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.

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## Pentobarbital *(BAN, rINN)*

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

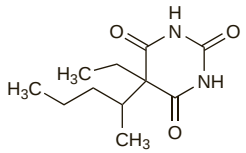
Пентобарбитал

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

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## Perazine Dimalonate

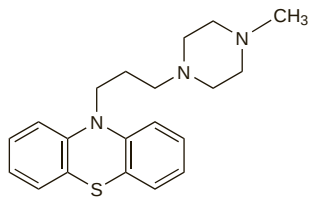
P-725 (perazine); Pemazine Dimalonate; Perazina, dimalonato de. 10-[3-(4-Methylpiperazin-1-yl)propyl]phenothiazine dimalonate.

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

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## 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.

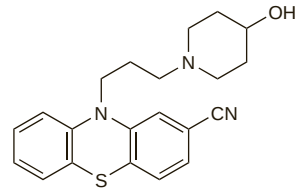
Перициазин

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

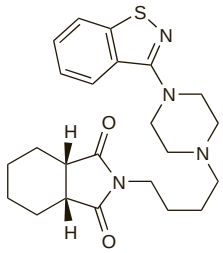
### Perospirone Hydrochloride *(rINNM)*

Hidrocloruro de perospirona; Pérospirone, Chlorhydrate de; Perospironi Hydrochloridum; SM-9018. *cis*-*N*-{4-[4-(1,2-Benzisothiazol-3-yl)-1-piperazinyl]butyl}-1,2-cyclohexanedicarboximide hydrochloride.

Пероспирона Гидрохлорид

$C_{23}H_{30}N_4O_2S,HCl$ = 463.0.

*CAS — 150915-41-6 (perospirone); 129273-38-7 (perospirone hydrochloride).*



*(perospirone)*

#### Profile

Perospirone is an antipsychotic used in the treatment of schizophrenia. Although it has been described as an atypical antipsychotic, the incidence of extrapyramidal effects may be rather higher than is usually seen with atypical drugs such as clozapine (p.981). Perospirone hydrochloride is given in usual oral doses of 12 to 48 mg daily in 3 divided doses.

◊ References.

1. Onrust SV, McClellan K. Perospirone. *CNS Drugs.* 2001; **15:** 329–37.

#### Preparations

**Proprietary Preparations** (details are given in Part 3)
***Jpn:*** Lullan.

## Perphenazine *(BAN, rINN)*

Perfenatsiini; Perfenazin; Perfenazina; Perfenazinas; Perfenazyna; Perphénazine; Perphenazinum. 2-{4-[3-(2-Chlorophenothiazin-10-yl)propyl]piperazin-1-yl}ethanol.

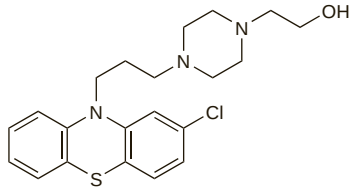
Перфеназин

$C_{21}H_{26}ClN_3OS$ = 404.0.

*CAS — 58-39-9.*

*ATC — N05AB03.*

*ATC Vet — QN05AB03.*



**Pharmacopoeias.** In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*. *Jpn* also includes the maleate.

**Ph. Eur. 6.2** (Perphenazine). A white or yellowish-white crystalline powder. Practically insoluble in water; soluble in alcohol; freely soluble in dichloromethane; dissolves in dilute solutions of hydrochloric acid. Protect from light.

**USP 31** (Perphenazine). A white to creamy-white odourless powder. M.p. 94° to 100°. Practically insoluble in water; soluble 1 in 7 of alcohol and 1 in 13 of acetone; freely soluble in chloroform. Store in airtight containers. Protect from light.

**Incompatibility.** Perphenazine has been reported to be incompatible with cefoperazone sodium[1] and with midazolam hydrochloride (see p.1007).

1. Gasca M, *et al.* Visual compatibility of perphenazine with various antimicrobials during simulated Y-site injection. *Am J Hosp Pharm* 1987; **44:** 574–5.

### Perphenazine Decanoate *(BANM, rINNM)*

Decanoato de perfenazina; Perphénazine, Décanoate de; Perphenazini Decanoas.

Перфеназина Деканоат

$C_{31}H_{44}ClN_3O_2S$ = 558.2.

*ATC — N05AB03.*

*ATC Vet — QN05AB03.*

### Perphenazine Enantate *(BANM, rINNM)*

Enantato de perfenazina; Perphénazine, Enantate de; Perphenazine Enanthate; Perphenazine Heptanoate; Perphenazini Enantas.

Перфеназина Энантат

$C_{28}H_{38}ClN_3O_2S$ = 516.1.

*CAS — 17528-28-8.*

*ATC — N05AB03.*

*ATC Vet — QN05AB03.*

### Adverse Effects, Treatment, and Precautions

As for Chlorpromazine, p.969. Perphenazine has been associated with a lower frequency of sedation, but a higher incidence of extrapyramidal effects.

**Breast feeding.** The American Academy of Pediatrics[1] considers that, although the effect of perphenazine on breast-fed infants is unknown, its use by mothers during breast feeding may be of concern since antipsychotics do appear in breast milk and thus could conceivably alter CNS function in the infant both in the short and long term.

The distribution of perphenazine into breast milk was studied[2] in a mother who was receiving oral perphenazine 24 mg daily, later reduced to 16 mg daily. Breast feeding was started after it was estimated that a breast-fed infant would ingest about 0.1% of a maternal dose. Treatment with perphenazine lasted for 3.5 months and during this period the child thrived normally and no drug-induced symptoms were seen.

1. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 28/04/04)
2. Olesen OV, *et al.* Perphenazine in breast milk and serum. *Am J Psychiatry* 1990; **147:** 1378–9.

### Interactions

As for Chlorpromazine, p.973.

### Pharmacokinetics

Perphenazine is well absorbed after oral doses and undergoes some first-pass metabolism, resulting in a relative bioavailability of about 60 to 80%. Peak plasma concentrations are achieved between 1 to 3 hours after ingestion. It is widely distributed and crosses the placenta. Perphenazine is extensively metabolised; up to 70% is excreted in the urine mainly as metabolites, with about 5% being excreted in the faeces. The plasma elimination half-life of perphenazine is between 9 and 12 hours. Perphenazine decanoate and perphenazine enantate are slowly absorbed from the site of intramuscular injection. They gradually release perphenazine into the body and are therefore suitable for use as depot injections.

◊ Perphenazine 5 or 6 mg given intravenously had a plasma half-life from 8.4 to 12.3 hours in a study of 4 schizophrenic patients and 4 healthy subjects.[1] Plasma-perphenazine concentrations varied considerably 3 to 5 hours after dosing; this was followed by an exponential elimination phase. Plasma concentrations were undetectable after a 6-mg oral dose in 4 healthy subjects and only low plasma concentrations of its sulfoxide metabolite could be detected; this was attributed to a marked first-pass effect. Systemic availability was also variable and poor in 4 schizophrenic patients given perphenazine 12 mg three times daily. However, it was considered that oral therapy should be given at 8-hour intervals. Intramuscular injection of perphenazine enantate 50 or 100 mg every 2 weeks gave plasma-perphenazine concentrations similar to those after continuous oral dosage, but high initial absorption in the first 2 to 3 days was associated with serious CNS adverse effects.

1. Hansen CE, *et al.* Clinical pharmacokinetic studies of perphenazine. *Br J Clin Pharmacol* 1976; **3:** 915–23.

**Metabolism.** In a study in 12 healthy subjects there was a clear difference in the disposition of a single oral dose of perphenazine between poor and extensive hydroxylators of debrisoquine.[1]

1. Dahl-Puustinen M-L, *et al.* Disposition of perphenazine is related to polymorphic debrisoquin hydroxylation in human beings. *Clin Pharmacol Ther* 1989; **46:** 78–81.

### Uses and Administration

Perphenazine is a phenothiazine with general properties similar to those of chlorpromazine (p.975). It has a piperazine side-chain. It is used in the treatment of various psychoses including schizophrenia (p.955) and mania (see Bipolar Disorder, p.372) as well as disturbed behaviour (p.954) and in the short-term, adjunctive management of severe anxiety (p.952). Perphenazine is also used for the management of postoperative or chemotherapy-induced nausea and vomiting (p.1700) and for the treatment of intractable hiccup (p.976).

Perphenazine is usually given orally and sometimes by intramuscular or intravenous injection as the base. Long-acting decanoate or enantate esters of perphenazine, available in some countries, are given by intramuscular injection.

The usual initial oral dose for the treatment of **schizophrenia, mania, and other psychoses** is 4 mg three times daily. The dose is adjusted according to response up to a usual maximum of 24 mg daily, although up to 64 mg daily has occasionally been used in hospitalised patients. Similar doses have been used for the management of **severe agitated or violent behaviour** or in **severe anxiety**. Perphenazine has sometimes been used in preparations with tricyclic antidepressants such as amitriptyline in the treatment of anxiety with depression.

For the **control of nausea and vomiting** the usual oral dose is 4 mg three times daily but up to 8 mg three times daily may be required.

Perphenazine may be given by deep *intramuscular* injection for control of acute psychotic symptoms or for severe nausea and vomiting. An initial dose of 5 or 10 mg is followed, if necessary, by 5 mg every 6 hours to a maximum of 15 to 30 mg daily.

Perphenazine, diluted to a concentration of 500 micrograms/mL in sodium chloride 0.9%, is occasionally given by *intravenous* injection in divided doses, not more than 1 mg being given every 1 to 2 minutes; the maximum intravenous dose is 5 mg. The intravenous route is usually reserved for the control of severe vomiting or intractable hiccup. Perphenazine has also been given by slow infusion.

The long-acting decanoate or enantate esters of perphenazine are given by deep intramuscular injection in doses ranging from about 50 to 300 mg of ester given at intervals of 2 to 4 weeks.

Perphenazine and its esters should be given in reduced doses to the elderly but it should be noted that they are not indicated for the management of agitation and restlessness in these patients.

◊ References.

1. Hartung B, *et al.* Perphenazine for schizophrenia. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2005 (accessed 14/04/05).

### Preparations

***BP 2008:*** Perphenazine Tablets;
***USP 31:*** Perphenazine and Amitriptyline Hydrochloride Tablets; Perphenazine Injection; Perphenazine Oral Solution; Perphenazine Syrup; Perphenazine Tablets.

**Proprietary Preparations** (details are given in Part 3)
***Austria:*** Decentan; ***Belg.:*** Trilafon†; ***Canad.:*** Trilafon; ***Denm.:*** Trilafon; ***Fin.:*** Peratsin; ***Fr.:*** Trilifan; ***Ger.:*** Decentan; ***Indon.:*** Trilafon; ***Israel:*** Perphenan; ***Ital.:*** Trilafon; ***Mex.:*** Leptopsique; Trilafon†; ***Neth.:*** Trilafon; ***Norw.:*** Trilafon; ***Philipp.:*** Trilafon; ***Pol.:*** Trilafon; ***S.Afr.:*** Trilafon†; ***Spain:*** Decentan; ***Swed.:*** Trilafon; ***Switz.:*** Trilafon; ***Thai.:*** Conazine; Pernamed; Pernazine; Perzine†; Porazine; ***UK:*** Fentazin; ***USA:*** Trilafon†.

**Multi-ingredient:** ***Arg.:*** Karile; Mutabon D†; ***Canad.:*** PMS-Levazine; Triavil†; ***Chile:*** Mutabon D†; ***Fin.:*** Pertriptyl; ***Gr.:*** Minitran; ***Indon.:*** Mutabon-D; Mutabon-M; ***Ital.:*** Mutabon; ***Mex.:*** Adepsique; ***Port.:*** Mutabon; ***S.Afr.:*** Etrafon†; ***Spain:*** Mutabase; ***Thai.:*** Anxipress-D†; Neuragon; Polybon; ***UK:*** Triptafen; ***USA:*** Etrafon; Triavil†.

## Phenazepam

Fenazepam. 7-Bromo-5-(2-chlorophenyl)-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one.

$C_{15}H_{10}BrClN_2O$ = 349.6.

*CAS — 51753-57-2.*