in the treatment of psychoses including schizophrenia. Doses are expressed in terms of the base; loxapine succinate 34 mg is equivalent to about 25 mg of loxapine.

The usual oral dose is 20 to 50 mg daily initially, in 2 divided doses, increased according to response over the next 7 to 10 days to 60 to 100 mg daily or more, in 2 to 4 divided doses; the maximum recommended dose is 250 mg daily. Maintenance doses are usually in the range of 20 to 60 mg daily, in divided doses. For the control of acute conditions it is given by intramuscular injection in daily doses of up to 300 mg in 2 or 3 divided doses. Reduced dosage may be required in elderly patients.

Loxapine has also been given orally and by intramuscular injection as the hydrochloride.

Disturbed behaviour. For a discussion of the use and limitations of antipsychotics such as loxapine in patients with disturbed behaviour, see p.954.

References.

1. Carlyle W, *et al.* Aggression in the demented patient: a double-blind study of loxapine versus haloperidol. *Int J Clin Psychopharmacol* 1993; **8:** 103–8.

Schizophrenia. A brief review of loxapine[1] found no conclusive evidence that it was particularly effective in patients with paranoid schizophrenia (p.955). A subsequent systematic review considered that the limited evidence did not indicate a clear difference in its effects from other antipsychotics.[2]

1. Anonymous. Clozapine and loxapine for schizophrenia. *Drug Ther Bull* 1991; **29:** 41–2.
2. Chakrabarti A, *et al.* Loxapine for schizophrenia. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2007 (accessed 19/03/08).

Preparations

USP 31: Loxapine Capsules.

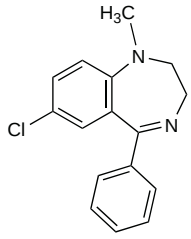
Proprietary Preparations (details are given in Part 3)
Canad.: Loxapac; ***Fr.:*** Loxapac; ***Gr.:*** Loxapac†; ***India:*** Loxapac; ***Spain:*** Desconex†; ***UK:*** Loxapac†; ***USA:*** Loxitane.

Medazepam *(BAN, rINN)*

Medatsepaami; Médazépam; Medazepamum. 7-Chloro-2,3-dihydro-1-methyl-5-phenyl-1*H*-1,4-benzodiazepine.

Медазепам

$C_{16}H_{15}ClN_2$ = 270.8.
CAS — 2898-12-6.
ATC — N05BA03.
ATC Vet — QN05BA03.



Pharmacopoeias. In *Jpn.*

Medazepam Hydrochloride *(USAN)*

Medazepam, hidrocloruro de; Ro-5-4556.

$C_{16}H_{15}ClN_2$,HCl = 307.2.
CAS — 2898-11-5.
ATC — N05BA03.
ATC Vet — QN05BA03.

Profile

Medazepam is a long-acting benzodiazepine with properties similar to those of diazepam (p.986). It has been given for the short-term treatment of anxiety disorders (p.952). A usual oral dose is 10 to 30 mg daily in divided doses; in severe conditions up to 60 mg daily has been given. Reduced doses should be given to elderly or debilitated patients.

Preparations

Proprietary Preparations (details are given in Part 3)
Cz.: Ansilan; Rusedal†; ***Ger.:*** Rudotel; Rusedal; ***Hung.:*** Nobrium; Rudotel; Rusedal; ***Pol.:*** Rudotel; ***Rus.:*** Rudotel (Рудотель).

Multi-ingredient: ***Ital.:*** Debrum; ***Spain:*** Nobritol; ***Turk.:*** Tanko-Buskas; Tranko-Buskas.

Medetomidine Hydrochloride *(BANM, USAN, rINNM)*

Hidrocloruro de medetomidina; Medetomidiinihydrokloridi; Médétomidine, Chlorhydrate de; Medetomidinhydroklorid; Medetomidini Hydrochloridum; MPV-785. (±)-4-[1-(2,3-Xylyl)ethyl]imidazole monohydrochloride.

Медетомидина Гидрохлорид

$C_{13}H_{16}N_2$,HCl = 236.7.
CAS — 86347-15-1 (medetomidine hydrochloride); 86347-14-0 (medetomidine).

Profile

Medetomidine is an α_2-adrenoceptor agonist with sedative, muscle relaxant, and analgesic properties. It is used as the hydrochloride in veterinary medicine.

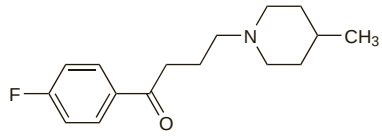
Its isomer dexmedetomidine (p.986) is used as the hydrochloride in intensive care.

Melperone Hydrochloride *(BANM, rINNM)*

FG-5111; Flubuperone Hydrochloride; Hidrocloruro de melperona; Melperon Hidroklorür; Melpérone, Chlorhydrate de; Melperoni Hydrochloridum; Methylperone Hydrochloride. 4′-Fluoro-4-(4-methylpiperidino)butyrophenone hydrochloride.

Мелперона Гидрохлорид

$C_{16}H_{22}FNO$,HCl = 299.8.
CAS — 3575-80-2 (melperone); 1622-79-3 (melperone hydrochloride).
ATC — N05AD03.
ATC Vet — QN05AD03.



(melperone)

Profile

Melperone is a butyrophenone with general properties similar to those of haloperidol (p.1000). It is given as the hydrochloride by mouth or by intramuscular injection for the management of psychoses such as schizophrenia (p.955) and in disturbed behaviour (p.954); doses are expressed as the hydrochloride. A usual oral dose is up to 400 mg daily in divided doses. In acute conditions it may be given intramuscularly in doses of 25 to 100 mg repeated to a usual maximum of 200 mg daily.

Cardiac arrhythmias. Melperone has been reported to have class III electrophysiologic and antiarrhythmic activity[1,2] but its clinical use as an antiarrhythmic would be limited by a high incidence of adverse effects.[2] For a discussion of the cardiovascular effects of antipsychotics in general, see under Chlorpromazine, p.970.

1. Møgelvang JC, *et al.* Antiarrhythmic properties of a neuroleptic butyrophenone, melperone, in acute myocardial infarction. *Acta Med Scand* 1980; **208:** 61–4.
2. Hui WKK, *et al.* Melperone: electrophysiologic and antiarrhythmic activity in humans. *J Cardiovasc Pharmacol* 1990; **15:** 144–9.

Pharmacokinetics. References.

1. Köppel C, *et al.* Gas chromatographic-mass spectrometric study of urinary metabolism of melperone. *J Chromatogr Biomed Appl* 1988; **427:** 144–50.

Schizophrenia. References[1-3] to the use of melperone in schizophrenia. It has been suggested that melperone should be considered as an atypical antipsychotic in view of the low incidence of extrapyramidal effects associated with its use.

1. Meltzer HY, *et al.* Melperone in the treatment of neuroleptic-resistant schizophrenia. *Psychiatry Res* 2001; **105:** 201–9.
2. Sumiyoshi T, *et al.* The effect of melperone, an atypical antipsychotic drug, on cognitive function in schizophrenia. *Schizophr Res* 2003; **59:** 7–16.
3. Sumiyoshi T, *et al.* A comparison of two doses of melperone, an atypical antipsychotic drug, in the treatment of schizophrenia. *Schizophr Res* 2003; **62:** 65–72.

Preparations

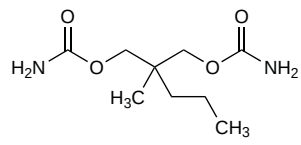
Proprietary Preparations (details are given in Part 3)
Austria: Buronil; Neuril†; ***Belg.:*** Buronil; ***Cz.:*** Buronil; ***Denm.:*** Buronil; ***Fin.:*** Buronil†; Melpax; ***Ger.:*** Eunerpan; Harmosin; Mel-Puren; Melneurin; Melperomerck; ***Port.:*** Bunil; ***Swed.:*** Buronil; ***Turk.:*** Buronon.

Meprobamate *(BAN, rINN)*

Meprobamaatti; Meprobamát; Meprobamat; Meprobamatas; Méprobamate; Meprobamato; Meprobamatum; Meprotanum. 2-Methyl-2-propyltrimethylene dicarbamate.

Мепробамат

$C_9H_{18}N_2O_4$ = 218.3.
CAS — 57-53-4.
ATC — N05BC01.
ATC Vet — QN05BC01.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of meprobamate: Miltown; Mother's little helper; Uncle Miltie.

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

Ph. Eur. 6.2 (Meprobamate). A white or almost white, crystalline or amorphous powder. Slightly soluble in water; freely soluble in alcohol.

USP 31 (Meprobamate). A white powder having a characteristic odour. Slightly soluble in water; freely soluble in alcohol and in acetone; practically insoluble or insoluble in ether. Store in airtight containers.

Dependence and Withdrawal

As for the barbiturates (see Amobarbital, p.962).

Adverse Effects and Treatment

Drowsiness is the most frequent adverse effect of meprobamate. Other effects include nausea, vomiting, diarrhoea, paraesthesia, weakness, and CNS effects such as headache, paradoxical excitement, dizziness, ataxia, and disturbances of vision. There may be hypotension, tachycardia, and cardiac arrhythmias. Hypersensitivity reactions occur occasionally. These may be limited to skin rashes, urticaria, and purpura or may be more severe with angioedema, bronchospasm, or anuria. Erythema multiforme or Stevens-Johnson syndrome, and exfoliative or bullous dermatitis have been reported.

Blood disorders including agranulocytosis, eosinophilia, leucopenia, thrombocytopenia, and aplastic anaemia have occasionally been reported.

Overdosage with meprobamate produces symptoms similar to those of barbiturate overdosage (see Amobarbital, p.962), and is managed similarly.

Overdosage. Two children aged 2 and 2.5 years recovered with conservative management alone after overdosage of meprobamate with bendroflumethiazide despite measured plasma-meprobamate concentrations of 170 and 158 micrograms/mL, respectively.[1] Although it had been recommended that haemoperfusion should be considered at plasma-meprobamate concentrations above 100 micrograms/mL, the authors considered that experience with adults suggested haemoperfusion should normally only be considered at plasma concentrations above 200 micrograms/mL.

1. Dennison J, *et al.* Meprobamate overdosage. *Hum Toxicol* 1985; **4:** 215–17.

Precautions

Meprobamate should be used with caution in patients with hepatic or renal impairment, depression, muscle weakness, and, as with all sedatives, in patients with impaired respiratory function. Meprobamate should be given with care to elderly or debilitated patients. Meprobamate may induce seizures in patients with a history of epilepsy.

Meprobamate may cause drowsiness; affected patients should not drive or operate machinery.

Breast feeding. The *BNF* considers that the use of meprobamate should be avoided in breast feeding mothers as concentrations in milk may exceed maternal plasma concentrations fourfold and may cause drowsiness in the infant.

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

Pregnancy. Studies on the use of meprobamate during pregnancy.

1. Milkovich L, van den Berg BJ. Effects of prenatal meprobamate and chlordiazepoxide hydrochloride on human embryonic and fetal development. *N Engl J Med* 1974; **291:** 1268–71.
2. Crombie DL, *et al.* Fetal effects of tranquilizers in pregnancy. *N Engl J Med* 1975; **293:** 198–9.
3. Hartz SC, *et al.* Antenatal exposure to meprobamate and chlordiazepoxide in relation to malformations, mental development, and childhood mortality. *N Engl J Med* 1975; **292:** 726–8.

Interactions

The sedative effects of meprobamate are enhanced by CNS depressants including alcohol. Meprobamate is capable of inducing hepatic microsomal enzyme systems involved in drug metabolism: the metabolism of other drugs may be enhanced if given concurrently.

Pharmacokinetics

Meprobamate is readily absorbed from the gastrointestinal tract and peak plasma concentrations occur 1 to 3 hours after ingestion. Meprobamate is widely distributed. It is extensively metabolised in the liver and is excreted in the urine mainly as an inactive hydroxylated metabolite and its glucuronide conjugate. About 10% of a dose is excreted unchanged. Meprobamate has a half-life reported to range from about 6 to 17 hours, although this may be prolonged after chronic use.

It diffuses across the placenta and appears in breast milk at concentrations of up to 4 times those in the maternal plasma.

Uses and Administration

Meprobamate is a carbamate with hypnotic, sedative, and some muscle relaxant properties, although in therapeutic doses its sedative effect rather than a direct action may be responsible for muscle relaxation. It has been used in the short-term treatment of anxiety disorders (p.952) and also for the short-term management of insomnia (p.957) but has largely been superseded by other drugs. Meprobamate has sometimes been used, alone or