Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Hung.:*** Demalgon.

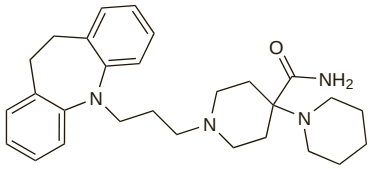
Carpipramine Hydrochloride *(rINNM)*

Carpipramine, Chlorhydrate de; Carpipramini Hydrochloridum; Hidrocloruro de carpipramina; PZ-1511. 1-[3-(10,11-Dihydro-5*H*-dibenz[*b,f*]azepin-5-yl)propyl]-4-piperidinopiperidine-4-carboxamide dihydrochloride monohydrate.

Карпипрамина Гидрохлорид

$C_{28}H_{38}N_4O,2HCl,H_2O$ = 537.6.

CAS — 5942-95-0 (carpipramine); 7075-03-8 (anhydrous carpipramine hydrochloride).



(carpipramine)

Profile

Carpipramine is structurally related both to imipramine (p.400) and to butyrophenones such as haloperidol (p.1000). It has been used in the management of anxiety disorders (p.952) and psychoses such as schizophrenia (p.955). Carpipramine is given as the hydrochloride although doses are expressed in terms of the base; carpipramine hydrochloride 60.2 mg is equivalent to about 50 mg of carpipramine. A usual oral dose is equivalent to 150 mg of the base daily in 2 or 3 divided doses, with a range of 50 to 400 mg daily.

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

Preparations

Proprietary Preparations (details are given in Part 3)

Fr.: Prazinil.

Chlordiazepoxide *(BAN, rINN)*

Chlordiazepoksidas; Chlordiazepoxid; Chlordiazépoxide; Chlordiazepoxidum; Chlorodiazepoksyd; Clordiazepóxido; Klooridiatsepoksidi; Klordiazepoksit; Klórdiazepoxid; Klordiazepoxid; Methaminodiazepoxide. 7-Chloro-2-methylamino-5-phenyl-3*H*-1,4-benzodiazepine 4-oxide.

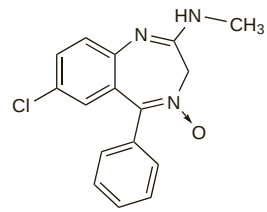
Хлордиазепоксид

$C_{16}H_{14}ClN_3O$ = 299.8.

CAS — 58-25-3.

ATC — N05BA02.

ATC Vet — QN05BA02.



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

Pharmacopoeias. In *Chin., Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Chlordiazepoxide). An almost white or light yellow, crystalline powder. It exhibits polymorphism. Practically insoluble in water; sparingly soluble in alcohol. Protect from light.
USP 31 (Chlordiazepoxide). A yellow, practically odourless, crystalline powder. Insoluble in water; soluble 1 in 50 of alcohol, 1 in 6250 of chloroform, and 1 in 130 of ether. Store in airtight containers. Protect from light.

Chlordiazepoxide Hydrochloride *(BANM, USAN, rINNM)*

Chlordiazepoksido hidrochloridas; Chlordiazepoksydu chlorowodorek; Chlordiazépoxide, chlorhydrate de; Chlordiazepoxidhydrochlorid; Chlordiazepoxidi hydrochloridum; Hidrocloruro de clordiazepóxido; Klooridiatsepoksidihydrokloridi; Klordiazepoksit Hidroklorür; Klórdiazepoxid-hidroklorid; Klordiazepoxidhydroklorid; Methaminodiazepoxide Hydrochloride; NSC-115748; Ro-5-0690.

Хлордиазепоксида Гидрохлорид

$C_{16}H_{14}ClN_3O,HCl$ = 336.2.
CAS — 438-41-5.
ATC — N05BA02.
ATC Vet — QN05BA02.

Pharmacopoeias. In *Eur.* (see p.vii) and *US*.
Ph. Eur. 6.2 (Chlordiazepoxide Hydrochloride). A white or slightly yellow, crystalline powder. It exhibits polymorphism. Soluble in water; sparingly soluble in alcohol. Protect from light.
USP 31 (Chlordiazepoxide Hydrochloride). A white or practically white, odourless, crystalline powder. Soluble in water; sparingly soluble in alcohol; insoluble in petroleum spirit. Store in airtight containers. Protect from light.

Dependence and Withdrawal

As for Diazepam, p.987.

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

Adverse Effects, Treatment, and Precautions

As for Diazepam, p.987.

Hepatic impairment. Progressive drowsiness began after 20 days of treatment with chlordiazepoxide in a woman with cirrhosis and hepatitis.[1] One week after stopping the drug the patient could not be roused, and full consciousness was not regained for another week. Accumulation of active metabolites of chlordiazepoxide may have been responsible for the prolonged stupor.

1. Barton K, *et al*. Chlordiazepoxide metabolite accumulation in liver disease. *Med Toxicol* 1989; **4:** 73–6.

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

Interactions

As for Diazepam, p.989.

Pharmacokinetics

Absorption of chlordiazepoxide is almost complete after oral doses; peak plasma concentrations are achieved after 1 to 2 hours. Absorption after intramuscular injection may be slow and erratic depending on the site of injection. Chlordiazepoxide is about 96% bound to plasma proteins. Reported values for the elimination half-life of chlordiazepoxide have ranged from about 5 to 30 hours, but its main active metabolite desmethyldiazepam (nordazepam, p.1012) has a half-life of several days. Other pharmacologically active metabolites of chlordiazepoxide include desmethylchlordiazepoxide, demoxepam, and oxazepam (p.1014). Chlordiazepoxide passes into the CSF and breast milk, and crosses the placenta. Unchanged drug and metabolites are excreted in the urine, mainly as conjugated metabolites.

◊ References.

1. Greenblatt DJ, *et al*. Clinical pharmacokinetics of chlordiazepoxide. *Clin Pharmacokinet* 1978; **3:** 381–94.

Uses and Administration

Chlordiazepoxide is a benzodiazepine with general properties similar to those of diazepam (p.992). It is used in the short-term treatment of anxiety disorders (p.952) and insomnia (p.957). Chlordiazepoxide is also used in muscle spasm (p.1887), in alcohol withdrawal syndrome (p.1626), and for premedication (p.1780).

Chlordiazepoxide is given orally as the hydrochloride or the base; the doses given refer equally to both. It may also be given by deep intramuscular or slow intravenous injection as the hydrochloride. Preparations formulated for intramuscular use are considered unsuitable for intravenous injection due to the formation of air bubbles in the solvent.

Elderly and debilitated patients should be given one-half or less of the usual adult dose.

The usual oral dose for the treatment of **anxiety** is up to 30 mg daily in divided doses; in severe conditions up to 100 mg daily has been given. For acute or severe anxiety an initial dose of 50 to 100 mg of the hydrochloride has been given by injection, followed if necessary by 25 to 50 mg three or four times daily.

For relief of **muscle spasm** a dose of 10 to 30 mg daily orally in divided doses is recommended, and 10 to 30 mg orally may be given before bedtime for insomnia associated with anxiety.

For the control of the acute symptoms of **alcohol withdrawal** chlordiazepoxide or chlordiazepoxide hydrochloride may be given in an oral dose of 25 to 100 mg repeated as needed up to a maximum of 300 mg daily. For severe symptoms treatment may be begun by injection of 50 to 100 mg, repeated if necessary after 2 to 4 hours.

Chlordiazepoxide hydrochloride has also been given for anaesthetic **premedication** in a dose of 50 to 100 mg intramuscularly one hour before surgery.

Preparations

BP 2008: Chlordiazepoxide Capsules; Chlordiazepoxide Hydrochloride Tablets;
USP 31: Chlordiazepoxide and Amitriptyline Hydrochloride Tablets; Chlordiazepoxide Hydrochloride and Clidinium Bromide Capsules; Chlordiazepoxide Hydrochloride Capsules; Chlordiazepoxide Hydrochloride for Injection; Chlordiazepoxide Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: OCM; ***Braz.:*** Psicosedin; ***Cz.:*** Defobin†; Elenium; ***Denm.:*** Klopoxid; Risolid; ***Fin.:*** Risolid; ***Ger.:*** Librium; Multum; Radepur; ***Gr.:*** Oasil; ***Hong Kong:*** Librium; ***Hung.:*** Elenium; Librium; ***India:*** Equilibrium; Librium; ***Indon.:*** Cetabrium; Librium; ***Irl.:*** Librium; ***Ital.:*** Librium; Reliberan†; ***Malaysia:*** Benpine; Klorpo†; ***Mex.:*** Kalmocaps†; ***NZ:*** Novapam; ***Pol.:*** Elenium; ***Port.:*** Paxium; ***Rus.:*** Elenium (Элениум); ***S.Afr.:*** Librium; ***Singapore:*** Benpine; Klorpo; ***Spain:*** Huberplex; Omnalio; ***Thai.:*** Benpine; Cozep; Epoxide†; ***UK:*** Librium; Tropium; ***USA:*** Libritabs†; Librium; Mitran†; Reposans†; ***Venez.:*** Eposal.

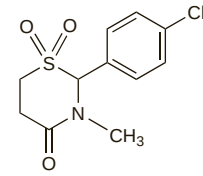
Multi-ingredient: ***Arg.:*** Libraxin; Plafonyl†; ***Austria:*** Limbitrol; ***Braz.:*** Limbitrol; Menotensil; ***Canad.:*** Apo-Chlorax; Librax; ***Chile:*** Aero Itan; Aerogastrol; Antalin; Garceptol; Gaseofin†; Gastrolen; Lerogin; Libraxin; Limbatrilin; Lironex†; Morelin; No-Ref; Profisin; Sedogastrol†; Tensoliv; Tiperin; Tranvagal†; ***Fin.:*** Klotriptyl; Librax; Limbitrol; ***Fr.:*** Librax; ***Gr.:*** Librax; ***Hong Kong:*** Bralix; Epilon; Librax; Medocalum†; ***India:*** Emotrip; Equirex; Normaxin; Spasrax; ***Indon.:*** Braxidin; Cliad; Klidibrax; Librax; Limbritol; Melidox; Neurogen; Renagas; Sanmag; Spasmium; ***Israel:*** Nirvaxal; ***Ital.:*** Diapatol; Librax; Limbitryl; Sedans; ***Malaysia:*** Apo-Chlorax†; Liblan; ***Port.:*** Librax; ***Rus.:*** Amixide (Амиксид); ***S.Afr.:*** Librax; Limbitrol; ***Singapore:*** Apo-Chlorax; Chlobax; Librax; Medocalum; ***Spain:*** Psico Blocan; ***Switz.:*** Librax; Librocol; Limbitrol; ***Thai.:*** Kenspa; Librax; Pobrax†; Tumax; Zepobrax†; ***Turk.:*** Klipaks; Libkol; Librax; ***USA:*** Clindex; Librax; Limbitrol; ***Venez.:*** Librax.

Chlormezanone *(BAN, rINN)*

Chlormethazanone; Chlormézanone; Chlormezanonum; Clormezanona; Kloorimetsanoni; Klormezanon. 2-(4-Chlorophenyl)-3-methylperhydro-1,3-thiazin-4-one 1,1-dioxide.

Хлормезанон

$C_{11}H_{12}ClNO_3S$ = 273.7.
CAS — 80-77-3.
ATC — M03BB02.
ATC Vet — QM03BB02.



Profile

Chlormezanone has been used in the treatment of anxiety disorders and insomnia. It was also used in conditions associated with painful muscle spasm, often in compound preparations with analgesics; its mechanism of action is not clear but is probably related to its sedative effect. Chlormezanone was withdrawn from use in many countries after reports of serious skin reactions (see below).

Effects on the skin. Chlormezanone was responsible for 5 of 86 cases of fixed drug eruption detected in a Finnish hospital from 1971 to 1980.[1] In the period from 1981 to 1985 chlormezanone was responsible for 1 out of 77 such eruptions.[2] In a case control study[3] comparing drug use in 245 patients hospitalised because of toxic epidermal necrolysis or Stevens-Johnson syndrome and 1147 controls, 13 patients and one control were found to have taken chlormezanone. From these figures a high crude relative risk of 62 was calculated; the excess risk was estimated to be 1.7 cases per million users per week.

1. Kauppinen K, Stubb S. Fixed eruptions: causative drugs and challenge tests. *Br J Dermatol* 1985; **112:** 575–8.