Cyclobarbital *(BAN, rINN)*

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

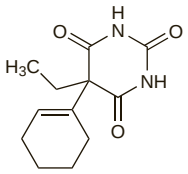
Циклобарбитал

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

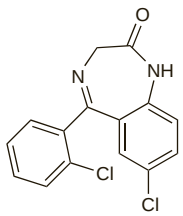
Delorazepam *(pINN)*

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.

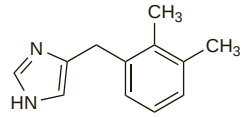
Detomidine Hydrochloride *(BANM, USAN, rINNM)*

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.

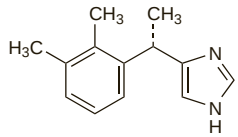
Дексмедетомидина Гидрохлорид

$C_{13}H_{16}N_2$,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.

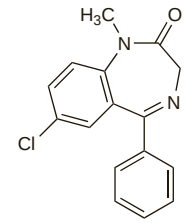
Диазепам

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