Systemic toxicity. Ten of 66 patients (29 males and 37 females) who received one drop of 2% cyclopentolate in each eye developed mild to moderate systemic toxicity; 9 of the 10 were female.[1] Toxic signs included physical weakness, nausea, lightheadedness, changes in emotional attitude, unprovoked weeping, and loss of equilibrium; tachycardia was always present but changes in blood pressure were insignificant. Spontaneous recovery occurred within 1 hour to several days.

As with atropine, it has been recommended that cyclopentolate eye drops should not be used during the first 3 months of life because of the possible association with development of amblyopia. Systemic toxicity has also been reported in neonates given ocular cyclopentolate.[2]

A 4-year-old boy with cerebral palsy and paraplegia suffered tonic-clonic seizures, facial flushing, and tachycardia 70 minutes after one drop of a 1% cyclopentolate solution was instilled into each eye to dilate his pupils.[3] The child had no history of convulsions and had received 1% cyclopentolate eye drops on 2 previous occasions without incident. In a more recent case,[4] a 23-month-old boy experienced a tonic-clonic seizure lasting 30 minutes after the use of cyclopentolate 1% and phenylephrine 10% eye drops. One drop of each was instilled into both eyes every 5 minutes for 3 doses; the seizure occurred 45 minutes after the last dose. The child was found to have low pseudocholinesterase activity, an enzyme likely to be involved in the metabolism of cyclopentolate.

1. Awan KJ. Adverse systemic reactions of topical cyclopentolate hydrochloride. *Ann Ophthalmol* 1976; **8:** 695–8.
2. Bauer CR, *et al*. Systemic cyclopentolate (Cyclogyl) toxicity in the newborn infant. *J Pediatr* 1973; **92:** 501–5.
3. Fitzgerald DA, *et al*. Seizures associated with 1% cyclopentolate eyedrops. *J Paediatr Child Health* 1990; **26:** 106–7.
4. Demayo AP, Reidenberg MM. Grand mal seizure in a child 30 minutes after Cyclogyl (cyclopentolate hydrochloride) and 10% Neo-Synephrine (phenylephrine hydrochloride) eye drops were instilled. Abstract: *Pediatrics* 2004; **113:** 1390–1. Full version: http://pediatrics.aappublications.org/cgi/reprint/113/5/e499 (accessed 24/11/05)

Interactions

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

Uses and Administration

Cyclopentolate hydrochloride is a tertiary amine antimuscarinic with actions similar to those of atropine (p.1219). It is used to produce mydriasis and cycloplegia (p.1874) for ophthalmic diagnostic procedures and also in the treatment of uveitis and iritis (p.1515). It acts more quickly than atropine and has a shorter duration of action; the maximum mydriatic effect is produced 30 to 60 minutes after instillation, and may persist for up to 24 hours or longer in some patients; the maximum cycloplegic effect is produced within 25 to 75 minutes and accommodation recovers within 6 to 24 hours.

For diagnostic procedures, instillation of a 0.5% ophthalmic solution of cyclopentolate hydrochloride, repeated after about 5 to 15 minutes, is usually sufficient for adults. Higher strengths have been used. For children a 1% solution is instilled similarly, although some recommend that strengths greater than 0.5% should not be used in infants and that cyclopentolate should not be used at all during the first 3 months of life.

In the treatment of uveitis and iritis, a 0.5% ophthalmic solution of cyclopentolate hydrochloride is instilled into the eye up to four times daily.

Deeply pigmented eyes are more resistant to pupillary dilatation and may require the use of a 1% solution.

Preparations

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

Proprietary Preparations (details are given in Part 3)

Arg.: Ciclopenal; ***Austral.:*** Cyclogyl; ***Belg.:*** Cyclogyl; Cyclopentol†; ***Braz.:*** Ciclolato; Ciclopleglico; ***Canad.:*** Cyclogyl; Diopentolate†; ***Chile:*** Cyclogyl; ***Cz.:*** Cyclogyl†; ***Denm.:*** Cyclogyl; ***Fin.:*** Oftan Sykloº†; ***Fr.:*** Skiacol; ***Ger.:*** Zykolat-EDO; ***Gr.:*** Cyclogyl; ***Hong Kong:*** Cyclogyl; ***Hung.:*** Humapent; ***India:*** Bell Pentolate; Cyclate; Cyclogyl; ***Irl.:*** Mydrilate; ***Ital.:*** Ciclolux; ***Malaysia:*** Colircusi Cicloplejico; Cyclogyl; ***Mex.:*** Refractyl; ***Neth.:*** Cyclogyl; Cyclomydri†; ***NZ:*** Cyclogyl; ***Port.:*** Cicloplegicedol; Midriodavi; ***S.Afr.:*** Cyclogyl; ***Singapore:*** Cyclogyl; ***Spain:*** Cicloplejico; ***Swed.:*** Cyclogyl; ***Switz.:*** Cyclogyl; ***Thai.:*** Cyclogyl; ***Turk.:*** Siklomid; Siklopleji; ***UK:*** Mydrilate; ***USA:*** Ak-Pentolate; Cyclogyl; Ocu-Pentolate; Pentolair; ***Venez.:*** Cicloftal†; Cyclogyl.

Multi-ingredient: ***Israel:*** Cyclopentolate†; ***Malaysia:*** Cyclomydril; ***Rus.:*** Cyclomed (Цикломед); ***S.Afr.:*** Cyclomydril; ***Singapore:*** Cyclomydril; ***USA:*** Cyclomydril.

Demecarium Bromide *(BAN, rINN)*

BC-48; Bromuro de demecario; Demecarii Bromidum; Démécarium, Bromure de; Demekariumbromid; Demekariumbromidi. *N,N′*-Decamethylenebis(*N,N,N*-trimethyl-3-methylcarbamoyloxyanilinium) dibromide.

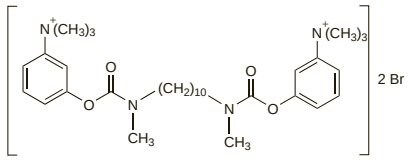
Демекария Бромид

$C_{32}H_{52}Br_2N_4O_4$ = 716.6.

CAS — 16505-84-3 (demecarium); 56-94-0 (demecarium bromide).

ATC — S01EB04.

ATC Vet — QS01EB04.



Pharmacopoeias. In *US*.

USP 31 (Demecarium Bromide). A white or slightly yellow, slightly hygroscopic, crystalline powder. Freely soluble in water and in alcohol; sparingly soluble in acetone; soluble in ether. pH of a 1% solution in water is between 5.0 and 7.0. Store in airtight containers. Protect from light.

Profile

Demecarium is a quaternary ammonium compound that is a reversible inhibitor of cholinesterase with a long duration of action similar to that of ecothiopate iodide (p.1881). It has been used as a 0.125 or 0.25% ophthalmic solution in the treatment of open-angle glaucoma and in the diagnosis and management of accommodative convergent strabismus.

Preparations

USP 31: Demecarium Bromide Ophthalmic Solution.

Proprietary Preparations (details are given in Part 3)
USA: Humorsol†.

Diclofenamide *(BAN, rINN)* ⊗

Dichlorphenamide; Diclofenamida; Diclofénamide; Diclofenamidum; Diklofenamid; Diklofenamidi. 4,5-Dichlorobenzene-1,3-disulphonamide.

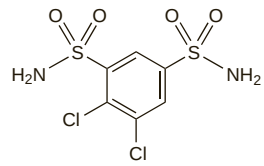
Диклофенамид

$C_6H_6Cl_2N_2O_4S_2$ = 305.2.

CAS — 120-97-8.

ATC — S01EC02.

ATC Vet — QS01EC02.



Pharmacopoeias. In *Chin., Jpn*, and *US*.

Profile

Diclofenamide is an inhibitor of carbonic anhydrase with properties similar to those of acetazolamide (p.1875). When given orally its effect begins within 1 hour and lasts for 6 to 12 hours.

Diclofenamide is used to reduce intra-ocular pressure in glaucoma (p.1873). The usual initial oral dose is 100 to 200 mg, then 100 mg every 12 hours until the desired response is obtained, followed by a maintenance dose of 25 to 50 mg one to three times daily. Diclofenamide sodium has been given by injection.

Preparations

USP 31: Dichlorphenamide Tablets.

Proprietary Preparations (details are given in Part 3)
Belg.: Oratrol†; ***Cz.:*** Oratrol†; ***Gr.:*** Oratrol†; ***Ital.:*** Antidrasi; Fenamide; Glaumid†; ***Spain:*** Glauconide; ***USA:*** Daranide†.

Dorzolamide Hydrochloride

(BANM, USAN, rINNM) ⊗

Dorzolamid Hidroklorür; Dorzolamide, chlorhydrate de; Dorzolamidi hydrochloridum; Hidrocloruro de dorzolamida; L-671152 (dorzolamide); MK-507; MK-0507. (4*S*,6*S*)-4-(Ethylamino)-5,6-dihydro-6-methyl-4*H*-thieno[2,3-*b*]thiopyran-2-sulphonamide 7,7-dioxide hydrochloride.

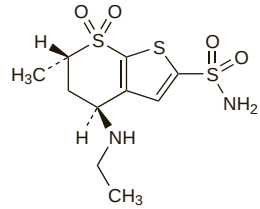
Дорзоламида Гидрохлорид

$C_{10}H_{16}N_2O_4S_3$,HCl = 360.9.

CAS — 120279-96-1 (dorzolamide); 130693-82-2 (dorzolamide hydrochloride).

ATC — S01EC03.

ATC Vet — QS01EC03.



(dorzolamide)

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

Ph. Eur. 6.2 (Dorzolamide Hydrochloride). A white or almost white, crystalline powder. Soluble in water; very slightly soluble in anhydrous alcohol; slightly soluble in methyl alcohol. It exhibits polymorphism.

USP 31 (Dorzolamide Hydrochloride). A white to off-white crystalline powder. Soluble in water. Store at 15° to 30°. Protect from light.

Adverse Effects and Precautions

Local ocular adverse effects may occur with dorzolamide eye drops and include conjunctivitis, keratitis, burning or stinging, eyelid inflammation or irritation, and blurred vision. Dorzolamide may be absorbed systemically, resulting in adverse effects and precautions similar to those of acetazolamide (see p.1875). Other adverse effects reported are headache, bitter taste, epistaxis, fatigue, and nausea.

Interactions

Systemic absorption may occur after topical application of dorzolamide to the eye and there is a theoretical possibility of interactions similar to those reported with acetazolamide (see p.1876).

Uses and Administration

Dorzolamide is a carbonic anhydrase inhibitor with actions similar to those of acetazolamide (p.1876). It is used in the management of open-angle glaucoma, pseudo-exfoliative glaucoma, and ocular hypertension (p.1873), either alone or as an adjunct to a topical beta blocker.

Dorzolamide is given as eye drops containing dorzolamide hydrochloride equivalent to 2% of the base. For monotherapy it is usually given three times daily; a twice-daily regimen is recommended when used with a beta blocker.

◊ References.

1. Martens-Lobenhoffer J, Banditt P. Clinical pharmacokinetics of dorzolamide. *Clin Pharmacokinet* 2002; **41:** 197–205.
2. Lesk MR, *et al*. Effectiveness and safety of dorzolamide-timolol alone or combined with latanoprost in open-angle glaucoma or ocular hypertension. *Ann Pharmacother* 2008; **42:** 498–504.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Biodrop†; Dorlamida; Poenglausil†; Trusopt; ***Austral.:*** Trusopt; ***Austria:*** Trusopt; ***Belg.:*** Trusopt; ***Braz.:*** Ocupress; Trusopt; ***Canad.:*** Trusopt; ***Chile:*** Glaucotensil; Trusopt; ***Cz.:*** Trusopt; ***Denm.:*** Trusopt; ***Fin.:*** Trusopt; ***Fr.:*** Trusopt; ***Ger.:*** Trusopt; ***Gr.:*** Trusopt; ***Hong Kong:*** Trusopt; ***Hung.:*** Trusopt; ***India:*** Dorzox; ***Irl.:*** Trusopt; ***Israel:*** Trusopt; ***Ital.:*** Trusopt; ***Malaysia:*** Trusopt; ***Mex.:*** Trusopt; ***Neth.:*** Trusopt; ***Norw.:*** Trusopt; ***NZ:*** Trusopt; ***Philipp.:*** Trusopt; ***Pol.:*** Trusopt; ***Port.:*** Trusopt; ***Rus.:*** Trusopt (Трусопт); ***S.Afr.:*** Trusopt; ***Singapore:*** Trusopt; ***Spain:*** Trusopt; ***Swed.:*** Trusopt; ***Switz.:*** Trusopt; ***Thai.:*** Trusopt; ***Turk.:*** Trusopt; ***UK:*** Trusopt; ***USA:*** Trusopt; ***Venez.:*** Dorzol; Glaucotensil D; Trusopt.

Multi-ingredient: ***Arg.:*** Cosopt; Dorlamida T; Dorzoflax†; Glaucotensil TD; Timed D; ***Austral.:*** Cosopt; ***Austria:*** Cosopt; Timsopt; ***Belg.:*** Cosopt; ***Braz.:*** Cosopt; ***Canad.:*** Cosopt; ***Chile:*** Cosopt; Dorsof T; Glaucotensil T; Glausolets Plus; Tiof Plus; ***Cz.:*** Cosopt; ***Denm.:*** Cosopt; ***Fin.:*** Cosopt; ***Fr.:*** Cosopt; ***Ger.:*** Cosopt; ***Gr.:*** Cosopt; Tesol†; ***Hong Kong:*** Cosopt; ***Hung.:*** Cosopt; ***Irl.:*** Cosopt; ***Israel:*** Cosopt; ***Ital.:*** Cosopt; ***Malaysia:*** Cosopt; ***Mex.:*** Cosopt; ***Neth.:*** Cosopt; ***Norw.:*** Cosopt; ***NZ:*** Cosopt; ***Philipp.:*** Cosopt; ***Pol.:*** Cosopt; ***Port.:*** Cosopt; Timosopt; ***S.Afr.:*** Cosopt; ***Singapore:*** Cosopt; ***Swed.:*** Cosopt; ***Switz.:*** Cosopt; ***Thai.:*** Cosopt; ***Turk.:*** Cosopt; ***UK:*** Cosopt; ***USA:*** Cosopt; ***Venez.:*** Cosopt; Dobet; Glaucotensil T.

Dyflos *(BAN)*

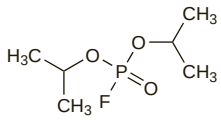
DFP; Difluorophate; Di-isopropyl Fluorophosphate; Di-isopropylfluorophosphonate; Fluostigmine; Isoflurofato; Isoflurophate. Di-isopropyl phosphorofluoridate.

$C_6H_{14}FO_3P$ = 184.1.

CAS — 55-91-4.

ATC — S01EB07.

ATC Vet — QS01EB07.



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

Dyflos 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 dyflos is very toxic. The eyes, nose, and mouth should be protected when handling dyflos, and contact with the skin should be avoided. Dyflos 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)*

Echothiophate Iodide; Ecostigmine Iodide; Écothiopate, Iodure d'; Ecothiopati Iodidum; Ekotiopaattijodidi; Ekotiopatjodid; Ioduro de ecotiopato; MI-217. (2-Diethoxyphosphinylthioethyl)trimethylammonium iodide.

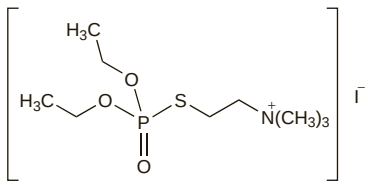
Экотиопата Йодид

$C_9H_{23}INO_3PS$ = 383.2.

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

ATC — S01EB03.

ATC Vet — QS01EB03.



Pharmacopoeias. In *Jpn* and *US*.

USP 31 (Echothiophate 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); subconjunctival 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: Echothiophate Iodide for Ophthalmic Solution.

Proprietary Preparations (details are given in Part 3)

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

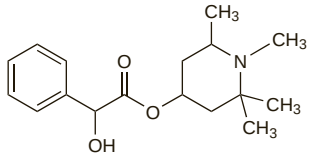
Eucatropine Hydrochloride *(BANM, rINNM)*

Clorhidrato de Euftalmina; Eucatropine, Chlorhydrate d'; Eucatropini Hydrochloridum; Eucatropinium 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).



(eucatropine)

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)*

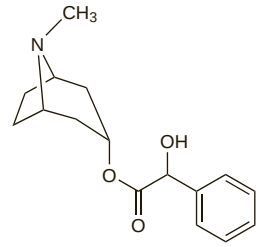
Homatropiini; Homatropin; Homatropina; Homatropinum. (1*R*,3*r*,5*S*)-Tropan-3-yl (*RS*)-mandelate.

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

CAS — 87-00-3.

ATC — S01FA05.

ATC Vet — QS01FA05.



Homatropine Hydrobromide *(BANM)*

Homatr. Hydrobrom.; Homatropiinihydrobromidi; Homatropina, hidrobromuro de; Homatropine, bromhydrate d'; Homatropin-hidrobromid; Homatropinhydrobromid; Homatropin-hydrobromid; Homatropini hydrobromidum; Homatropinium Bromide; Homatropino hidrobromidas; Homatropinum Bromatum; Homatropiny bromowodorek; Omatropina Bromidrato; Oxtolyltropine Hydrobromide; Tropyl 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)*

Homatropiinimetyylibromidi; Homatropine Methobromide; Homatropine, méthylbromure d'; Homatropini methylbromidum; Homatropin-methylbromid; Homatropin-metilbromid; Homatropinmetylbromid; Homatropino metilbromidas; Methylhomatropinium Bromatum; Methylhomatropinium Bromide; Metilbromuro de homatropina. (1*R*,3*r*,5*S*)-3-[(±)-Mandeloyloxy]-8-methyltropanium bromide.

Гоматропина Метилбромид

$C_{16}H_{21}NO_3$,CH_3Br = 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 children[1] and the elderly[2,3] given homatropine eye drops.

1. Hoefnagel D. Toxic effects of atropine and homatropine eyedrops 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