

if necessary 5 to 10 minutes later. In the treatment of uveitis (p.1515), the eye drops should be instilled two or three times daily, or up to every 3 to 4 hours if required.

The *BNFC* recommends that eye drops containing 0.5% homatropine hydrobromide are used once daily or on alternate days for uveitis in children aged 3 months to 2 years; older children may be given 1 or 2% eye drops twice daily.

Homatropine has also been used as the quaternary ammonium methobromide derivative in the treatment of gastrointestinal spasm and as an adjunct in peptic ulcer disease; homatropine methobromide has also been included in preparations used for the treatment of coughs.

Preparations

BP 2008: Homatropine Eye Drops;

USP 31: Homatropine Hydrobromide Ophthalmic Solution; Homatropine Methylobromide Tablets; Hydrocodone Bitartrate and Homatropine Methylobromide Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Antiespasmodico; Dallapasma; Espasmotropin; Paratropina; **Braz.:** Espasmo Flatol; Novotropina; **Gr.:** Nopar; **Malaysia:** Homa†; **Mex.:** Homasedin†; Homogin; Infalfren Simple; Pasmolit; **Spain:** Homatrop; **Venez.:** Litropina.

Multi-ingredient: **Arg.:** Antispaquina; Asestor; Bellatotal; Bibol Leloup; Bilosan Compuesto†; Carbon Tabs; Colistop; Dimaval; Espasmo Ibupirac†; Espasmo†; Factor AG Antiespasmodico; Hepatodirectol; Ibupirac Fem; Opoenterol†; Paratropina Antigas; Paratropina Compuesta; Sumal; Zimerol; **Braz.:** Analgosedan†; Asmatron†; Atapec†; Belacodid†; Bromalgin†; Calmazin†; Codeverin†; Dipirol†; Enterobion†; Espasalgon†; Espasmo Colic†; Espasmo Luftal; Etaverol†; Flagass Baby; Marsoni†; Migrane; Naquinto†; Pasmalgin†; Plencodan†; Sedalene; Sedalin; Spasmotropin; Tropinal; Vagoplex†; **Chile:** Codelasa; **Hung.:** Bilagit†; Neo-Bilagit; Ridol†; Troparinum; **India:** Dysfur-M†; **Mex.:** Bontal; Contefur†; Coralzul; Dialgin; Facetin-D; Fuzoty†; Neopecsul; Neoxil; Sultroquin†; Tasakal†; Threchop; Trior†; Yodozona; **Philipp.:** Creamalin HM; **Spain:** Cortenema; **Thai.:** Polyzyme-†; **USA:** Hycodan; Hydromet; Hydropane; Tussigon; **Venez.:** Frevagt; Metilfedrin†.

Latanoprost (BAN, USAN, rINN)

Latanoprost; Latanoprostum; PhXA-41; XA-41. Isopropyl (Z)-7-((1*R*,2*R*,3*R*,5*S*)-3,5-dihydroxy-2-[(3*R*)-3-hydroxy-5-phenylpentyl]cyclopentyl)-5-heptenoate.

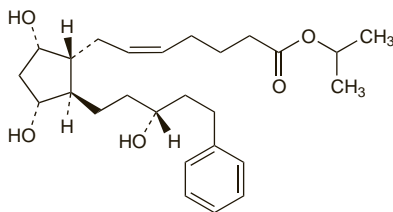
Латанопро́ст

$C_{26}H_{40}O_5 = 432.6$.

CAS — 130209-82-4.

ATC — S01EE01.

ATC Vet — QS01EE01.



Adverse Effects and Precautions

Latanoprost eye drops may produce a gradual increase in the amount of brown pigment in the iris, due to increased melanin content of melanocytes. This change in eye colour is most evident in patients with mixed colour irises, and may be permanent in some patients. The onset of iris pigmentation is usually within the first 8 months of treatment, rarely during the second or third year, and has not been seen after the fourth year of treatment. Darkening, thickening, and lengthening of eye lashes may occur and are reversible upon stopping treatment. Darkening of the palpebral skin has been reported rarely. Ocular irritation, conjunctival hyperaemia, transient punctate epithelial erosions and eyelid oedema may occur; there have also been rare reports of iritis and/or uveitis, and macular oedema. Systemic effects may also occur, see below for further details. Dizziness, headache, arthralgia, and myalgia have also been reported.

Effects on the eyes. Latanoprost has been associated with various adverse effects on the eyes, including case reports of cystoid macular oedema¹ and bilateral optic disc oedema.² Licensed product information states that reports of macular oedema have mainly occurred in aphakic patients, in pseudophakic patients with torn posterior lens capsule or anterior chamber lenses, or in patients with risk factors for cystoid macular oedema such as those with diabetic retinopathy or retinal vein occlusion.

Herpes simplex dendritic keratitis developed in 2 patients during latanoprost therapy.³ The author suggested that the biochemical changes in the cornea caused by latanoprost may predispose to herpes keratitis.

1. Wardrop DRA, Wishart PK. Latanoprost and cystoid macular oedema in a pseudophakic. *Br J Ophthalmol* 1998; **82**: 843–4.
2. Stewart O, et al. Bilateral optic disc oedema associated with latanoprost. *Br J Ophthalmol* 1999; **83**: 1092–3.
3. Ekatomatis P. Herpes simplex dendritic keratitis after treatment with latanoprost for primary open angle glaucoma. *Br J Ophthalmol* 2001; **85**: 1008–9.

Systemic effects. The use of latanoprost eye drops has been associated with systemic adverse reactions. In a case report¹ of 2 patients with latanoprost-associated hypertension the authors mentioned that other events including peripheral and facial oedema, dyspnoea, exacerbation of asthma, tachycardia, and chest pain or angina pectoris had been reported. Another case report² also referred to exacerbation of angina. Although a study³ involving 24 stable asthmatics found that latanoprost eye drops had no effect on pulmonary function or asthma symptoms, UK licensed product information recommends caution in patients with asthma.

1. Peak AS, Sutton BM. Systemic adverse effects associated with topically applied latanoprost. *Ann Pharmacother* 1998; **32**: 504–5.
2. Mitra M, et al. Exacerbation of angina associated with latanoprost. *BMJ* 2001; **323**: 783.
3. Hedner J, et al. Latanoprost and respiratory function in asthmatic patients: randomized, double-masked, placebo-controlled crossover evaluation. *Arch Ophthalmol* 1999; **117**: 1305–9.

Interactions

Paradoxical increases in intra-ocular pressure have been reported after the concomitant ophthalmic use of 2 prostaglandin analogues. UK licensed product information states that the use of 2 or more prostaglandin analogues or derivatives is not recommended.

Uses and Administration

Latanoprost is a synthetic analogue of dinoprost (prostaglandin $F_{2\alpha}$) that is used to reduce intra-ocular pressure in patients with open-angle glaucoma and ocular hypertension (p.1873). Reduction of intra-ocular pressure starts about 3 to 4 hours after instillation and is maximal after 8 to 12 hours; pressure reduction lasts for at least 24 hours. A 0.005% ophthalmic solution is instilled once daily, preferably in the evening.

References

1. Patel SS, Spencer CM. Latanoprost: a review of its pharmacological properties, clinical efficacy and tolerability in the management of primary open-angle glaucoma and ocular hypertension. *Drugs Aging* 1996; **9**: 363–78.
2. Einarson TR, et al. Meta-analysis of the effect of latanoprost and brimonidine on intraocular pressure in the treatment of glaucoma. *Clin Ther* 2000; **22**: 1502–15.
3. Zhang WY, et al. Meta-analysis of randomised controlled trials comparing latanoprost with timolol in the treatment of patients with open angle glaucoma or ocular hypertension. *Br J Ophthalmol* 2001; **85**: 983–90.
4. Feldman RM. An evaluation of the fixed-combination of latanoprost and timolol for use in open-angle glaucoma and ocular hypertension. *Expert Opin Pharmacother* 2004; **5**: 909–21.
5. Bayer A, et al. Clinical predictors of latanoprost treatment effect. *J Glaucoma* 2005; **14**: 260–3.
6. Diestelhorst M, Larsson LI. European-Canadian Latanoprost Fixed Combination Study Group. A 12-week, randomized, double-masked, multicenter study of the fixed combination of latanoprost and timolol in the evening versus the individual components. *Ophthalmology* 2006; **113**: 70–6.
7. Fung AT, et al. Meta-analysis of randomised controlled trials comparing latanoprost with brimonidine in the treatment of open-angle glaucoma, ocular hypertension or normal-tension glaucoma. *Br J Ophthalmol* 2007; **91**: 62–8.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Glaucostat; Klonaprost; Latanoflax; Louten; Ocuprost†; Paraiop; Tanarof; Xalatan; **Austral.:** Xalatan; **Austria:** Xalatan; **Belg.:** Xalatan; **Braz.:** Xalatan; **Canada.:** Xalatan; **Chile:** Gaax; Latof; Louten; Xalatan; **Cz.:** Xalatan; **Denm.:** Xalatan; **Fin.:** Xalatan; **Fr.:** Xalatan; **Ger.:** Xalatan; **Gr.:** Xalatan; **Hong Kong:** Xalatan; **Hung.:** Xalatan; **India:** 9P†; **Indon.:** Xalatan; **Irl.:** Xalatan; **Israel:** Xalatan; **Ital.:** Xalatan; **Malaysia:** Xalatan; **Mex.:** Gaap Ofteno; Latsol; Xalatan; **Neth.:** Xalatan; **Norw.:** Xalatan; **NZ:** Xalatan; **Philipp.:** Xalatan; **Pol.:** Xalatan; **Port.:** Xalatan; **Rus.:** Xalatan (Ксалаван); **S.Afr.:** Xalatan; **Singapore:** Xalatan; **Spain:** Xalatan; **Swed.:** Xalatan; **Switz.:** Xalatan; **Thai.:** Xalatan; **Turk.:** Xalatan; **UK:** Xalatan; **USA:** Xalatan; **Venez.:** Gaap Ofteno; Laprost; Latanoprest; Xalatan.

Multi-ingredient: **Arg.:** Louten T; Ocuprostim; Xalacom; **Austral.:** Xalacom; **Austria:** Xalacom; **Belg.:** Xalacom; **Braz.:** Xalacom; **Canada.:** Xalacom; **Chile:** Gaax T; Latof-T; Xalacom; **Cz.:** Xalacom; **Denm.:** Xalacom; **Fin.:** Xalacom; **Fr.:** Xalacom; **Ger.:** Xalacom; **Gr.:** Xalacom; **Hong Kong:** Xalacom; **Hung.:** Xalacom; **Indon.:** Xalacom; **Irl.:** Xalacom; **Israel:** Xalacom; **Ital.:** Xalacom; **Malaysia:** Xalacom; **Mex.:** Xalacom; **Neth.:** Xalacom; **Norw.:** Xalacom; **NZ:** Xalacom; **Philipp.:** Xalacom; **Pol.:** Xalacom; **Port.:** Tavu; Xalacom; **Rus.:** Xalacom (Ксааком); **S.Afr.:** Xalacom; **Singapore:** Xalacom; **Spain:** Xalacom; **Swed.:** Xalacom; **Switz.:** Xalacom; **Thai.:** Xalacom; **UK:** Xalacom; **Venez.:** Xalacom.

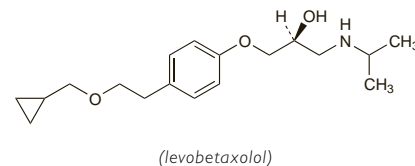
Levobetaxolol Hydrochloride (USAN, rINN) ⊗

AL-1577A (levobetaxolol or levobetaxolol hydrochloride); Hidrocloruro de levobetaxolol; Lévoβétaxolol, Chlorhydrate de; Levobetaxololi Hydrochloridum. (–)-(S)-1-*p*-[2-(Cyclopropylmethoxy)ethyl]phenoxy]-3-isopropylaminopropan-2-ol hydrochloride.

Левобетаксолола Гидрохлорид

$C_{18}H_{29}NO_3 \cdot HCl = 343.9$.

CAS — 93221-48-8 (levobetaxolol); 116209-55-3 (levobetaxolol hydrochloride).



(levobetaxolol)

Profile

Levobetaxolol, the *S*-isomer of betaxolol (p.1231) is a cardioselective beta blocker (p.1225). It is reported to lack intrinsic sympathomimetic activity and to have no significant membrane-stabilising properties.

Levobetaxolol has been used as the hydrochloride to reduce raised intra-ocular pressure in open-angle glaucoma and ocular hypertension.

Preparations

Proprietary Preparations (details are given in Part 3)

USA: Betaxof†.

Levobunolol Hydrochloride

(BANM, USAN, rINN) ⊗

(–)-Bunolol Hydrochloride; *l*-Bunolol Hydrochloride; Hidrocloruro de levobunolol; Lévoβunolol, Chlorhydrate de; Levobunolol Hidroklorür; Levobunololihydroklorid; Levobunololi Hydrochloridum; Levobunololihydrokloridi; W-7000A. (–)-5-(3-*tert*-Butylamino-2-hydroxypropoxy)-1,2,3,4-tetrahydronaphthalen-1-one hydrochloride.

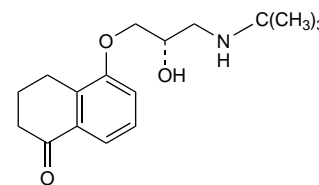
Левобунолола Гидрохлорид

$C_{17}H_{25}NO_3 \cdot HCl = 327.8$.

CAS — 47141-42-4 (levobunolol); 27912-14-7 (levobunolol hydrochloride).

ATC — S01ED03.

ATC Vet — QS01ED03.



(levobunolol)

Pharmacopoeias. In Br and US.

BP 2008 (Levobunolol Hydrochloride). A white or pinkish-white crystalline powder. Freely soluble in water; sparingly soluble in alcohol. A 5% solution in water has a pH of between 4.5 and 6.5. Protect from light.

USP 31 (Levobunolol Hydrochloride). A white odourless crystalline powder. Soluble in water and in methyl alcohol; slightly soluble in alcohol and in chloroform. A 5% solution in water has a pH between 4.5 and 6.5.

Adverse Effects, Treatment, and Precautions

As for Beta Blockers, p.1226.

Interactions

The interactions associated with beta blockers are discussed on p.1228.

Pharmacokinetics

Some systemic absorption is reported to occur after topical application to the eye. After oral doses levobunolol is rapidly and almost completely absorbed from the gastrointestinal tract. It is extensively metabolised

in the liver; the principal metabolite, dihydrolevobunolol, is reported to possess beta-blocking activity. The metabolites and some unchanged drug are excreted in the urine.

Uses and Administration

Levobunolol is a non-cardioselective beta blocker (p.1225). It is reported to lack intrinsic sympathomimetic activity and membrane-stabilising properties.

Levobunolol is used as the hydrochloride to reduce raised intra-ocular pressure in open-angle glaucoma and ocular hypertension (p.1873). It begins to act 1 hour after instillation with maximal effect seen between 2 and 6 hours; the effect may be maintained for up to 24 hours. Levobunolol hydrochloride is usually used as a 0.5% ophthalmic solution instilled once or twice daily; alternatively a 0.25% solution may be instilled twice daily.

Preparations

BP 2008: Levobunolol Eye Drops;
USP 31: Levobunolol Hydrochloride Ophthalmic Solution.

Proprietary Preparations (details are given in Part 3)

Arg.: Betagan; **Levunolol:** Betagan; **Austria:** Vistagan; **Belg.:** Betagan; **Braz.:** B-Tablock; Betagan; **Canad.:** Betagan; Ophtho-Bunolol†; **Chile:** Betagen; **Cz.:** Vistagan; **Denm.:** Betagan; **Fr.:** Betagan; **Ger.:** Vistagan; **Gr.:** Pentila†; Vistagan; **Hong Kong:** Betagan; **Hung.:** Vistagan; **Irl.:** Betagan; **Israel:** Betagan; **Ital.:** Vistagan; **Malaysia:** Betagan†; **Mex.:** Betagan; **Neth.:** Betagan; **NZ:** Betagan; **Port.:** Betagan; **S.Afr.:** Betagan; **Singapore:** Betagan; **Spain:** Betagan; **Switz.:** Vistagan; **Thai.:** Betagan; **Turk.:** Betagan; **UK:** Betagan; **USA:** Ak-Beta; Betagan; **Venez.:** Vistagan.

Multi-ingredient: **Canad.:** Probeta†.

Methazolamide (BAN, rINN) ⊗

Metazolamidum; Méthazolamide; Methazolamidum. *N*-(4-Methyl-2-sulphamoyl-Δ²-1,3,4-thiadiazolin-5-ylidene)acetamide.

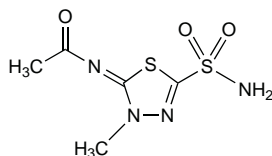
Метазолами́д

C₅H₈N₄O₃S₂ = 236.3.

CAS — 554-57-4.

ATC — S01EC05.

ATC Vet — QS01EC05.



Pharmacopoeias. In US.

USP 31 (Methazolamide). A white or faintly yellow crystalline powder with a slight odour. Very slightly soluble in water and in alcohol; slightly soluble in acetone; soluble in dimethylformamide. Protect from light.

Adverse Effects and Precautions

As for Acetazolamide, p.1875.

Hypersensitivity. Cholestatic hepatitis with jaundice, rash, and subsequent pure red cell aplasia was associated with methazolamide in a patient.¹ Drug-induced hypersensitivity was suspected as the cause of the reaction.

1. Krivoy N, *et al.* Methazolamide-induced hepatitis and pure RBC aplasia. *Arch Intern Med* 1981; **141**: 1229–30.

Pharmacokinetics

Methazolamide is absorbed from the gastrointestinal tract more slowly than acetazolamide. It has been reported not to be extensively bound to plasma protein, and to have a half-life of about 14 hours. About 15 to 30% of the dose is excreted in the urine; the fate of the remainder is unknown.

Uses and Administration

Methazolamide is an inhibitor of carbonic anhydrase with actions similar to those of acetazolamide (p.1876). It is used in the treatment of glaucoma (p.1873) in oral doses of 50 to 100 mg two or three times daily. Its action is less prompt but of longer duration than that of acetazolamide, lasting for 10 to 18 hours.

The diuretic activity of methazolamide is less pronounced than that of acetazolamide.

Preparations

USP 31: Methazolamide Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Glaumeta†; **Canad.:** Neptazane†; **Israel:** Neptazane†; **Thai.:** Neptazane†; **USA:** GlaucoTabs†; MZM†.

Metipranolol (BAN, USAN, rINN) ⊗

BMOI-004; Methipranolol; Métipranolol; Metipranololum; VUAB-6453 (SPOFA); VUFB-6453. 1-(4-Acetoxy-2,3,5-trimethylphenoxy)-3-isopropylaminopropan-2-ol; 4-(2-Hydroxy-3-isopropylaminoproxy)-2,3,6-trimethylphenyl acetate.

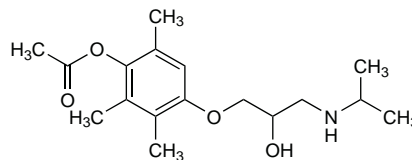
Метипранолол

C₁₇H₂₇NO₄ = 309.4.

CAS — 22664-55-7.

ATC — S01ED04.

ATC Vet — QS01ED04.



NOTE. MPR is a code approved by the BP 2008 for use on single unit doses of eye drops containing metipranolol where the individual container may be too small to bear all the appropriate labelling information.

Pharmacopoeias. In Br.

BP 2008 (Metipranolol). A white crystalline powder. Practically insoluble in water; soluble in alcohol, in acetone, and in methyl alcohol; dissolves in dilute mineral acids. The filtrate of a 2.5% suspension in water has a pH of 9.0 to 10.0. Protect from light.

Adverse Effects, Treatment, and Precautions

As for Beta Blockers, p.1226.

Conjunctivitis, conjunctival leucoplakia, transient stinging, as well as other ocular adverse effects have been reported with metipranolol eye drops. Granulomatous anterior uveitis has been reported rarely; a high incidence reported in the UK may have been associated with changes induced by radiation sterilisation of metipranolol eye drops in their final container, but this preparation is no longer available.

Interactions

The interactions associated with beta blockers are discussed on p.1228.

Uses and Administration

Metipranolol is a non-cardioselective beta blocker (p.1225). It is reported to be largely lacking in intrinsic sympathomimetic activity and membrane-stabilising properties.

Metipranolol is used to reduce raised intra-ocular pressure in the management of open-angle glaucoma and ocular hypertension (p.1873). Eye drops usually containing metipranolol 0.1 or 0.3% are used twice daily.

Metipranolol has also been used by mouth in the management of cardiovascular disorders.

Preparations

BP 2008: Metipranolol Eye Drops.

Proprietary Preparations (details are given in Part 3)

Austria: Beta-Optiole; **Belg.:** Beta-Optiole; **Cz.:** Trimepranol; **Ger.:** Betamann; **Ital.:** Turoptin; **Malaysia:** Beta-Optiole†; **Neth.:** Beta-Optiole; **Philipp.:** Beta-Optiole; **Pol.:** Betamann; **Port.:** Beta-Optiole; **S.Afr.:** Beta-Optiole; **Singapore:** Beta-Optiole†; **Switz.:** Turoptin†; **Thai.:** Beta-Optiole†; **Turk.:** Turoptin; **USA:** OptiPranolol.

Multi-ingredient: **Austria:** Betacarpin; **Belg.:** Normoglaucou; **Cz.:** Tri-mecryton†; **Ger.:** Normoglaucou; **Torlat†; Tri-Torlat†; Gr.:** Beta Optiole; **Ripix†; Hong Kong:** Torlat†; **Ital.:** Ripix; **Malaysia:** Normoglaucou†; **Neth.:** Normoglaucou; **Pol.:** Normoglaucou; **Port.:** Normoglaucou; **Singapore:** Normoglaucou†; **Switz.:** Ripix; **Thai.:** Normoglaucou†.

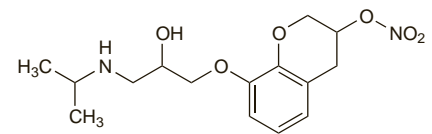
Nipradilol (rINN) ⊗

K-351; Nipradilolum; Nipradolol. 8-[2-Hydroxy-3-(isopropylamino)propoxy]-3-chromanol 3-nitrate.

Нипрадилол

C₁₅H₂₂N₂O₆ = 326.3.

CAS — 81486-22-8.



Profile

Nipradilol is a non-cardioselective beta blocker (p.1225). It is also reported to have direct vasodilating activity. It is used in the management of glaucoma and ocular hypertension (p.1873); eye drops containing nipradilol 0.05% are instilled twice daily.

Preparations

Proprietary Preparations (details are given in Part 3)

Jpn.: Hypadil.

Paraoxon

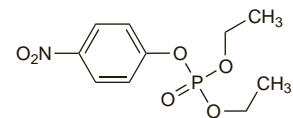
E-600. Diethyl *p*-nitrophenyl phosphate.

C₁₀H₁₄NO₆P = 275.2.

CAS — 311-45-5.

ATC — S01EB10.

ATC Vet — QS01EB10.



Profile

Paraoxon is a potent inhibitor of cholinesterase activity that has been used with other miotics in the treatment of glaucoma. It is the active metabolite of the organophosphorus insecticide parathion (p.2048) and therefore produces similar toxicity but with a faster onset.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: **Ital.:** Mios.

Physostigmine (BAN)

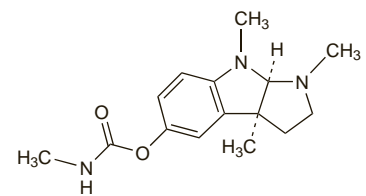
Eserine; Fisostigmina; Fysostigmiini; Fysostigmin; Physostigminum. (3a,5,8aR)-1,2,3,3a,8,8a-Hexahydro-1,3a,8-trimethylpyrrolo[2,3-*b*]indol-5-yl methylcarbamate.

C₁₅H₂₁N₃O₂ = 275.3.

CAS — 57-47-6.

ATC — S01EB05; V03AB19.

ATC Vet — QA03AX90; QA03FA90; QS01EB05; QV03AB19.



Description. An alkaloid obtained from the calabar bean (ordeal bean; chopnut), the seed of *Physostigma venenosum* (Leguminosae).

Pharmacopoeias. In US.

USP 31 (Physostigmine). An alkaloid usually obtained from the dried ripe seed of *Physostigma venenosum* (Leguminosae). It is a white, odourless, microcrystalline powder which acquires a red tint on exposure to heat, light, or air, or on contact with traces of metals. M.p. not lower than 103°. Slightly soluble in water; freely soluble in alcohol; very soluble in chloroform and in dichloromethane; soluble in fixed oils and in benzene. Store in airtight containers. Protect from light.

Physostigmine Salicylate (BANM)

Eserine Salicylate; Ésérine, salicylate d'; Eserini salicylas; Ezerino salicilatas; Fisostigmina, salicilato de; Fiszostigmino salicilatas; Fiszostigminy salicylan; Fiszostigmin-szalicilát; Fyszostigmiinisalicylaatti; Fyszostigminsalicylat; Fyszostigmin-salicylát; Physostig. Sal.; Physostigmine Monosalicylate; Physostigmini salicylas.

C₁₅H₂₁N₃O₂·C₇H₆O₃ = 413.5.

CAS — 57-64-7.

ATC — S01EB05; V03AB19.

ATC Vet — QS01EB05; QV03AB19.