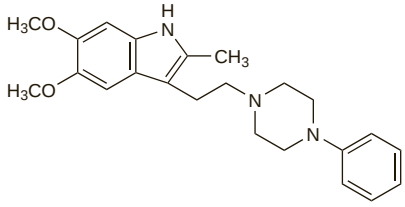
Oxypertine *(BAN, USAN, rINN)*

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

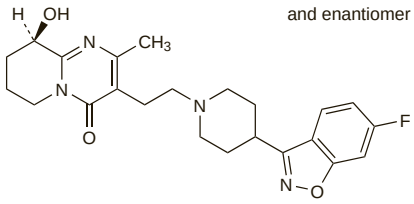
Oxypertine is an indole derivative with general properties similar to those of the phenothiazine, chlorpromazine (p.969). It has been given orally in the treatment of psychoses including schizophrenia, mania, and disturbed behaviour, and in severe anxiety.

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.

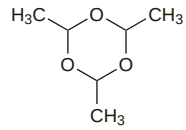
Preparations

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.

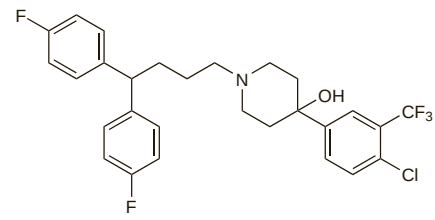
Proprietary Preparations (details are given in Part 3)
USA: Paral.

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