Profile
Pipazetate hydrochloride is a centrally acting cough suppressant that also has some peripheral actions in non-productive cough (p.1547). It has been given by mouth and rectally.

Overdosage. A healthy 4-year-old child became somnolent and agitated, with convulsions, followed by coma, after swallowing an unknown number of tablets containing pipazetate; cardiac arrhythmias also developed.[1] Fatal toxicity has also been reported in children.[2,3]

1. da Silva OA, Lopez M. Pipazethate—acute childhood poisoning. *Clin Toxicol* 1977; **11:** 455–8.
2. Bonavita V, *et al*. Accidental lethal pipazethate poisoning in a child. *Z Rechtsmed* 1982; **89:** 145–8.
3. Soto E, *et al*. Pipazethate lethality in a baby. *Vet Hum Toxicol* 1993; **35:** 41.

Preparations
Proprietary Preparations (details are given in Part 3)
Braz.: Selvigon; ***Ital.:*** Selvjgon; ***Mex.:*** Selvigon; ***Thai.:*** Transpulmin†.

Poppy Capsule
Dormideiras; Fruit du Pavot; Fruto de adormidera; Mohnfrucht; Papaveris Capsula; Poppy Heads.

Маковая Коробочка

Pharmacopoeias. In *Chin.*

Profile
Poppy capsule consists of dried fruits of *Papaver somniferum* (Papaveraceae), collected before dehiscence has occurred, containing very small amounts of morphine with traces of other opium alkaloids. It is mildly sedative and has been used as a liquid extract or syrup in cough mixtures.

Preparations
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Belg.:*** Sedemol; Sulfa-Sedemol; ***Braz.:*** Malvodon.

Prenoxdiazine Hydrochloride *(rINNM)*
Hidrocloruro de prenoxdiazina; HK-256; Prenoxdiazin Hydrochloride; Prénoxdiazine, Chlorhydrate de; Prenoxdiazini Hydrochloridum. 3-(2,2-Diphenylethyl)-5-(2-piperidinoethyl)-1,2,4-oxadiazole hydrochloride.

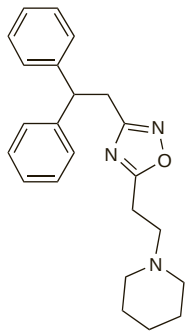
Преноксдиазина Гидрохлорид

$C_{23}H_{27}N_3O,HCl$ = 397.9.

CAS — 47543-65-7 (prenoxdiazine); 37671-82-2 (prenoxdiazine hibenzate); 982-43-4 (prenoxdiazine hydrochloride).

ATC — R05DB18.

ATC Vet — QR05DB18.



(prenoxdiazine)

Profile
Prenoxdiazine hydrochloride is a peripherally acting cough suppressant for non-productive cough (p.1547) that has been given orally. Prenoxdiazine hibenzate has also been used.

Preparations
Proprietary Preparations (details are given in Part 3)
Cz.: Libexin†; ***Hung.:*** Libexin; Rhinathiol Tusso; ***India:*** Libexin; ***Rus.:*** Libexin (Либексин).

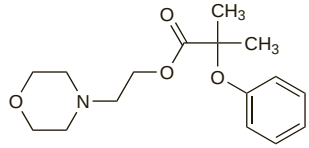
Multi-ingredient: ***Ital.:*** Broncofluid; Libexin Mucolitico.

Promolate *(rINN)*
Morphethylbutyne; Promolato; Promolatum. 2-Morpholinoethyl 2-methyl-2-phenoxypropionate.

Промолат

$C_{16}H_{23}NO_4$ = 293.4.

CAS — 3615-74-5.



Profile
Promolate is a cough suppressant that has been given rectally to infants.

Preparations
Proprietary Preparations (details are given in Part 3)
Chile: Atusil.

Pseudoephedrine *(BAN, rINN)*
d-Ψ-Ephedrine; *d*-Isoephedrine; Pseudoefedriini; Pseudoefedrin; Pseudoefedrina; Pseudoéphédrine; Pseudoephedrinum. (+)-(1*S*,2*S*)-2-Methylamino-1-phenylpropan-1-ol.

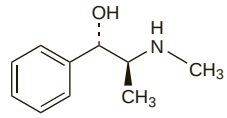
Псевдоэфедрин

$C_{10}H_{15}NO$ = 165.2.

CAS — 90-82-4.

ATC — R01BA02.

ATC Vet — QR01BA02.



Description. Pseudoephedrine is an alkaloid obtained from *Ephedra* spp.

Pseudoephedrine Hydrochloride
(BANM, USAN, rINNM)

Hidrocloruro de pseudoefedrina; Pseudoefedriinihydrokloridi; Pseudoefedrin-hydrochlorid; Pseudoefedrinhydroklorid; Pseudoefedrino hidrochloridas; Pseudoéphédrine, chlorhydrate de; Pseudoephedrini hydrochloridum; Psödoefedrin Hidroklorür; Pszeudoefedrin-hidroklorid.

Псевдоэфедрина Гидрохлорид

$C_{10}H_{15}NO,HCl$ = 201.7.

CAS — 345-78-8.

ATC — R01BA02.

ATC Vet — QR01BA02.

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

Ph. Eur. 6.2 (Pseudoephedrine Hydrochloride). A white or almost white, crystalline powder or colourless crystals. Freely soluble in water and in alcohol; sparingly soluble in dichloromethane. Protect from light.

USP 31 (Pseudoephedrine Hydrochloride). A fine, white to off-white crystalline powder, having a faint characteristic odour. Soluble 1 in 0.5 of water, 1 in 3.6 of alcohol, 1 in 91 of chloroform, and 1 in 7000 of ether. pH of a 5% solution in water is between 4.6 and 6.0. Store in airtight containers. Protect from light.

Pseudoephedrine Sulfate *(USAN, rINNM)*
Pseudoéphédrine, Sulfate de; Pseudoephedrine Sulphate *(BANM)*; Pseudoephedrini Sulfas; Sch-4855; Sulfato de pseudoefedrina.

Псевдоэфедрина Сульфат

$(C_{10}H_{15}NO)_2,H_2SO_4$ = 428.5.

CAS — 7460-12-0.

ATC — R01BA02.

ATC Vet — QR01BA02.

Pharmacopoeias. In *US*.

USP 31 (Pseudoephedrine Sulfate). Odourless, white crystals or crystalline powder. Freely soluble in alcohol. pH of a 5% solution in water is between 5.0 and 6.5. Store in airtight containers. Protect from light.

Adverse Effects and Precautions
As for Ephedrine, p.1558. The commonest adverse effects of pseudoephedrine include tachycardia, anxiety, restlessness, and insomnia; skin rashes and urinary retention have occasionally occurred. Hallucinations have been reported rarely, particularly in children.

◊ In response to reports in the USA of overdosages associated with cough and cold medications, the CDC and the National Association of Medical Examiners investigated deaths in infants aged under 12 months associated with such use; 3 cases were identified. All 3 infants had high concentrations of pseudoephedrine in postmortem blood samples, 2 had detectable blood concentrations of dextromethorphan and paracetamol, and 1 was also found to have detectable concentrations of doxylamine. None of the deaths were determined to be intentional. Two infants had evidence of respiratory infection upon autopsy; no cardiac abnormalities were found in any of the infants.[1]

1. CDC. Infant deaths associated with cough and cold medications—two States, 2005. *MMWR* 2007; **56:** 1–4. Also available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5601a1.htm (accessed 19/04/07)

Abuse. Acute psychosis and visual and tactile hallucinations have been reported[1] in an 18-year-old male after intravenous misuse of pseudoephedrine hydrochloride. Pseudoephedrine has also been used for the illicit manufacture of street stimulants such as metamfetamine (p.2158).

For reference to toxic effects after long-term use of over-the-counter preparations containing sympathomimetics, such as pseudoephedrine, see under Ephedrine, p.1558.

1. Sullivan G. Acute psychosis following intravenous abuse of pseudoephedrine: a case report. *J Psychopharmacol* 1996; **10:** 324–5.

Breast feeding. The American Academy of Pediatrics[1] states that, although usually compatible with breast feeding, preparations used by breast-feeding mothers that contain pseudoephedrine with dexbrompheniramine maleate have resulted in crying, irritability, and poor sleep patterns in the infant.

The concentrations of pseudoephedrine and triprolidine in plasma and breast milk of 3 mothers for up to 48 hours after ingestion of a preparation containing pseudoephedrine hydrochloride 60 mg with triprolidine hydrochloride 2.5 mg have been studied.[2] Concentrations of pseudoephedrine in milk were consistently higher than in plasma; the half-life in both fluids was between 4.2 and 7.0 hours. Assuming a generous milk secretion of 500 mL over 12 hours it was calculated that the excreted dose was the equivalent of 250 to 330 micrograms of pseudoephedrine base, or 0.5 to 0.7% of the dose ingested by the mothers. Triprolidine did not appear to be concentrated in breast milk. The amounts of pseudoephedrine and triprolidine distributed into breast milk were probably not high enough to warrant cessation of breast feeding.

A small, randomised, crossover study concluded that a single dose of 60 mg pseudoephedrine hydrochloride decreased 24-hour milk production by 24%. The authors of the study suggested that pseudoephedrine might be of benefit for suppressing excess milk production.[3]

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 05/01/07)
2. Findlay JWA, *et al*. Pseudoephedrine and triprolidine in plasma and breast milk of nursing mothers. *Br J Clin Pharmacol* 1984; **18:** 901–6.
3. Aljazaf K, *et al*. Pseudoephedrine: effects on milk production in women and estimation of infant exposure via breastmilk. *Br J Clin Pharmacol* 2003; **56:** 18–24.

Convulsions. A child who suffered a generalised seizure after ingesting a large quantity of pseudoephedrine hydrochloride tablets was believed to be the first report of convulsions associated with overdose of a preparation containing the drug as a single ingredient.[1]

1. Clark RF, Curry SC. Pseudoephedrine dangers. *Pediatrics* 1990; **85:** 389–90.

Effects on the gastrointestinal tract. Ischaemic colitis has been reported[1-3] after acute or chronic use of pseudoephedrine in combination cold and allergy preparations. In one case[3] the authors suggested that use with tramadol may have contributed to adrenergic vasoconstriction by inhibition of noradrenaline reuptake.

1. Dowd J, *et al*. Ischemic colitis associated with pseudoephedrine: four cases. *Am J Gastroenterol* 1999; **94:** 2430–4.
2. Lichtenstein GR, Yee NS. Ischemic colitis associated with decongestant use. *Ann Intern Med* 2000; **132:** 682.
3. Traino AA, *et al*. Probable ischemic colitis caused by pseudoephedrine with tramadol as a possible contributing factor. *Ann Pharmacother* 2004; **38:** 2068–70.

Effects on mental function. Adverse mental effects (particularly in children) have been associated with combination preparations containing pseudoephedrine.[1-5] See also Abuse, above.

1. Leighton KM. Paranoid psychosis after abuse of Actifed. *BMJ* 1982; **284:** 789–90.
2. Sankey RJ, *et al*. Visual hallucinations in children receiving decongestants. *BMJ* 1984; **288:** 1369.
3. Stokes MA. Visual hallucinations in children receiving decongestants. *BMJ* 1984; **288:** 1540.