6. Timmer CJ, Sitsen JM. Pharmacokinetic evaluation of gepirone immediate-release capsules and gepirone extended-release tablets in healthy volunteers. *J Pharm Sci* 2003; **92:** 1773–8.
7. Amsterdam JD, *et al.* Sustained efficacy of gepirone-IR in major depressive disorder: a double-blind placebo substitution trial. *J Psychiatr Res* 2004; **38:** 259–65.
8. Alpert JE, *et al.* Gepirone extended-release treatment of anxious depression: evidence from a retrospective subgroup analysis in patients with major depressive disorder. *J Clin Psychiatry* 2004; **65:** 1069–75.
9. Keller MB, *et al.* Relapse prevention with gepirone ER in outpatients with major depression. *J Clin Psychopharmacol* 2005; **25:** 79–84.

Glutethimide *(BAN, rINN)*

Glutéthimide; Glutethimidum; Glutetimid; Glutetimida; Glutetimide; Glutetimidi. 2-Ethyl-2-phenylglutarimide; 3-Ethyl-3-phenylpiperidine-2,6-dione.

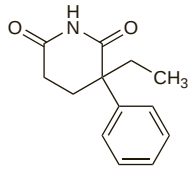
Глутетимид

$C_{13}H_{15}NO_2$ = 217.3.

CAS — 77-21-4.

ATC — N05CE01.

ATC Vet — QN05CE01.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of glutethimide: CIBAs; D; Doors; Goofers.

Profile

Glutethimide is a piperidinedione hypnotic and sedative with effects broadly similar to those of the barbiturates (see Amobarbital, p.961). It also has antimuscarinic properties. It has been given for the short-term management of insomnia but it has been superseded by other drugs.

Abuse. A warning of the hazards associated with the abuse of glutethimide in a combination with codeine termed 'loads'.[1]

1. Sramek JJ, Khajawall A. "Loads". *N Engl J Med* 1981; **305:** 231.

Porphyria. Glutethimide has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Hung.:*** Tardyl†.

Halazepam *(BAN, USAN, rINN)*

Halatsepaami; Halazépam; Halazepamum; Sch-12041. 7-Chloro-1,3-dihydro-5-phenyl-1-(2,2,2-trifluoroethyl)-1,4-benzodiazepin-2-one.

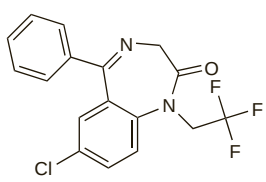
Галазепам

$C_{17}H_{12}ClF_3N_2O$ = 352.7.

CAS — 23092-17-3.

ATC — N05BA13.

ATC Vet — QN05BA13.



Profile

Halazepam is a benzodiazepine with general properties similar to those of diazepam (p.986). It has been given for the short-term treatment of anxiety disorders (p.952) in usual oral doses of 20 to 40 mg every 6 to 8 hours.

Preparations

Proprietary Preparations (details are given in Part 3)

Port.: Pacinone; ***Spain:*** Alapryl.

Haloperidol *(BAN, USAN, rINN)*

Aloperidolo; Halopéridol; Haloperidoli; Haloperidolis; Haloperidolum; McN-JR-1625; R-1625. 4-[4-(4-Chlorophenyl)-4-hydroxypiperidino]-4′-fluorobutyrophenone.

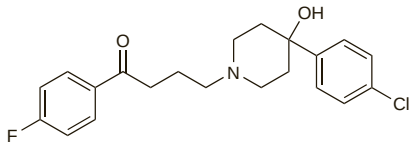
Галоперидол

$C_{21}H_{23}ClFNO_2$ = 375.9.

CAS — 52-86-8.

ATC — N05AD01.

ATC Vet — QN05AD01.



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

Ph. Eur. 6.2 (Haloperidol). A white or almost white powder. Practically insoluble in water; slightly soluble in alcohol, in dichloromethane, and in methyl alcohol. Protect from light.

USP 31 (Haloperidol). A white to faintly yellowish amorphous or microcrystalline powder. Practically insoluble in water; soluble 1 in 60 of alcohol, 1 in 15 of chloroform, and 1 in 200 of ether. A saturated solution is neutral to litmus. Store in airtight containers. Protect from light.

Dilution. See Incompatibility, below.

Incompatibility. A precipitate formed after dilution of haloperidol (as the lactate) in sodium chloride 0.9% injection when the final haloperidol concentration was 1 mg/mL or higher.[1]

Undiluted haloperidol (5 mg/mL) injection has been reported to be incompatible with heparin sodium (diluted in sodium chloride 0.9% or glucose 5% injection),[2] sodium nitroprusside (diluted in glucose 5%),[1] cefmetazole sodium,[3] and diphenhydramine.[4] A mixture of equal volumes of sargramostim 10 micrograms/mL and haloperidol (as the lactate) 200 micrograms/mL resulted in a precipitate at 4 hours.[5]

1. Outman WR, Monolakis J. Visual compatibility of haloperidol lactate with 0.9% sodium chloride injection or injectable critical-care drugs during simulated Y-site injection. *Am J Hosp Pharm* 1991; **48:** 1539–41.
2. Solomon DA, Nasinnyk KK. Compatibility of haloperidol lactate and heparin sodium. *Am J Hosp Pharm* 1982; **39:** 843–4.
3. Hutchings SR, *et al.* Compatibility of cefmetazole sodium with commonly used drugs during Y-site delivery. *Am J Health-Syst Pharm* 1996; **53:** 2185–8.
4. Ukhun IA. Compatibility of haloperidol and diphenhydramine in a hypodermic syringe. *Ann Pharmacother* 1995; **29:** 1168–9.
5. Trissel LA, *et al.* Visual compatibility of sargramostim with selected antineoplastic agents, anti-infectives, or other drugs during simulated Y-site injection. *Am J Hosp Pharm* 1992; **49:** 402–6.

Stability. A combination of the stabilisers benzyl alcohol and vanillin could protect haloperidol from photodegradation.[1]

1. Thoma K, Klimek R. Photostabilisation of drugs in dosage forms without protection from packaging materials. *Int J Pharmaceutics* 1991; **67:** 169–75.

Haloperidol Decanoate *(BANM, USAN, rINNM)*

Decanoato de haloperidol; Halopéridol, décanoate d'; Haloperidoldekanoat; Haloperidol-dekanoát; Haloperidoli decanoas; Haloperidolidekanoaatti; Haloperidolio dekanoatas; R-13672.

Галоперидола Деканоат

$C_{31}H_{41}ClFNO_3$ = 530.1.

CAS — 74050-97-8.

ATC — N05AD01.

ATC Vet — QN05AD01.

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

Ph. Eur. 6.2 (Haloperidol Decanoate). A white or almost white powder. It melts at about 42°. Practically insoluble in water; very soluble in alcohol, in dichloromethane, and in methyl alcohol. Store at a temperature below 25°. Protect from light.

Adverse Effects, Treatment, and Precautions

As for Chlorpromazine, p.969. Haloperidol is less likely to cause sedation, hypotension, or antimuscarinic effects, but is associated with a higher incidence of extrapyramidal effects. Haloperidol should be used with great care in children and adolescents as they may be at increased risk of severe dystonic reactions; patients with hyperthyroidism may also be at increased risk.

Breast feeding. The American Academy of Pediatrics[1] considers that the use of haloperidol by mothers during breast feeding may be of concern, since there have been reports of decline in developmental scores in breast-fed infants. Licensed product information also reports that there have been isolated cases of extrapyramidal effects in breast-fed infants.

The concentration of haloperidol in breast milk of one mother given a mean daily dose of about 30 mg for 6 days was reported to be 5 nanograms/mL; on day 12 the concentration 9 hours after a 12-mg dose was 2 nanograms/mL.[2]

1. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 28/04/04)
2. Stewart RB, *et al.* Haloperidol excretion in human milk. *Am J Psychiatry* 1980; **137:** 849–50.

Convulsions. For mention of haloperidol as one of the antipsychotics suitable for patients at risk of seizures, see p.969.

Effects on the liver. Liver dysfunction with jaundice and eosinophilia developed in a 15-year-old male 4 weeks after starting haloperidol and benzatropine mesilate.[1] The drugs were stopped 2 weeks later but some symptoms lasted for 28 months. The reaction was suggestive of a drug-induced hypersensitivity reaction and haloperidol was the most likely cause. Haloperidol-induced liver injury was considered to be rare.

1. Dincsoy HP, Saelinger DA. Haloperidol-induced chronic cholestatic liver disease. *Gastroenterology* 1982; **83:** 694–700.

Overdosage. Symptoms of haloperidol overdosage in children have ranged from the expected, such as drowsiness, restlessness, confusion, marked extrapyramidal symptoms, and hypothermia,[1,2] to unexpected reactions such as bradycardia (possibly secondary to hypothermia)[1] and an episode of severe, delayed hypertension.[3]

Torsade de pointes has followed overdosage in adults (for references, see Effects on the Cardiovascular System under Chlorpromazine, p.970).

1. Scialli JVK, Thornton WE. Toxic reactions from a haloperidol overdose in two children: thermal and cardiac manifestations. *JAMA* 1978; **239:** 48–9.
2. Sinaniotis CA, *et al.* Acute haloperidol poisoning in children. *J Pediatr* 1978; **93:** 1038–9.
3. Cummingham DG, Challapalli M. Hypertension in acute haloperidol poisoning. *J Pediatr* 1979; **95:** 489–90.

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

Retroperitoneal fibrosis. Obstructive uropathy was noted in a 45-year-old woman given haloperidol 5 to 15 mg daily for 8 years.[1] Benzatropine was also taken during that time, and in the previous 5 years she had taken chlorpromazine and fluphenazine. A diagnosis of retroperitoneal fibrosis was made and was tentatively associated with long-term antipsychotic therapy.

1. Jeffries JJ, *et al.* Retroperitoneal fibrosis and haloperidol. *Am J Psychiatry* 1982; **139:** 1524–5.

Toxic encephalopathy. A report[1] of possible toxic encephalopathy after use of high intravenous doses of haloperidol. The patient, who had a history of bipolar disorder and cerebrovascular accident, had been given increasing intravenous doses of haloperidol (up to 270 mg daily) to control post-surgical agitation. The encephalopathy had resolved 8 days after stopping haloperidol.

1. Maxa JL, *et al.* Possible toxic encephalopathy following high-dose intravenous haloperidol. *Ann Pharmacother* 1997; **31:** 736–7.

Interactions

As for Chlorpromazine, p.973.

Haloperidol must be used with extreme caution in patients receiving lithium; an encephalopathic syndrome has been reported after their use together (see p.405).

Pharmacokinetics

Haloperidol is readily absorbed from the gastrointestinal tract. It is metabolised in the liver and is excreted in the urine and, via the bile, in the faeces; there is evidence of enterohepatic recycling. Owing to first-pass metabolism in the liver, plasma concentrations after oral doses are lower than those after intramuscular injection. Moreover, there is wide intersubject variation in plasma concentrations of haloperidol. In practice, however, no strong correlation has been found between plasma concentrations of haloperidol and its therapeutic effect. Paths of metabolism of haloperidol include oxidative *N*-dealkylation and reduction of the ketone group to form an alcohol known as reduced haloperidol. Haloperidol has been reported to have a plasma elimination half-life ranging from about 12 to 38 hours after oral doses. Haloperidol is about 92% bound to plasma proteins. It is widely distributed in the body and crosses the blood-brain barrier. Haloperidol is distributed into breast milk.

The decanoate ester of haloperidol is very slowly absorbed from the site of injection and is therefore suitable for depot injection. It is gradually released into the bloodstream where it is rapidly hydrolysed to haloperidol.

◊ References.

1. Kudo S, Ishizaki T. Pharmacokinetics of haloperidol: an update. *Clin Pharmacokinet* 1999 **37:** 435–56.

Metabolites. The clinical significance of the reduced metabolite of haloperidol has been much debated.[1,2] Its activity appears to be substantially less than that of the parent drug but there is some evidence for re-oxidation of reduced haloperidol to haloperidol.[1-3] Some studies suggest that nonresponders to haloperidol have elevated ratios of reduced haloperidol to haloperidol in the plasma, although other workers have reported contrary findings.[2] Pyridinium metabolites resulting from oxidation of haloperidol have been detected in the urine and there is concern that they may be neurotoxic in a manner similar to MPTP (see Parkinsonism, p.791), a compound which can induce irreversible parkinsonism.[4]

1. Sramek JJ, *et al.* Neuroleptic plasma concentrations and clinical response: in search of a therapeutic window. *Drug Intell Clin Pharm* 1988; **22:** 373–80.
2. Froemming JS, *et al.* Pharmacokinetics of haloperidol. *Clin Pharmacokinet* 1989; **17:** 396–423.
3. Chakraborty BS, *et al.* Interconversion between haloperidol and reduced haloperidol in healthy volunteers. *Eur J Clin Pharmacol* 1989; **37:** 45–8.
4. Eyles DW, *et al.* Quantitative analysis of two pyridinium metabolites of haloperidol in patients with schizophrenia. *Clin Pharmacol Ther* 1994; **56:** 512–20.

Therapeutic drug monitoring. Measurement of concentrations of haloperidol or reduced haloperidol in scalp hair has been suggested as a useful means of monitoring compliance.[1,2] Evidence for the existence of any relationship between plasma concentrations of haloperidol and therapeutic effect in schizophrenia has been discussed.[3]

1. Uematsu T, *et al.* Human scalp hair as evidence of individual dosage history of haloperidol: method and retrospective study. *Eur J Clin Pharmacol* 1989; **37:** 239–44.
2. Matsuno H, *et al.* The measurement of haloperidol and reduced haloperidol in hair as an index of dosage history. *Br J Clin Pharmacol* 1990; **29:** 187–94.
3. Ulrich S, *et al.* The relationship between serum concentration and therapeutic effect of haloperidol in patients with acute schizophrenia. *Clin Pharmacokinet* 1998; **34:** 227–63.

Uses and Administration

Haloperidol is a butyrophenone with general properties similar to those of the phenothiazine, chlorpromazine (p.975). It is an antipsychotic with actions most closely resembling those of phenothiazines with a piperazine side-chain.

Haloperidol is used in the treatment of various psychoses including schizophrenia (p.955) and mania (see Bipolar Disorder, p.372), and in behaviour disturbances (p.954), in Tourette's syndrome and severe tics (p.954), in intractable hiccups (p.976), and in severe anxiety (p.952), including for the sedation of patients in intensive care (p.957) or palliative care. Haloperidol has also been used for its antiemetic effect in the management of nausea and vomiting of various causes (p.1700).

Haloperidol is usually given orally or by injection as the base or intramuscularly as the long-acting decanoate ester. Some haloperidol preparations are prepared with the aid of lactic acid and may be stated to contain haloperidol lactate. Doses are expressed in terms of the equivalent amount of haloperidol. Haloperidol decanoate 141 mg is equivalent to about 100 mg of haloperidol. Dosages should be reduced in elderly or debilitated patients; a usual starting dose is half the normal adult dose. Doses at the lower end of the scale are also advised for adolescents.

The usual initial *oral* dose for the treatment of **psychoses** and associated behavioural disorders is 0.5 to 5 mg two or three times daily. In severe or resistant psychoses up to 30 mg daily is recommended in the UK, whereas in the USA doses of up to 100 mg daily are allowed; doses above 100 mg daily have rarely been used. The dose should be reduced gradually according to response. Maintenance doses as low as 3 to 10 mg daily may be sufficient. A suitable initial oral dose for children is 25 to 50 micrograms/kg daily in 2 divided doses, increased cautiously, if necessary. A maximum daily dose of 10 mg has been recommended in the UK but in the USA the suggested maximum daily dose is 150 micrograms/kg as the manufacturer has stated that there is little evidence of behaviour improvement with daily doses of more than 6 mg.

For the control of acute psychotic conditions, haloperidol may be given *intramuscularly* in doses of 2 to 10 mg; subsequent doses may be given hourly, until symptoms are controlled, although dosage intervals of 4 to 8 hours may be adequate, up to a maximum of 18 mg daily. For the emergency control of very severely disturbed patients, an initial intramuscular dose of no more than 18 mg is recommended. The *intravenous* route may also be used.

In patients already stabilised on an oral dose of haloperidol and requiring long-term therapy the long-acting decanoate ester may be given by *deep intramuscular* injection. The usual initial dose is the equivalent of 10 to 20 times the total daily oral dose of haloperidol, up to a maximum of 100 mg; if more than 100 mg is required for an initial dose the excess should be given after 3 to 7 days. Subsequent doses, usually given every 4 weeks, may be increased in steps of 50 mg to up to 300 mg or more, according to the patient's requirements, both dose and dose interval being adjusted as required.

In the management of **nausea and vomiting** haloperidol has been given in a dose of 0.5 to 2 mg by *intramuscular* injection; alternatively, an *oral* dose of 1 mg daily may be given. In palliative care haloperidol 1.5 mg may be given orally once or twice daily, increased if necessary to 5 to 10 mg daily given in divided doses; alternatively, it may be given by *subcutaneous* infusion (via a syringe driver) in doses of 2.5 to 10 mg over 24 hours. The *intravenous* route has also been used.

A starting *oral* dose of 0.5 to 1.5 mg three times daily has been suggested for the management of **Tourette's syndrome** and severe **tics**. Up to about 30 mg daily may be needed in Tourette's syndrome, although requirements vary considerably and the dose must be very carefully adjusted to obtain the optimum response; a maintenance dose of 4 mg daily is effective for most patients.

For intractable **hiccups** a suggested *oral* dose is 1.5 mg given 3 times daily adjusted according to response.

An *oral* dose of 500 micrograms twice daily has been used as adjunctive treatment in the short-term management of severe **anxiety disorders**.

In palliative care, haloperidol has been given in an *oral* dose of 1 to 3 mg every 8 hours for the treatment of **restlessness and confusion**. It may also be given as a *subcutaneous* infusion in a dose of 5 to 15 mg over 24 hours.

Ballism. Dopamine-blocking antipsychotics such as haloperidol may sometimes be needed for the management of patients with ballism (p.953) when symptoms are severe.

Chorea. For a discussion of the management of various choreas, including mention of the use of haloperidol, see p.953.

Dystonia. Antipsychotics such as phenothiazines, haloperidol, or pimozide are sometimes useful in the treatment of idiopathic dystonia (p.809) in patients who have failed to respond to other drugs. However, they often act non-specifically and there is the risk of adding drug-induced extrapyramidal disorders to the dystonia being treated (see Extrapyramidal Disorders under Adverse Effects of Chlorpromazine, p.971).

Schizophrenia. Systematic reviews[1,2] of the use of haloperidol for schizophrenia (p.955) concluded that it appears to be of similar efficacy to chlorpromazine although it is associated with a high incidence of extrapyramidal adverse effects. An earlier systematic review[3] considered that the limited evidence did not indicate any advantages of giving haloperidol in doses greater than 7.5 mg daily to patients with uncomplicated acute schizophrenia.

1. Joy CB, *et al.* Haloperidol versus placebo for schizophrenia. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2006 (accessed 19/03/08).
2. Leucht C, *et al.* Haloperidol versus chlorpromazine for schizophrenia. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2008 (accessed 19/03/08).
3. Waraich PS, *et al.* Haloperidol dose for the acute phase of schizophrenia. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2002 (accessed 19/03/08).

Sneezing. Report[1] of a patient whose intractable sneezing was controlled by haloperidol given in doses of up to 5 mg twice daily. Symptoms recurred when treatment was stopped after 5 weeks but responded again to 5 mg three times daily. On gradual reduction of dosage over 6 months the patient had no recurrence and had remained symptom-free after 6 months without medication.

1. Davison K. Pharmacological treatment for intractable sneezing. *BMJ* 1982; **284:** 1163–4.

Stuttering. Stuttering (stammering) is a disorder that affects the fluency of speech. Developmental stuttering usually occurs in early childhood and is more common in boys than girls. While stuttering may cease in some children after only a few months, it may become a chronic condition in others. Stuttering that starts during adulthood is rarer and may be the result of a neurological insult. It should also be remembered that stuttering may be drug induced. While stuttering may be greatly improved with intensive speech training the effectiveness of other forms of management such as hypnosis, psychotherapy, counselling, and drug therapy has been largely unconvincing.[1] Although many drugs have been used to treat stuttering a review of the literature[2] indicated that there were few adequate studies of their efficacy. Haloperidol was considered to be the most well studied drug and its efficacy had been shown by several double-blind placebo-controlled studies. However, most patients needed to continue taking haloperidol to maintain improvement but few did so because of its adverse effects. Double-blind studies have on the whole failed to confirm reports of benefit for drugs such as bethanechol, beta blockers, and calcium-channel blockers although isolated patients may have marked improvement. Other drugs that have been studied and which might be of benefit include clomipramine,[3] SSRIs,[4] and atypical antipsychotics[4] such as olanzapine and risperidone; local anaesthetics and injections of botulinum toxin have also been tried.

1. Andrews G, *et al.* Stuttering. *JAMA* 1988; **260:** 1445.
2. Brady JP, *et al.* The pharmacology of stuttering: a critical review. *Am J Psychiatry* 1991; **148:** 1309–16.
3. Gordon CT, *et al.* A double-blind comparison of clomipramine and desipramine in the treatment of developmental stuttering. *J Clin Psychiatry* 1995; **56:** 238–42.
4. Costa D, Kroll R. Stuttering: an update for physicians. *Can Med Assoc J* 2000; **162:** 1849–55.

Taste disorders. For reference to the use of haloperidol in the treatment of taste disorders, see Chlorpromazine, p.977.

Tourette's syndrome. Many patients with Tourette's syndrome (p.954) do not require medication but when treatment is needed dopamine antagonists such as the antipsychotics haloperidol or pimozide are most commonly used. They often decrease the frequency and severity of tics and may improve any accompanying behavioural disturbances. However, superiority of either drug in terms of efficacy or adverse effects has not been clearly demonstrated.[1,2] Because of the potential for acute and long-term adverse effects it is usually recommended that doses are titrated to be as low as possible; the aim of treatment is not necessarily to control symptoms completely. Medication can often be stopped after a few years.

1. Shapiro E, *et al.* Controlled study of haloperidol, pimozide, and placebo for the treatment of Gilles de la Tourette's syndrome. *Arch Gen Psychiatry* 1989; **46:** 722–30.
2. Sallee FR, *et al.* Relative efficacy of haloperidol and pimozide in children and adolescents with Tourette's disorder. *Am J Psychiatry* 1997; **154:** 1057–62.

Preparations

BP 2008: Haloperidol Capsules; Haloperidol Injection; Haloperidol Oral Solution; Haloperidol Tablets; Strong Haloperidol Oral Solution;
USP 31: Haloperidol Injection; Haloperidol Oral Solution; Haloperidol Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Enabran; Halopidol; Halozen; Limerix; Neupram; Zetorital†; ***Austral.:*** Haldol; Serenace; ***Austria:*** Haldol; ***Belg.:*** Haldol; ***Braz.:*** Decan Haloper; Haldol; Halo; Haloper; Loperidol; Uni Haloper; ***Canad.:*** Haldol†; Novo-Peridol; Peridol†; ***Chile:*** Alternus; Haldol; ***Denm.:*** Serenase; ***Fin.:*** Serenase; ***Fr.:*** Haldol; ***Ger.:*** Haldol; Haloneural†; Haloper; Sigaperidol†; ***Gr.:*** Aloperidin; Sevium; ***Hong Kong:*** Haldol; Serenace; ***India:*** Cizoren†; Serenace; ***Indon.:*** Dores; Govotil; Haldol; Lodomer; Serenace; ***Irl.:*** Haldol; Serenace; ***Israel:*** Haldol; Haloper; Pericate; Peridor; ***Ital.:*** Haldol; Serenase; ***Malaysia:*** Avant†; Manace; Serenace†; ***Mex.:*** Haldol; Haloperil; Hispadol; Kepsidol; Pulsit; ***Neth.:*** Haldol; ***Norw.:*** Haldol; ***NZ:*** Haldol; Serenace; ***Philipp.:*** Haldol; Seredol; Serenace; ***Pol.:*** Decaldol; ***Port.:*** Haldol; Serenelfi†; ***Rus.:*** Haloper (Галопр)†; Senorm (Сенорм); ***S.Afr.:*** Serenace; ***Singapore:*** Serenace†; ***Swed.:*** Haldol; ***Switz.:*** Haldol; Sigaperidol†; ***Thai.:*** H-Tab; Haldol; Halo-P†; Halomed; Halopol; Haricon; Haridol; Perida; Polyhadon; Schizopol†; Tensidol†; ***Turk.:*** Norodol; Sedaperidol; ***UK:*** Dozic; Haldol; Serenace; ***USA:*** Haldol; ***Venez.:*** Haldol; Tiplac.

Multi-ingredient: ***Fr.:*** Vesadol†.

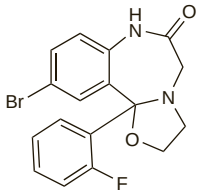
Haloxazolam *(rINN)*

Haloxazolamum. 10-Bromo-11b-(2-fluorophenyl)-2,3,7,11b-tetrahydrooxazolo[3,2-*d*][1,4]benzodiazepin-6(5*H*)-one.

Галоксазолам

$C_{17}H_{14}BrFN_2O_2$ = 377.2.

CAS — 59128-97-1.



Pharmacopoeias. In *Jpn.*

Profile

Haloxazolam is a benzodiazepine with general properties similar to those of diazepam (p.986). It has been given orally as a hypnotic in the short-term management of insomnia.

Hexobarbital *(BAN, rINN)*

Enhexymalum; Enimal; Heksobarbitaali; Heksobarbitalis; Hexobarbitál; Hexobarbitalum; Hexobarbitone; Methexenyl; Methylcyclohexenylmethyl-barbitursäure; Methylhexabarbital. 5-(Cyclohex-1-enyl)-1,5-dimethylbarbituric acid.

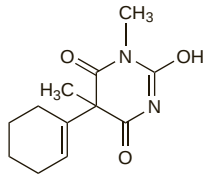
Гексобарбитал

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

CAS — 56-29-1.

ATC — N01AF02; N05CA16.

ATC Vet — QN01AF02; QN05CA16.



NOTE. The name ciclobarbital (see Cyclobarbital, p.986) has sometimes been applied to hexobarbital.

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

Ph. Eur. 6.2 (Hexobarbital). A white or almost white, crystalline powder. Very slightly soluble in water; sparingly soluble in alcohol. Forms water-soluble compounds with alkali hydroxides and carbonates and with ammonia.

Hexobarbital Sodium *(BANM, rINNM)*

Enhexymalnatrium; Hexenalum; Hexobarbital sódico; Hexobarbital Sodique; Hexobarbitalum Natricum; Hexobarbitone Sodium; Natrii Hexobarbitalum; Sodium Hexobarbital; Soluble Hexobarbitone. Sodium 5-(cyclohex-1-enyl)-1,5-dimethylbarbiturate.

Натрий Гексобарбитал

$C_{12}H_{15}N_2NaO_3$ = 258.2.

CAS — 50-09-9.

ATC — N01AF02; N05CA16.

ATC Vet — QN01AF02; QN05CA16.

Profile

Hexobarbital is a barbiturate with the general properties of amobarbital (p.961). It has been used as a hypnotic and sedative but barbiturates are no longer considered appropriate for such purposes.

Preparations

Proprietary Preparations (details are given in Part 3)
Hung.: Novopan†.

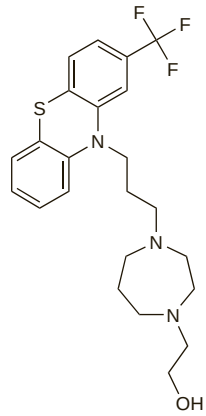
Homofenazine Hydrochloride *(rINNM)*

D-775 (homofenazine); HFZ (homofenazine); Hidrocloruro de homofenazina; Homoféназine, Chlorhydrate d'; Homofenazini Hydrochloridum. 2-{Hexahydro-4-[3-(2-trifluoromethylphenothiazin-10-yl)propyl]-1,4-diazepin-1-yl}ethanol dihydrochloride.

Гомофеназина Гидрохлорид

$C_{23}H_{28}F_3N_3OS,2HCl$ = 524.5.

CAS — 3833-99-6 (homofenazine); 1256-01-5 (homofenazine hydrochloride).



(homofenazine)

Profile

Homofenazine hydrochloride is a phenothiazine with general properties similar to those of chlorpromazine (p.969). It has been used in the management of neuropsychiatric disorders.

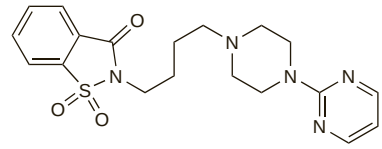
Ipsapirone Hydrochloride *(BANM, USAN, rINNM)*

Bay-q-7821; Hidrocloruro de ipsapirona; Ipsapirone, Chlorhydrate d'; Ipsapironi Hydrochloridum; TVX-Q-7821. 2-[4-(4-Pyrimidin-2-ylpiperazin-1-yl)butyl]-1,2-benzothiazol-3(2*H*)-one 1,1-dioxide hydrochloride.

Ипсапирона Гидрохлорид

$C_{19}H_{23}N_5O_3S,HCl$ = 437.9.

CAS — 95847-70-4 (ipsapirone); 92589-98-5 (ipsapirone hydrochloride).



(ipsapirone)

Profile

Ipsapirone is structurally related to buspirone (p.965). It has been investigated as the hydrochloride for the treatment of anxiety disorders and depression.

Action. Ipsapirone is a partial agonist at serotonin (hydroxytryptamine, 5-HT) receptors of the 5-HT_{1A} subtype. For reference to the actions and potential uses of such drugs, see Buspirone, p.966.

References.

1. Cutler NR, *et al.* A double-blind, placebo-controlled study comparing the efficacy and safety of ipsapirone versus lorazepam in patients with generalized anxiety disorder: a prospective multicenter trial. *J Clin Psychopharmacol* 1993; **13:** 429–37.
2. Fuhr U, *et al.* Absorption of ipsapirone along the human gastrointestinal tract. *Br J Clin Pharmacol* 1994; **38:** 83–6.
3. Mandos LA, *et al.* Placebo-controlled comparison of the clinical effects of rapid discontinuation of ipsapirone and lorazepam after 8 weeks of treatment for generalized anxiety disorder. *Int Clin Psychopharmacol* 1995; **10:** 251–6.
4. Lapierre YD, *et al.* A Canadian multicenter study of three fixed doses of controlled-release ipsapirone in outpatients with moderate to severe major depression. *J Clin Psychopharmacol* 1998; **18:** 268–73.

Ketazolam *(BAN, USAN, rINN)*

Ketatsolaami; Kétazolam; Ketazolamum; U-28774. 11-Chloro-8,12b-dihydro-2,8-dimethyl-12b-phenyl-4*H*-[1,3]oxazino[3,2-*d*][1,4]benzodiazepine-4,7(6*H*)-dione.

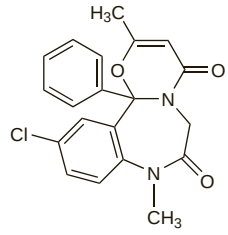
Кетазолам

$C_{20}H_{17}ClN_2O_3$ = 368.8.

CAS — 27223-35-4.

ATC — N05BA10.

ATC Vet — QN05BA10.



Profile

Ketazolam is a long-acting benzodiazepine with general properties similar to those of diazepam (p.986). It is given in the short-term treatment of anxiety (p.952) in usual oral doses of 15 to 60 mg daily, either in divided doses or as a single dose at night. Reduced doses may be required in elderly or debilitated patients.

◊ References.

1. Angelini G, *et al.* Ketazolam, a new long-acting benzodiazepine, in the treatment of anxious patients: a multicenter study of 2,056 patients. *Curr Ther Res* 1989; **45:** 294–304.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Ansieten; ***Belg.:*** Solatran†; ***Chile:*** Ansietil; Sedatival; ***Ital.:*** Anseren; ***Port.:*** Unakalm; ***S.Afr.:*** Solatran; ***Spain:*** Marcen; Sedotime; ***Switz.:*** Solatran.

Levomepromazine *(BAN, USAN, rINN)*

CL-36467; CL-39743; Levomepromatsiini; Levomepromazin; Levomepromazina; Lévomépromazine; Levomepromazinum; Methotrimeprazine; RP-7044; SKF-5116; XP-03. (–)-*NN*-Dimethyl-3-(2-methoxyphenothiazin-10-yl)-2-methylpropylamine; 3-(2-Methoxyphenothiazin-10-yl)-2-methylpropyldimethylamine.

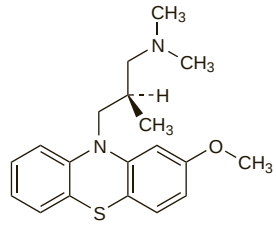
Левомепромазин

$C_{19}H_{24}N_2OS$ = 328.5.

CAS — 60-99-1.

ATC — N05AA02.

ATC Vet — QN05AA02.



Pharmacopoeias. In *US.* Also in *BP(Vet).*

BP(Vet) 2008 (Levomepromazine). A white or slightly cream-coloured crystalline powder. Practically insoluble in water; slightly soluble in alcohol; freely soluble in ether. Protect from light.

USP 31 (Methotrimeprazine). A fine white, practically odourless, crystalline powder. Soluble 1 in 10 of water, of alcohol, and of methyl alcohol, and 1 in 2 of chloroform; freely soluble in ether; sparingly soluble in alcohol at 25° but freely soluble in boiling alcohol. Store at a temperature of 25°, excursions permitted between 15° and 30°. Protect from light.

Levomepromazine Hydrochloride

(BANM, USAN, rINNM)

Hidrocloruro de levomepromazina; Levomepromatsiinihydrokloridi; Levomepromazin hydrochlorid; Lévomépromazine, chlorhydrate de; Levomepromazin-hidroklorid; Levomepromazinhydroklorid; Levomepromazini hydrochloridum; Levomepromazino hidrochloridas; Lewomepromazyny chlorowodorek; Methotrimeprazine Hydrochloride.

Левомепромазина Гидрохлорид

$C_{19}H_{24}N_2OS,HCl$ = 364.9.

CAS — 4185-80-2; 1236-99-3.

ATC — N05AA02.

ATC Vet — QN05AA02.

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

Ph. Eur. 6.2 (Levomepromazine Hydrochloride). A white or very slightly yellow, slightly hygroscopic crystalline powder. It deteriorates on exposure to air and light. Freely soluble in water and in alcohol. Store in airtight containers. Protect from light.

Incompatibility. Levomepromazine hydrochloride is reported to be incompatible with alkaline solutions.