with impairment of cardiac function, hypokalaemia, or other electrolyte imbalance. It is recommended that a baseline ECG is performed in all patients before use of droperidol.

Uses and Administration

Droperidol is a butyrophenone with general properties similar to those of haloperidol (p.1001). The duration of action of droperidol has been reported to last about 2 to 4 hours although alteration of alertness may last for up to 12 hours.

One manufacturer of droperidol (*Janssen-Cilag*) voluntarily withdrew it from the market worldwide in March 2001 after reports of QT prolongation, serious ventricular arrhythmias, or sudden death in association with its use. However, in the USA, droperidol remained available from other manufacturers although its use was restricted to the management of nausea and vomiting after surgical or diagnostic procedures in patients who fail to show an adequate response to other treatments. It is also still available, in some other countries, for use as a premedicant, as an adjunct in anaesthesia, and for the control of agitated patients in acute psychoses and in mania. Droperidol has been used in the management of chemotherapy-induced nausea and vomiting. It has also been used with an opioid analgesic such as fentanyl citrate to maintain patients in a state of neuroleptanalgesia in which they are calm and indifferent to the surroundings and able to cooperate with the surgeon. The longer duration of action of droperidol must be kept in mind when using it with such opioid analgesics.

For the prevention of postoperative **nausea and vomiting** a maximum initial dose of 2.5 mg intramuscularly or intravenously has been given; additional doses of 1.25 mg may be given if necessary. Children aged 2 years and over have been given a maximum initial dose of 100 micrograms/kg intramuscularly or intravenously.

◊ References.

1. McKeage K, *et al*. Intravenous droperidol: a review of its use in the management of postoperative nausea and vomiting. *Drugs* 2006; **66:** 2123–47.

Preparations

BP 2008: Droperidol Injection; Droperidol Tablets;
USP 31: Droperidol Injection.

Proprietary Preparations (details are given in Part 3)
Austral.: Droleptan; ***Belg.:*** Dehydrobenzperidol; ***Braz.:*** Droperdal; ***Cz.:*** Dehydrobenzperidol†; Xomolix; ***Denm.:*** Dehydrobenzperidol; ***Fin.:*** Dehydrobenzperidol; ***Fr.:*** Droleptan; ***Gr.:*** Dehydrobenzperidol†; Droleptan; ***India:*** Droperol; ***Ital.:*** Sintodian†; ***Neth.:*** Dehydrobenzperidol; ***NZ:*** Droleptan; ***Port.:*** Dehidrobenzperidol; Xomolix; ***S.Afr.:*** Paxical; ***Spain:*** Dehidrobenzperidol†; ***Swed.:*** Dridol; ***Thai.:*** Dehydrobenzperidol†; ***USA:*** Inapsine.

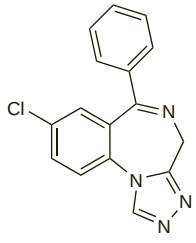
Multi-ingredient: ***Arg.:*** Disifelit; ***Braz.:*** Nilperidol; ***Ital.:*** Leptofen.

Estazolam *(USAN, rINN)*

Abbott-47631; D-40TA; Estatsolaami; Estazolamum. 8-Chloro-6-phenyl-4*H*-1,2,4-triazolo[4,3-*a*]-1,4-benzodiazepine.

Эстазолам

$C_{16}H_{11}ClN_4$ = 294.7.
CAS — 29975-16-4.
ATC — N05CD04.
ATC Vet — QN05CD04.



Pharmacopoeias. In *Chin.* and *Jpn.*

Dependence and Withdrawal

As for Diazepam, p.987.

Adverse Effects, Treatment, and Precautions

As for Diazepam, p.987.

Interactions

As for Diazepam, p.989.

Pharmacokinetics

Peak plasma concentrations of estazolam are reached on average within 2 hours of oral doses. Estazolam is about 93% protein bound. Reported mean elimination half-lives have generally been in the range of 10 to 24 hours. Estazolam is extensively metabolised, mainly to 4-hydroxyestazolam and 1-oxoestazolam, which are considered inactive. These metabolites are excreted, either free or conjugated, in the urine with small amounts detected in the faeces. Only a small proportion of a dose is excreted as unchanged drug.

Uses and Administration

Estazolam is a short-acting benzodiazepine with general properties similar to those of diazepam (p.992). It is given as a hypnotic in the short-term management of insomnia (p.957) in usual oral doses of 1 to 2 mg at night. Small or debilitated elderly patients may be given an initial dose of 0.5 mg.

Preparations

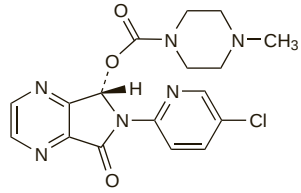
Proprietary Preparations (details are given in Part 3)
Arg.: Somnatrol†; ***Braz.:*** Noctal; ***Denm.:*** Domnamid†; ***Fr.:*** Nuctalon; ***Indon.:*** Esilgan; ***Ital.:*** Esilgan; ***Jpn:*** Eurodin; ***Mex.:*** Tasedan; ***Philipp.:*** Esilgan; ***Port.:*** Kainever; ***USA:*** Prosom†.

Eszopiclone *(USAN, rINN)*

Eszopiclona; Eszopiclonum; (*S*)-Zopiclone; (+)-Zopiclone. (+)-(5*S*)-6-(5-Chloropyridin-2-yl)-7-oxo-6,7-dihydro-5*H*-pyrrolo[3,4-*b*]pyrazin-5-yl 4-methylpiperazine-1-carboxylate.

Эзопикльон

$C_{17}H_{17}ClN_6O_3$ = 388.8.
CAS — 138729-47-2.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of eszopiclone: Sleepeasy.

Profile

Eszopiclone is the (+)-isomer of zopiclone (p.1039) and is used similarly as a hypnotic in the short-term management of insomnia.

The usual oral dose is 2 mg immediately before bedtime; if appropriate, the dose may be started at or increased to 3 mg. In elderly patients who have difficulty falling asleep, the initial dose is 1 mg; this may be increased to 2 mg. For elderly patients who have difficulty staying asleep, the starting dose is 2 mg.

The starting dose should be reduced in patients taking potent inhibitors of the cytochrome P450 isoenzyme CYP3A4; a dose not exceeding 1 mg is recommended which may then be increased to 2 mg. For doses in patients with hepatic impairment, see below.

◊ Reviews.

1. Melton ST, *et al*. Eszopiclone for insomnia. *Ann Pharmacother* 2005; **39:** 1659–66.
2. Halas CJ. Eszopiclone. *Am J Health-Syst Pharm* 2006; **63:** 41–8.

Administration in hepatic impairment. The starting oral dose of eszopiclone should be reduced to 1 mg at bedtime in patients with severe hepatic impairment. No dose adjustment is necessary in patients with mild to moderate impairment.

Preparations

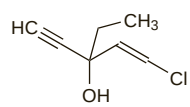
Proprietary Preparations (details are given in Part 3)
Arg.: Inductal; ***USA:*** Lunesta.

Ethchlorvynol *(BAN, rINN)*

β-Chlorovinyl Ethyl Ethynyl Carbinol; Etclorvinol; Éthchlorvynol; *E*-Ethchlorvynol; Ethchlorvynolum; Etkloorivinoli; Etklorvinol. 1-Chloro-3-ethylpent-1-en-4-yn-3-ol.

Этхлорвинол

C_7H_9ClO = 144.6.
CAS — 113-18-8.
ATC — N05CM08.
ATC Vet — QN05CM08.



Pharmacopoeias. In *US*.
USP 31 (Ethchlorvynol). A colourless to yellow, slightly viscous liquid having a characteristic pungent odour. It darkens on exposure to air and light. Immiscible with water; miscible with most organic solvents. Store in airtight containers of glass or polyethylene, using polyethylene-lined closures. Protect from light.

Dependence and Withdrawal

Prolonged use of ethchlorvynol may lead to dependence similar to that with barbiturates (see Amobarbital, p.962).

Adverse Effects

Adverse effects of ethchlorvynol include gastrointestinal disturbances, dizziness, headache, unwanted sedation and other symptoms of CNS depression such as ataxia, facial numbness, blurred vision, and hypotension. Hypersensitivity reactions include skin rashes, urticaria, and occasionally, thrombocytopenia and cholestatic jaundice. Idiosyncratic reactions include excitement, severe muscular weakness, and syncope without marked hypotension.

Acute overdosage is characterised by prolonged deep coma, respiratory depression, hypothermia, hypotension, and relative bradycardia. Pancytopenia and nystagmus have occurred.

Pulmonary oedema has followed abuse by intravenous injection.

Treatment of Adverse Effects

Treatment is as for barbiturate overdose (see Amobarbital, p.962). Haemoperfusion may be of value in the treatment of severe poisoning with ethchlorvynol.

Precautions

Ethchlorvynol should be used with caution in patients with hepatic or renal impairment or with depression, in patients with severe uncontrolled pain, and, as with all sedatives, in those with impaired respiratory function. It may cause drowsiness; affected patients should not drive or operate machinery.

Excessively rapid absorption of ethchlorvynol in some patients has been reported to produce giddiness and ataxia; this may be reduced by giving it with food.

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

Interactions

The effect of ethchlorvynol may be enhanced by alcohol, barbiturates, and other CNS depressants. Ethchlorvynol has been reported to decrease the effects of coumarin anticoagulants.

Tricyclic antidepressants. Transient delirium has been reported from the use of ethchlorvynol with *amitriptyline* but details of such an interaction do not appear to have been published in the literature.

Pharmacokinetics

Ethchlorvynol is readily absorbed from the gastrointestinal tract, peak plasma concentrations usually occurring within 2 hours of ingestion. It is widely distributed in body tissues and is extensively metabolised in the liver, and possibly to some extent in the kidneys. It has a biphasic plasma half-life with a rapid initial phase and a terminal phase reported to last from 10 to 20 hours. Ethchlorvynol is excreted mainly in the urine as metabolites and their conjugates. Ethchlorvynol crosses the placenta.

Uses and Administration

Ethchlorvynol is a hypnotic and sedative with some anticonvulsant and muscle relaxant properties. It is given for the short-term management of insomnia (p.957) but has been largely superseded by other drugs. Use for periods greater than one week is not recommended. The usual oral hypnotic dose is 500 mg at night but doses ranging from 200 mg to 1 g have been given. Taking doses with food has been recommended—see Precautions, above.

Preparations

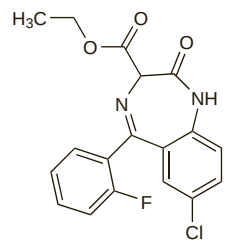
USP 31: Ethchlorvynol Capsules.

Ethyl Loflazepate *(rINN)*

CM-6912; Éthyle, Loflazépate d'; Ethylis Loflazepas; Loflazepato de etilo. Ethyl 7-chloro-5-(2-fluorophenyl)-2,3-dihydro-2-oxo-1*H*-1,4-benzodiazepine-3-carboxylate.

Этил Лофлазепат

$C_{18}H_{14}ClFN_2O_3$ = 360.8.
CAS — 29177-84-2.
ATC — N05BA18.
ATC Vet — QN05BA18.



Profile

Ethyl loflazepate is a long-acting benzodiazepine derivative with general properties similar to those of diazepam (p.986). It is used in the short-term treatment of anxiety disorders (p.952) in usual oral doses of 1 to 3 mg daily in a single dose or in divided doses.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Victan†; ***Belg.:*** Victan; ***Fr.:*** Victan; ***Jpn:*** Meilax; ***Mex.:*** Victan; ***Port.:*** Victan; ***Thai.:*** Victan.

Etifoxine Hydrochloride *(BANM, rINNM)*

Etifoxin Hydrochloride; Étifoxine, Chlorhydrate d'; Etifoxini Hydrochloridum; Hidrocloruro de etifoxina; Hoe-36801. 6-Chloro-4-methyl-4-phenyl-3,1-benzoxazin-2-yl(ethyl)amine hydrochloride.

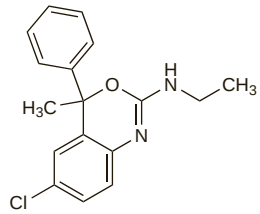
Этифоксина Гидрохлорид

$C_{17}H_{17}ClN_2O,HCl$ = 337.2.

CAS — 21715-46-8 (etifoxine); 56776-32-0 (etifoxine hydrochloride).

ATC — N05BX03.

ATC Vet — QN05BX03.



(etifoxine)

Profile

Etifoxine hydrochloride is an anxiolytic used for the short-term treatment of anxiety (p.952). It is given in usual oral doses of 150 or 200 mg daily in 2 or 3 divided doses.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Stresam.

Etizolam *(rINN)*

AHR-3219; Étizolam; Etizolamum; Y-7131. 4-(2-Chlorophenyl)-2-ethyl-9-methyl-6*H*-thieno[3,2-*f*]-s-triazolo[4,3-*a*][1,4]diazepine.

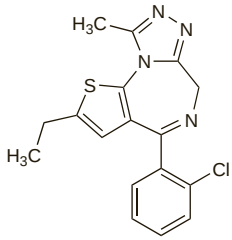
Этизолам

$C_{17}H_{15}ClN_4S$ = 342.8.

CAS — 40054-69-1.

ATC — N05BA19.

ATC Vet — QN05BA19.



Pharmacopoeias. In *Jpn.*

Profile

Etizolam is a short-acting benzodiazepine derivative with general properties similar to those of diazepam (p.986). It is given for the short-term treatment of insomnia (p.957) and anxiety disorders (p.952) in oral doses of up to 3 mg daily in divided doses or as a single dose at night.

Preparations

Proprietary Preparations (details are given in Part 3)
Ital.: Depas; Pasaden; ***Jpn:*** Depas.

Febarbamate *(rINN)*

Fébarbamate; Febarbamato; Febarbamatum; Go-560. 1-(3-Butoxy-2-carbamoyloxypropyl)-5-ethyl-5-phenylbarbituric acid.

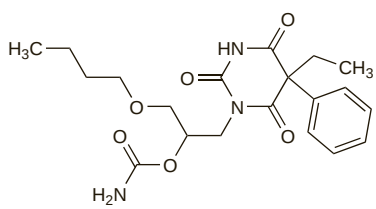
Фебарбамат

$C_{20}H_{27}N_3O_6$ = 405.4.

CAS — 13246-02-1.

ATC — M03BA05.

ATC Vet — QM03BA05.



Profile

Febarbamate is a barbiturate with general properties similar to those of amobarbital (p.961). It has been used in the management of anxiety, insomnia, and alcohol withdrawal symptoms. However, barbiturates are no longer considered appropriate in the management of these conditions.

Tetrabamate, a complex of febarbamate, difebarbamate, and phenobarbital, has been used similarly but was associated with the development of hepatitis.

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Hung.:*** Atrium†.

Fluanisone *(BAN, rINN)*

Fluanison; Fluanisona; Fluanisoni; Fluanisonum; Haloanisone; MD-2028; R-2028; R-2167. 4′-Fluoro-4-[4-(2-methoxyphenyl)piperazin-1-yl]butyrophenone.

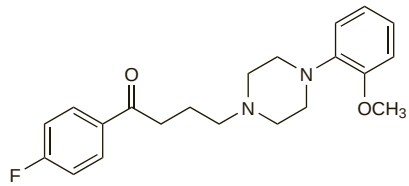
Флуанизон

$C_{21}H_{25}FN_2O_2$ = 356.4.

CAS — 1480-19-9.

ATC — N05AD09.

ATC Vet — QN05AD09.



Pharmacopoeias. In *BP(Vet).*

BP(Vet) 2008 (Fluanisone). White or almost white to buff-coloured, odourless or almost odourless crystals or powder. It exhibits polymorphism. M.p. 72° to 76°. Practically insoluble in water; freely soluble in alcohol, in chloroform, in ether, and in dilute solutions of organic acids. Protect from light.

Profile

Fluanisone is a butyrophenone with general properties similar to those of haloperidol (p.1000). It has been used in the management of agitated states in psychiatric patients and as anaesthetic premedication.

Fluanisone is used in veterinary medicine for neuroleptanalgesia.

Fludiazepam *(rINN)*

Fludiazépam; Fludiazepamum; ID-540. 7-Chloro-5-(2-fluorophenyl)-1,3-dihydro-1-methyl-2*H*-1,4-benzodiazepin-2-one.

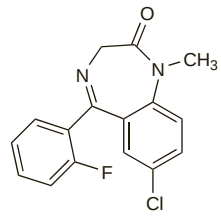
Флудиазепам

$C_{16}H_{12}ClFN_2O$ = 302.7.

CAS — 3900-31-0.

ATC — N05BA17.

ATC Vet — QN05BA17.



Pharmacopoeias. In *Jpn.*

Profile

Fludiazepam is a short-acting benzodiazepine with general properties similar to those of diazepam (p.986). It has been used in the short-term treatment of anxiety disorders.

Flunitrazepam *(BAN, USAN, rINN)*

Flunitratsepaami; Flunitrazépam; Flunitrazepám; Flunitrazepamas; Flunitrazepamum; Ro-5-4200. 5-(2-Fluorophenyl)-1,3-dihydro-1-methyl-7-nitro-1,4-benzodiazepin-2-one.

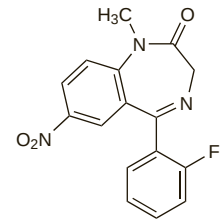
Флунитразепам

$C_{16}H_{12}FN_3O_3$ = 313.3.

CAS — 1622-62-4.

ATC — N05CD03.

ATC Vet — QN05CD03.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of flunitrazepam:
Benzo; Circles; Date rape drug; Forget me drug; Forget pill; Forget-me pill; Forget-Me-Pill; Getting roached; La Rocha; La Roche; Lunch money drug; Mexican valium; Pingus; R2; R-2; Reynolds; Rib; Rick James Biatch; Roach 2; Roach-2; Roaches; Roachies; Roapies; Robutal; Rochas dos; Roche; Roches; Rolpes; Roofie; Roofies; Roopies; Rope; Rophies; Rophy; Ropies; Roples; Ropples; Row-shay; Ruffies; Ruffles; Sedexes; Wolfies.

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

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

Dependence and Withdrawal

As for Diazepam, p.987.

Adverse Effects, Treatment, and Precautions

As for Diazepam, p.987.

Abuse. A WHO review[1] concluded that flunitrazepam had a moderate abuse potential that might be higher than that of other benzodiazepines. It was reported that there was current evidence of widespread abuse of flunitrazepam among drug abusers, particularly among those who used opioids or cocaine.

Flunitrazepam is tasteless and odourless and has been misused to incapacitate the victim and produce amnesia in sexual assaults[2] and drug-facilitated rape ('date rape').[3] A 1-mg dose may produce impairment for 8 to 12 hours.[4] Some manufacturers have incorporated a blue dye into flunitrazepam tablets to increase visibility when placed into drinks but caution is still necessary as it has been reported that blue tropical drinks and punches are being used to overcome this.[3]

1. WHO expert committee on drug dependence: twenty-ninth report. *WHO Tech Rep Ser 856* 1995. Available at: http://libdoc.who.int/trs/WHO_TRS_856.pdf (accessed 21/08/08)
2. Simmons MM, Cupp MJ. Use and abuse of flunitrazepam. *Ann Pharmacother* 1998; **32:** 117–19.
3. National Institute on Drug Abuse. Rohypnol and GHB (issued May 2006). Available at: http://www.nida.nih.gov/PDF/Infofacts/Rohypnol06.pdf (accessed 21/08/08)
4. Smith KM, *et al.* Club drugs: methylenedioxymethamphetamine, flunitrazepam, ketamine hydrochloride, and γ-hydroxybutyrate. *Am J Health-Syst Pharm* 2002; **59:** 1067–76.

Breast feeding. Concentrations in breast milk the morning after a single evening 2-mg dose of flunitrazepam were considered to be too low to produce clinical effects in breast-fed infants, although accumulation in the milk might occur after repeated use.[1]

1. Kanto J, *et al.* Placental transfer and breast milk levels of flunitrazepam. *Curr Ther Res* 1979; **26:** 539–46.

Local reactions. Of 43 patients given a single intravenous dose of flunitrazepam 1 to 2 mg, two had local thrombosis 7 to 10 days later.[1] The incidence was lower than in those given diazepam [in solution]. However, there was little difference in the incidence of local reactions after intravenous use of flunitrazepam and diazepam in another study.[2]

1. Hegarty JE, Dundee JW. Sequelae after the intravenous injection of three benzodiazepines—diazepam, lorazepam, and flunitrazepam. *BMJ* 1977; **2:** 1384–5.
2. Mikkelsen H, *et al.* Local reactions after iv injections of diazepam, flunitrazepam and isotonic saline. *Br J Anaesth* 1980; **52:** 817–19.

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

Interactions

As for Diazepam, p.989.

Pharmacokinetics

Flunitrazepam is readily absorbed from the gastrointestinal tract. About 77 to 80% is bound to plasma proteins. It is extensively metabolised in the liver and excreted mainly in the urine as metabolites (free or conjugated). Its principal metabolites are 7-aminoflunitrazepam and *N*-desmethylflunitrazepam; *N*-desmethylflunitrazepam is reported to be pharmacologically active. The elimination half-life of flunitrazepam