relatively few published comparisons with other atypical antipsychotics, but one systematic review[8] concluded that there was little to differentiate between olanzapine and risperidone apart from their adverse effects; risperidone was particularly associated with movement disorders and sexual dysfunction while olanzapine induced rapid weight gain. Another study has suggested that olanzapine is not inferior to clozapine.[9] Olanzapine's efficacy in the treatment of patients with refractory schizophrenia remains to be determined; a small, randomised study found it to be no more effective than haloperidol.[10]

1. Beasley CM, *et al.* Olanzapine HGAD Study Group. Olanzapine versus placebo and haloperidol: acute phase results of the North American double-blind olanzapine trial. *Neuropsychopharmacology* 1996; **14:** 111–23.
2. Beasley C, *et al.* Olanzapine versus haloperidol: long-term results of the multi-center international trial. *Eur Neuropsychopharmacol* 1996; **6** (suppl 3): 59.
3. Beasley CM, *et al.* Olanzapine versus haloperidol: acute phase results of the international double-blind olanzapine trial. *Eur Neuropsychopharmacol* 1997; **7:** 125–37.
4. Tollefson GD, *et al.* Olanzapine versus haloperidol in the treatment of schizophrenia and schizoaffective and schizophreniform disorders: results of an international collaborative trial. *Am J Psychiatry* 1997; **154:** 457–65.
5. Bhana N, *et al.* Olanzapine: an updated review of its use in the management of schizophrenia. *Drugs* 2001; **61:** 111–61.
6. Duggan L, *et al.* Olanzapine for schizophrenia. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2005 (accessed 24/05/05).
7. Hamilton SH, *et al.* Olanzapine versus placebo and haloperidol: quality of life and efficacy results of the North American double-blind trial. *Neuropsychopharmacology* 1998; **18:** 41–9.
8. Jayaram MB, *et al.* Risperidone versus olanzapine for schizophrenia. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2006 (accessed 16/01/07).
9. Naber D, *et al.* Randomized double blind comparison of olanzapine vs clozapine on subjective well-being and clinical outcome in patients with schizophrenia. *Acta Psychiatr Scand* 2005; **111:** 106–15.
10. Buchanan RW, *et al.* Olanzapine treatment of residual positive and negative symptoms. *Am J Psychiatry* 2005; **162:** 124–9.

Stuttering. Although olanzapine may be of benefit in the treatment of stuttering (p.1001),[1,2] it has been associated with reports of stuttering in 6 adult patients with schizophrenia or depression.[3]

1. Lavid N, *et al.* Management of child and adolescent stuttering with olanzapine: three case reports. *Ann Clin Psychiatry* 1999; **11:** 233–6.
2. Maguire GA, *et al.* Olanzapine in the treatment of developmental stuttering: a double-blind, placebo-controlled trial. *Ann Clin Psychiatry* 2004; **16:** 63–7.
3. Bär KJ, *et al.* Olanzapine- and clozapine-induced stuttering: a case series. *Pharmacopsychiatry* 2004; **37:** 131–4.

Tourette's syndrome. When drug treatment is required for tics and behavioural disturbances in Tourette's syndrome (see Tics, p.954) haloperidol or pimozide are commonly used but atypical antipsychotics, including olanzapine, are increasingly being tried.[1-4]

1. Stamenkovic M, *et al.* Effective open-label treatment of tourette's disorder with olanzapine. *Int Clin Psychopharmacol* 2000; **15:** 23–8.
2. Onofrj M, *et al.* Olanzapine in severe Gilles de la Tourette syndrome: a 52-week double-blind cross-over study vs. low-dose pimozide. *J Neurol* 2000; **247:** 443–6.
3. Budman CL, *et al.* An open-label study of the treatment efficacy of olanzapine for Tourette's disorder. *J Clin Psychiatry* 2001; **62:** 290–4.
4. Stephens RJ, *et al.* Olanzapine in the treatment of aggression and tics in children with Tourette's syndrome: a pilot study. *J Child Adolesc Psychopharmacol* 2004; **14:** 255–66.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Midax; Zyprexa; ***Austral.:*** Zyprexa; ***Austria:*** Zyprexa; ***Belg.:*** Zyprexa; ***Braz.:*** Zyprexa; ***Canad.:*** Zyprexa; ***Chile:*** Olvin; Zyprexa; ***Cz.:*** Zalasta; Zyprexa; ***Denm.:*** Zyprexa; ***Fin.:*** Zyprexa; ***Fr.:*** Zyprexa; ***Ger.:*** Zyprexa; ***Gr.:*** Zyprexa; ***Hong Kong:*** Zyprexa; ***Hung.:*** Zyprexa; ***India:*** Joyzol; Olexar; Ozapin; Psycholanz; ***Indon.:*** Zyprexa; ***Irl.:*** Zyprexa; ***Israel:*** Zyprexa; ***Ital.:*** Zyprexa; ***Malaysia:*** Zyprexa; ***Mex.:*** Zyprexa; ***Neth.:*** Zyprexa; ***Norw.:*** Zyprexa; ***NZ:*** Zyprexa; ***Philipp.:*** Zyprexa; ***Pol.:*** Olzapin; Zalasta; Zolafren; Zyprexa; ***Port.:*** Olapin; Zalasta; Zolafren; Zyprexa; ***Rus.:*** Zyprexa (Зипрекса); ***S.Afr.:*** Zyprexa; ***Singapore:*** Zyprexa; ***Spain:*** Zyprexa; ***Swed.:*** Zyprexa; ***Switz.:*** Zyprexa; ***Thai.:*** Zyprexa; ***Turk.:*** Zyprexa; ***UK:*** Zyprexa; ***USA:*** Zyprexa; ***Venez.:*** Zyprexa.

Multi-ingredient: ***Arg.:*** Combined†; Symbyax†; ***Chile:*** Symbyax; ***Mex.:*** Symbyax; ***USA:*** Symbyax.

Oxazepam *(BAN, USAN, rINN)*

Oksatsepaami; Oksazeoam; Oksazepam; Oksazepamas; Oxazépam; Oxazepám; Oxazepamum; Wy-3498. 7-Chloro-1,3-dihydro-3-hydroxy-5-phenyl-1,4-benzodiazepin-2-one.

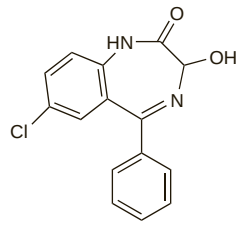
Оксазепам

$C_{15}H_{11}ClN_2O_2$ = 286.7.

CAS — 604-75-1.

ATC — N05BA04.

ATC Vet — QN05BA04.



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

Ph. Eur. 6.2 (Oxazepam). A white or almost white crystalline powder. Practically insoluble in water; slightly soluble in alcohol. Protect from light.

USP 31 (Oxazepam). A creamy-white to pale yellow, practically odourless powder. Practically insoluble in water; soluble 1 in 220 of alcohol, 1 in 270 of chloroform, and 1 in 2200 of ether. pH of a 2% suspension in water is between 4.8 and 7.0.

Dependence and Withdrawal

As for Diazepam, p.987.

◊ For the purpose of withdrawal regimens, 15 mg of oxazepam is considered equivalent to about 5 mg of diazepam.

Adverse Effects, Treatment, and Precautions

As for Diazepam, p.987.

Hepatic impairment. All benzodiazepines should be used with caution in patients with hepatic impairment, but short-acting ones such as oxazepam may be preferred.

Seven patients with acute viral hepatitis, 6 with cirrhosis of the liver, and 16 age-matched healthy control subjects took a single dose of oxazepam 15 or 45 mg orally.[1] Urinary excretion rates and plasma elimination patterns were unaltered in patients with acute and chronic parenchymal liver disease. Oxazepam 15 mg orally was also given three times daily for 2 weeks to 2 healthy subjects and to 2 patients with cirrhosis and did not appear to accumulate in any of the four.

1. Shull HJ, *et al.* Normal disposition of oxazepam in acute viral hepatitis and cirrhosis. *Ann Intern Med* 1976; **84:** 420–5.

Porphyria. Oxazepam is considered to be unsafe in patients with porphyria although there is conflicting experimental evidence of porphyrinogenicity.

Renal impairment. Pharmacokinetic studies suggest that, in general, the dosage of oxazepam does not need adjusting in patients with renal impairment.[1-3]

1. Murray TG, *et al.* Renal disease, age, and oxazepam kinetics. *Clin Pharmacol Ther* 1981; **30:** 805–9.
2. Busch U, *et al.* Pharmacokinetics of oxazepam following multiple administration in volunteers and patients with chronic renal disease. *Arzneimittelforschung* 1981; **31:** 1507–11.
3. Greenblatt DJ, *et al.* Multiple-dose kinetics and dialyzability of oxazepam in renal insufficiency. *Nephron* 1983; **34:** 234–8.

Thyroid disorders. There was a reduction in half-life and an increase in the apparent oral clearance of oxazepam in 7 hyperthyroid patients.[1] In 6 hypothyroid patients there was no overall change in oxazepam elimination, although 5 of the 6 complained of drowsiness despite a relatively low dose (15 mg).

1. Scott AK, *et al.* Oxazepam pharmacokinetics in thyroid disease. *Br J Clin Pharmacol* 1984; **17:** 49–53.

Interactions

As for Diazepam, p.989.

Pharmacokinetics

Oxazepam is well absorbed from the gastrointestinal tract and reaches peak plasma concentrations about 2 hours after ingestion. It crosses the placenta and has been detected in breast milk. Oxazepam is about 85 to 97% bound to plasma proteins and has been reported to have an elimination half-life ranging from about 3 to 21 hours. It is largely metabolised to the inactive glucuronide which is excreted in the urine.

Pregnancy. The placental passage of oxazepam and its metabolism in 12 women given a single dose of oxazepam 25 mg during labour has been studied.[1] Oxazepam was readily absorbed and peak plasma concentrations were in the same range as those reported in healthy males and non-pregnant females given the same dose, although the plasma half-life (range 5.3 to 7.8 hours in 8 subjects studied) was shorter than that reported for non-pregnant subjects. Oxazepam was detected in the umbilical vein of all 12 patients with the ratio between umbilical to maternal vein concentration of oxazepam reaching a value of about 1.35 and remaining constant beyond a dose-delivery time of 3 hours. All of the babies had a normal Apgar score value. The oxazepam plasma half-life in the newborns was about 3 to 4 times that of the mothers, although in 3 the plasma concentration of oxazepam conjugate rose during the first 6 to 10 hours after delivery indicating the ability of the neonate to conjugate oxazepam.

1. Tomson G, *et al.* Placental passage of oxazepam and its metabolism in mother and newborn. *Clin Pharmacol Ther* 1979; **25:** 74–81.

Uses and Administration

Oxazepam is a short-acting benzodiazepine with general properties similar to those of diazepam (p.992). It is used in the short-term management of anxiety disorders (p.952) and insomnia (p.957) associated with anxiety. Oxazepam is also used for the control of symptoms associated with alcohol withdrawal (p.1626). Oxazepam is usually given as the base but the hemisuccinate has been used in some multi-ingredient preparations.

The usual oral dose of oxazepam for the treatment of anxiety or for control of symptoms of alcohol withdrawal is 15 to 30 mg three or four times daily. A suggested initial dose for elderly or debilitated patients is 10 mg three times daily increased if necessary up to 10 to 20 mg three or four times daily. For the treatment of insomnia associated with anxiety oxazepam 15 to 25 mg may be given one hour before retiring; up to 50 mg may occasionally be necessary.

Administration in renal impairment. For a suggestion that dosage adjustment of oxazepam may not be necessary in patients with renal impairment, see Renal Impairment, above.

Preparations

BP 2008: Oxazepam Tablets;
USP 31: Oxazepam Capsules; Oxazepam Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Pausafren T; ***Austral.:*** Alepam; Murelax; Serepax; ***Austria:*** Adumbran; Anxiolit; Oxahexal; Praxiten; ***Belg.:*** Seresta; Tranquo; ***Chile:*** Serepax†; ***Denm.:*** Alopam; Oxabenz; Oxapax; Serepax; ***Fin.:*** Alopam†; Opamox; Oxamin; Oxepam†; ***Fr.:*** Seresta; ***Ger.:*** Adumbran; Azutranquil†; durazepam; Mirfudorm; Noctazepam†; Oxa; Praxiten; Sigacalm†; Uskan; ***India:*** Serepax; ***Israel:*** Vaben; ***Ital.:*** Limbial; Serpax; ***Neth.:*** Seresta; ***Norw.:*** Alopam; Sobril; ***NZ:*** Ox-Pam; ***Pol.:*** Oxam; ***Port.:*** Serenal; ***Rus.:*** Tazepam (Тазепам); ***S.Afr.:*** Medopam; Noripam; Purata; Serepax; ***Spain:*** Adumbran†; ***Swed.:*** Oxascand; Sobril; ***Switz.:*** Anxiolit; Seresta; ***USA:*** Serax; ***Venez.:*** Anastil†.

Multi-ingredient: ***Arg.:*** Cavodan†; Pankreoflat Sedante†; ***Austria:*** Anxiolit plus; ***Chile:*** Novalona; ***Port.:*** Sedioton†; ***Spain:*** Novo Aerofil Sedante†; Suxidina; ***Venez.:*** Vuscobras.

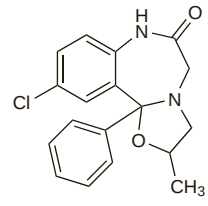
Oxazolam *(rINN)*

Oxazolamum; Oxazolazepam. 10-Chloro-2,3,7,11b-tetrahydro-2-methyl-11b-phenyloxazolo[3,2-*d*][1,4]benzodiazepin-6(5*H*)-one.

Оксазолам

$C_{18}H_{17}ClN_2O_2$ = 328.8.

CAS — 24143-17-7.



Pharmacopoeias. In *Jpn.*

Profile

Oxazolam is a long-acting benzodiazepine with general properties similar to those of diazepam (p.986). It has been given by mouth for the short-term treatment of anxiety disorders.

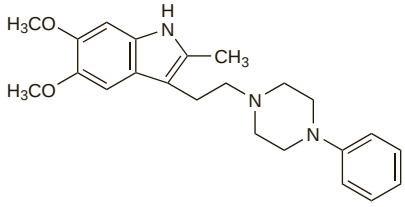
Oxazolam has also been used as a premedicant in general anaesthesia.

Oxypertine *(BAN, USAN, rINN)*

Oksipertiini; Oxipertin; Oxipertina; Oxypertinum; Win-18501-2. 5,6-Dimethoxy-2-methyl-3-[2-(4-phenylpiperazin-1-yl)ethyl]-indole.

Оксипертин

$C_{23}H_{29}N_3O_2$ = 379.5.
CAS — 153-87-7 (oxypertine); 40523-01-1 (oxypertine hydrochloride).
ATC — N05AE01.
ATC Vet — QN05AE01.



Profile

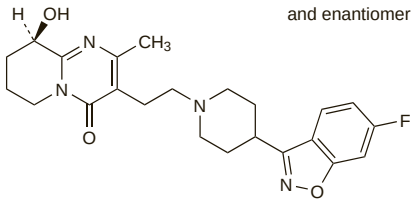
Oxypertine is an indole derivative with general properties similar to those of the phenothiazine, chlorpromazine (p.969). It has been given orally in the treatment of psychoses including schizophrenia, mania, and disturbed behaviour, and in severe anxiety.

Paliperidone *(USAN, rINN)*

9-Hydroxyrisperidone; Paliperidona; Palipéridone; Paliperidonum; RO-76477. (±)-3-{2-[4-(6-Fluoro-1,2-benzisoxazol-3-yl)piperidino]ethyl}-6,7,8,9-tetrahydro-9-hydroxy-2-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one.

Палиперидон

$C_{23}H_{27}FN_4O_3$ = 426.5.
CAS — 144598-75-4.
ATC — N05AX13.
ATC Vet — QN05AX13.



Paliperidone Palmitate *(USAN, rINNM)*

Palipéridone, Palmitate de; Paliperidoni Palmitas; Palmitato de paliperidona; RO-92670. (9*RS*)-3-{2-[4-(6-Fluoro-1,2-benzisoxazol-3-yl)piperidin-1-yl]ethyl}-2-methyl-4-oxo-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-9-yl hexadecanoate.

Палиперидона Палмитат

$C_{39}H_{57}FN_4O_4$ = 664.9.
CAS — 199739-10-1.

Profile

Paliperidone is a benzisoxazole derivative and is the major active metabolite of the atypical antipsychotic risperidone (p.1024). It is reported to be an antagonist at dopamine D_2, serotonin ($5\text{-}HT_2$), adrenergic (α_1 and α_2), and histamine (H_1) receptors. It is used in the treatment of schizophrenia.

The recommended oral dose of paliperidone is 6 mg once daily as a modified-release preparation; doses may range from 3 to 12 mg daily. US licensed product information recommends that dose increases are made in small steps of 3 mg at intervals of more than 5 days.

For details of dose reductions in patients with renal impairment, see below.

Paliperidone palmitate is being developed as a long-acting intramuscular formulation.

Administration in renal impairment. The plasma concentrations of paliperidone are increased in patients with renal impairment. The usual oral daily dosage (see above) should therefore be adjusted according to creatinine clearance (CC).

In the UK, licensed product information recommends the following doses:

- CC 50 to 80 mL/minute: initially 3 mg once daily, may be increased thereafter according to response and tolerance
- CC 30 to 50 mL/minute: 3 mg once daily
- CC 10 to 30 mL/minute: initially 3 mg on alternate days which may be increased thereafter to 3 mg once daily after clinical reassessment

However, US licensed product information recommends the following maximum doses:

- CC 50 to 80 mL/minute: 6 mg once daily
- CC 10 to 50 mL/minute: 3 mg once daily

Paliperidone has not been studied in patients with a CC of less than 10 mL/minute; UK product information does not recommend its use in such patients.

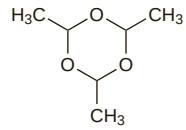
Preparations

Proprietary Preparations (details are given in Part 3)
Cz.: Invega; ***Fr.:*** Invega; ***Port.:*** Invega; ***UK:*** Invega; ***USA:*** Invega.

Paraldehyde

Paracetaldehyde; Paraldehid; Paraldehidas; Paraldehído; Paraldehit; Paraldehyd; Paraldéhyde; Paraldehydi; Paraldehydum. The trimer of acetaldehyde; 2,4,6-Trimethyl-1,3,5-trioxane.

$(C_2H_4O)_3$ = 132.2.
CAS — 123-63-7.
ATC — N05CC05.
ATC Vet — QN05CC05.



Pharmacopoeias. In *Eur.* (see p.vii) and *US.*

Ph. Eur. 6.2 (Paraldehyde). A colourless or slightly yellow, transparent liquid. It solidifies on cooling to form a crystalline mass. It may contain a suitable amount of an antoxidant. Relative density 0.991 to 0.996. F.p. is 10° to 13°; not more than 10% distils below 123° and not less than 95% below 126°. Soluble in water but less soluble in boiling water; miscible with alcohol and with volatile oils. Store in small well-filled airtight containers. Protect from light.

USP 31 (Paraldehyde). A colourless transparent liquid with a strong characteristic, but not unpleasant or pungent, odour. It is subject to oxidation to form acetic acid. It may contain a suitable stabiliser. Specific gravity is about 0.99. It has a congealing temperature of not lower than 11° and distils completely between 120° and 126°. Soluble 1 in 10 of water v/v, but only 1 in 17 of boiling water v/v; miscible with alcohol, with chloroform, with ether, and with volatile oils. Store in well-filled airtight containers of not more than 30 mL at a temperature not exceeding 25°. Protect from light. It must not be used more than 24 hours after opening the container.

Incompatibility. Paraldehyde exerts a solvent action upon rubber, polystyrene, and styrene-acrylonitrile copolymer and should not be given in plastic syringes made with these materials.

An evaluation of the compatibility of paraldehyde with plastic syringes and needle hubs concluded that, if possible, all-glass syringes should be used with paraldehyde.[1] Needles with plastic hubs could be used. Polypropylene syringes with rubber-tipped plastic plungers (*Plastipak*), or glass syringes with natural rubber-tipped plastic plungers (*Glaspak*) were acceptable only for the immediate administration or measurement of paraldehyde doses.

1. Johnson CE, Vigoreaux JA. Compatibility of paraldehyde with plastic syringes and needle hubs. *Am J Hosp Pharm* 1984; **41:** 306–8.

Stability. Paraldehyde decomposes on storage, particularly after the container has been opened. Partly decomposed paraldehyde is **dangerous** if given. It must not be used if it has a brownish colour or a sharp penetrating odour of acetic acid.

Dependence and Withdrawal

Prolonged use of paraldehyde may lead to dependence, especially in alcoholics. Features of dependence and withdrawal are similar to those of barbiturates (see Amobarbital, p.962).

Adverse Effects and Treatment

Paraldehyde decomposes on storage and deaths from corrosive poisoning have followed the use of such material. Paraldehyde has an unpleasant taste and imparts a smell to the breath; it may cause skin rashes.

Oral or rectal use of paraldehyde may cause gastric or rectal irritation. Intramuscular injection is painful and associated with tissue necrosis, sterile abscesses, and nerve damage. Intravenous use is extremely hazardous since it may cause pulmonary oedema and haemorrhage, hypotension and cardiac dilatation, and circulatory collapse; thrombophlebitis is also associated with intravenous use.

Overdosage results in rapid laboured breathing owing to damage to the lungs and to acidosis. Nausea and vomiting may follow an overdose by mouth. Respiratory depression and coma as well as hepatic and renal damage may occur. Treatment is as for barbiturate overdose (see Amobarbital, p.962).

Precautions

Paraldehyde should not be given to patients with gastric disorders and it should be used with caution, if at all, in patients with bronchopulmonary disease or hepatic impairment. It should not be given rectally in the presence of colitis. Old paraldehyde must never be used.

Paraldehyde must be well diluted before oral or rectal use; if it is deemed essential to give paraldehyde intravenously it must be well diluted and given very slowly with extreme caution (see also Adverse Effects, above and Uses, below). Intramuscular injections may be given undiluted but care should be taken to avoid nerve damage. Plastic syringes should be avoided (see Incompatibility, above).

Interactions

The sedative effects of paraldehyde are enhanced by CNS depressants such as alcohol, barbiturates, and other sedatives. A few case reports suggest that disulfiram may enhance the toxicity of paraldehyde; use together is not recommended.

Pharmacokinetics

Paraldehyde is generally absorbed readily, although absorption is reported to be slower after rectal than after oral or intramuscular doses. It is widely distributed and has a reported half-life of 4 to 10 hours. About 80% of a dose is metabolised in the liver probably to acetaldehyde, which is oxidised by aldehyde dehydrogenase to acetic acid. Unmetabolised drug is largely excreted unchanged through the lungs; only small amounts appear in the urine. It crosses the placental barrier and is distributed into breast milk.

Uses and Administration

Paraldehyde is a hypnotic and sedative with antiepileptic effects. However, because of the hazards associated with its use, its tendency to react with plastic, and the risks associated with its deterioration, it has largely been superseded by other drugs. It is still occasionally used to control status epilepticus (p.469) resistant to conventional treatment. Given rectally or intramuscularly it causes little respiratory depression and is therefore useful where facilities for resuscitation are poor.

At low temperature it solidifies to form a crystalline mass. If it solidifies, the whole should be liquefied before use.

A usual dose for adults is 10 to 20 mL given rectally as a 10% solution in sodium chloride 0.9% solution or diluted with 1 or 2 parts of oil. Doses of 5 to 10 mL are also occasionally given intramuscularly up to a maximum of 20 mL daily with not more than 5 mL being given at any one site. In the UK it is licensed for intramuscular use in children; however, the *BNFC* advocates use of the rectal route instead, diluted as above. Recommended single daily doses by either route are:

- up to 3 months, 0.5 mL (the *BNFC* suggests a single rectal dose of 0.4 mL/kg (maximum of 0.5 mL) in those under 1 month)
- 3 to 6 months, 1 mL
- 6 to 12 months, 1.5 mL
- 1 to 2 years, 2 mL
- 3 to 5 years, 3 to 4 mL
- 6 to 12 years, 5 to 6 mL

Paraldehyde has been given by slow intravenous infusion in specialist centres with intensive care facilities but this route is not usually recommended; it must be diluted in sodium chloride 0.9% before use.

Paraldehyde has been given orally; it should always be well diluted to avoid gastric irritation.

Preparations

BP 2008: Paraldehyde Injection.

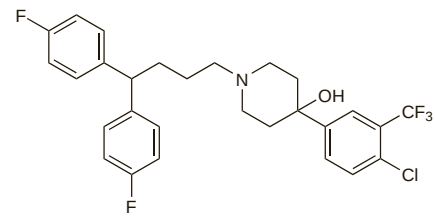
Proprietary Preparations (details are given in Part 3)
USA: Paral.

Penfluridol *(BAN, USAN, rINN)*

McN-JR-16341; Penfluridoli; Penfluridolum; R-16341. 4-(4-Chloro-3-trifluoromethylphenyl)-1-[3-(*p,p'*-difluorobenzhydryl)propyl]piperidin-4-ol.

Пенфлуридол

$C_{28}H_{27}ClF_5NO$ = 524.0.
CAS — 26864-56-2.
ATC — N05AG03.
ATC Vet — QN05AG03.



Pharmacopoeias. In *Chin.*

Profile

Penfluridol is a diphenylbutylpiperidine antipsychotic and shares the general properties of the phenothiazine, chlorpromazine (p.969). After oral doses it has a prolonged duration of action that