BNF

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Emergency Supply of PoM at Patient's Request[1]

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[2] 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 five days' treatment except when the prescription-only medicine is:
- (i) 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 phenobarbitone or phenobarbitone sodium for the treatment of epilepsy: for details see *Medicines, Ethics and Practice*, No. 12, London, Pharmaceutical Press, 1994 (and subsequent editions as available).

ROYAL PHARMACEUTICAL SOCIETY'S GUIDELINES

(1) The pharmacist should consider the medical consequences, if any, of **not** supplying.

(2) The pharmacist should identify the patient by means of documentary evidence and/or personal knowledge.

(3) The doctor who prescribed on a previous occasion should be identified and contacted, if possible.

(4) The patient should be asked whether the doctor has stopped the treatment.

(5) The patient should be asked whether any other medicine is being taken at the same time to check drug interactions.

(6) An emergency supply should not be made if the item requested was prescribed previously more than six months prior to the request. Variations may be made in the case of illnesses which occur infrequently, e.g. hay fever, asthma attack, or migraine.

(7) Consideration should be given to providing less than five days' supply if this is justified.

(8) Labelling should be clear and legible and there should be some suitable identification of emergency supply entries in the prescription book.

1. For emergency supply at the request of a doctor see *Medicines, Ethics and Practice*, No. 12, London, Pharmaceutical Press, 1994 (and subsequent editions as available).
2. The doctor must be a UK-registered doctor.

Plasma concentrations in the BNF are expressed in mass units per litre (e.g. mg/litre). The approximate equivalent in terms of amount of substance units (e.g. micromol/litre) is given in brackets.

Approximate Conversions and Units

lb	*kg*
1	0.45
2	0.91
3	1.36
4	1.81
5	2.27
6	2.72
7	3.18
8	3.63
9	4.08
10	4.54
11	4.99
12	5.44
13	5.90
14	6.35

stones	*kg*
1	6.35
2	12.70
3	19.05
4	25.40
5	31.75
6	38.10
7	44.45
8	50.80
9	57.15
10	63.50
11	69.85
12	76.20
13	82.55
14	88.90
15	92.95

ml	*fl. oz*
50	1.8
100	3.5
150	5.3
200	7.0
500	17.6
1000	35.2

Mass

1 kilogram (kg)	= 1000 grams (g)
1 gram (g)	= 1000 milligrams (mg)
1 milligram (mg)	= 1000 micrograms
1 microgram	= 1000 nanograms
1 nanogram	= 1000 picograms

Volume

1 litre	= 1000 millilitres (mL)
1 millilitre	= 1000 microlitres
1 pint	~ 568 mL

Other units

1 kilocalorie (kcal)	= 4186.8 joules (J)
1000 kilocalories (kcal)	= 4.1868 megajoules (MJ)
1 megajoule (MJ)	= 238.8 kilocalories (kcal)
1 millimetre of mercury (mmHg)	= 133.3 pascals (Pa)
1 kilopascal (kPa)	= 7.5 mmHg (pressure)

Controlle Dependei

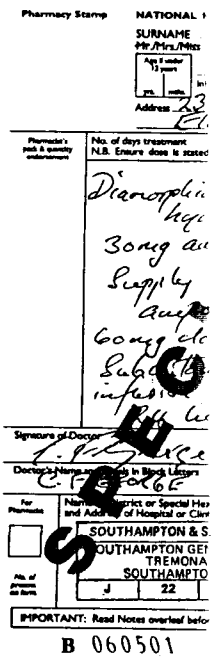
PRESCRIPTIONS. Prepar the prescription requi Drugs Regulations 198 in schedules 2 and 3, a the BNF by the symb The principal legal medical prescriptions a

Prescriptions ordering to prescription require *dated*[1] by the pres prescriber's *address*. Th state *in the prescriber's* otherwise so as to be in

1. The name and addres
2. In the case of a prepa appropriate the strength
3. The total quantity number of dose units, *in*
4. The dose.[5]

A prescription may or dispensed by instalme instalments and the inte be specified.[6] Prescripti the same form are **not** p

It is an offence fo incomplete prescription allowed to dispense a the information require prescription. Failure to c concerning the writing



B 060501

Controlled Drugs and Drug Dependence

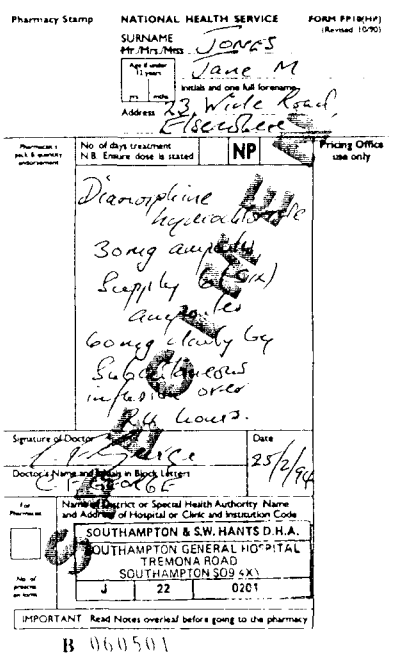
PRESCRIPTIONS. Preparations which are subject to the prescription requirements of the Misuse of Drugs Regulations 1985, i.e. preparations specified in schedules 2 and 3, are distinguished throughout the BNF by the symbol **CD** (Controlled Drugs). The principal legal requirements relating to medical 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*;
4. The dose.[5]

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.[6] Prescriptions ordering 'repeats' on the same form are **not** permitted.

It is an offence for a doctor 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.


Pharmacy Stamp
NATIONAL HEALTH SERVICE
FORM FP10(HP) (Revised 10/90)
SURNAME Jones
Mr./Mrs./Miss
Jane M
Address 23 Wade Road Elsewhere
No. of days treatment N.B. Ensure dose is stated
NP
Pricing Office use only
Diamorphine hydrochloride
30mg ampoules
Supply (6 (six)
ampoules
30mg/ml Gly
Subcutaneous
infusion
24 hours.
Signature of Doctor
Date 25/2/94
Doctor's Name and Address in Block Letters
Name of District or Special Health Authority Name and Address of Hospital or Clinic and Institution Code
SOUTHAMPTON & S.W. HANTS D.H.A.
SOUTHAMPTON GENERAL HOSPITAL
TREMONA ROAD
SOUTHAMPTON SO9 4XY
J 22 0201
IMPORTANT Read Notes overleaf before going to the pharmacy
B 066501

DEPENDENCE AND MISUSE. The prevalence of drug dependence and misuse in Great Britain, particularly amongst young people, continues to give cause for concern to teachers, social workers, and the police, as well as doctors.

The most serious drugs of addiction are **diamorphine** (heroin), **morphine**, and the **synthetic opioids**; illicit **cocaine** is now also a problem.

Despite marked reduction in the prescribing of **amphetamines** there is concern that abuse of illicitly produced amphetamine and related compounds is widespread.

The principal **barbiturates** are now Controlled Drugs, but phenobarbitone and 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 phenobarbitone and phenobarbitone sodium are available under the emergency supply regulations (p. 6).

Cannabis (Indian hemp) has no approved medicinal use and cannot be prescribed by doctors (except under licence from the Home Secretary). Its use is illegal but has become widespread in certain sections of society. Cannabis is a mild hallucinogen seldom accompanied by a desire to increase the dose; withdrawal symptoms are unusual. **Lysergide** (lysergic acid diethylamide;

1. A prescription is valid for 13 weeks from the date stated thereon.
2. Unless the prescriber has been specifically exempted from this requirement or unless the prescription contains no controlled drug other than phenobarbitone or phenobarbitone 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. 'Tenuate Dospan') 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. The instruction 'one as directed' constitutes a dose but 'as directed' does not.
6. A special form, FP10(HP)(addl. in Scotland HBP(A)), is available to doctors in NHS drug treatment centres for prescribing cocaine, dextromoramide, diamorphine, dipipanone, methadone, morphine, or pethidine by instalments for addicts. In Scotland general practitioners can prescribe by instalments on form GP10. In England and Wales forms FP10 and FP10(HP) are not suitable for this purpose but form FP10(MDA) is available. **Important:** in all cases a special licence is necessary to prescribe cocaine, diamorphine, or dipipanone for addicts except for treatment of organic disease or injury; for details see p. 9

LSD) is a much more potent hallucinogen; its use can lead to severe psychotic states in which life may be at risk.

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. A doctor should therefore be wary of prescribing for strangers and may be able to get information about suspected opioid addicts from the Home Office (for details see p. 9).

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 071-273 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 control. For clearance in the country to be visited it would be necessary to approach that country's embassy or High Commission in the UK.

The Misuse of Drugs Act, 1971

This Act was passed in 1971 to provide more flexible and more comprehensive control over the misuse of drugs of all kinds than was possible under the earlier Dangerous Drugs Act. The Act as amended 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, 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 benzphetamine and chlorphentermine, buprenorphine, diethylpropion, mazindol, meprobamate, pemoline, pipradrol, and most benzodiazepines

The Misuse of Drugs Regulations 1985 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, quinalbarbitone, glutethimide, amphetamine, and cocaine and are subject to the full controlled drug requirements relating to prescriptions, safe custody, the need to keep registers, etc. (unless exempted in schedule 5).

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

Schedule 4 includes 34 benzodiazepines and pemoline which are subject to minimal control. In particular, controlled drug prescription requirements do not apply and they are not subject to safe custody.

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 Addicts

The Misuse of Drugs (Notification of and Supply to Addicts) Regulations 1973 require that any doctor who attends a person who the doctor considers or has reasonable grounds to suspect, is addicted to any of the 14 notifiable drugs (see below) shall, within seven days of the attendance, furnish in writing particulars of that person to:

Chief Medical Officer,
Home Office, Drugs Branch,
Queen Anne's Gate,
London SW1H 9AT.

The drugs to which the Regulations apply are:

Cocaine	Methadone
Dextromoramide	Morphine
Diamorphine	Opium
Dipipanone	Oxycodone
Hydrocodone	Pethidine
Hydromorphone	Phenazocine
Levorphanol	Pirritramide

Note. Dipipanone is only legally available as Diconal® Tablets. These have been much misused by opioid addicts in recent years; only medical practitioners with a special licence may now prescribe them for addicts to treat addiction. Doctors and others should be suspicious of young people who ask for them, especially as temporary residents.

Particulars[1] to be notified to the Chief Medical Officer are:

Name and address
Sex
Date of birth
National Health Service number (if known)
Date of attendance
Name of drugs of addiction
Whether patient injects any drug (whether or not notifiable)

Notification must be confirmed annually in writing if the patient is still being treated by the practitioner. Notified information is incorporated in an Index of Addicts which is maintained in the Home Office and information from this is available on a confidential basis to doctors; in fact, it is good medical practice to check all new cases of addiction or suspected addiction with the Index before prescribing or supplying controlled drugs since this is a safeguard against addicts obtaining supplies simultaneously from two or more doctors. Enquiries can be made either in writing to the Chief Medical Officer or, preferably, by telephoning 071-273 2213. To keep notified information confidential, such enquiries are normally answered by means of a return telephone call. The reply will come from lay staff who are not qualified to give guidance on the clinical handling of cases; a recorded telephone service is available for out-of-office hours.

The preceding paragraph applies only to medical practitioners in England, Scotland, and Wales. In Northern Ireland notification should be sent to:

Chief Medical Officer
Department of Health and Social Services
Dundonald House
Belfast BT4 3SF
Enquiries should also be made to that Department, telephone 0232 650111 extension 227

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

The Misuse of Drugs (Notification of and Supply to Addicts) Regulations 1973 also provide that only medical practitioners who hold a special licence issued by the Home Secretary may prescribe diamorphine, dipipanone (Diconal®), or cocaine for addicts; 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 prescription-writing guidelines, see p. 7.

1 Only the particulars of which the doctor has knowledge need be notified immediately; the remainder may be notified at a later date. Private doctors, police surgeons and prison medical officers may continue to notify the Home Office using form HS2 A/B(Rev), available from their Family Health Services Authority (FHSA) or their Health Board in Scotland.

All other doctors, including general practitioners, hospital doctors and those practising in treatment centres, should use notification forms which can be obtained from their Regional Health Authority Drugs Misuse Database administration.

Adverse Reactions to Drugs

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

CSM
Freepost
London SW8 5BR
(071-627 3291)

Yellow prepaid lettercards for reporting are available from the above address or by dialling 100 and asking for 'CSM Freefone'; also, forms are bound in this book (inside back cover).

A 24-hour Freefone service is now available to all parts of the United Kingdom, for doctors seeking advice and information on adverse reactions; it may be obtained by dialling 100 and asking for 'CSM Freefone'. Outside office hours a telephone-answering machine will take messages.

The following regional centres also collect data:

CSM Mersey
Freepost
Liverpool L3 3AB
(051-236 4620 Extn 2126)

CSM Wales
Freepost
Cardiff CF4 1ZZ
(0222 744181 Direct Line)

CSM Northern
Freepost 1085
Newcastle upon Tyne
NE1 1BR
(091-232 1525 Direct Line)

CSM West Midlands
Freepost
Birmingham B15 1BR
[No telephone number]

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

ADROIT

Adverse Drug Reactions On-line Information Tracking (ADROIT) has now been introduced to facilitate the monitoring of adverse drug reactions.

NEWER DRUGS. These are indicated by the sign ▼. Doctors are asked to report *all* suspected reactions (i.e. any adverse or any unexpected event, however minor, which could conceivably be attributed to the drug). Reports should be made despite uncertainty about a causal relationship, irrespective of whether the reaction is well recognized, and even if other drugs have been given concurrently.

ESTABLISHED DRUGS. Doctors 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 risk/benefit ratios to be compared with other drugs of a similar class. For established drugs doctors are asked not to report well-known, relatively minor side-effects, such as dry mouth with tricyclic antidepressants, constipation with opioids, or nausea with digoxin.

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. Doctors are asked to be particularly alert to 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.

Vaccines. Doctors are asked to report all suspected reactions to both new and established vaccines. The balance between risks and benefits needs to be kept under continuous review.

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. It is very important to recognise allergy and idiosyncrasy as 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*; remember that interactions may occur.
4. Age and hepatic or renal disease may alter the metabolism or excretion of drugs, so that much smaller doses may need to be prescribed. Pharmacogenetic factors may also be responsible for variations in the rate of 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 Defect Medicines Report Centre operates a 24-hour service to assist with the investigation of problems arising from licensed medicinal products thought to be defective, and to co-ordinate 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 Defect Medicines Report Centre
Medicines Control Agency
Room 1801, Market Towers
1 Nine Elms Lane
London SW8 5NQ
071-273 0574 (weekdays 8.30 am–5.30 pm)
or 071-210 5368 or 5371 (any other time)

Prescribing in Terminal Care

In recent years there has been increased interest in providing better treatment and support for patients with terminal illness. The aim is to keep them as comfortable, alert, and free of pain as possible. If patients are to end their days in serenity it may also be necessary to direct attention to emotional, financial, social, or family problems. The patient's minister or the hospital chaplain may give invaluable help.

DOMICILIARY CARE. If they wish, whenever possible, patients should end their days in their own homes. Although families may at first be afraid of caring for the patient at home, they will usually do so if extra support from district nursing services and social services is provided. Families may be reassured if an assurance is given that the patient will be admitted to a hospital or hospice if they cannot cope.

HOSPITAL OR HOSPICE CARE. The most important lesson to be drawn from the experience of hospices is that both doctors and nurses must give time to listen to the patient. This gives great support and comfort to a patient who may otherwise suffer intolerable loneliness. Often problems come to light that can easily be dealt with—adjusting a blind in the late afternoon, an irritating noise to be avoided, drinks to be placed in easier reach, someone to read the newspaper, or the TV to be replaced by radio. The staff should not exclude the family from contributing to the patient's care; if prevented they may be resentful or subsequently suffer a feeling of guilt.

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 always more effective in preventing the development of pain than in the relief of established pain.

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 indomethacin (see section 10.1.1) are valuable and if necessary can be given rectally. **Corticosteroids** or **radiotherapy** are also often useful for pain due to bone metastases.

Morphine is the most useful of the **opioid analgesics**. In addition to relief of pain, it confers a state of euphoria and mental detachment.

ORAL ROUTE. Morphine is given *by mouth* as an oral solution 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 it should be increased by 50%, the aim being to choose the lowest dose which prevents pain. Although a dose of 5–20 mg is usually adequate there should be no hesitation in increasing it to 30–60 mg or occasionally to 90–150 mg or higher if necessary. If pain occurs between doses the next dose due is increased; in the interim an additional dose is given.

Modified-release tablets of morphine (MST Continus® tablets or Oramorph® SR tablets) are an alternative to the oral solution; they have the advantage that they need only be taken every 12 hours. The starting dose of MST Continus® tablets or Oramorph® SR tablets is usually 10–20 mg every 12 hours if no other analgesic (or only paracetamol) has previously been taken, 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 MST Continus® tablets or Oramorph® SR tablets can alternatively be found 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 tablet (divided into two portions for 12-hourly administration). The first dose of the modified-release tablet is given 4 hours after the last dose of the oral solution[1].

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 only about a quarter to a third of the oral dose of morphine; *subcutaneous infusion via syringe driver* can be useful (for details, see p.14).

RECTAL ROUTE. Morphine is also available for *rectal administration* as suppositories; alternatively **oxycodone** suppositories can be obtained on special order.

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.14.

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

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.

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.

NERVE PAIN. 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.

Dysaesthetic or stabbing pain resulting from *nerve irritation* may be reduced by amitriptyline 25–75 mg at night, or by carbamazepine 200 mg 3 times daily.

Nerve blocks may be considered when pain is localised to a specific area.

MISCELLANEOUS CONDITIONS

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.

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

DYSPNOEA. *Dyspnoea* may be relieved by regular oral morphine hydrochloride (or sulphate) solution 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. 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. 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 (see section 1.1.1). 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.

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

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 (see sections 1.6.2 and 1.6.3).

FUNGATING GROWTH. *Fungating growth* may be treated by cleansing with a mixture of 1 part of 4% povidone-iodine skin cleanser solution and 4 parts of liquid paraffin. Oral administration of metronidazole (see section 5.1.11) may eradicate the anaerobic bacteria responsible for the odour of fungating tumours; topical application (see section 13.10.1.2) is also used.

CAPILLARY BLEEDING. *Capillary bleeding* may be reduced by applying gauze soaked in adrenaline solution (1 in 1000).

DRY MOUTH. *Dry mouth* may be associated with candidiasis which can be treated by nystatin oral suspension or pastilles, amphotericin lozenges, or miconazole oral gel after food; alternatively, fluconazole can be given by mouth (see section 5.2). Dry mouth can also be a side-effect of morphine.

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

CONVULSIONS. Patients with *cerebral tumours* or *uraemia* may be susceptible to convulsions. Prophylactic treatment with phenytoin or carbamazepine (see 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 phenobarbitone by injection 50–200 mg twice daily is continued as prophylaxis. For the use of midazolam by *subcutaneous infusion* using a syringe driver, see next page.

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 very common in patients with advanced cancer. The cause should be diagnosed before treatment with anti-emetics (see section 4.6) is started.

Nausea and vomiting may also occur in the initial stages of morphine therapy but can be prevented by

giving an anti-emetic such as haloperidol or prochlorperazine. An anti-emetic is usually only necessary for the first 4 or 5 days therefore fixed-combination opioid preparations containing an anti-emetic are not recommended since they lead to unnecessary anti-emetic therapy (often with undesirable drowsiness). For the administration of anti-emetics by *subcutaneous infusion* using a syringe driver, see below.

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 (see 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.

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.

Methotrimeprazine causes sedation in about 50% of patients; it is given in a *subcutaneous infusion dose* of 25–200 mg/24 hours.

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 30–60 mg/24 hours.

BOWEL COLIC OR 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).

RESTLESSNESS AND CONFUSION. **Haloperidol** has little sedative effect; it is given in a *subcutaneous infusion dose* of 5–30 mg/24 hours.

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 20–40 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 on the next page gives the approximate doses of *morphine by mouth* (as oral solution or standard 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 terminal 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 **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]
Dexamethasone[2]
Haloperidol[3]
Hyoscine butylbromide
Hyoscine hydrobromide
Methotrimeprazine
Metoclopramide[4]
Midazolam

1. Cyclizine may precipitate at concentrations above 20mg/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.

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. Tenderness or swelling at the site of injection is not in itself an indication for change, but pain or obvious inflammation is.

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	70 mg	400 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.

POLYPHARMACY. Elderly patients are apt to receive multiple drugs for their multiple diseases. This greatly increases the risk of drug interactions as well as other adverse reactions. 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.

FORM OF MEDICINE. 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 advisable to prescribe 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 drug-induced parkinsonism, postural hypotension, and mental 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 relatives and a home visit may be needed to establish exactly what is being taken.

SUSCEPTIBILITY. The ageing nervous system shows increased *susceptibility* to many commonly used drugs, such as opioid analgesics, benzodiazepines, and antiparkinsonian drugs, all of which must be used with caution.

PHARMACOKINETICS

While drug distribution and metabolism may be significantly altered, the most important effect of age is reduction in renal clearance, frequently aggravated by the effects of prostatism, nephrosclerosis, or chronic urinary tract infection. Many aged patients thus possess only *limited reserves of renal function, 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.

The net result of pharmacokinetic changes is that tissue concentrations are commonly increased by over 50%, and aged and debilitated patients may show even larger changes.

ADVERSE REACTIONS

Adverse reactions often present in the elderly in a vague and non-specific fashion. *Mental 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 (see 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.

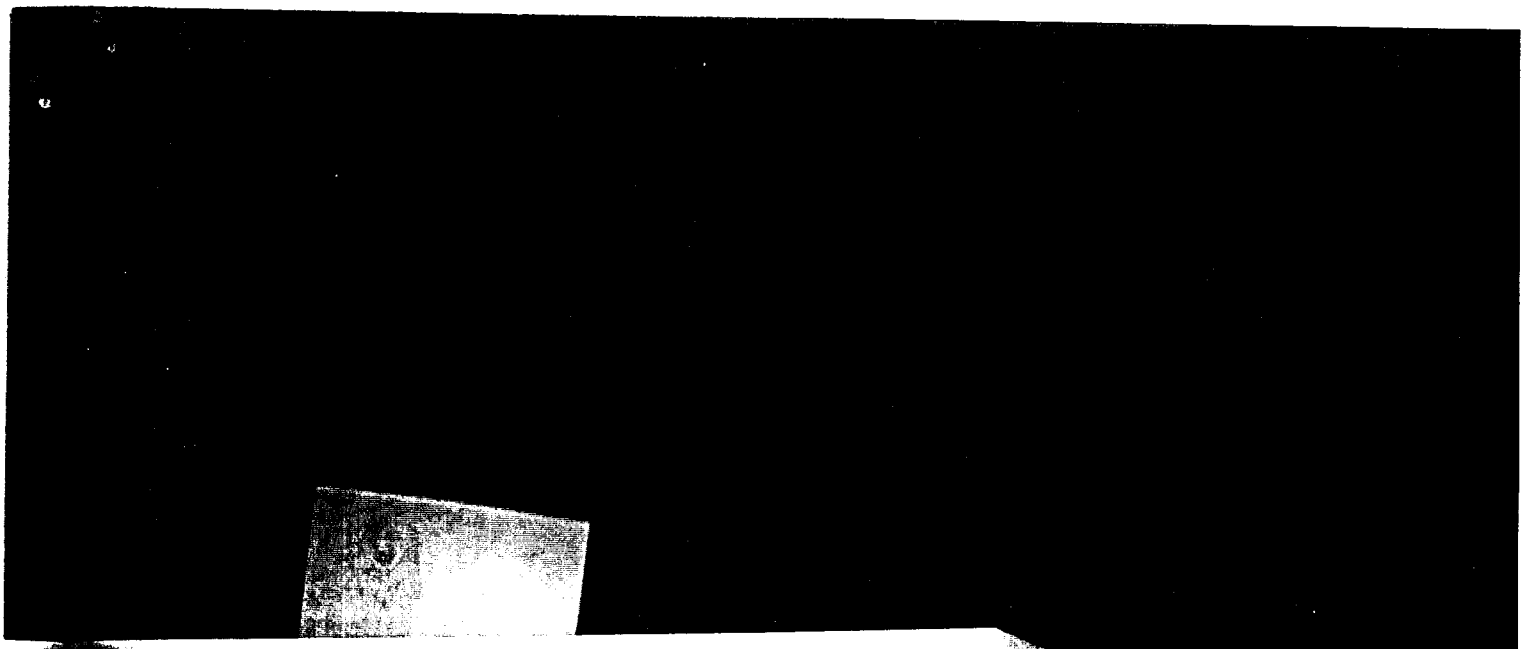
DIURETICS. Diuretics are overprescribed in old age and should **not** be used on a long-term basis to treat simple gravitational oedema which will usually respond to increased movement, raising the legs, and support stockings. A few days of diuretic treatment may speed the clearing of the oedema but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

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

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 is often inadequate, and toxicity is common in those given 250 micrograms).

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 one must always pose the question of 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. chlorpropamide) should be avoided altogether.

REVIEW REGULARLY. Review repeat prescriptions regularly. It may be possible to stop the drug (e.g. digoxin can often be withdrawn) or it may be necessary to reduce the dose to match diminishing renal function.

SIMPLIFY. Simplify regimens. Elderly patients can not normally cope with more than three different drugs and, ideally, these should not be given more than 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.

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 but sometimes a home help, neighbour, or a sheltered-housing warden.