously, but to replace a weaker opioid analgesic (such as co-proxamol) the starting dose is usually 20–30 mg every 12 hours. Increments should be made to the dose, not to the frequency of administration, which should remain at every 12 hours.

The effective dose of modified-release preparations can alternatively be determined by giving the oral solution of morphine every 4 hours in increasing doses until the pain has been controlled, and then transferring the patient to the same total 24-

hour dose of morphine given as the modified-release preparation (divided into two portions for 12-hourly administration). The first dose of the modified-release preparation is given 4 hours after the last dose of the oral solution.[1]

Morphine, as oral solution or standard formulation tablets, should be prescribed for breakthrough pain; the dose should be about one-sixth of the total daily dose of oral morphine.

PARENTERAL ROUTE. If the patient becomes unable to swallow, the equivalent intramuscular dose of morphine is half the oral solution dose; in the case of the modified-release tablets it is half the total 24-hour dose (which is then divided into 6 portions to be given every 4 hours). **Diamorphine** is preferred for injection because, being more soluble, it can be given in a smaller volume. The equivalent intramuscular (or subcutaneous) dose of diamorphine is approximately a third of the oral dose of morphine. *Subcutaneous infusion* of diamorphine via syringe driver can be useful (for details, see p. 15).

If the patient can resume taking medicines by mouth, then oral morphine may be substituted for subcutaneous infusion of diamorphine; see table of equivalent doses of morphine on p. 17 for equivalences between the two opioids.

RECTAL ROUTE. Morphine is also available for *rectal administration* as suppositories; alternatively **oxycodone** suppositories can be obtained on special order. A modified-release preparation of morphine for once-daily administration is available as a rectal tampon (*Moraxen*®). The dose is calculated in the same way as modified-release preparations given by the oral route (see above).

TRANSDERMAL ROUTE. Transdermal preparations of fentanyl are available (section 4.7.2). Careful conversion from oral morphine to transdermal fentanyl is necessary. The following 24-hour doses of morphine are considered to be equivalent to the fentanyl patches shown:

Morphine salt 90 mg daily ≡ fentanyl '25' patch
Morphine salt 180 mg daily ≡ fentanyl '50' patch
Morphine salt 270 mg daily ≡ fentanyl '75' patch
Morphine salt 360 mg daily ≡ fentanyl '100' patch

Morphine (as oral solution or standard formulation tablets) is given for breakthrough pain.

GASTRO-INTESTINAL PAIN. The pain of *bowel colic* may be reduced by loperamide 2–4 mg 4 times daily. Hyoscine hydrobromide may also be helpful, given sublingually at a dose of 300 micrograms 3 times daily as *Kwells*® (Roche Consumer Health) tablets. For the dose by subcutaneous infusion using a syringe driver, see p. 16.

Gastric distension pain due to pressure on the stomach may be helped by a preparation incorporating an antacid with an antiflatulent (section 1.1.1) and by domperidone 10 mg 3 times daily before meals.

MUSCLE SPASM. The pain of muscle spasm can be helped by a muscle relaxant such as diazepam 5–10 mg daily or baclofen 5–10 mg 3 times daily.

1. Studies have indicated that administration of the last dose of the *oral solution* with the first dose of the *modified-release tablets* is not necessary.

NEUROPATHIC PAIN. Patients with neuropathic pain (section 4.7.3) may benefit from a trial of a tricyclic antidepressant for several weeks. An anticonvulsant may be added or substituted if pain persists; gabapentin is licensed for neuropathic pain (section 4.8.1)

Pain due to nerve compression may be reduced by a corticosteroid such as dexamethasone 8 mg daily, which reduces oedema around the tumour, thus reducing compression.

Nerve blocks may be considered when pain is localised to a specific area. **Transcutaneous electrical nerve stimulation** (TENS) may also help.

Miscellaneous conditions

Non-licensed indications or routes

Several recommendations in this section involve non-licensed indications or routes.

RAISED INTRACRANIAL PRESSURE. Headache due to raised intracranial pressure often responds to a high dose of a corticosteroid, such as dexamethasone 16 mg daily for 4 to 5 days, subsequently reduced to 4–6 mg daily if possible; dexamethasone should be given before 6 p.m. to reduce the risk of insomnia.

INTRACTABLE COUGH. Intractable cough may be relieved by moist inhalations or by regular administration of oral morphine in an initial dose of 5 mg every 4 hours. Methadone linctus should be avoided because it has a long duration of action and tends to accumulate.

DYSPNOEA. Dyspnoea may be relieved by regular oral morphine in carefully titrated doses, starting at 5 mg every 4 hours. Diazepam 5–10 mg daily may be helpful; a corticosteroid, such as dexamethasone 4–8 mg daily, may also be helpful if there is bronchospasm or partial obstruction.

EXCESSIVE RESPIRATORY SECRETION. Excessive respiratory secretion (death rattle) may be reduced by subcutaneous injection of hyoscine hydrobromide 400–600 micrograms every 4 to 8 hours; care must however be taken to avoid the discomfort of dry mouth. For the dose by subcutaneous infusion using a syringe driver, see next page.

RESTLESSNESS AND CONFUSION. Restlessness and confusion may require treatment with haloperidol 1–3 mg by mouth every 8 hours. Chlorpromazine 25–50 mg by mouth every 8 hours is an alternative, but causes more sedation. Levomepromazine (methotrimeprazine) is also used occasionally for restlessness. For the dose by subcutaneous infusion using a syringe driver, see next page.

HICCUP. Hiccup due to gastric distension may be helped by a preparation incorporating an antacid with an antiflatulent (section 1.1). If this fails, metoclopramide 10 mg every 6 to 8 hours by mouth or by intramuscular injection can be added; if this also fails, chlorpromazine 10–25 mg every 6 to 8 hours can be tried.

ANOREXIA. Anorexia may be helped by prednisolone 15–30 mg daily or dexamethasone 2–4 mg daily.

CONSTIPATION. Constipation is a very common cause of distress and is almost invariable after administration of an opioid. It should be prevented if possible by the regular administration of laxatives; a faecal softener with a peristaltic stimulant (e.g. co-danthramer), or lactulose solution with a senna preparation should be used (section 1.6.2 and section 1.6.3).

FUNGATING GROWTH. Fungating growth may be treated by regular dressing and oral administration of metronidazole; topical application of metronidazole is also used.

CAPILLARY BLEEDING. Capillary bleeding may be reduced by applying gauze soaked in adrenaline (epinephrine) solution 1 mg/mL (1 in 1000).

DRY MOUTH. Dry mouth may be relieved by good mouth care and measures such as the sucking of ice or pineapple chunks or the use of artificial saliva (section 12.3.5); dry mouth associated with candidiasis can be treated by oral preparations of nystatin or miconazole (section 12.3.2); alternatively, fluconazole can be given by mouth (section 5.2). Dry mouth may be caused by certain medication including opioids, antimuscarinic drugs (e.g. hyoscine), antidepressants and some anti-emetics; if possible, an alternative preparation should be considered.

PRURITUS. Pruritus, even when associated with obstructive jaundice, often responds to simple measures such as application of emollients (section 13.2.1). In the case of obstructive jaundice, further measures include administration of colestyramine or an anabolic steroid, such as stanozolol 5–10 mg daily; antihistamines can be helpful (section 3.4.1).

CONVULSIONS. Patients with cerebral tumours or uraemia may be susceptible to convulsions. Prophylactic treatment with phenytoin or carbamazepine (section 4.8.1) should be considered. When oral medication is no longer possible, diazepam as suppositories 10–20 mg every 4 to 8 hours, or phenobarbital by injection 50–200 mg twice daily is continued as prophylaxis. For the use of midazolam by subcutaneous infusion using a syringe driver, see below.

DYSPHAGIA. A corticosteroid such as dexamethasone 8 mg daily may help, temporarily, if there is an obstruction due to tumour. See also under Dry Mouth.

NAUSEA AND VOMITING. Nausea and vomiting are common in patients with advanced cancer. Ideally, the cause should be determined before treatment with anti-emetics (section 4.6) is started.

Nausea and vomiting may occur with opioid therapy particularly in the initial stages but can be prevented by giving an anti-emetic such as haloperidol or metoclopramide. An anti-emetic is usually necessary only for the first 4 or 5 days and therefore combined preparations containing an opioid with an anti-emetic are not recommended because they lead to unnecessary anti-emetic therapy (and associated side-effects when used long-term).

Metoclopramide has a prokinetic action and is used in a dose of 10 mg 3 times daily by mouth for nausea and vomiting associated with gastritis, gastric stasis, and functional bowel obstruction. Drugs with antimuscarinic effects antagonise prokinetic drugs and, where possible, should not therefore be used concurrently.

Haloperidol is used in a dose of 1.5 mg daily (or twice daily if nausea continues) by mouth for most chemical causes of vomiting (e.g. hypercalcaemia, renal failure).

Cyclizine is given in a dose of 50 mg up to 3 times daily by mouth. It is used for nausea and vomiting due to mechanical bowel obstruction, raised intracranial pressure, and motion sickness.

Anti-emetic therapy should be reviewed every 24 hours; it may be necessary to substitute the anti-emetic or to add another one.

Levomepromazine (methotrimeprazine) 12.5–25 mg daily by mouth may be used if first-line anti-emetics are inadequate. Dexamethasone 8–16 mg daily by mouth may be used as an adjunct.

For the administration of anti-emetics by subcutaneous infusion using a syringe driver, see below.

For the treatment of nausea and vomiting associated with cancer chemotherapy, see section 8.1.

INSOMNIA. Patients with advanced cancer may not sleep because of discomfort, cramps, night sweats, joint stiffness, or fear. There should be appropriate treatment of these problems before hypnotics are used. Benzodiazepines, such as temazepam, may be useful (section 4.1.1).

HYPERCALCAEMIA. See section 9.5.1.2.

Syringe drivers

Although drugs can usually be administered *by mouth* to control the symptoms of advanced cancer, the parenteral route may sometimes be necessary. If the parenteral route is necessary, repeated administration of *intramuscular injections* can be difficult in a cachectic patient. This has led to the use of a portable syringe driver to give a *continuous subcutaneous infusion*, which can provide good control of symptoms with little discomfort or inconvenience to the patient.

Syringe driver rate settings. Staff using syringe drivers should be **adequately trained** and different rate settings should be **clearly identified** and **differentiated**; incorrect use of syringe drivers is a common cause of drug errors.

Indications for the **parenteral route** are:

- the patient is unable to take medicines by mouth owing to *nausea and vomiting, dysphagia, severe weakness*, or *coma*;
- there is *malignant bowel obstruction* in patients for whom further surgery is inappropriate (avoiding the need for an intravenous infusion or for insertion of a nasogastric tube);
- occasionally when the patient *does not wish* to take regular medication by mouth.

NAUSEA AND VOMITING. Haloperidol is given in a *subcutaneous infusion* dose of 2.5–10 mg/24 hours.

Levomepromazine (methotrimeprazine) causes sedation in about 50% of patients; it is given in a *subcutaneous infusion dose* of 25–200 mg/24 hours, although lower doses of 5–25 mg/24 hours may be effective with less sedation.

Cyclizine is particularly liable to precipitate if mixed with diamorphine or other drugs (see under Mixing and Compatibility, below); it is given in a *subcutaneous infusion dose* of 150 mg/24 hours.

Metoclopramide may cause skin reactions; it is given in a *subcutaneous infusion dose* of 30–100 mg/24 hours.

Octreotide (section 8.3.4.3), which stimulates water and electrolyte absorption and inhibits water secretion in the small bowel, can be used by subcutaneous infusion, in a dose of 300–600 micrograms/24 hours to reduce intestinal secretions and vomiting.

BOWEL COLIC AND EXCESSIVE RESPIRATORY SECRETIONS. Hyoscine hydrobromide effectively reduces respiratory secretions and is sedative (but occasionally causes paradoxical agitation); it is given in a *subcutaneous infusion dose* of 0.6–2.4 mg/24 hours.

Hyoscine butylbromide is effective in bowel colic, is less sedative than hyoscine hydrobromide, but is not always adequate for the control of respiratory secretions; it is given in a *subcutaneous infusion dose* of 20–60 mg/24 hours (**important:** this dose of *hyoscine butylbromide* must not be confused with the much lower dose of *hyoscine hydrobromide*, above).

Glycopyrronium 0.6–1.2 mg/24 hours may also be used.

RESTLESSNESS AND CONFUSION. Haloperidol has little sedative effect; it is given in a *subcutaneous infusion dose* of 5–15 mg/24 hours.

Levomepromazine (methotrimeprazine) has a sedative effect; it is given in a *subcutaneous infusion dose* of 50–200 mg/24 hours.

Midazolam is a sedative and an antiepileptic, and is therefore suitable for a very restless patient; it is given in a *subcutaneous infusion dose* of 20–100 mg/24 hours.

CONVULSIONS. If a patient has previously been receiving an antiepileptic *or* has a primary or secondary cerebral tumour *or* is at risk of convulsion (e.g. owing to uraemia) antiepileptic medication should not be stopped. Midazolam is the benzodiazepine antiepileptic of choice for *continuous subcutaneous infusion*, and is given in a dose of 20–40 mg/24 hours.

PAIN CONTROL. Diamorphine is the preferred opioid since its high solubility permits a large dose to be given in a small volume (see under Mixing and Compatibility, below). The table below gives the approximate doses of *morphine by mouth* (as oral solution or standard formulation tablets or as modified-release tablets) equivalent to *diamorphine by injection* (intramuscularly or by subcutaneous infusion).

MIXING AND COMPATIBILITY. The general principle that injections should be given into separate sites (and should not be mixed) does not apply to the use of syringe drivers in palliative care. Provided that there is evidence of compatibility, selected injections can be mixed in syringe drivers. Not all types of medication can be used in a subcutaneous infusion. In particular, chlorpromazine, prochlorperazine and diazepam are **contra-indicated** as they cause skin reactions at the injection site; to a lesser extent cyclizine and levomepromazine (methotrimeprazine) may also sometimes cause local irritation.

In theory injections dissolved in water for injections are more likely to be associated with pain (possibly owing to their hypotonicity). The use of physiological saline (sodium chloride 0.9%) however increases the likelihood of precipitation when more than one drug is used; moreover subcutaneous infusion rates are so slow (0.1–0.3 mL/hour) that pain is not usually a problem when water is used as a diluent.

Diamorphine can be given by subcutaneous infusion in a strength of up to 250 mg/mL; up to a strength of 40 mg/mL either *water for injections* or *physiological saline* (sodium chloride 0.9%) is a suitable diluent—above that strength only *water for injections* is used (to avoid precipitation).

The following can be mixed with *diamorphine:*

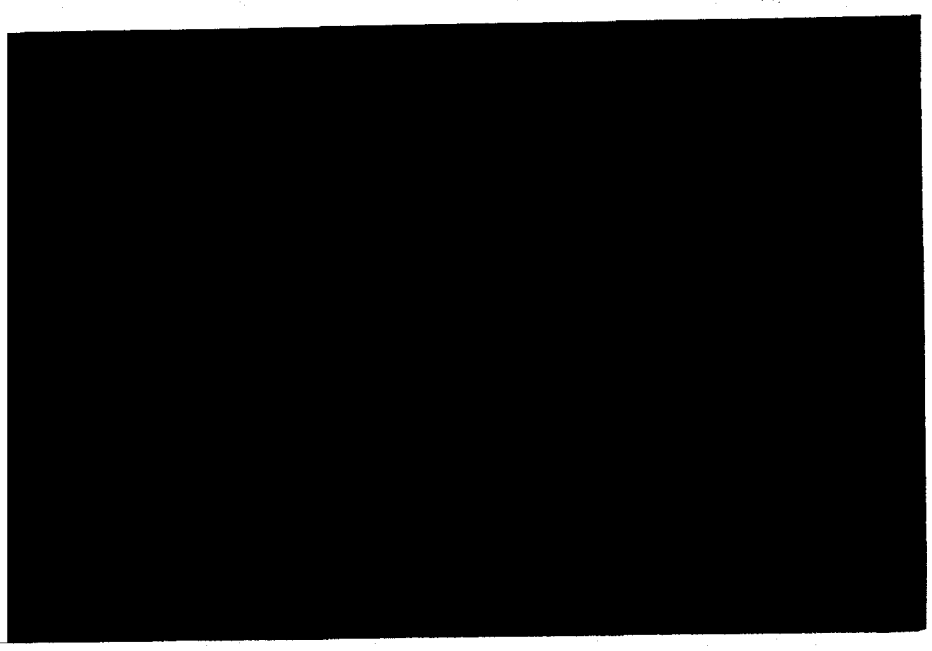
Cyclizine[1]	Hyoscine hydrobromide
Dexamethasone[2]	Levomepromazine
Haloperidol[3]	Metoclopramide[4]
Hyoscine butylbromide	Midazolam

Subcutaneous infusion solution should be monitored regularly both to check for precipitation (and discoloration) and to ensure that the infusion is running at the correct rate.

PROBLEMS ENCOUNTERED WITH SYRINGE DRIVERS. The following are problems that may be encountered with syringe drivers and the action that should be taken:

- if the subcutaneous infusion runs *too quickly* check the rate setting and the calculation;
- if the subcutaneous infusion runs *too slowly* check the start button, the battery, the syringe driver, the cannula, and make sure that the injection site is not inflamed;
- if there is an *injection site reaction* make sure that the site does not need to be changed—firmness or swelling at the site of injection is not in itself an indication for change, but pain or obvious inflammation is.

1. Cyclizine may precipitate at concentrations above 10 mg/mL *or* in the presence of physiological saline *or* as the concentration of diamorphine relative to cyclizine increases; mixtures of diamorphine and cyclizine are also liable to precipitate after 24 hours.
2. Special care is needed to avoid precipitation of dexamethasone when preparing.
3. Mixtures of haloperidol and diamorphine are liable to precipitate after 24 hours if haloperidol concentration is above 2 mg/mL.
4. Under some conditions metoclopramide may become discoloured; such solutions should be discarded.



Equivalent doses of morphine sulphate by mouth (as oral solution or standard tablets or as *modified release* tablets) or of diamorphine hydrochloride by intramuscular injection or by subcutaneous infusion

These equivalences are approximate only and may need to be adjusted according to response

ORAL MORPHINE		PARENTERAL DIAMORPHINE	
Morphine sulphate oral solution or standard tablets	Morphine sulphate modified release tablets	Diamorphine hydrochloride by intramuscular injection	Diamorphine hydrochloride by subcutaneous infusion
every 4 hours	**every 12 hours**	**every 4 hours**	**every 24 hours**
5 mg	20 mg	2.5 mg	15 mg
10 mg	30 mg	5 mg	20 mg
15 mg	50 mg	5 mg	30 mg
20 mg	60 mg	7.5 mg	45 mg
30 mg	90 mg	10 mg	60 mg
40 mg	120 mg	15 mg	90 mg
60 mg	180 mg	20 mg	120 mg
80 mg	240 mg	30 mg	180 mg
100 mg	300 mg	40 mg	240 mg
130 mg	400 mg	50 mg	300 mg
160 mg	500 mg	60 mg	360 mg
200 mg	600 mg	80 mg	480 mg

If breakthrough pain occurs give a subcutaneous (preferable) or intramuscular injection of diamorphine equivalent to one-sixth of the total 24-hour subcutaneous infusion dose. It is kinder to give an intermittent bolus injection *subcutaneously*—absorption is smoother so that the risk of adverse effects at peak absorption is avoided (an even better method is to use a subcutaneous butterfly needle).

To minimise the risk of infection no individual subcutaneous infusion solution should be used for longer than 24 hours.

Prescribing for the elderly

Old people, especially the very old, require special care and consideration from prescribers. *Medicines for Older People*, a component document of the National Service Framework for Older People,[1] describes how to maximise the benefits of medicines and how to avoid excessive, inappropriate, or inadequate consumption of medicines by older people.

POLYPHARMACY. Elderly patients often receive multiple drugs for their multiple diseases. This greatly increases the risk of drug interactions as well as adverse reactions, and may affect compliance (see Taking medicines to best effect under General guidance). Moreover, symptoms such as headache, sleeplessness, and lightheadedness which may be associated with social stress, as in widowhood, loneliness, and family dispersal can lead to further prescribing, especially of psychotropics. The use of drugs in such cases can at best be a poor substitute for effective social measures and at worst pose a serious threat from adverse reactions. Whilst unnecessary medication should be avoided, elderly patients should not be denied effective treatments such as those for stroke prophylaxis in atrial fibrillation or for osteoporosis.

FORM OF MEDICINE. Frail elderly patients may have difficulty swallowing tablets; if left in the mouth, ulceration may develop. They should always be encouraged to take their tablets or capsules with enough fluid, and in some cases it may be helpful to discuss with the patient the possibility of prescribing the drug as a liquid if available.

MANIFESTATIONS OF AGEING. In very old subjects, manifestations of normal ageing may be mistaken for disease and lead to inappropriate prescribing. For example, drugs such as prochlorperazine are commonly misprescribed for giddiness due to age-related loss of postural stability. Not only is such treatment ineffective but the patient may experience serious side effects such as parkinsonism, postural hypotension, and confusion.

SELF MEDICATION. Self-medication with over-the-counter products or with drugs prescribed for a previous illness (or even for another person) may be an added complication. Discussion with both the patient and relatives as well as a home visit may be needed to establish exactly what is being taken.

SENSITIVITY. The ageing nervous system shows increased *susceptibility* to many commonly used drugs, such as opioid analgesics, benzodiazepines, antipsychotics, and antiparkinsonian drugs, all of which must be used with caution. Similarly, other organs may also be more susceptible to the effects of drugs such as antihypertensives and NSAIDs.

1. Department of Health. National Service Framework for Older People. London: Department of Health, March 2001

Pharmacokinetics

The most important effect of age is reduction in renal clearance. Many aged patients thus *excrete drugs slowly*, and are *highly susceptible to nephrotoxic drugs*. Acute illness may lead to rapid reduction in renal clearance, especially if accompanied by dehydration. Hence, a patient stabilised on a drug with a narrow margin between the therapeutic and the toxic dose (e.g. digoxin) may rapidly develop adverse effects in the aftermath of a myocardial infarction or a respiratory-tract infection. Metabolism of drugs in the liver may be reduced in the elderly. Furthermore, body composition alters with increasing age and may affect the distribution of drugs.

The net result of pharmacokinetic changes is that the tissue concentration of a drug is commonly increased by over 50%, and debilitated patients may show even larger changes.

Adverse reactions

Adverse reactions often present in the elderly in a vague and non-specific fashion. *Confusion* is often the presenting symptom (caused by almost any of the commonly used drugs). Other common manifestations are *constipation* (with antimuscarinics and many tranquillisers) and postural *hypotension* and *falls* (with diuretics and many psychotropics).

HYPNOTICS. Many hypnotics with long half-lives have serious hangover effects of drowsiness, unsteady gait, and even slurred speech and confusion. Those with short half-lives should be used but they too can present problems (section 4.1.1). Short courses of hypnotics are occasionally useful for helping a patient through an acute illness or some other crisis but every effort must be made to avoid dependence. Benzodiazepines impair balance, which may result in falls.

DIURETICS. Diuretics are overprescribed in old age and should **not** be used on a long-term basis to treat simple gravitational oedema which will usually respond to increased movement, raising the legs, and support stockings. A few days of diuretic treatment may speed the clearing of the oedema but it should rarely need continued drug therapy.

NSAIDs. Bleeding associated with *aspirin* and *other NSAIDs* is more common in the elderly who are more likely to have a fatal or serious outcome. NSAIDs are also a special hazard in patients with cardiac disease or renal impairment which may again place older patients at particular risk.

Owing to the *increased susceptibilty of the elderly* to the *side-effects of NSAIDs* the following recommendations are made:

- for *osteoarthritis*, *soft-tissue lesions* and *back pain* first try measures such as weight reduction (if obese), warmth, exercise and use of a walking stick;
- for *osteoarthritis*, *soft-tissue lesions*, *back pain* and *pain in rheumatoid arthritis*, paracetamol should be used first and can often provide adequate pain relief;
- alternatively, a low-dose NSAID (e.g. ibuprofen up to 1.2 g daily may be given;
- for pain relief when either drug is inadequate, paracetamol in a full dose plus a low-dose NSAID may be given;
- if necessary, the NSAID dose can be increased or an opioid analgesic given with paracetamol;
- do not give two NSAIDs at the same time.

For advice on prophylaxis of NSAID-induced peptic ulcers if continued NSAID treatment is necessary, see section 1.3.

OTHER DRUGS. Other drugs which commonly cause adverse reactions are *antiparkinsonian drugs*, *antihypertensives*, *psychotropics*, and *digoxin*. The usual maintenance dose of digoxin in very old patients is 125 micrograms daily (62.5 micrograms in those with renal disease); lower doses are often inadequate but toxicity is common in those given 250 micrograms daily.

Drug-induced blood disorders are much more common in the elderly. Therefore drugs with a tendency to cause bone marrow depression (e.g. *co-trimoxazole*, *mianserin*) should be avoided unless there is no acceptable alternative.

The elderly generally require a lower maintenance dose of *warfarin* than younger adults; once again, the outcome of bleeding tends to be more serious.

Guidelines

First always question whether a drug is indicated at all.

LIMIT RANGE. It is a sensible policy to prescribe from a limited range of drugs and to be thoroughly familiar with their effects in the elderly.

REDUCE DOSE. Dosage should generally be substantially lower than for younger patients and it is common to start with about 50% of the adult dose. Some drugs (e.g. long-acting antidiabetic drugs such as glibenclamide and chlorpropamide) should be avoided altogether.

REVIEW REGULARLY. Review repeat prescriptions regularly. In many patients it may be possible to stop some drugs, provided that clinical progress is monitored. It may be necessary to reduce the dose of some drugs as renal function declines.

SIMPLIFY REGIMENS. Elderly patients benefit from simple treatment regimens. Only drugs with a clear indication should be prescribed and whenever possible given once or twice daily. In particular, regimens which call for a confusing array of dosage intervals should be avoided.

EXPLAIN CLEARLY. Write full instructions on every prescription (*including* repeat prescriptions) so that containers can be properly labelled with full directions. Avoid imprecisions like 'as directed'. Child-resistant containers may be unsuitable.

REPEATS AND DISPOSAL. Instruct patients what to do when drugs run out, and also how to dispose of any that are no longer necessary. Try to prescribe matching quantities.

If these guidelines are followed most elderly people will cope adequately with their own medicines. If not then it is essential to enrol the help of a third party, usually a relative or a friend.