verse effects, clozapine therapy should be introduced gradually, beginning with low doses and increasing according to response.

In the treatment of **schizophrenia**, including reducing the risk of suicidal behaviour, the usual oral dose is 12.5 mg once or twice on the first day followed by 25 mg once or twice on the second day. Thereafter the daily dosage may be increased gradually in steps of 25 to 50 mg to achieve a daily dose of up to 300 mg within 14 to 21 days (in the USA, up to 450 mg daily is permitted by the end of 2 weeks). Subsequent increases in steps of 50 to 100 mg may be made once or twice weekly; a daily dosage of 900 mg should not be exceeded. Once a therapeutic response has been obtained, a gradual reduction of dosage to a suitable maintenance dose is recommended; most patients respond to 200 to 450 mg daily. The total daily dose is given in divided doses; a larger portion may be given at night. Daily maintenance doses of 200 mg or less may be given as a single dose in the evening. If clozapine is to be withdrawn, this should be done gradually over a 1- to 2-week period. However, immediate withdrawal with careful observation is essential if neutropenia develops or if myocarditis or cardiomyopathy is suspected (see Precautions, above).

Elderly patients may require lower doses of clozapine and it is recommended that treatment should start with a dose of 12.5 mg on the first day and that subsequent dose increments should be restricted to 25 mg.

For patients who are restarting treatment after an interval of more than 2 days, 12.5 mg may be given once or twice on the first day. If this dose is well tolerated it may be possible to increase the dosage more quickly than when first starting. However, patients who have had respiratory or cardiac arrest with initial dosing, but were then successfully titrated to a therapeutic dose, should be re-titrated with extreme caution after a break of even 24 hours. Additional monitoring of blood cell counts may also be required if treatment is interrupted, see Treatment Break, under Monitoring, above.

It is recommended that oral therapy with other antipsychotics should be withdrawn gradually before treatment with clozapine is started.

Clozapine has also been given by intramuscular injection.

In the management of treatment-resistant **psychoses in Parkinson's disease**, the initial oral dose of clozapine is no more than 12.5 mg once daily in the evening. Thereafter, the daily dosage may be increased in increments of 12.5 mg up to twice a week; a dose of 50 mg daily should not be reached before the end of the second week. The usual dose ranges from 25 to 37.5 mg daily. Increases in the daily dose above 50 mg should only be made in exceptional cases in increments of 12.5 mg at weekly intervals up to a maximum of 100 mg daily. The total daily dose should preferably be given as a single dose in the evening. Dosage of antiparkinsonian drugs may be increased when there has been complete remission of psychotic symptoms after at least 2 weeks of clozapine therapy. If psychotic symptoms recur after increases in antiparkinsonian therapy, the dose of clozapine may need to be increased in line with the above guidance. As in patients with schizophrenia, planned withdrawal of clozapine in patients with Parkinson's disease should also be gradual in decrements of 12.5 mg over 1 to 2 weeks.

Action. Antipsychotics are thought to work through inhibition of dopamine D_2-receptors (see p.975), but this hypothesis fails to explain the activity of the atypical antipsychotics such as clozapine. How clozapine produces its antipsychotic activity is not clear; it has a high affinity for a number of different receptors.[1]

1. Kerwin RW. The new atypical antipsychotics: a lack of extrapyramidal side-effects and new routes in schizophrenia research. *Br J Psychiatry* 1994; **164:** 141–8.

Administration. There has been controversy over the bioequivalence or otherwise of different brands of clozapine. Although some reports indicate that it is perfectly possible to switch from branded to generic clozapine,[1-4] the need for monitoring and concerns about any requirement for retitration of doses (because of potential lack of bioequivalence[5]) have to be taken into account. There have been a few reports of exacerbation of psychotic symptoms in patients who were switched to a generic formulation.[6,7]

1. Sajbel TA, *et al.* Converting patients from brand-name clozapine to generic clozapine. *Ann Pharmacother* 2001; **35:** 281–4.
2. Makela EH, *et al.* Branded versus generic clozapine for treatment of schizophrenia. *Ann Pharmacother* 2003; **37:** 350–3.
3. Stoner SC, *et al.* A program to convert patients from trade-name to generic clozapine. *Pharmacotherapy* 2003; **23:** 806–10.
4. Bazire S, Burton V. Generic clozapine in schizophrenia: what is all the fuss about? *Pharm J* 2004; **273:** 720–1.
5. Lam YW, *et al.* Branded versus generic clozapine: bioavailability comparison and interchangeability issues. *J Clin Psychiatry* 2001; **62** (suppl 5): 18–22.
6. Kluznik JC, *et al.* Clinical effects of a randomized switch of patients from clozaril to generic clozapine. *J Clin Psychiatry* 2001; **62** (suppl 5): 14–17.
7. Mofsen R, Balter J. Case reports of the reemergence of psychotic symptoms after conversion from brand-name clozapine to a generic formulation. *Clin Ther* 2001; **23:** 1720–31.

Bipolar disorder. Clozapine is of benefit for the treatment of mania in patients with bipolar disorder (p.372), and the use of atypical antipsychotics in the management of such patients is increasing. However, the adverse effects of clozapine may restrict its use.

Dementia. Although atypical antipsychotics such as clozapine have been tried in elderly patients with dementia, the licensing authorities in the USA now recommend against such use, see under Precautions, above. For further discussion of the management of disturbed behaviour, see p.954.

Parkinsonism. Clozapine is used as an alternative to classical antipsychotics in the management of **treatment-resistant psychoses** in patients with Parkinson's disease (p.791). Some neurologists even consider clozapine to be the antipsychotic of choice in these patients,[1] although this remains to be determined. A review[2] in 1994 considered that there was little evidence to support clozapine as first choice given the quality of the available studies and the need for extensive monitoring. However a subsequent double-blind, placebo-controlled study[3] showed that low-dose clozapine treatment (up to 50 mg daily) significantly improved drug-induced psychosis without worsening parkinsonism. Adverse effects noted in this study were generally mild, although in the clozapine group of 30 patients, there was 1 report of leucopenia. A similar study also reported benefit,[4] although 7 of 32 patients noted some aggravation of parkinsonism, usually mild and transient, while receiving clozapine. Adverse effects reported from other individuals have also included a patient with parkinsonism who had worsening of psychotic symptoms when her dose of clozapine was increased,[5] and the sudden return of psychosis in another patient with parkinsonism whose psychosis was successfully treated with clozapine for 5 years.[6]

Low-dose clozapine (about 40 mg daily) also appears to be of benefit in the management of **levodopa-induced dyskinesias** in patients with severe Parkinson's disease.[7]

1. Klein C, *et al.* Clozapine in Parkinson's disease psychosis: 5-year follow-up review. *Clin Neuropharmacol* 2003; **26:** 8–11.
2. Pfeiffer C, Wagner ML. Clozapine therapy for Parkinson's disease and other movement disorders. *Am J Hosp Pharm* 1994; **51:** 3047–53.
3. The Parkinson Study Group. Low-dose clozapine for the treatment of drug-induced psychosis in Parkinson's disease. *N Engl J Med* 1999; **340:** 757–63.
4. The French Clozapine Parkinson Study Group. Clozapine in drug-induced psychosis in Parkinson's disease. *Lancet* 1999; **353:** 2041–2.
5. Auzou P, *et al.* Worsening of psychotic symptoms by clozapine in Parkinson's disease. *Lancet* 1994; **344:** 955.
6. Greene P. Clozapine therapeutic plunge in patient with Parkinson's disease. *Lancet* 1995; **345:** 1172–3.
7. Durif F, *et al.* Clozapine improves dyskinesias in Parkinson disease: a double-blind, placebo-controlled study. *Neurology* 2004; **62:** 381–8.

Schizophrenia. Clozapine is an effective antipsychotic for the management of schizophrenia (p.955) but its use is limited by its blood toxicity. Its effectiveness and superiority over classical antipsychotics was shown in a multicentre study.[1] Patients refractory to at least 3 different antipsychotics and who failed to improve after a single-blind trial of haloperidol, were randomised, double-blind, to treatment for 6 weeks with either clozapine up to 900 mg daily, or chlorpromazine hydrochloride up to 1800 mg daily with benzatropine mesilate up to 6 mg daily. Of the 267 patients included in the evaluation, 5 of 141 (4%) improved with chlorpromazine and benzatropine, and 38 of 126 (30%) improved with clozapine. Clozapine was superior to chlorpromazine in the treatment of negative as well as positive symptoms. Reviews[2,3] of clozapine indicate that these findings have been well replicated both in subsequent studies and in clinical practice. It is, however, unclear for how long clozapine should be tried: although 1 study[4] identified new responses up to 12 months after starting therapy, others have indicated that if improvement was not seen within the first 6 to 24 weeks, it was unlikely to occur.[2,5]

Clozapine is also used to reduce suicide risk in patients with refractory chronic schizophrenia.[6] The reported suicide rate of 0.05% per year in 6300 patients in the UK given clozapine since 1990 was considered to be tenfold less than expected.[7] A subsequent study[8] found it to be more effective than olanzapine in preventing suicide attempts in patients with schizophrenia or schizoaffective disorder at high risk.

Clozapine has shown consistent clinical benefit in schizophrenic patients with persistent aggressive or violent behaviour.[2,9] Whether this is due to a sedative effect, a specific antiaggressive action, or just reflects an overall improvement in psychosis is unknown.

Clozapine has been advocated for use in schizophrenic patients with moderate to severe tardive dyskinesia. It is still unclear whether clozapine can itself cause tardive dyskinesia but some patients with established tardive dyskinesia have experienced improvement in their symptoms when using clozapine.[10,11]

1. Kane J, *et al.* Clozapine for the treatment-resistant schizophrenic: a double-blind comparison with chlorpromazine. *Arch Gen Psychiatry* 1988; **45:** 789–96.
2. Buckley PF. New dimensions in the pharmacologic treatment of schizophrenia and related psychoses. *J Clin Pharmacol* 1997; **37:** 363–78. Correction. *ibid.* 1998; **38:** 27.
3. Wahlbeck K, *et al.* Clozapine versus typical neuroleptic medication for schizophrenia. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 1999 (accessed 24/05/05).
4. Meltzer HY, *et al.* A prospective study of clozapine in treatment-resistant schizophrenic patients I: preliminary report. *Psychopharmacology (Berl)* 1989; **99:** S68–S72.
5. Conley RR, *et al.* Time to clozapine response in a standardized trial. *Am J Psychiatry* 1997; **154:** 1243–7.
6. Meltzer HY, Okayli G. Reduction of suicidality during clozapine treatment of neuroleptic-resistant schizophrenia: impact on risk-benefit assessment. *Am J Psychiatry* 1995; **152:** 183–90.
7. Kerwin RW. Clozapine: back to the future for schizophrenia research. *Lancet* 1995; **345:** 1063–4.
8. Meltzer HY, *et al.* Clozapine treatment for suicidality in schizophrenia: International Suicide Prevention Trial (InterSePT). *Arch Gen Psychiatry* 2003; **60:** 82–91. Correction. *ibid.* 735.
9. Volavka J, *et al.* Overt aggression and psychotic symptoms in patients with schizophrenia treated with clozapine, olanzapine, risperidone, or haloperidol. *J Clin Psychopharmacol* 2004; **24:** 225–8.
10. Tamminga CA, *et al.* Clozapine in tardive dyskinesia: observations from human and animal model studies. *J Clin Psychiatry* 1994; **55** (suppl B): 102–6.
11. Nair C, *et al.* Dose-related effects of clozapine on tardive dyskinesia among "treatment-refractory" patients with schizophrenia. *Biol Psychiatry* 1996; **39:** 529–30.

Preparations

USP 31: Clozapine Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Lapenax; Sequax; ***Austral.:*** Clopine; Clozaril; ***Austria:*** Lanolept; Leponex; ***Belg.:*** Leponex; ***Braz.:*** Leponex; Zolapin†; ***Canad.:*** Clozaril; ***Chile:*** Leponex; ***Cz.:*** Leponex; ***Denm.:*** Leponex; ***Fin.:*** Froidir; Leponex; ***Fr.:*** Leponex; ***Ger.:*** Elcrit; Leponex; ***Gr.:*** Leponex; ***Hong Kong:*** Clozaril; ***Hung.:*** Leponex; ***India:*** Lozapin; Sizopin; ***Indon.:*** Clozaril; Sizoril; ***Irl.:*** Clozaril; ***Israel:*** Leponex; Lozapine; ***Ital.:*** Leponex; ***Malaysia:*** Clozaril; Zapine; ***Mex.:*** Clopsine; Leponex; ***Neth.:*** Leponex; ***Norw.:*** Leponex; ***NZ:*** Clopine; Clozaril; ***Philipp.:*** Leponex; ***Pol.:*** Klozapol; Leponex; ***Port.:*** Leponex; Ozapim; ***Rus.:*** Leponex (Лепонекс); ***S.Afr.:*** Cloment; Leponex; ***Singapore:*** Clozaril; ***Spain:*** Leponex; ***Swed.:*** Leponex; ***Switz.:*** Clopin; Leponex; ***Thai.:*** Cloril; Clozaril; ***Turk.:*** Leponex; ***UK:*** Clozaril; Denzapine; Zaponex; ***USA:*** Clozaril; FazaClo; Fazalco†; ***Venez.:*** Leponex.

Cyamemazine *(rINN)*

Ciamemazina; Cyamémazine; Cyamemazinum; Cyamepromazine; RP-7204. 10-(3-Dimethylamino-2-methylpropyl)phenothiazine-2-carbonitrile.

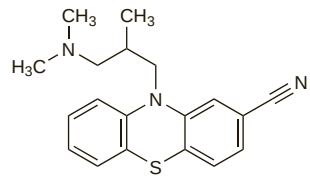
Циамемазин

$C_{19}H_{21}N_3S$ = 323.5.

CAS — 3546-03-0 (cyamemazine); 93841-82-8 (cyamemazine tartrate).

ATC — N05AA06.

ATC Vet — QN05AA06.



Profile

Cyamemazine is a phenothiazine with general properties similar to those of chlorpromazine (p.969). It is used in the management of a variety of psychiatric disorders including anxiety disorders (p.952) and aggressive behaviour (p.954).

Cyamemazine has been given orally as the base or the tartrate and by injection as the base. Doses are expressed in terms of the base; cyamemazine tartrate 36.6 mg is equivalent to about 25 mg of cyamemazine. Oral doses have ranged from 25 to 600 mg daily, depending on the individual and the condition being treated; the daily dosage is given in 2 or 3 divided doses. Doses given by intramuscular injection have ranged from 25 to 200 mg daily.

Cyamemazine should be given in reduced dosage to elderly patients; the parenteral route is not recommended for the elderly.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Tercian; ***Port.:*** Tercian.

Cyclobarbital *(BAN, rINN)*

Ciclobarbital; Cyclobarbitalum; Cyclobarbitone; Cyklobarbital; Ethylhexabital; Hexemalum; Syklobarbitaali. 5-(Cyclohex-1-enyl)-5-ethylbarbituric acid.

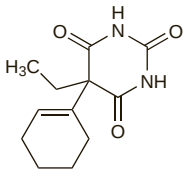
Циклобарбитал

$C_{12}H_{16}N_2O_3$ = 236.3.

CAS — 52-31-3.

ATC — N05CA10.

ATC Vet — QN05CA10.



NOTE. The name ciclobarbital has sometimes been applied to hexobarbital.

Cyclobarbital Calcium *(BANM, rINNM)*

Calcii Cyclobarbitalum; Ciclobarbital cálcico; Ciclobarbital Calcium; Cyclobarbital Calcique; Cyclobarbitalum Calcicum; Cyclobarbitone Calcium; Cyklobarbital wapniowy; Hexemalcalcium. Calcium 5-(cyclohex-1-enyl)-5-ethylbarbiturate.

Кальций Циклобарбитал

$(C_{12}H_{15}N_2O_3)_2Ca$ = 510.6.

CAS — 5897-20-1.

ATC — N05CA10.

ATC Vet — QN05CA10.

Pharmacopoeias. In *Pol.*

Profile

Cyclobarbital is a barbiturate with general properties similar to those of amobarbital (p.961). The calcium salt has been used as a hypnotic but barbiturates are no longer considered appropriate for such purposes.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: *Rus.:* Reladorm (Реладорм).

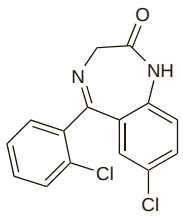
Delorazepam *(pINN)*

Chlordesmethyldiazepam; Clordesmethyldiazepam; Délorazépam; Delorazepamum. 7-Chloro-5-(2-chlorophenyl)-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one.

Делоразепам

$C_{15}H_{10}Cl_2N_2O$ = 305.2.

CAS — 2894-67-9.



Profile

Delorazepam is a long-acting benzodiazepine with general properties similar to those of diazepam (p.986). It has been used in the short-term treatment of anxiety disorders, insomnia, and epilepsy, and for premedication.

Administration in hepatic or renal impairment. The pharmacokinetics of total delorazepam were unchanged in patients with renal failure undergoing haemodialysis compared with controls.[1] However, the apparent volume of distribution of unbound drug was smaller and the clearance slower. The volume of distribution and clearance of unchanged drug was also reduced in patients with liver disease.[2]

1. Sennesael J, *et al.* Pharmacokinetics of intravenous and oral chlordesmethyldiazepam in patients on regular haemodialysis. *Eur J Clin Pharmacol* 1991; **41:** 65–8.
2. Bareggi SR, *et al.* Effects of liver disease on the pharmacokinetics of intravenous and oral chlordesmethyldiazepam. *Eur J Clin Pharmacol* 1995; **48:** 265–8.

Preparations

Proprietary Preparations (details are given in Part 3)

Ital.: Dadumir; En.

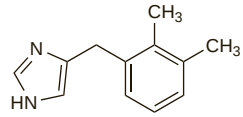
Detomidine Hydrochloride *(BANM, USAN, rINNM)*

Demotidini Hydrochloridum; Detomidiinihydrokloridi; Detomidin hydrochlorid; Détomidine, chlorhydrate de; Detomidin-hidroklorid; Detomidinhydroklorid; Detomidini hydrochloridum; Hidrocloruro de detomidina; MPV-253-All. 4-(2,3-Dimethylbenzyl)imidazole hydrochloride.

Детомидина Гидрохлорид

$C_{12}H_{14}N_2$,HCl = 222.7.

CAS — 76631-46-4 (detomidine); 90038-01-0 (detomidine hydrochloride).



(detomidine)

Pharmacopoeias. In *Eur.* (see p.vii) for veterinary use only.

Ph. Eur. 6.2 (Detomidine Hydrochloride for Veterinary Use; Detomide Hydrochloride BP(Vet) 2008). A white or almost white, hygroscopic, crystalline powder. Soluble in water; freely soluble in alcohol; practically insoluble in acetone; very slightly soluble in dichloromethane. Protect from moisture.

Profile

Detomidine is an α_2-adrenoceptor agonist with sedative, muscle relaxant, and analgesic properties. It is used as the hydrochloride in veterinary medicine.

Dexmedetomidine Hydrochloride

(BANM, USAN, rINNM)

Deksmedetomidin Hidroklorür; Dexmédétomidine, Chlorhydrate de; Dexmedetomidini Hydrochloridum; Hidrocloruro de dexmedetomidina; MPV-1440 (dexmedetomidine). (*S*)-4-[1-(2,3-Xylyl)ethyl]imidazole hydrochloride.

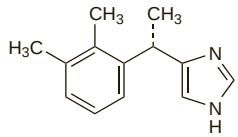
Дексмедетомидина Гидрохлорид

$C_{13}H_{16}N_2$,HCl = 236.7.

CAS — 113775-47-6 (dexmedetomidine); 145108-58-3 (dexmedetomidine hydrochloride).

ATC — N05CM18.

ATC Vet — QN05CM18.



(dexmedetomidine)

Adverse Effects and Precautions

The most frequently observed adverse effect with dexmedetomidine is hypotension. Other common adverse effects include hypertension, nausea and vomiting, bradycardia, tachycardia, fever, hypoxia, and anaemia. Patients should be continuously monitored during use. Dexmedetomidine should be used with caution in patients with advanced heart block, or hepatic or renal impairment, or in the elderly.

Interactions

The effects of other CNS depressants may be enhanced by dexmedetomidine. Dexmedetomidine may also increase the effects of other vasodilators or drugs such as cardiac glycosides, that have negative chronotropic effects.

Pharmacokinetics

Dexmedetomidine is about 94% protein bound, but this has been reported to be significantly decreased in patients with hepatic impairment. Dexmedetomidine is almost completely metabolised by direct glucuronidation or by cytochrome P450 isoenzymes. It is excreted mainly as metabolites in the urine and faeces. The terminal elimination half-life is about 2 hours.

◊ References.

1. Scheinin H, *et al.* Pharmacodynamics and pharmacokinetics of intramuscular dexmedetomidine. *Clin Pharmacol Ther* 1992; **52:** 537–46.
2. Kivistö KT, *et al.* Pharmacokinetics and pharmacodynamics of transdermal dexmedetomidine. *Eur J Clin Pharmacol* 1994; **46:** 345–9.
3. De Wolf AM, *et al.* The pharmacokinetics of dexmedetomidine in volunteers with severe renal impairment. *Anesth Analg* 2001; **93:** 1205–9.
4. Anttila M, *et al.* Bioavailability of dexmedetomidine after extravascular doses in healthy subjects. *Br J Clin Pharmacol* 2003; **56:** 691–3.

Uses and Administration

Dexmedetomidine is a selective alpha$_2$-adrenergic receptor agonist with anxiolytic, analgesic, and sedative properties. It is used for the sedation of mechanically ventilated patients in intensive care. Dexmedetomidine is given as the hydrochloride, but doses are expressed in terms of the base. Dexmedetomidine hydrochloride 118 micrograms is equivalent to about 100 micrograms of dexmedetomidine.

It is given in sodium chloride 0.9% by intravenous infusion in a loading dose equivalent to 1 microgram/kg of dexmedetomidine over 10 minutes, followed by a maintenance infusion of 0.2 to 0.7 micrograms/kg per hour for up to 24 hours. Reduced doses may be necessary in patients with hepatic or renal impairment, or in the elderly.

The racemate, medetomidine (p.1006), is used as the hydrochloride in veterinary medicine.

◊ References.

1. Venn RM, *et al.* Preliminary UK experience of dexmedetomidine, a novel agent for postoperative sedation in the intensive care unit. *Anaesthesia* 1999; **54:** 1136–42.
2. Bhana N, *et al.* Dexmedetomidine. *Drugs* 2000; **59:** 263–8.
3. Coursin DB, *et al.* Dexmedetomidine. *Curr Opin Crit Care* 2001; **7:** 221–6.
4. Bekker A, Sturaitis MK. Dexmedetomidine for neurological surgery. *Neurosurgery* 2005; **57** (suppl): 1–10.
5. Szumita PM, *et al.* Sedation and analgesia in the intensive care unit: evaluating the role of dexmedetomidine. *Am J Health-Syst Pharm* 2007; **64:** 37–44.
6. Gerlach AT, Dasta JF. Dexmedetomidine: an updated review. *Ann Pharmacother* 2007; **41:** 245–53. Correction. *ibid.*; 530–1.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Precedex; ***Austral.:*** Precedex; ***Braz.:*** Precedex; ***Cz.:*** Precedex; ***Hong Kong:*** Precedex; ***Israel:*** Precedex; ***Malaysia:*** Precedex; ***Mex.:*** Precedex; ***NZ:*** Precedex; ***Pol.:*** Precedex; ***Singapore:*** Precedex†; ***Thai.:*** Precedex; ***Turk.:*** Precedex; ***USA:*** Precedex; ***Venez.:*** Precedex†.

Diazepam *(BAN, USAN, rINN)*

Diatsepaami; Diazépam; Diazepám; Diazepamas; Diazepamum; LA-III; NSC-77518; Ro-5-2807; Wy-3467. 7-Chloro-1,3-dihydro-1-methyl-5-phenyl-2*H*-1,4-benzodiazepin-2-one.

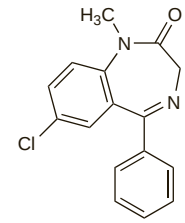
Диазепам

$C_{16}H_{13}ClN_2O$ = 284.7.

CAS — 439-14-5.

ATC — N05BA01.

ATC Vet — QN05BA01.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of diazepam:
Benzo; Blue; Blues; Drunk pills; La Roche; Ludes; Mother's little helper; Mother's little helpers; Pami; Roaches; Roachies; Roche; V; V's blues; Vallies; Vals.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.*

Ph. Eur. 6.2 (Diazepam). A white or almost white, crystalline powder. Very slightly soluble in water; soluble in alcohol. Protect from light.

USP 31 (Diazepam). An off-white to yellow, practically odourless, crystalline powder. Soluble 1 in 333 of water, 1 in 16 of alcohol, 1 in 2 of chloroform, and 1 in 39 of ether. Store in airtight containers. Protect from light.

Incompatibility. Incompatibility has been reported between diazepam and several other drugs. Manufacturers of diazepam injection (*Roche* and others) have advised against its admixture with other drugs.

Sorption. Substantial adsorption of diazepam onto some plastics may cause problems when giving the drug by continuous intravenous infusion. More than 50% of diazepam in solution may be adsorbed onto the walls of PVC infusion bags and their use should, therefore, be avoided. Giving sets should contain the minimum amount of PVC tubing and should not contain a cellulose propionate volume-control chamber. Suitable materials for infusion containers, syringes, and giving sets for diazepam include glass, polyolefin, polypropylene, and polyethylene.

References.

1. Cloyd JC, *et al.* Availability of diazepam from plastic containers. *Am J Hosp Pharm* 1980; **37:** 492–6.
2. Parker WA, MacCara ME. Compatibility of diazepam with intravenous fluid containers and administration sets. *Am J Hosp Pharm* 1980; **37:** 496–500.