Naphcon-A; Opcon-A; ***Hung.:*** Fervex; Neo Citran; ***India:*** Avil Expectorant; Cosavil; Dristan Nasal Drops; ***Indon.:*** Flamergi; Isotic Azora; Naphcon-A; ***Israel:*** Tussosedan; ***Ital.:*** Nafcon A†; Senodin-AN; Stillergy; Tetramil; Triaminic; Triaminicflu; ***Malaysia:*** Naphcon-A; ***Mex.:*** Eyrasil; Istasol; Mirus; Opcon-A; Solutina; ***NZ:*** Naphcon-A; Visine Allergy; ***Philipp.:*** Deconcon A; Naphcon-A; Optaphen; ***Pol.:*** Fervex; Theraflu ExtraGRIP; ***Rus.:*** Rinzasip (Ринзасип); TheraFlu Flu and Cold (ТераФлю от Гриппа и Простуды Экстра); ***S.Afr.:*** Calasthetic; Coff-Up; Degoran; Dristan Decongestant Nasal Mist; ***Singapore:*** Naphcon-A; ***Switz.:*** Neo Citran Grippe/refroidissement; ***Thai.:*** Naphcon-A; ***Turk.:*** Antibeksin; ***UAE:*** Histol Exp; ***USA:*** Dristan Nasal Spray; Nafazair A†; Naphazoline Plus; Naphcon-A; Naphoptic-A; Ocuhist; Opcon-A; Poly-Histine†; Scot-Tussin Original 5-Action; TheraFlu Cold & Cough; Tussirex; Visine-A; ***Venez.:*** Robitessin AC†; Soluclear; Tempragrip.

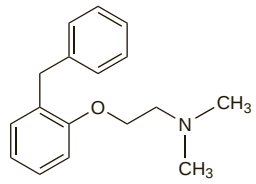
Phenyltoloxamine Citrate *(BANM, rINNM)*

C-5581H (phenyltoloxamine); Citrato de feniltoloxamina; Phényltoloxamine, Citrate de; Phenyltoloxamini Citras; Phenyltolyloxamine Citrate; PRN (phenyltoloxamine). 2-(2-Benzylphenoxy)-*NN*-dimethylethylamine dihydrogen citrate.

Фенилтолоксамина Цитрат

$C_{17}H_{21}NO,C_6H_8O_7$ = 447.5.

CAS — 92-12-6 (phenyltoloxamine); 1176-08-5 (phenyltoloxamine citrate).



(phenyltoloxamine)

Pharmacopoeias. In *US.*

USP 31 (Phenyltoloxamine Citrate). A white crystalline powder. Very soluble in boiling water; slightly soluble in cold water and in alcohol; practically insoluble in cold acetone, in solvent ether, and in toluene. pH of a 1% solution in water is between 3.2 and 4.2.

Profile

Phenyltoloxamine citrate, a monoethanolamine derivative, is a sedating antihistamine (p.561). It is usually given orally in combination preparations with a decongestant or analgesic. Phenyltoloxamine citrate has been used in nasal preparations. Phenyltoloxamine polistirex has also been given orally.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Austria:*** Codipront; ***Braz.:*** Afebrin†; Setux; Setux Expectorante; ***Canad.:*** Omni-Tuss†; Tussionex; ***Chile:*** Codipront†; Matinor; Rinofrim†; Sinutab; Tossin†; ***Cz.:*** Codipront†; ***Fr.:*** Biocidan; Netux†; ***Ger.:*** Codipront†; ***Hong Kong:*** Codipront; ***Indon.:*** Codipront; Codipront cum Expectorant; ***Israel:*** Codivis; ***Ital.:*** Codipront†; ***Philipp.:*** Sinutab; ***Port.:*** Codipront; ***S.Afr.:*** Adco-Sinal Co; Dequa-Flu; Pholtex Linctus; Sinustop; Sinustop with Codeine; Sinutab; Sinutab with Codeine; Suncodin; ***Singapore:*** Codipront†; ***Spain:*** Codipront†; ***Switz.:*** Codipront; Codipront cum Expectorans†; ***Thai.:*** Codipront†; ***Turk.:*** Benzoleks; ***USA:*** Aceta-Gesic; Anabar; Be-Flex Plus; BP Poly-650; By-Ache; Cafgesic Forte; Chlorex-A; Combiflex; Combiflex ES; Comhist LA; Durabac Forte; Duraxin; Flextra; Hyflex; Lagesic; Levacet; Lobac; Major-gesic; Mobigesic; Momentum; Nalex-A; Pain-gesic; Percogesic; Phenylgesic; Poly-Histine†; Relagesic; Staflex; Tetra-Mag; ***Venez.:*** Codipront; Efoxamina†.

Pimethixene *(rINN)*

BP-400; Piméthixène; Pimethixenum; Pimetixene; Pimetixeno. 9-(1-Methyl-4-piperidylidene)thioxanthene.

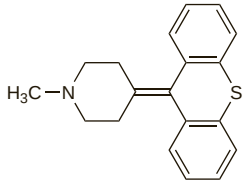
Пиметиксен

$C_{19}H_{19}NS$ = 293.4.

CAS — 314-03-4.

ATC — R06AX23.

ATC Vet — QR06AX23.



Profile

Pimethixene is reported to be a sedating antihistamine (p.561) and an inhibitor of serotonin. It is given to children in usual oral doses of about 1.8 to 5.5 mg daily for coughs. It has been used as a sedative and for the treatment of respiratory disorders.

Preparations

Proprietary Preparations (details are given in Part 3)

Braz.: Ansiotex; Muricalm; Sonin†; ***Fr.:*** Calmixene.

Multi-ingredient: ***Braz.:*** Santussal.

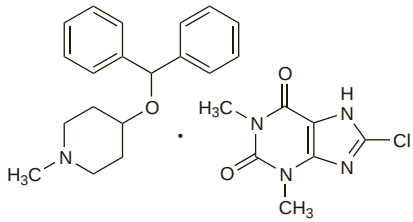
Piprinhydrinate *(BAN, rINN)*

Diphenylpyraline Teoclate; Diphenylpyraline Theoclate; Piprinhidrinato; Piprinhydrinatum. The diphenylpyraline salt of 8-chlorotheophylline; 4-Benzhydryloxy-1-methylpiperidine salt of 8-chlorotheophylline.

Пипрингидринат

$C_{19}H_{23}NO,C_7H_7ClN_4O_2$ = 496.0.

CAS — 606-90-6.



Profile

Piprinhydrinate, a piperidine derivative, is an antihistamine (p.561) given orally as an ingredient of compound preparations for the symptomatic relief of coughs and the common cold.

Preparations

Proprietary Preparations (details are given in Part 3)

Hong Kong: Plokon†; ***Thai.:*** Plokon.

Multi-ingredient: ***Austria:*** Waldheim Influvidon; ***Ger.:*** Kolton grippale N†.

Promethazine *(BAN, rINN)*

Prometatsiini; Prometazin; Prometazina; Prométhazine; Promethazinum. Dimethyl (1-methyl-2-phenothiazin-10-ylethyl)amine.

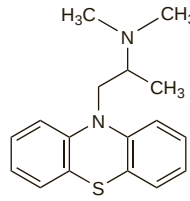
Прометазин

$C_{17}H_{20}N_2S$ = 284.4.

CAS — 60-87-7.

ATC — D04AA10; R06AD02.

ATC Vet — QD04AA10; QR06AD02.



Promethazine Hydrochloride *(BANM, rINNM)*

Diprazinum; Hidrocloruro de prometazina; Proazamine Chloride; Prometatsiinihydrokloridi; Prometazin Hidroklorür; Prometazin-hidroklorid; Prometazinhydroklorid; Prometazino hidrochloridas; Prometazyny chlorowodorek; Prométhazine, chlorhydrate de; Promethazin-hydrochlorid; Promethazini hydrochloridum; Promethazinium Chloride.

Прометазина Гидрохлорид

$C_{17}H_{20}N_2S$,HCl = 320.9.

CAS — 58-33-3.

ATC — D04AA10; R06AD02.

ATC Vet — QD04AA10; QR06AD02.

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

Ph. Eur. 6.2 (Promethazine Hydrochloride). A white or faintly yellowish, crystalline powder. Very soluble in water; freely soluble in alcohol and in dichloromethane. A 10% solution in water has a pH of 4.0 to 5.0. Protect from light.

USP 31 (Promethazine Hydrochloride). A white to faint yellow, practically odourless, crystalline powder. Slowly oxidises and acquires a blue colour on prolonged exposure to air. Freely soluble in water, in hot dehydrated alcohol, and in chloroform; practically insoluble in acetone, in ether, and in ethyl acetate. pH of a 5% solution in water is between 4.0 to 5.0. Store in airtight containers. Protect from light.

Adsorption. The adsorption of promethazine hydrochloride onto various glass and plastic containers and infusion systems has been studied.[1-4] Factors affecting the degree of adsorption included the particular material tested and the pH of the solution.

1. Kowaluk EA, *et al.* Interactions between drugs and polyvinyl chloride infusion bags. *Am J Hosp Pharm* 1981; **38:** 1308–14.
2. Kowaluk EA, *et al.* Interactions between drugs and intravenous delivery systems. *Am J Hosp Pharm* 1982; **39:** 460–7.
3. Rhodes RS, *et al.* Stability of meperidine hydrochloride, promethazine hydrochloride, and atropine sulfate in plastic syringes. *Am J Hosp Pharm* 1985; **42:** 112–5.
4. Martens HJ, *et al.* Sorption of various drugs in polyvinyl chloride, glass, and polyethylene-lined infusion containers. *Am J Hosp Pharm* 1990; **47:** 369–73.

Incompatibility. Solutions of promethazine hydrochloride are incompatible with alkaline substances, which precipitate the insoluble promethazine base. Compounds reported to be incompatible with promethazine hydrochloride include aminophylline, barbiturates, benzylpenicillin salts, carbenicillin sodium, chloramphenicol sodium succinate, chlorothiazide sodium, cefmetazole sodium, cefoperazone sodium, cefotetan disodium, dimenhydrinate, doxorubicin hydrochloride (in a liposomal formulation), furosemide, heparin sodium, hydrocortisone sodium succinate, meticillin sodium, morphine sulfate, nalbuphine hydrochloride, and some contrast media and parenteral nutrient solutions.

Promethazine Teoclate *(BAN, rINN)*

Prométhazine, Téoclate de; Promethazine Theoclate; Promethazini Teoclas; Teoclato de prometazina. The promethazine salt of 8-chlorotheophylline .

Прометазина Теоклат

$C_{17}H_{20}N_2S,C_7H_7ClN_4O_2$ = 499.0.

CAS — 17693-51-5.

ATC — D04AA10; R06AD02.

ATC Vet — QD04AA10; QR06AD02.

Pharmacopoeias. In *Br.*

BP 2008 (Promethazine Teoclate). A white or almost white, odourless or almost odourless powder. Very slightly soluble in water; sparingly soluble in alcohol; freely soluble in chloroform; practically insoluble in ether. Protect from light.

Adverse Effects

As for the sedating antihistamines in general, p.561.

Cardiovascular adverse effects are more commonly seen after injection, and bradycardia, tachycardia, transient minor increases in blood pressure, and occasional hypotension have all been reported with promethazine hydrochloride. Jaundice and blood dyscrasias have been reported, and extrapyramidal effects may occur at high doses.

Venous thrombosis has been reported at the site of intravenous injections, and arteriospasm and gangrene may follow inadvertent intra-arterial injection.

Overdosage. A toxic neurological syndrome, which included CNS depression, acute excitomotor manifestations, ataxia and visual hallucinations, plus peripheral antimuscarinic effects developed in 2 children aged 44 months and 16 months after topical application of a 2% promethazine cream providing between 12.9 and 26 mg/kg.[1] The older child had also received hydroxyzine 10 mg orally 1 hour earlier.

1. Shawn DH, McGuigan MA. Poisoning from dermal absorption of promethazine. *Can Med Assoc J* 1984; **130:** 1460–1.

Sudden infant death syndrome. Although some early reports raised the possibility of an association between the use of phenothiazine antihistamines and the sudden infant death syndrome (SIDS) this has not been confirmed. Following an initial report that 4 of 7 infants with SIDS had been given alimemazine before death and that a series of severe apnoeic crises had been observed in the twin of a SIDS victim given promethazine,[1] the same workers studied 52 SIDS victims, 36 near-miss infants (those who had experienced severe unexplained episodes of cyanosis or pallor during sleep), and 175 control subjects to investigate the role of nasopharyngitis and phenothiazines in this syndrome.[2] They found that there was no difference in the incidence of nasopharyngitis between the 3 groups, but the proportion of infants given phenothiazines was higher in both the SIDS group (23%) and the near-miss group (22%) than in the control group (2%). In a subsequent study,[3] they found that the incidence of central and obstructive sleep apnoeas was increased in 4 healthy infants given promethazine for 3 days, although the duration of the attacks was unaltered and generally short, with a range of 3 to 10 seconds. A report on behalf of the European Commission,[4] stated that no link between sudden deaths in infants and drug use had been confirmed by national drug monitoring centres. It was likely that the risk of apnoea was associated with all sedative drugs, especially in overdose.[4] Previously, phenothiazine-induced hyperthermia had been proposed as a contributory factor in SIDS.[5]

For general precautions regarding the use of antihistamines in children, see p.562.

1. Kahn A, Blum D. Possible role of phenothiazines in sudden infant death. *Lancet* 1979; **ii:** 364–5.