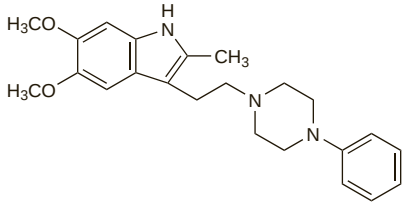
Oxypertine *(BAN, USAN, rINN)*

Oksipertiini; Oxipertin; Oxipertina; Oxypertinum; Win-18501-2. 5,6-Dimethoxy-2-methyl-3-[2-(4-phenylpiperazin-1-yl)ethyl]-indole.

Оксипертин

$C_{23}H_{29}N_3O_2$ = 379.5.
CAS — 153-87-7 (oxypertine); 40523-01-1 (oxypertine hydrochloride).
ATC — N05AE01.
ATC Vet — QN05AE01.



Profile

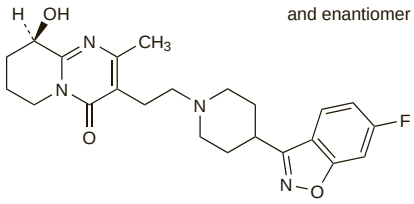
Oxypertine is an indole derivative with general properties similar to those of the phenothiazine, chlorpromazine (p.969). It has been given orally in the treatment of psychoses including schizophrenia, mania, and disturbed behaviour, and in severe anxiety.

Paliperidone *(USAN, rINN)*

9-Hydroxyrisperidone; Paliperidona; Palipéridone; Paliperidonum; RO-76477. (±)-3-{2-[4-(6-Fluoro-1,2-benzisoxazol-3-yl)piperidino]ethyl}-6,7,8,9-tetrahydro-9-hydroxy-2-methyl-4*H*-pyrido[1,2-*a*]pyrimidin-4-one.

Палиперидон

$C_{23}H_{27}FN_4O_3$ = 426.5.
CAS — 144598-75-4.
ATC — N05AX13.
ATC Vet — QN05AX13.



Paliperidone Palmitate *(USAN, rINNM)*

Palipéridone, Palmitate de; Paliperidoni Palmitas; Palmitato de paliperidona; RO-92670. (9*RS*)-3-{2-[4-(6-Fluoro-1,2-benzisoxazol-3-yl)piperidin-1-yl]ethyl}-2-methyl-4-oxo-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-9-yl hexadecanoate.

Палиперидона Палмитат

$C_{39}H_{57}FN_4O_4$ = 664.9.
CAS — 199739-10-1.

Profile

Paliperidone is a benzisoxazole derivative and is the major active metabolite of the atypical antipsychotic risperidone (p.1024). It is reported to be an antagonist at dopamine D_2, serotonin ($5\text{-}HT_2$), adrenergic (α_1 and α_2), and histamine (H_1) receptors. It is used in the treatment of schizophrenia.

The recommended oral dose of paliperidone is 6 mg once daily as a modified-release preparation; doses may range from 3 to 12 mg daily. US licensed product information recommends that dose increases are made in small steps of 3 mg at intervals of more than 5 days.

For details of dose reductions in patients with renal impairment, see below.

Paliperidone palmitate is being developed as a long-acting intramuscular formulation.

Administration in renal impairment. The plasma concentrations of paliperidone are increased in patients with renal impairment. The usual oral daily dosage (see above) should therefore be adjusted according to creatinine clearance (CC).

In the UK, licensed product information recommends the following doses:

- CC 50 to 80 mL/minute: initially 3 mg once daily, may be increased thereafter according to response and tolerance
- CC 30 to 50 mL/minute: 3 mg once daily
- CC 10 to 30 mL/minute: initially 3 mg on alternate days which may be increased thereafter to 3 mg once daily after clinical reassessment

However, US licensed product information recommends the following maximum doses:

- CC 50 to 80 mL/minute: 6 mg once daily
- CC 10 to 50 mL/minute: 3 mg once daily

Paliperidone has not been studied in patients with a CC of less than 10 mL/minute; UK product information does not recommend its use in such patients.

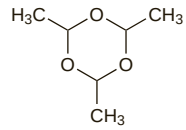
Preparations

Proprietary Preparations (details are given in Part 3)
Cz.: Invega; ***Fr.:*** Invega; ***Port.:*** Invega; ***UK:*** Invega; ***USA:*** Invega.

Paraldehyde

Paracetaldehyde; Paraldehid; Paraldehidas; Paraldehído; Paraldehit; Paraldehyd; Paraldéhyde; Paraldehydi; Paraldehydum. The trimer of acetaldehyde; 2,4,6-Trimethyl-1,3,5-trioxane.

$(C_2H_4O)_3$ = 132.2.
CAS — 123-63-7.
ATC — N05CC05.
ATC Vet — QN05CC05.



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

Ph. Eur. 6.2 (Paraldehyde). A colourless or slightly yellow, transparent liquid. It solidifies on cooling to form a crystalline mass. It may contain a suitable amount of an antoxidant. Relative density 0.991 to 0.996. F.p. is 10° to 13°; not more than 10% distils below 123° and not less than 95% below 126°. Soluble in water but less soluble in boiling water; miscible with alcohol and with volatile oils. Store in small well-filled airtight containers. Protect from light.

USP 31 (Paraldehyde). A colourless transparent liquid with a strong characteristic, but not unpleasant or pungent, odour. It is subject to oxidation to form acetic acid. It may contain a suitable stabiliser. Specific gravity is about 0.99. It has a congealing temperature of not lower than 11° and distils completely between 120° and 126°. Soluble 1 in 10 of water v/v, but only 1 in 17 of boiling water v/v; miscible with alcohol, with chloroform, with ether, and with volatile oils. Store in well-filled airtight containers of not more than 30 mL at a temperature not exceeding 25°. Protect from light. It must not be used more than 24 hours after opening the container.

Incompatibility. Paraldehyde exerts a solvent action upon rubber, polystyrene, and styrene-acrylonitrile copolymer and should not be given in plastic syringes made with these materials.

An evaluation of the compatibility of paraldehyde with plastic syringes and needle hubs concluded that, if possible, all-glass syringes should be used with paraldehyde.[1] Needles with plastic hubs could be used. Polypropylene syringes with rubber-tipped plastic plungers (*Plastipak*), or glass syringes with natural rubber-tipped plastic plungers (*Glaspak*) were acceptable only for the immediate administration or measurement of paraldehyde doses.

1. Johnson CE, Vigoreaux JA. Compatibility of paraldehyde with plastic syringes and needle hubs. *Am J Hosp Pharm* 1984; **41:** 306–8.

Stability. Paraldehyde decomposes on storage, particularly after the container has been opened. Partly decomposed paraldehyde is **dangerous** if given. It must not be used if it has a brownish colour or a sharp penetrating odour of acetic acid.

Dependence and Withdrawal

Prolonged use of paraldehyde may lead to dependence, especially in alcoholics. Features of dependence and withdrawal are similar to those of barbiturates (see Amobarbital, p.962).

Adverse Effects and Treatment

Paraldehyde decomposes on storage and deaths from corrosive poisoning have followed the use of such material. Paraldehyde has an unpleasant taste and imparts a smell to the breath; it may cause skin rashes.

Oral or rectal use of paraldehyde may cause gastric or rectal irritation. Intramuscular injection is painful and associated with tissue necrosis, sterile abscesses, and nerve damage. Intravenous use is extremely hazardous since it may cause pulmonary oedema and haemorrhage, hypotension and cardiac dilatation, and circulatory collapse; thrombophlebitis is also associated with intravenous use.

Overdosage results in rapid laboured breathing owing to damage to the lungs and to acidosis. Nausea and vomiting may follow an overdose by mouth. Respiratory depression and coma as well as hepatic and renal damage may occur. Treatment is as for barbiturate overdose (see Amobarbital, p.962).

Precautions

Paraldehyde should not be given to patients with gastric disorders and it should be used with caution, if at all, in patients with bronchopulmonary disease or hepatic impairment. It should not be given rectally in the presence of colitis. Old paraldehyde must never be used.

Paraldehyde must be well diluted before oral or rectal use; if it is deemed essential to give paraldehyde intravenously it must be well diluted and given very slowly with extreme caution (see also Adverse Effects, above and Uses, below). Intramuscular injections may be given undiluted but care should be taken to avoid nerve damage. Plastic syringes should be avoided (see Incompatibility, above).

Interactions

The sedative effects of paraldehyde are enhanced by CNS depressants such as alcohol, barbiturates, and other sedatives. A few case reports suggest that disulfiram may enhance the toxicity of paraldehyde; use together is not recommended.

Pharmacokinetics

Paraldehyde is generally absorbed readily, although absorption is reported to be slower after rectal than after oral or intramuscular doses. It is widely distributed and has a reported half-life of 4 to 10 hours. About 80% of a dose is metabolised in the liver probably to acetaldehyde, which is oxidised by aldehyde dehydrogenase to acetic acid. Unmetabolised drug is largely excreted unchanged through the lungs; only small amounts appear in the urine. It crosses the placental barrier and is distributed into breast milk.

Uses and Administration

Paraldehyde is a hypnotic and sedative with antiepileptic effects. However, because of the hazards associated with its use, its tendency to react with plastic, and the risks associated with its deterioration, it has largely been superseded by other drugs. It is still occasionally used to control status epilepticus (p.469) resistant to conventional treatment. Given rectally or intramuscularly it causes little respiratory depression and is therefore useful where facilities for resuscitation are poor.

At low temperature it solidifies to form a crystalline mass. If it solidifies, the whole should be liquefied before use.

A usual dose for adults is 10 to 20 mL given rectally as a 10% solution in sodium chloride 0.9% solution or diluted with 1 or 2 parts of oil. Doses of 5 to 10 mL are also occasionally given intramuscularly up to a maximum of 20 mL daily with not more than 5 mL being given at any one site. In the UK it is licensed for intramuscular use in children; however, the *BNFC* advocates use of the rectal route instead, diluted as above. Recommended single daily doses by either route are:

- up to 3 months, 0.5 mL (the *BNFC* suggests a single rectal dose of 0.4 mL/kg (maximum of 0.5 mL) in those under 1 month)
- 3 to 6 months, 1 mL
- 6 to 12 months, 1.5 mL
- 1 to 2 years, 2 mL
- 3 to 5 years, 3 to 4 mL
- 6 to 12 years, 5 to 6 mL

Paraldehyde has been given by slow intravenous infusion in specialist centres with intensive care facilities but this route is not usually recommended; it must be diluted in sodium chloride 0.9% before use.

Paraldehyde has been given orally; it should always be well diluted to avoid gastric irritation.

Preparations

BP 2008: Paraldehyde Injection.

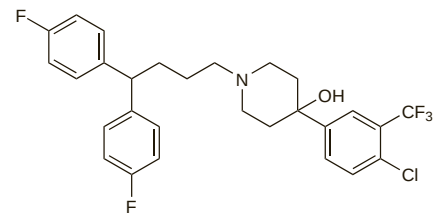
Proprietary Preparations (details are given in Part 3)
USA: Paral.

Penfluridol *(BAN, USAN, rINN)*

McN-JR-16341; Penfluridoli; Penfluridolum; R-16341. 4-(4-Chloro-3-trifluoromethylphenyl)-1-[3-(*p,p'*-difluorobenzhydryl)propyl]piperidin-4-ol.

Пенфлуридол

$C_{28}H_{27}ClF_5NO$ = 524.0.
CAS — 26864-56-2.
ATC — N05AG03.
ATC Vet — QN05AG03.



Pharmacopoeias. In *Chin.*

Profile

Penfluridol is a diphenylbutylpiperidine antipsychotic and shares the general properties of the phenothiazine, chlorpromazine (p.969). After oral doses it has a prolonged duration of action that

lasts for about a week. It is used in the treatment of psychoses including schizophrenia (p.955).

The usual oral dose of penfluridol for the treatment of chronic psychoses is 20 to 60 mg once a week. Doses of up to 250 mg once a week may be required in severe or resistant conditions.

Schizophrenia. A systematic review[1] concluded that penfluridol appears to have a similar efficacy and adverse effects profile to other classical antipsychotics used in the treatment of schizophrenia (p.955). The authors also suggested that penfluridol, in a weekly oral dose of 40 to 80 mg, is a suitable alternative, particularly for patients who do not respond to daily oral medication or adapt well to depot drugs.

1. Soares BGO, Lima MS. Penfluridol for schizophrenia. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2006 (accessed 19/03/08).

Preparations

Proprietary Preparations (details are given in Part 3)

Austria: Semap; ***Belg.:*** Semap; ***Braz.:*** Semap; ***Cz.:*** Semap†; ***Denm.:*** Semap; ***Fr.:*** Semap†; ***Gr.:*** Flupidol; ***Israel:*** Semap; ***Mex.:*** Semap; ***Neth.:*** Semap; ***Switz.:*** Semap.

Pentobarbital *(BAN, rINN)*

Aethaminalum; Mebubarbital; Mebumal; Pentobarbitaali; Pentobarbitál; Pentobarbitalis; Pentobarbitalum; Pentobarbitone. 5-Ethyl-5-(1-methylbutyl)barbituric acid.

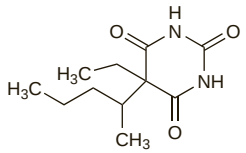
Пентобарбитал

$C_{11}H_{18}N_2O_3$ = 226.3.

CAS — 76-74-4.

ATC — N05CA01.

ATC Vet — QN05CA01; QN51AA01.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of pentobarbital:
Blockbuster; Menish; Nebbies; Nembies; Nemish; Nemmies; Nimbies; Nimby; Yellow; Yellow bullets; Yellow dolls; Yellow jackets; Yellow submarines; Yellows.

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

Ph. Eur. 6.2 (Pentobarbital). Colourless crystals or a white or almost white, crystalline powder. Very slightly soluble in water; freely soluble in dehydrated alcohol. It forms water-soluble compounds with alkali hydroxides and carbonates, and with ammonia.

USP 31 (Pentobarbital). A white or practically white, practically odourless, fine powder. Very slightly soluble in water and in carbon tetrachloride; soluble 1 in 4.5 of alcohol, 1 in 4 of chloroform, and 1 in 10 of ether; very soluble in acetone and in methyl alcohol; soluble in benzene. Store in airtight containers.

Pentobarbital Calcium *(BANM, rINNM)*

Calcii Pentobarbitalum; Pentobarbital cálcico; Pentobarbital Calcique; Pentobarbitone Calcium. Calcium 5-ethyl-5-(1-methylbutyl)barbiturate.

Кальций Пентобарбитал

$(C_{11}H_{17}N_2O_3)_2Ca$ = 490.6.

ATC — N05CA01.

ATC Vet — QN05CA01.

Pharmacopoeias. In *Jpn.*

Pentobarbital Sodium *(BANM, rINNM)*

Aethaminalum-Natrium; Ethaminal Sodium; Mebumalnatrium; Natrii Pentobarbitalum; Pentobarbitaalinatrium; Pentobarbital sódico; Pentobarbital sodique; Pentobarbital sodná sůl; Pentobarbitalio natrio druska; Pentobarbitalnatrium; Pentobarbitál-nátrium; Pentobarbitalum natricum; Pentobarbitone Sodium; Sodium Pentobarbital; Soluble Pentobarbitone. Sodium 5-ethyl-5-(1-methylbutyl)barbiturate.

Натрий Пентобарбитал

$C_{11}H_{17}N_2NaO_3$ = 248.3.

CAS — 57-33-0.

ATC — N05CA01.

ATC Vet — QN05CA01.

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

Ph. Eur. 6.2 (Pentobarbital Sodium). A white or almost white, hygroscopic, crystalline powder. Very soluble in water. A 10% solution in water has a pH of 9.6 to 11.0 when freshly prepared. Store in airtight containers.

USP 31 (Pentobarbital Sodium). White, crystalline granules or white powder. Is odourless or has a slight characteristic odour. Very soluble in water; freely soluble in alcohol; practically insoluble in ether. pH of a 10% solution in water is between 9.8 and 11.0. Solutions decompose on standing, the decomposition being accelerated at higher temperatures. Store in airtight containers.

Incompatibility. Pentobarbital may be precipitated from preparations containing pentobarbital sodium, depending on the concentration and pH. Pentobarbital sodium has, therefore, been reported to be incompatible with many other drugs particularly acids and acidic salts.

Dependence and Withdrawal

As for Amobarbital, p.962.

Adverse Effects, Treatment, and Precautions

As for Amobarbital, p.962.

Interactions

As for Amobarbital, p.962.

Pharmacokinetics

Pentobarbital is well absorbed from the gastrointestinal tract after oral or rectal doses, and is reported to be about 60 to 70% bound to plasma proteins. The elimination half-life appears to be dose-dependent and reported values have ranged from 15 to 50 hours. Pentobarbital is metabolised in the liver, mainly by hydroxylation, and excreted in the urine mainly as metabolites.

Uses and Administration

Pentobarbital is a barbiturate that has been used as a hypnotic and sedative. It has general properties and uses similar to those of amobarbital (p.962). It has been used as a sedative and in the short-term management of insomnia (p.957) but barbiturates are not considered appropriate for such purposes. Pentobarbital sodium has also been used for premedication in anaesthetic procedures (p.1780), but barbiturates for pre-operative sedation have been replaced by other drugs. Pentobarbital is usually given as the sodium salt, although pentobarbital itself and its calcium salt have both been used.

A usual oral dose of pentobarbital sodium for insomnia was 100 to 200 mg, given at bedtime. Usual parenteral doses for other indications were 150 to 200 mg as a single intramuscular dose or 100 mg by slow intravenous injection.

Cerebrovascular disorders. For reference to the use of barbiturate-induced coma in the management of patients with cerebral ischaemia, see under Thiopental, p.1796. See also p.1181 for reference to the use of barbiturates in the management of raised intracranial pressure.

Status epilepticus. General anaesthesia may be used to control refractory tonic-clonic status epilepticus (p.469). A short-acting barbiturate such as thiopental is usually used, but pentobarbital has been used similarly.

Preparations

BP 2008: Pentobarbital Tablets;
USP 31: Pentobarbital Elixir; Pentobarbital Sodium Capsules; Pentobarbital Sodium Injection.

Proprietary Preparations (details are given in Part 3)

Canad.: Nembutal†; ***Denm.:*** Mebumal; ***Hong Kong:*** Nembutal†; ***S.Afr.:*** Sopental; ***Thai.:*** Nembutal†; ***USA:*** Nembutal.

Multi-ingredient: ***Arg.:*** Dimaval; ***Canad.:*** Cafergot-PB†; ***USA:*** Cafatine-PB.

Perazine Dimalonate

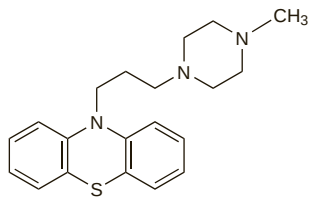
P-725 (perazine); Pemazine Dimalonate; Perazina, dimalonato de. 10-[3-(4-Methylpiperazin-1-yl)propyl]phenothiazine dimalonate.

$C_{20}H_{25}N_3S,2C_3H_4O_4$ = 547.6.

CAS — 84-97-9 (perazine); 14777-25-4 (perazine dimalonate).

ATC — N05AB10.

ATC Vet — QN05AB10.



(perazine)

Pharmacopoeias. *Pol.* includes only an injection of the dimalonate. It also includes a monograph for Perazine Dimaleate.

Profile

Perazine dimalonate is a phenothiazine with general properties similar to those of chlorpromazine (p.969) and is used for the treatment of psychotic conditions. It has a piperazine side-chain. It is given orally as the dimalonate although doses are expressed in terms of the base; perazine dimalonate 40.3 mg is equivalent to about 25 mg of perazine. Usual doses are the equivalent of 50 to 600 mg of the base daily; up to 1000 mg daily has been given in resistant cases. It has also been given intramuscularly.

Perazine dimaleate given orally has been used similarly.

Adverse effects. A report of 5 patients receiving perazine dimalonate who developed acute axonal neuropathies of superficial nerve fibres after exposure to sunlight.[1]

1. Roelcke U, *et al.* Acute neuropathy in perazine-treated patients after sun exposure. *Lancet* 1992; **340:** 729–30.

Preparations

Proprietary Preparations (details are given in Part 3)

Ger.: Taxilan; ***Pol.:*** Perazin; Perazyna; Pernazinum.

Pericyazine *(BAN)*

Periciazine *(pINN)*; Periciazin; Periciazina; Péricyazine; Periciazinum; Perisiatsiini; Propericiazine; RP-8909; SKF-20716. 10-[3-(4-Hydroxypiperidino)propyl]phenothiazine-2-carbonitrile; 1-[3-(2-Cyanophenothiazin-10-yl)propyl]piperidin-4-ol.

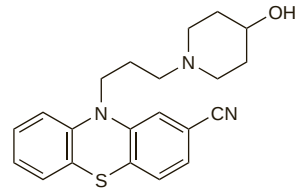
Перициазин

$C_{21}H_{23}N_3OS$ = 365.5.

CAS — 2622-26-6.

ATC — N05AC01.

ATC Vet — QN05AC01.



Adverse Effects, Treatment, and Precautions

As for Chlorpromazine, p.969. Sedation and orthostatic hypotension may be marked.

Interactions

As for Chlorpromazine, p.973.

Uses and Administration

Pericyazine is a phenothiazine with general properties similar to those of chlorpromazine (p.975). It has a piperidine side-chain. It is used in the treatment of psychoses including schizophrenia (p.955) and disturbed behaviour (p.954), and in the short-term management of severe anxiety (p.952).

Pericyazine is usually given as the base but the mesilate and tartrate have also been used.

The usual oral dose for the treatment of severe anxiety, agitation, aggression, or impulsive behaviour is 15 to 30 mg daily given in 2 divided doses, the larger amount in the evening. In schizophrenia and severe psychoses initial doses of 75 mg daily may be given in divided doses, increased if necessary, at weekly intervals by increments of 25 mg, to a maximum of 300 mg daily.

A recommended initial oral dose in children aged over 1 year is 500 micrograms daily for a child weighing 10 kg; for heavier children this initial dose may be increased by 1 mg for each additional 5 kg, to a maximum total of 10 mg daily. Thereafter the dose may be gradually increased according to response but the daily maintenance dose should not exceed twice the initial dose.

Elderly patients should be given reduced doses: a recommended initial dose is 5 to 10 mg daily for anxiety or disturbed behaviour and 15 to 30 mg daily for schizophrenia or psychosis, both in divided doses.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Neuleptil; ***Austral.:*** Neulactil; ***Austria:*** Neuleptil; ***Braz.:*** Neuleptil; ***Canad.:*** Neuleptil; ***Chile:*** Neuleptil; ***Cz.:*** Neuleptil†; ***Denm.:*** Neulactil; ***Fin.:*** Neulactil; ***Fr.:*** Neuleptil; ***Gr.:*** Neuleptil; ***Hong Kong:*** Neulactil; ***Irl.:*** Neulactil†; ***Israel:*** Neuleptil; ***Ital.:*** Neuleptil; ***Neth.:*** Neuleptil; ***NZ:*** Neulactil; ***Rus.:*** Neuleptil (Неулептил); ***S.Afr.:*** Neulactil†; ***Spain:*** Nemactil; ***UK:*** Neulactil; ***Venez.:*** Neuleptil.