

Dyflon (BAN)

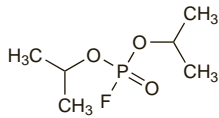
DFF; Difluorophate; Di-isopropyl Fluorophosphate; Di-isopropylfluorophosphonate; Fluostigmine; Isoflurofate; Isoflurophate; Di-isopropyl phosphorofluoridate.

$C_6H_{14}FO_3P = 184.1$.

CAS — 55-91-4.

ATC — S01E07.

ATC Vet — QS01E07.

**Pharmacopoeias.** In *US*.

USP 31 (Isoflurophate). A clear, colourless, or faintly yellow liquid. Specific gravity about 1.05. Sparingly soluble in water; soluble in alcohol and in vegetable oils. It is decomposed by moisture with the evolution of hydrogen fluoride. Store at 8° to 15° in sealed containers.

Profile

Dyflon is an irreversible inhibitor of cholinesterases with actions similar to those of ecothiopate iodide (below). It has been used mainly in the treatment of open-angle glaucoma, particularly in aphakic patients and when other drugs have proved inadequate; it has usually been given as a 0.025% ophthalmic ointment. It was also used in the diagnosis and management of accommodative convergent strabismus.

Handling. The vapour of dyflon is very toxic. The eyes, nose, and mouth should be protected when handling dyflon, and contact with the skin should be avoided. Dyflon can be removed from the skin by washing with soap and water. Contaminated material should be immersed in a 2% aqueous solution of sodium hydroxide for several hours.

Preparations

USP 31: Isoflurophate Ophthalmic Ointment.

Ecothiopate Iodide (BAN, rINN)

Ecothiopate Iodide; Ecostigmine Iodide; Écothiopate, Iodure d'; Ecothiopatī Iodidum; Ekotiopaattijodidi; Ekotiopatjodid; Ioduro de ecothiopato; M1-217. (2-Diethoxyphosphinylthioethyl)trimethylammonium iodide.

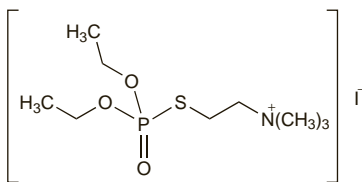
Экотиопата Йодид

$C_9H_{23}INO_3PS = 383.2$.

CAS — 6736-03-4 (ecothiopate); 513-10-0 (ecothiopate iodide).

ATC — S01E03.

ATC Vet — QS01E03.

**Pharmacopoeias.** In *Jpn* and *US*.

USP 31 (Ecothiopate Iodide). A white, crystalline, hygroscopic solid having a slight mercaptan-like odour. Soluble 1 in 1 of water, 1 in 25 of dehydrated alcohol, and 1 in 3 of methyl alcohol; practically insoluble in other organic solvents. Its solutions in water have a pH of about 4. Store in airtight containers preferably at a temperature below 0°. Protect from light.

Adverse Effects

As for Neostigmine, p.631. For adverse effects of miotics, see also Pilocarpine, p.1885.

Ecothiopate is an irreversible cholinesterase inhibitor; its action, and hence its adverse effects, may be prolonged.

Plasma and erythrocyte cholinesterases may be reduced by treatment with eye drops of ecothiopate or other long-acting anticholinesterases, and systemic toxicity occurs more frequently than with shorter-acting miotics. Acute iritis, retinal detachment, or precipitation of acute glaucoma may occasionally occur, and iris cysts (especially in children) or lens opacities may develop on prolonged treatment.

Treatment of Adverse Effects

To treat the systemic effects of poisoning, atropine sulfate may be given parenterally with pralidoxime chloride as for intoxication with organophosphorus insecticides (see p.1460); subcon-

junctival injection of pralidoxime has been used to reverse severe ocular adverse effects. Supportive treatment, including assisted ventilation, should be given as necessary.

To prevent or reduce development of iris cysts in patients receiving ecothiopate eye drops, phenylephrine eye drops may be given simultaneously.

Precautions

As for Neostigmine, p.632. For precautions of miotics, see also under Pilocarpine, p.1885. In general, as with other long-acting anticholinesterases, ecothiopate should be used only where therapy with other drugs has proved ineffective. Ecothiopate iodide should not be used in patients with iodine hypersensitivity.

Interactions

As for Neostigmine, p.632. The possibility of an interaction remains for a considerable time after stopping long-acting anticholinesterases such as ecothiopate.

Uses and Administration

Ecothiopate is an irreversible inhibitor of cholinesterase; its actions are similar to those of neostigmine (p.632) but much more prolonged. Its miotic action begins within 1 hour of its application and may persist for 1 to 4 weeks; it causes a reduction in intra-ocular pressure, which is maximal after 24 hours and may persist for days or weeks.

Ecothiopate iodide is used mainly in the treatment of open-angle glaucoma (p.1873), particularly in aphakic patients and when other drugs have proved inadequate. It is given as drops of a 0.03 to 0.25% ophthalmic solution. Licensed product information states that 2 daily doses are preferred to allow for diurnal variations in intra-ocular pressure, although it has also been given once daily or on alternate days. It is advisable to give the single dose or one of the 2 daily doses at bedtime.

Ecothiopate iodide eye drops are also used in the diagnosis and management of accommodative convergent strabismus (p.1874).

Preparations

USP 31: Ecothiopate Iodide for Ophthalmic Solution.

Proprietary Preparations (details are given in Part 3)

Austral: Phospholine Iodide†; **Austria:** Phospholinjodid†; **USA:** Phospholine Iodide†.

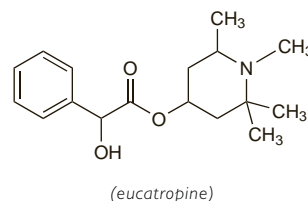
Eucatropine Hydrochloride (BANM, rINNM)

Clorhidrato de Eufalmina; Eucatropine, Chlorhydrate d'; Eucatropini Hydrochloridum; Eucatropinum Chloride; Hidrocloruro de eucatropina. 1,2,2,6-Tetramethyl-4-piperidyl mandelate hydrochloride.

Эукатропина Гидрохлорид

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

CAS — 100-91-4 (eucatropine); 536-93-6 (eucatropine hydrochloride).

**Pharmacopoeias.** In *US*.

USP 31 (Eucatropine Hydrochloride). A white, odourless, granular powder. Very soluble in water; freely soluble in alcohol and in chloroform; insoluble in ether. Its solutions are neutral to litmus. Store in airtight containers. Protect from light.

Profile

Eucatropine hydrochloride is a tertiary amine antimuscarinic that has been used as a mydriatic. It has little or no effect on accommodation.

Preparations

USP 31: Eucatropine Hydrochloride Ophthalmic Solution.

Homatropine (BAN)

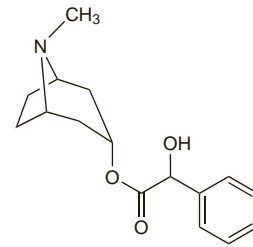
Homatropini; Homatropin; Homatropina; Homatropinum. (1R,3r,5S)-Tropan-3-yl (RS)-mandelate.

$C_{16}H_{21}NO_3 = 275.3$.

CAS — 87-00-3.

ATC — S01FA05.

ATC Vet — QS01FA05.

**Homatropine Hydrobromide** (BANM)

Homatr. Hydrobrom.; Homatropinihydrobromidi; Homatropina, hidrobromuro de; Homatropine, bromhydrate d'; Homatropin-hidrobromid; Homatropinhydrobromid; Homatropinhydrobromid; Homatropini hydrobromidum; Homatropinum Bromide; Homatropino hidrobromidas; Homatropinum Bromatum; Homatropiny bromowodorek; Omotropina Bromidrat; Oxtolyltropine Hydrobromide; Tropy Mandelate Hydrobromide.

$C_{16}H_{21}NO_3.HBr = 356.3$.

CAS — 51-56-9.

ATC — S01FA05.

ATC Vet — QS01FA05.

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

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

Ph. Eur. 6.2 (Homatropine Hydrobromide). A white or almost white, crystalline powder or colourless crystals. Freely soluble in water; sparingly soluble in alcohol. A 5% solution in water has a pH of 5.0 to 6.5. Protect from light.

USP 31 (Homatropine Hydrobromide). White crystals or a white crystalline powder. Soluble 1 in 6 of water, 1 in 40 of alcohol, and 1 in 420 of chloroform; insoluble in ether. pH of a 2% solution in water is between 5.7 and 7.0. Store in airtight containers. Protect from light.

Homatropine Methylbromide (BANM, rINN)

Homatropiniimetylibromidi; Homatropine Methylbromide; Homatropine, méthylbromure d'; Homatropini methylbromidum; Homatropin-methylbromid; Homatropin-metilbromid; Homatropinmetylibromid; Homatropine methylbromidas; Methylhomatropinum Bromatum; Methylhomatropinum Bromide; Metilbromuro de homatropina. (1R,3r,5S)-3-[(±)-Mandeloyloxy]-8-methyltropanium bromide.

Гоматропина Метилбромид

$C_{16}H_{21}NO_3.CH_2Br = 370.3$.

CAS — 80-49-9.

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

Ph. Eur. 6.2 (Homatropine Methylbromide). A white or almost white, crystalline powder or colourless crystals. Freely soluble in water; soluble in alcohol. A 5% solution in water has a pH of 4.5 to 6.5. Protect from light.

USP 31 (Homatropine Methylbromide). A white, odourless, powder that slowly darkens on exposure to light. Very soluble in water; freely soluble in alcohol and in acetone containing about 20% of water; practically insoluble in acetone and in ether. pH of a 1% solution in water is between 4.5 and 6.5. Store in airtight containers. Protect from light.

Adverse Effects, Treatment, and Precautions

As for Atropine Sulfate, p.1219.

Ophthalmic use. Antimuscarinic toxicity (including ataxia, restlessness, excitement, hallucinations) has been reported in children¹ and the elderly^{2,3} given homatropine eye drops.

1. Hoefnagel D. Toxic effects of atropine and homatropine eye drops in children. *N Engl J Med* 1961; **264**: 168-71.
2. Reid D, Fulton JD. Tachycardia precipitated by topical homatropine. *BMJ* 1989; **299**: 795-6.
3. Tune LE, et al. Anticholinergic delirium caused by topical homatropine ophthalmologic solution: confirmation by anticholinergic radioreceptor assay in two cases. *J Neuropsychiatr Clin Neurosci* 1992; **4**: 195-7.

Interactions

As for antimuscarinics in general (see Atropine Sulfate, p.1220).

Uses and Administration

Homatropine is a tertiary amine antimuscarinic with effects similar to those of atropine (p.1219). It is used as the hydrobromide, also a tertiary amine, to produce mydriasis and cycloplegia (p.1874); its actions are more rapid and of shorter duration than those of atropine, but it is less potent and has a relatively weak cycloplegic effect. In general, onset of action is between 30 and 60 minutes, and recovery within 1 to 3 days. Homatropine hydrobromide is generally used as a 1, 2, or 5% ophthalmic solution. For the determination of refraction, instillation may be repeated