

Pharmacopoeias. In *US*.

USP 31 (Methdilazine Hydrochloride). A light tan crystalline powder having a slight characteristic odour. Soluble 1 in 2 of water and of alcohol, 1 in 6 of chloroform, and 1 in 1 of 0.1N hydrochloric acid and of 0.1N sodium hydroxide solution; practically insoluble in ether. pH of a 1% solution in water is between 4.8 and 6.0. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

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

Interactions

As for the sedating antihistamines in general, p.563.

Uses and Administration

Methdilazine, a phenothiazine derivative, is a sedating antihistamine with antimuscarinic and sedative activity. Methdilazine is also reported to have serotonin-antagonist properties.

Methdilazine hydrochloride is used for the symptomatic relief of hypersensitivity reactions and particularly for the control of pruritic skin disorders (p.565). An oral dose of 8 mg has been given 2 to 4 times daily. Methdilazine base has been used in similar doses. For children's doses, see below.

Administration in children. Methdilazine hydrochloride has been used in children for symptomatic relief of hypersensitivity reactions and particularly for the control of pruritic skin disorders. Oral doses of 4 mg given 2 to 4 times daily have been used in children aged 3 to 12 years. However, lower daily doses have also been used: children aged 3 to 6 years may be given 300 micrograms/kg daily (maximum 8 mg daily) and those aged 6 to 12 years, 4 mg twice daily.

Preparations

USP 31: Methdilazine Hydrochloride Syrup; Methdilazine Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)

Austral.: Dilosyn†; **Denm.:** Tacryl†; **India:** Dilosyn.

Multi-ingredient: **India:** Dilosyn Expectorant.

Mizolastine (*BAN, rINN*)

Mitsolastini; Mizolastin; Mizolastina; Mizolastinum; SL-85.0324-00. 2-[[1-[1-(4-Fluorobenzyl)-1H-benzimidazol-2-yl]-4-piperidyl(methyl)amino]pyrimidin-4(1H)-one.

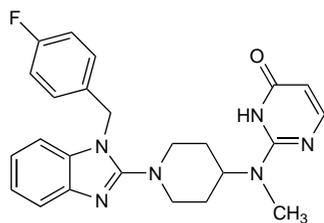
Мизоластин

$C_{24}H_{25}FN_6O = 432.5$.

CAS — 108612-45-9.

ATC — R06AX25.

ATC Vet — QR06AX25.

**Adverse Effects and Precautions**

As for the non-sedating antihistamines in general, p.561. Mizolastine has only a weak potential to prolong the QT interval (see also Arrhythmias, p.562) and has not been associated with arrhythmias. However, the manufacturers have warned against the use of mizolastine in patients with significant cardiac or hepatic disease, with hypokalaemia or other electrolyte imbalance, or with known or suspected QT prolongation. Use with drugs liable to interfere with the hepatic metabolism of mizolastine or with other potentially arrhythmogenic drugs should also be avoided (see under Interactions, below).

Interactions

As for the non-sedating antihistamines in general, p.563. Moderate increases in plasma concentrations of mizolastine have been reported with erythromycin and ketoconazole; use with macrolide antibacterials or sys-

temic imidazole antifungals is contra-indicated by the manufacturer. They also advise against use of mizolastine with drugs known to prolong the QT interval, such as class I and III antiarrhythmics.

Other potent inhibitors of or substrates for the hepatic metabolism of mizolastine include cimetidine, ciclosporin, and nifedipine; caution is advised if given together.

Pharmacokinetics

Mizolastine is rapidly absorbed from the gastrointestinal tract with peak plasma concentrations being reached after about 1.5 hours. Plasma protein binding is about 98%. The mean elimination half-life is about 13 hours. Mizolastine is mainly metabolised by glucuronidation although other metabolic pathways are involved, including metabolism by the cytochrome P450 isoenzyme CYP3A4, with the formation of inactive hydroxylated metabolites.

◇ References.

- Rosenzweig P, *et al.* Pharmacodynamics and pharmacokinetics of mizolastine (SL 85.0324), a new non-sedative H₁ antihistamine. *Ann Allergy* 1992; **69**: 135-9.
- Lebrun-Vignes B, *et al.* Clinical pharmacokinetics of mizolastine. *Clin Pharmacokinet* 2001; **40**: 501-7.

Uses and Administration

Mizolastine is a non-sedating antihistamine with a long duration of action. It does not have significant antimuscarinic actions; it is reported to have mast-cell stabilising properties. Mizolastine is used for the symptomatic relief of allergic conditions including rhinitis (p.565), conjunctivitis (p.564), and skin disorders such as urticaria (p.565). The oral dose is 10 mg daily.

◇ References.

- Leynadier F, *et al.* Efficacy and safety of mizolastine in seasonal allergic rhinitis. *Ann Allergy Asthma Immunol* 1996; **76**: 163-8.
- Brostoff J, *et al.* Efficacy of mizolastine, a new antihistamine, compared with placebo in the treatment of chronic idiopathic urticaria. *Allergy* 1996; **51**: 320-5.
- Stern MA, *et al.* Can an antihistamine delay appearance of hay-fever symptoms when given prior to pollen season? *Allergy* 1997; **52**: 440-4.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Mistamine†; **Austria:** Mizoll; **Belg.:** Mistamine†; Mizollen; **Chile:** Mistamine†; **Cz.:** Mizollen†; **Denm.:** Mizoll; **Fin.:** Mizollen†; **Fr.:** Mizollen; **Ger.:** Mizollen; Zolim; **Gr.:** Mizollen; Oriens; **Hung.:** Mizollen†; **India:** Elina; **Irl.:** Mistamine†; **Israel:** Mizollen; **Ital.:** Mizollen; Zolistam; **Mex.:** Mistamine; **Neth.:** Mizollen; **Pol.:** Mizollen; **Port.:** Mistamine†; Mizollen; Zolistam; **S.Afr.:** Mizollen; **Spain:** Mistamine†; Mizollen; Zolistan; **Swed.:** Mizollen; **Switz.:** Mistamine†; Mizollen; **UK:** Mizollen.

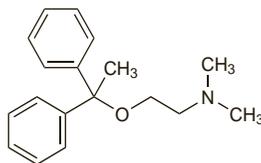
Moxastine Teoclate (*rINN*)

Mephenhydramine Theoclate; Mephenhydrinate; Moxastine, Téoclate de; Moxastine Theoclate; Moxastini Teoclas; Teoclate de moxastina. 2-(1,1-Diphenylethoxy)-N,N-dimethylethylamine 8-chlorotheophyllinate.

Моксастина Теоклат

$C_{18}H_{23}NO_6Cl_4 = 472.0$.

CAS — 3572-74-5 (moxastine); 21661-62-1 (moxastine teoclate).



(moxastine)

Profile

Moxastine teoclate is an antihistamine with antiemetic properties. It is used to treat nausea and vertigo associated with Ménière's disease and other vestibular disorders, and for the prevention and treatment of motion sickness.

Preparations

Proprietary Preparations (details are given in Part 3)

Cz.: Kinedryl.

Multi-ingredient: **Cz.:** Nokinal†.

Niaprazine (*rINN*)

1709-CERM; Niaprazina; Niaprazinum. N-[3-(4-p-Fluorophenyl)piperazin-1-yl)-1-methylpropyl]nicotinamide.

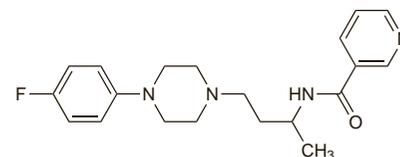
Ниапразин

$C_{20}H_{25}FN_4O = 356.4$.

CAS — 27367-90-4.

ATC — N05CM16.

ATC Vet — QN05CM16.

**Profile**

Niaprazine, a piperazine derivative, is an antihistamine (p.561) used in children for its sedative and hypnotic properties. The usual oral dose is 1 mg/kg at night.

Preparations

Proprietary Preparations (details are given in Part 3)

Fr.: Napron; **Ital.:** Napron.

Olopatadine Hydrochloride (*BAN, USAN, rINN*)

ALO-4943A; Hidrocloruro de olopatadina; KW-4679; Olopatadin Hidroklorür; Olopatadine, Chlorhydrate d'; Olopatadini Hydrochloridum. 11-[(Z)-3-(Dimethylamino)propylidene]-6,11-dihydrodibenz[e,j]oxepin-2-acetic acid hydrochloride.

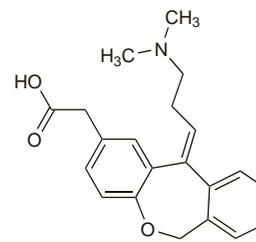
Олопатадина Гидрохлорид

$C_{21}H_{23}NO_3 \cdot HCl = 373.9$.

CAS — 113806-05-6 (olopatadine); 140462-76-6 (olopatadine hydrochloride).

ATC — R01AC08; S01GX09.

ATC Vet — Q501GX09.



(olopatadine)

Adverse Effects and Precautions

As for the antihistamines in general, p.561. Headache and stinging or burning of the eye have occurred after ocular use.

Uses and Administration

Olopatadine hydrochloride is an antihistamine with mast-cell stabilising properties. It is used twice daily as eye drops containing the equivalent of 0.1% of olopatadine base in the treatment of allergic conjunctivitis (p.564) in adults and children aged three years and over.

◇ References.

- Anonymous. Olopatadine for allergic conjunctivitis. *Med Lett Drugs Ther* 1997; **39**: 108-9.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Patanol; **Austral.:** Patanol; **Belg.:** Opatanol; **Braz.:** Patanol; **Canad.:** Patanol; **Chile:** Patanol; **Cz.:** Opatanol; **Denm.:** Opatanol; **Fin.:** Opatanol; **Fr.:** Opatanol; **Ger.:** Opatanol; **Gr.:** Opatanol; **Hong Kong:** Patanol; **Hung.:** Opatanol; **Indon.:** Patanol; **Irl.:** Opatanol; **Israel:** Patanol; **Ital.:** Opatanol; **Jpn.:** Allelock; **Malaysia:** Patanol; **Mex.:** Patanol; **Neth.:** Opatanol; **Norw.:** Opatanol; **NZ:** Patanol; **Philipp.:** Patanol; **Port.:** Opatanol; **Rus.:** Opatanol (Опатанол); **S.Afr.:** Patanol; **Singapore:** Patanol; **Spain:** Opatanol; **Swed.:** Opatanol; **Switz.:** Opatanol; **Thai.:** Patanol; **Turk.:** Patanol; **UK:** Opatanol; **USA:** Pataday; Patanol; **Venez.:** Patanol.

Oxatomide (BAN, USAN, rINN)

Oksatomidi; Oxatomid; Oxatomida; Oxatomidum; R-35443. 1-[3-(4-Benzhydryl)piperazin-1-yl)propyl]benzimidazolin-2-one.

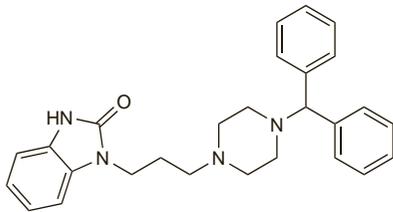
ОКСАТОМИД

$C_{27}H_{30}N_4O = 426.6$.

CAS — 60607-34-3.

ATC — R06AE06.

ATC Vet — QR06AE06.

**Profile**

Oxatomide, a piperazine derivative, is a sedating antihistamine (p.561) that has also been reported to have mast-cell stabilising properties. It is used for the symptomatic relief of allergic conditions including urticaria (p.565), rhinitis (p.565), and conjunctivitis (p.564). Oxatomide is given as the anhydrous substance or as the monohydrate; doses are expressed as the anhydrous substance. Oxatomide monohydrate 1.04 mg is equivalent to about 1 mg of anhydrous oxatomide. The usual oral dose is 30 mg twice daily. The hydrate has also been applied topically but, as with other antihistamines, there is a risk of sensitisation.

Effects on the nervous system. Acute dystonic reactions and long-lasting impaired consciousness were associated with oxatomide therapy in 6 children.¹ Impaired consciousness varied from lethargy and somnolence to a clinical picture resembling encephalitis and persisted for 2 days or more in 3 patients. Plasma-oxatomide concentrations were measured in 3 patients and found to be high, although 2 of these had been given the recommended dose.

1. Casteels-Van Daele M, *et al.* Acute dystonic reactions and long-lasting impaired consciousness associated with oxatomide in children. *Lancet* 1986; **i**: 1204-5.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Cenacert†; Fensedy†; **Tinset;** **Austria:** Tinset†; **Belg.:** Tinset†; **Chile:** Tinset†; **Fr.:** Tinset†; **Gr.:** Tinset†; **Hong Kong:** Tinset†; **Indon.:** Oxtin†; **Italy:** Tinset†; **Jpn.:** Celtect†; **Mex.:** Tinset†; **Neth.:** Tinset†; **Port.:** Tinset†; **S.Afr.:** Tinset†; **Spain:** Cobiona; Oxatokey†; **Thai.:** Tinset.

Multi-ingredient Arg.: Causalon Bronqual; Causalon Grip; Letondal.

Oxomemazine (rINN)

Oxomemazina; Oxomémazine; Oxomemazinum; RP-6847; Tri-mepazine 55-Dioxide. 10-(3-Dimethylamino-2-methylpropyl)phenothiazine 5,5-dioxide.

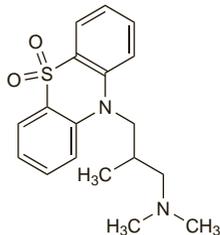
ОКСОМЕАЗИН

$C_{18}H_{22}N_2O_2S = 330.4$.

CAS — 3689-50-7.

ATC — R06AD08.

ATC Vet — QR06AD08.

**Oxomemazine Hydrochloride** (rINN)

Hidrocloruro de oxomemazina; Oxomémazine, Chlorhydrate d'; Oxomemazini Hydrochloridum.

ОКСОМЕАЗИНА Гидрохлорид

$C_{18}H_{22}N_2O_2S \cdot HCl = 366.9$.

CAS — 4784-40-1.

ATC — R06AD08.

ATC Vet — QR06AD08.

Pharmacopoeias. In *Fr.*

Profile

Oxomemazine, a phenothiazine derivative, is a sedating antihistamine (p.561) used for the symptomatic relief of hypersensitivity reactions and in pruritic skin disorders (p.565). It is also an

ingredient of compound preparations for the symptomatic treatment of coughs and the common cold (p.564).

Oxomemazine has been given orally in doses ranging from about 5 to 13 mg daily in divided doses. It has also been given by the rectal route. Oxomemazine hydrochloride has been used similarly by mouth.

Preparations

Proprietary Preparations (details are given in Part 3)

Fr.: Toplexil†; **Neth.:** Toplexil.

Multi-ingredient Belg.: Toplexil†; **Braz.:** Expec; Iodesin; Iodeto de Potassium Composto†; KI-Expectorante; Tirasoset†; **Toplexil;** **Tussol†;** **Indon.:** Comtusi; **Toplexil;** **Israel:** Oxacatin; **Toplexil;** **Switz.:** Toplexil.

Phenindamine Tartrate (BAN, USAN, rINN)

Phenindamine Acid Tartrate; Phénindamine, Tartrate de; Phenindamini Tartras; Phenindaminium Tartrate; Tartrato de fenindamina. 1,2,3,4-Tetrahydro-2-methyl-9-phenyl-2-azafluorene hydrogen tartrate; 2,3,4,9-Tetrahydro-2-methyl-9-phenyl-1H-indeno[2,1-c]pyridine hydrogen tartrate.

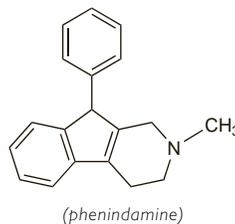
Фениндамина Тартрат

$C_{19}H_{19}N \cdot C_4H_6O_6 = 411.4$.

CAS — 82-88-2 (phenindamine); 569-59-5 (phenindamine tartrate).

ATC — R06AX04.

ATC Vet — QR06AX04.

**Pharmacopoeias.** In *Br.*

BP 2008 (Phenindamine Tartrate). A white or almost white, odourless or almost odourless, voluminous powder. Sparingly soluble in water; slightly soluble in alcohol; practically insoluble in chloroform and in ether. A 1% solution in water has a pH of 3.4 to 3.9. Protect from light.

Adverse Effects and Precautions

As for the sedating antihistamines in general, p.561. Phenindamine tartrate may have a stimulant effect in certain individuals; to avoid the possibility of insomnia patients may be advised to take the last dose of the day several hours before retiring.

Interactions

As for the sedating antihistamines in general, p.563.

Uses and Administration

Phenindamine, a piperidine derivative, is a sedating antihistamine; however it may be mildly stimulating in certain individuals. It is used as the tartrate for the symptomatic relief of allergic conditions including urticaria (p.565) and rhinitis (p.565), and as an ingredient of compound preparations for coughs and the common cold (p.564).

Phenindamine tartrate is given in oral doses of 25 mg every 4 to 6 hours, up to a maximum of 150 mg daily. Children over 6 years of age have been given half these doses.

Preparations

Proprietary Preparations (details are given in Part 3)

USA: Nolahist.

Multi-ingredient USA: P-V-Tussin.

Pheniramine (BAN, rINN)

Feniramiini; Feniramin; Feniramina; Phéniramine; Pheniraminum; Prophepyridamine. *NN*-Dimethyl-3-phenyl-3-(2-pyridyl)propylamine.

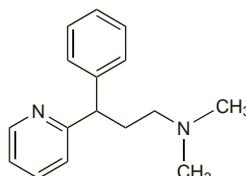
Фенирамин

$C_{16}H_{20}N_2 = 240.3$.

CAS — 86-21-5.

ATC — R06AB05.

ATC Vet — QR06AB05.

**Pheniramine Aminosalicilate** (BAN, rINN)

Aminosalicilato de feniramina; Pheniramine *p*-Aminosalicilate; Pheniramine 4-Aminosalicilate; Phéniramine, Aminosalicilate de; Pheniramine Para-aminosalicilate; Pheniramiini Aminosalicilas. Pheniramine 4-amino-2-hydroxybenzoate.

Фенирамина Аминосалисилат

$C_{16}H_{20}N_2 \cdot C_7H_7NO_3 = 393.5$.

CAS — 3269-83-8.

ATC — R06AB05.

ATC Vet — QR06AB05.

Pheniramine Maleate (BAN, USAN, rINN)

Feniramiinimaleaatti; Feniramin Hidrojen Maleat; Feniramin Maleat; Feniramin maleinát; Feniraminmaleat; Feniramin-maleát; Feniraminomaleatas; Maleato de feniramina; Phéniramine, maléate de; Pheniramiini maleas; Pheniraminium Maleate; Prophepyridamine Maleate. Pheniramine hydrogen maleate.

Фенирамина Малеат

$C_{16}H_{20}N_2 \cdot C_4H_4O_4 = 356.4$.

CAS — 132-20-7.

ATC — R06AB05.

ATC Vet — QR06AB05.

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

Ph. Eur. 6.2 (Pheniramine Maleate). A white or almost white, crystalline powder. Very soluble in water; freely soluble in alcohol, in dichloromethane, and in methyl alcohol. M.p. 106° to 109°. A 1% solution in water has a pH of 4.5 to 5.5. Protect from light.

USP 31 (Pheniramine Maleate). A white crystalline powder having a faint amine-like odour. Soluble in water and in alcohol. pH of a 1% solution in water is between 4.5 and 5.5.

Adverse Effects and Precautions

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

Abuse. References to the abuse of oral pheniramine.

1. Jones IH, *et al.* Pheniramine as an hallucinogen. *Med J Aust* 1973; **1**: 382-6.

2. Csillag ER, Landauer AA. Alleged hallucinogenic effect of a toxic overdose of an antihistamine preparation. *Med J Aust* 1973; **1**: 653-4.

3. Buckley NA, *et al.* Pheniramine—a much abused drug. *Med J Aust* 1994; **160**: 188-92.

Pregnancy. For discussion of the use of antihistamines, including pheniramine, in pregnancy, see p.563.

Interactions

As for the sedating antihistamines in general, p.563.

Pharmacokinetics

◇ The pharmacokinetics of pheniramine and its metabolites, *N*-desmethylpheniramine and *N*-didesmethylpheniramine, were investigated in 6 healthy subjects.¹ After oral doses of pheniramine aminosalicilate, peak-plasma pheniramine concentrations were reached in 1 to 2.5 hours. The terminal half-life ranged between 8 and 17 hours after intravenous doses (pheniramine maleate) and 16 and 19 hours after oral doses. The total recovery of pheniramine as unchanged drug and metabolites from the urine was 68 to 94% of the intravenous dose and 70 to 83% of the oral dose.

1. Witte PU, *et al.* Pharmacokinetics of pheniramine (Avil) and metabolites in healthy subjects after oral and intravenous administration. *Int J Clin Pharmacol Ther Toxicol* 1985; **23**: 59-62.

Uses and Administration

Pheniramine, an alkylamine derivative, is a sedating antihistamine with antimuscarinic and moderate sedative properties.

It is used as the maleate for the symptomatic relief of allergic conditions including urticaria and angioedema (p.565), rhinitis (p.565), and conjunctivitis (p.564), and in pruritic skin disorders (p.565). It has also been used for its antiemetic properties in the prevention and control of motion sickness (p.564). Pheniramine maleate is used as an ingredient of compound preparations for the symptomatic treatment of coughs and the common cold (p.564). It is also used in combination with a decongestant in eye and nasal preparations.

Pheniramine maleate is given as a syrup in usual oral doses of 15 to 30 mg two or three times daily. It may also be given as a tablet in doses up to about 45 mg three times daily. In some countries pheniramine maleate has been given parenterally.

The aminosalicilate, the hydrochloride, and the tannate have also been used.

Preparations

USP 31: Naphazoline Hydrochloride and Pheniramine Maleate Ophthalmic Solution.

Proprietary Preparations (details are given in Part 3)

Austral.: Avil; Fenamine†; **Austria:** Avil; **India:** Avil; **Indon.:** Avil; **Ital.:** In-histon†; **Mex.:** Histatext†; **NZ:** Avil†; **Turk.:** Avil; **UAE:** Histol.

Multi-ingredient Arg.: Mira Klonal; Mirus; Refenax Colirio; **Austral.:** Avil Decongestant; Naphcon-A; Visine Allergy with Antihistamine; **Austria:** Neo Citran; **Belg.:** Naphcon-A; **Braz.:** Claril; **Canada:** Ak Vernacon; Calmylin Ace; Citron Chaud DM; Diopticon A; Diorouge; Dristan; Hot Lemon; Hot Lemon Cough and Colds Relief DM; Hot Lemon Relief; Hot Lemon Relief for Cough and Cold; Naphcon-A; Neo Citran A†; Neo Citran Calorie Reduced†; Neo Citran Colds & Flu; Neo Citran DM†; Neo Citran Extra Strength; Neo Citran†; Opcon-A; Pulmorphan; Pulmorphan Pediatric; Robitussin AC; Robitussin with Codeine†; Visine Advance Allergy; **Chile:** Clarimir F; Dessolets; Miral; Mirust†; Naphcon-A; **Cz.:** Fervex; **Fr.:** Fervex; **Ger.:** Konjunktival Thilo†; Rhinosovil†; **Hong Kong:** Konjunktival†;