dence of acute mountain sickness by about 50%. Acetazolamide may also have some benefit in relieving symptoms once they have developed although experience is limited. It does not prevent or protect against pulmonary or cerebral oedema.

1. Dumont L, *et al.* Efficacy and harm of pharmacological prevention of acute mountain sickness: quantitative systematic review. *BMJ* 2000; **321:** 267–72.
2. Basnyat B, *et al.* Efficacy of low-dose acetazolamide (125 mg BID) for the prophylaxis of acute mountain sickness: a prospective, double-blind, randomized, placebo-controlled trial. *High Alt Med Biol* 2003; **4:** 45–52.

Macular oedema. For mention of the use of acetazolamide to treat macular oedema associated with uveitis, see Uveitis, p.1515.

Ménière's disease. In Ménière's disease (p.564) high concentrations of carbonic anhydrase are found in the labyrinth, and acetazolamide, a carbonic anhydrase inhibitor, has been tried for both diagnosis and treatment.[1] A dose of 500 mg by intravenous injection has been suggested for diagnosis of fluctuating Ménière's disease.[1] Oral treatment with the drug, however, has not been particularly effective and has been associated with a high incidence of adverse effects.[2]

1. Brookes GB. Ménière's disease: a practical approach to management. *Drugs* 1983; **25:** 77–89.
2. Brookes GB, Booth JB. Oral acetazolamide in Ménière's disease. *J Laryngol Otol* 1984; **98:** 1087–95.

Neuromuscular disorders. Acetazolamide may be of benefit in some neuromuscular disorders, including hypokalaemic periodic paralysis (p.1670). Doses of 375 to 500 mg daily were effective in 2 patients with severe paralysis and were well tolerated.[1] Preliminary observations in 5 other patients showed a striking improvement in 3. In a further 12 patients,[2] doses of 125 mg were given three times daily to children and 250 mg two to six times daily to adults. There was dramatic improvement in 10 of the 12 and this lasted for up to 43 months. Chronic weakness between attacks in 10 patients was improved in 8.

Acetazolamide may reduce the frequency of attacks in patients with hyperkalaemic periodic paralysis (p.1669). It has also been used in episodic ataxia.[3]

1. Resnick JS, *et al.* Acetazolamide prophylaxis in hypokalemic periodic paralysis. *N Engl J Med* 1968; **278:** 582–6.
2. Griggs RC, *et al.* Acetazolamide treatment of hypokalemic periodic paralysis: prevention of attacks and improvement of persistent weakness. *Ann Intern Med* 1970; **73:** 39–48.
3. Melberg A, *et al.* Loss of control after a cup of coffee. *Lancet* 1997; **350:** 1220.

Raised intracranial pressure. Acetazolamide has been used to reduce raised intracranial pressure (p.1181). It has a role in the management of idiopathic intracranial hypertension. It has also been tried in the treatment of immunocompromised patients with chronically raised intracranial pressure due to cryptococcal meningitis,[1] although a controlled trial[2] was terminated early due to serious adverse events possibly due to additive toxicity with amphotericin. However, acetazolamide was used successfully for long-term treatment in 2 immunocompetent patients[3] with raised intracranial pressure following fungal meningitis.

The *BNFC* suggests an initial dose of 8 mg/kg of acetazolamide 3 times daily for the treatment of raised intracranial pressure in children aged 1 month to 12 years; the dose may be increased to a maximum of 100 mg/kg daily as necessary. Acetazolamide may be given orally or by slow intravenous injection.

1. Johnston SRD, *et al.* Raised intracranial pressure and visual complications in AIDS patients with cryptococcal meningitis. *J Infect* 1992; **24:** 185–9.
2. Newton PN, *et al.* A randomized, double-blind, placebo-controlled trial of acetazolamide for the treatment of elevated intracranial pressure in cryptococcal meningitis. *Clin Infect Dis* 2002; **35:** 769–72.
3. Patel S, *et al.* Acetazolamide therapy and intracranial pressure. *Clin Infect Dis* 2002; **36:** 538.

Preparations

BP 2008: Acetazolamide Tablets;
USP 31: Acetazolamide for Injection; Acetazolamide Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Diamox; ***Austral.:*** Diamox; ***Austria:*** Diamox; ***Belg.:*** Diamox; ***Braz.:*** Diamox; Zolamox; ***Canad.:*** Diamox; ***Cz.:*** Diluran; ***Denm.:*** Diamox†; ***Fin.:*** Diamox; Odemin; ***Fr.:*** Defiltran; Diamox; ***Ger.:*** Diamox; Diuramid; Glaupax; ***Gr.:*** Diamox; ***Hong Kong:*** Diamox; ***Hung.:*** Huma-Zolamide; ***India:*** Diamox; ***Indon.:*** Diamox; ***Irl.:*** Diamox; ***Israel:*** Diamox†; Uramox; ***Ital.:*** Diamox; ***Mex.:*** Aceta-Diazol; Akezol; Diamox†; ***Neth.:*** Diamox; Glaupax†; ***Norw.:*** Diamox; ***NZ:*** Diamox; ***Philipp.:*** Cetamid; Diamox; ***Pol.:*** Diuramid; ***Port.:*** Carbinib; ***Rus.:*** Diacarb (Диакарб); ***S.Afr.:*** Azomid; Diamox; ***Spain:*** Edemox; ***Swed.:*** Diamox†; ***Switz.:*** Diamox; Glaupax; ***Thai.:*** Diamox; ***Turk.:*** Diazomid; ***UK:*** Diamox; ***USA:*** Dazamide†; Diamox; ***Venez.:*** Diamox†.

Acetylcholine Chloride *(BAN, rINN)*

Aceticholino chloridas; Acetilkolin-klorid; Acetylcholin chlorid; Acétylcholine, chlorure d'; Acetylcholini chloridum; Acetylkolinklorid; Acetylocholiny chlorek; Asetilkolin Klorür; Asetyylikoliinikloridi; Cloruro de acetilcolina. (2-Acetoxyethyl)trimethylammonium chloride.

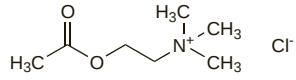
Ацетилхолина Хлорид

$C_7H_{16}ClNO_2$ = 181.7.

CAS — 51-84-3 (acetylcholine); 60-31-1 (acetylcholine chloride).

ATC — S01EB09.

ATC Vet — QS01EB09.



Pharmacopoeias. In *Eur.* (see p.vii) and *US*.
Jpn includes Acetylcholine Chloride for Injection.
Ph. Eur. 6.2 (Acetylcholine Chloride). A very hygroscopic, white or almost white crystalline powder or colourless crystals. Very soluble in water; freely soluble in alcohol; slightly soluble in dichloromethane. Protect from light.
USP 31 (Acetylcholine Chloride). White or off-white crystals or crystalline powder. Very soluble in water; freely soluble in alcohol; insoluble in ether. It is decomposed by hot water and by alkalis. Store in airtight containers.

Adverse Effects

Because it is rapidly hydrolysed in the body by cholinesterases the toxicity of acetylcholine is normally relatively low.

Systemic adverse effects of the choline esters include nausea and vomiting, abdominal pain, flushing, sweating, salivation, lachrymation, rhinorrhoea, eructation, diarrhoea, urinary frequency, headache, bradycardia, peripheral vasodilatation leading to hypotension, and bronchoconstriction.

Ocular adverse effects after local application of choline esters to the eye include corneal oedema, clouding, and decompensation, persistent bullous keratopathy, retinal detachment, and postoperative iritis.

Treatment of Adverse Effects

Atropine sulfate may be given intravenously, intramuscularly, or subcutaneously to control the muscarinic and most nicotinic effects of the choline esters. Supportive treatment may be required.

Precautions

Choline esters are generally contra-indicated for *systemic use* in intestinal or urinary obstruction or where increased muscular activity of the urinary or gastrointestinal tract is liable to be harmful. They are also contra-indicated in asthma and obstructive airways disease, in cardiovascular disorders including bradycardia or heart block and recent myocardial infarction, and in hypotension, vagotonia, epilepsy, parkinsonism, hyperthyroidism, peptic ulceration, and pregnancy. Choline esters should not be given by the intravenous or intramuscular routes as very severe muscarinic adverse effects are liable to occur, calling for emergency treatment with atropine.

Although acetylcholine is normally rapidly hydrolysed in the body, systemic effects have followed *topical application* of choline esters to the eye, albeit rarely, and caution is advisable in the above conditions.

Interactions

As for Neostigmine, p.632. Acetylcholine is hydrolysed in the body by cholinesterase and its effects are markedly prolonged and enhanced if given after anticholinesterases.

Beta blockers. Severe bronchospasm with subsequent pulmonary oedema was reported[1] after intra-ocular injection of acetylcholine chloride in a patient also receiving *metoprolol* by mouth.

1. Rasch D, *et al.* Bronchospasm following intraocular injection of acetylcholine in a patient taking metoprolol. *Anesthesiology* 1983; **59:** 583–5.

NSAIDs. According to licensed product information for acetylcholine chloride ophthalmic preparations, there have been reports that acetylcholine and carbachol were ineffective when used in patients treated with topical (ophthalmic) NSAIDs.

Uses and Administration

Acetylcholine is an endogenous chemical transmitter with a very wide range of actions in the body (see below). It is used as a miotic to reduce postoperative rises in intra-ocular pressure associated with cataract surgery, penetrating keratoplasty, iridectomy, and other anterior segment surgery (see p.1873) but is ineffective when applied topically as it is hydrolysed more rapidly than it can penetrate the cornea. Doses of 0.5 to 2 mL of a freshly prepared 1% solution of acetylcholine chloride are therefore instilled directly into the anterior chamber of the eye (intracameral instillation). Miosis occurs within seconds and lasts for about 20 minutes. A second application may be made if prolonged miosis is required.

Action. Acetylcholine is a powerful quaternary ammonium parasympathomimetic but its action is transient as it is rapidly destroyed by cholinesterase. It is released from postganglionic parasympathetic nerves and also from some postganglionic sympathetic nerves to produce peripheral actions which correspond to those of muscarine. It is accordingly a vasodilator and cardiac depressant, a stimulant of the vagus and the parasympathetic nervous system, and it has a tonic action on smooth muscle. It also increases lachrymal, salivary, and other secretions. All the muscarinic actions of acetylcholine are abolished by atropine.

Acetylcholine also has actions that correspond to those of nicotine and is accordingly a stimulant of skeletal muscle, the autonomic ganglia, and the adrenal medulla. The nicotinic actions of acetylcholine on skeletal muscle are blocked by competitive neuromuscular blockers; they are also inhibited by massive doses or discharge of acetylcholine itself, which has clinical application in relation to the mode of action of suxamethonium (p.1912).

Drugs that mimic or enhance the actions of acetylcholine in the body are known as **parasympathomimetics** and may be classified into 2 distinct pharmacological groups:

- **cholinergic agonists**, such as bethanechol, carbachol, methacholine, and pilocarpine which act directly on effector cells to mimic the effects of acetylcholine. They are sometimes referred to as cholinomimetics or true parasympathomimetics; some such as bethanechol, carbachol, and methacholine are choline esters
- **anticholinesterases** (cholinesterase inhibitors) which inhibit the enzymic hydrolysis of acetylcholine by acetylcholinesterase and other cholinesterases, thereby prolonging and enhancing its actions in the body. They may be classified by the length of time taken to restore active enzyme following binding of enzyme to drug. The 'reversible' anticholinesterases such as ambenonium, neostigmine, physostigmine, and pyridostigmine generally produce enzyme inhibition for a few hours, whereas 'irreversible' anticholinesterases such as dyflos and ecothiopate produce extremely prolonged inhibition, and return of cholinesterase activity depends on synthesis of new enzyme. Centrally acting reversible anticholinesterases include donepezil, galantamine, rivastigmine, and tacrine

Drugs such as fampridine and guanidine, which enhance the release of acetylcholine from nerve terminals, also have similar effects.

Diagnosis and testing. ***AUTONOMIC FAILURE.*** Acetylcholine has been used in a sweat-spot test for autonomic neuropathy in diabetic patients.[1] An area on the dorsum of the foot is painted with iodine and starch, followed by intradermal injection of acetylcholine into the centre of the area. Sweat produced in response to acetylcholine reacts with the iodine and starch to produce fine black dots corresponding to the pores of the sweat glands; a normal response is indicated by a uniform distribution of dark spots whereas in diabetic autonomic neuropathy this pattern is lost to a varying degree. A similar test has been carried out[2] to assess sympathetic nerve function and therefore predict the success of lumbar sympathectomy in patients with critical limb ischaemia.

1. Ryder REJ, *et al.* Acetylcholine sweatspot test for autonomic denervation. *Lancet* 1988; **i:** 1303–5.
2. Altomare DF. Acetylcholine sweat test: an effective way to select patients for lumbar sympathectomy. *Lancet* 1994; **344:** 976–8.

Preparations

USP 31: Acetylcholine Chloride for Ophthalmic Solution.

Proprietary Preparations (details are given in Part 3)
Austral.: Miochol; ***Belg.:*** Miochole; ***Canad.:*** Miochol-E; Miochol†; ***Chile:*** Miochol-E†; ***Fin.:*** Miochol-E; ***Fr.:*** Miochole; ***Ger.:*** Miochol-E; ***Gr.:*** Miochol-E; ***Hong Kong:*** Miochol-E; ***Indon.:*** Miochol-E; ***Irl.:*** Miochol; ***Israel:*** Miochol; Miochol-E; ***Ital.:*** Miochol-E; Miovisin; ***Mex.:*** Iloc; ***Neth.:*** Miochol; ***NZ:*** Miochol; ***Port.:*** Miochol; ***S.Afr.:*** Covochol; Miochol; ***Singapore:*** Miochol-E†; ***Swed.:*** Miochol-E; ***Switz.:*** Miochol; ***Thai.:*** Miochol†; ***Turk.:*** Miochol-E; ***UK:*** Miochol; ***USA:*** Miochol.

Apraclonidine Hydrochloride

(BANM, USAN, rINNM)

AL-02145 (apraclonidine); *p*-Aminoclonidine Hydrochloride; Aplonidine Hydrochloride; Apraclonidine, chlorhydrate d'; Apraclonidini hydrochloridum; Hidrocloruro de apraclonidina; NC-14. 2-[(4-Amino-2,6-dichlorophenyl)imino]imidazolidine hydrochloride; 2,6-Dichloro-*N*^{1}-imidazolidin-2-ylidene-*p*-phenylenediamine hydrochloride.

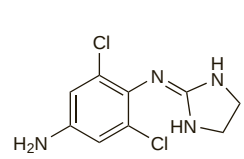
Апраклонидина Гидрохлорид

$C_9H_{10}Cl_2N_4,HCl$ = 281.6.

CAS — 66711-21-5 (apraclonidine); 73218-79-8 (apraclonidine hydrochloride).

ATC — S01EA03.

ATC Vet — QS01EA03.



(apraclonidine)

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

Pharmacopoeias. In *US*.
USP 31 (Apraclonidine Hydrochloride). A white to off-white, odourless to practically odourless powder. Soluble 1 in 34 of water, 1 in 74 of alcohol, and 1 in 13 of methyl alcohol; insoluble in chloroform, in ethyl acetate, and in hexanes. pH of a 1% solution in water is between 5.0 and 6.6. Store in airtight containers. Protect from light.

Adverse Effects and Precautions
Adverse effects after perioperative instillation of apraclonidine into the eye include hyperaemia, lid retraction, and mydriasis. Some patients may develop an exaggerated reduction in intra-ocular pressure. On regular instillation an ocular intolerance reaction may occur, characterised by hyperaemia, ocular pruritus, increased lachrymation, ocular discomfort, and oedema of the lids and conjunctiva; treatment should be stopped if these symptoms occur. Other adverse effects reported include dry mouth and nose, conjunctivitis, conjunctival blanching, blurred vision, asthenia, headache, and taste disturbances.

Systemic absorption can occur after application to the eye and may result in adverse effects similar to those of clonidine (p.1247). Cardiovascular effects have been reported; therefore apraclonidine should be used with caution in patients with severe cardiovascular disease, including hypertension, and in patients with a history of vasovagal attacks. Drowsiness may also occur. Depression has rarely been associated with use of apraclonidine and it should be used with caution in depressed patients.

Interactions
Systemic absorption may occur after topical application of apraclonidine to the eye and there is a theoretical possibility of interactions similar to those reported with clonidine (p.1248). Since the effects of apraclonidine on circulating catecholamines are unknown, licensed product information recommends that MAOIs should not be given with apraclonidine; tricyclic and related antidepressants and systemic sympathomimetics should also be avoided or used with caution.

Uses and Administration
Apraclonidine is an alpha$_2$-adrenoceptor agonist derived from clonidine (p.1247). It reduces intra-ocular pressure when instilled into the eye and is used in patients undergoing eye surgery, and as an adjunct in the management of glaucoma (p.1873). The reduction in intra-ocular pressure begins within an hour of instillation and is maximal after about 3 to 5 hours.

Apraclonidine is used as the hydrochloride, but the strength of an ophthalmic solution is usually expressed in terms of the base. Apraclonidine hydrochloride 11.5 mg is equivalent to about 10 mg of apraclonidine.

To control or prevent a postoperative increase in intraocular pressure in patients undergoing anterior segment laser surgery, a 1% solution is instilled into the eye one hour before surgery and again immediately upon completion of surgery.

For short-term adjunctive therapy in patients with raised intra-ocular pressure not controlled by conventional therapy, a 0.5% solution may be instilled three times daily.

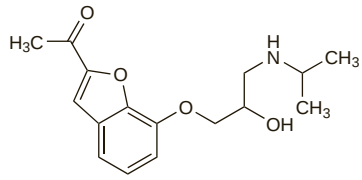
There is a loss of effect over time (tachyphylaxis) with apraclonidine and the benefit in most patients lasts for less than a month.

Preparations
USP 31: Apraclonidine Ophthalmic Solution.

Proprietary Preparations (details are given in Part 3)
Arg.: Iopidine†; ***Austral.:*** Iopidine; ***Austria:*** Iopidine; ***Belg.:*** Iopidine; ***Braz.:*** Iopidine†; ***Canad.:*** Iopidine; ***Chile:*** Iopidine†; ***Cz.:*** Iopidine†; ***Denm.:*** Iopidine; ***Fin.:*** Iopidine; ***Fr.:*** Iopidine; ***Ger.:*** Iopidine; ***Gr.:*** Iopidine; ***Hong Kong:*** Iopidine; ***India:*** Alfadrops; ***Irl.:*** Iopidine; ***Israel:*** Iopidine; ***Ital.:*** Iopidine; ***Jpn:*** Iopidine†; ***Malaysia:*** Iopidine†; ***Mex.:*** Iopidine; ***Neth.:*** Iopidine; ***Norw.:*** Iopidine; ***NZ:*** Iopidine†; ***Port.:*** Iopidine; ***S.Afr.:*** Iopidine; ***Singapore:*** Iopidine; ***Spain:*** Iopimax; ***Swed.:*** Iopidine; ***Switz.:*** Iopidine; ***Turk.:*** Iopidine; ***UK:*** Iopidine; ***USA:*** Iopidine; ***Venez.:*** Iopidine†.

Befunolol Hydrochloride *(rINNM)* ⊗
Béfunolol, Chlorhydrate de; Befunololi Hydrochloridum; BFE-60; Hidrocloruro de befunolol. 7-[2-Hydroxy-3-(isopropylamino)propoxy]-2-benzofuranyl methyl ketone hydrochloride.

Бефунолола Гидрохлорид
$C_{16}H_{21}NO_4$,HCl = 327.8.
CAS — 39552-01-7 (befunolol); 39543-79-8 (befunolol hydrochloride).
ATC — S01ED06.
ATC Vet — QS01ED06.



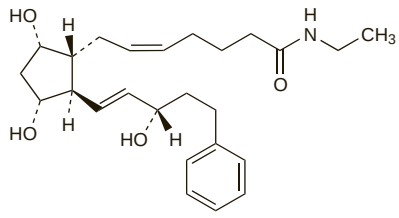
(befunolol)

Profile
Befunolol is a beta blocker (p.1225). It is used as the hydrochloride in the management of ocular hypertension and open-angle glaucoma (p.1873). Eye drops containing befunolol hydrochloride 0.25%, 0.5%, or 1% are instilled twice daily.

Preparations
Proprietary Preparations (details are given in Part 3)
Austria: Glauconex†; ***Gr.:*** Thilonium†; ***Ital.:*** Betaclar; ***Jpn:*** Bentos; ***Mon.:*** Bentos.

Bimatoprost *(BAN, USAN, rINN)*
AGN-192024; Bimatoprostum. (*Z*)-7-{(1*R*,2*R*,3*R*,5*S*)-3,5-Dihydroxy-2-[(1*E*,3*S*)-3-hydroxy-5-phenyl-1-pentenyl]cyclopentyl}-*N*-ethyl-5-heptenamide.

Биматопрост
$C_{25}H_{37}NO_4$ = 415.6.
CAS — 155206-00-1.
ATC — S01EE03.
ATC Vet — QS01EE03.



Adverse Effects and Precautions
As for Latanoprost, p.1882. Ocular pruritus is common. Hypertension and headache also commonly occur.

Pharmacokinetics
Small amounts of bimatoprost are absorbed from eye drops, with peak blood concentrations seen within 10 minutes of dosing. Bimatoprost is metabolised by oxidation, de-ethylation and glucuronidation and is excreted mainly in the urine with about 25% appearing in the faeces. The elimination half-life is 45 minutes.

Uses and Administration
Bimatoprost is a synthetic prostamide, a fatty-acid amide that is structurally related to dinoprost (prostaglandin F_2). It is used to reduce intra-ocular pressure in the treatment of open-angle glaucoma and ocular hypertension (p.1873). Reduction in pressure starts about 4 hours after instillation and is maximal within 8 to 12 hours; the effect lasts for at least 24 hours. It is given once daily in the evening as a 0.03% ophthalmic solution.

◊ References.

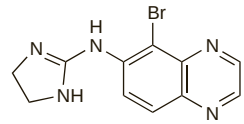
1. Sherwood M, *et al.* Six-month comparison of bimatoprost once-daily and twice-daily with timolol twice-daily in patients with elevated intraocular pressure. *Surv Ophthalmol* 2001; **45** (suppl 4): S361–S368.
2. Brandt JD, *et al.* Comparison of once- or twice-daily bimatoprost with twice-daily timolol in patients with elevated IOP: a 3-month clinical trial. *Ophthalmology* 2001; **108:** 1023–31.
3. Whitcup SM, *et al.* A randomised, double masked, multicentre clinical trial comparing bimatoprost and timolol for the treatment of glaucoma and ocular hypertension. *Br J Ophthalmol* 2003; **87:** 57–62.
4. Cantor LB, *et al.* Intraocular pressure-lowering efficacy of bimatoprost 0.03% and travoprost 0.004% in patients with glaucoma or ocular hypertension. *Br J Ophthalmol* 2006; **90:** 1370–3.

Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Lumigan; ***Austral.:*** Lumigan; ***Austria:*** Lumigan; ***Belg.:*** Lumigan; ***Braz.:*** Lumigan; ***Canad.:*** Lumigan; ***Chile:*** Lumigan; ***Cz.:*** Lumigan; ***Denm.:*** Lumigan; ***Fin.:*** Lumigan; ***Fr.:*** Lumigan; ***Ger.:*** Lumigan; ***Gr.:*** Lumigan; ***Hong Kong:*** Lumigan; ***Hung.:*** Lumigan; ***India:*** Lumigan; ***Irl.:*** Lumigan; ***Israel:*** Lumigan; ***Ital.:*** Lumigan; ***Malaysia:*** Lumigan†; ***Mex.:*** Lumigan; ***Neth.:*** Lumigan; ***Norw.:*** Lumigan; ***NZ:*** Lumigan; ***Philipp.:*** Lumigan; ***Pol.:*** Lumigan; ***Port.:*** Lumigan; ***S.Afr.:*** Lumigan; ***Singapore:*** Lumigan; ***Spain:*** Lumigan; ***Swed.:*** Lumigan; ***Switz.:*** Lumigan; ***Thai.:*** Lumigan; ***Turk.:*** Lumigan; ***UK:*** Lumigan; ***USA:*** Lumigan; ***Venez.:*** Lumigan.

Multi-ingredient: ***Cz.:*** Ganfort; ***Gr.:*** Ganfort; ***Port.:*** Ganfort; ***UK:*** Ganfort.

Brimonidine Tartrate *(BANM, USAN, rINNM)*
AGN-190342-LF; Brimonidin Tartrat; Brimonidine, Tartrate de; Brimonidini Tartras; Tartrato de brimonidina; UK-14304-18. 5-Bromo-6-(2-imidazolin-2-ylamino)quinoxaline D-tartrate.

Бримонидина Тартрат
$C_{11}H_{10}BrN_5,C_4H_6O_6$ = 442.2.
CAS — 59803-98-4 (brimonidine); 79570-19-7 (brimonidine tartrate).
ATC — S01EA05.
ATC Vet — QS01EA05.



(brimonidine)

Adverse Effects and Precautions
As for Apraclonidine Hydrochloride, p.1878.

In children. Systemic adverse effects, occasionally severe,[1] have been reported in children treated with brimonidine eye drops. In one study[2] adverse effects were reported in 70 of 83 children given adjunctive brimonidine, the most common effects being lethargy and excessive sleepiness; other effects included ocular irritation and blurred vision. Hypothermia occurred in a few cases, mainly in older children. Effects suggesting CNS depression, such as cyanosis and breathing difficulty, were rare, and were most likely in children less than 6 years of age or weighing less than 20 kg. Alternative medication should be considered in this group. In the UK, licensed product information contra-indicates use in neonates and infants under 2 years of age; use in children under 12 years of age is not recommended.

1. Sztajnbok J. Failure of naloxone to reverse brimonidine-induced coma in an infant. *J Pediatr* 2002; **140:** 485–6.
2. Al-Shahwan S, *et al.* Side-effect profile of brimonidine tartrate in children. *Ophthalmology* 2005; **112:** 2143–8.

Interactions
As for Apraclonidine Hydrochloride, p.1878.

Uses and Administration
Brimonidine is an alpha$_2$-adrenoceptor agonist with actions and uses similar to those of apraclonidine (p.1878). It is used to lower intra-ocular pressure in patients with open-angle glaucoma or ocular hypertension (p.1873), as an alternative or adjunct to topical beta blocker therapy. It may also be used as adjunctive therapy in patients with raised intra-ocular pressure not controlled by topical monotherapy with other drugs such as latanoprost and travoprost. The reduction in intra-ocular pressure is maximal about 2 hours after topical use.

In the management of glaucoma or ocular hypertension, eye drops containing brimonidine tartrate 0.1, 0.15, or 0.2% are instilled two or three times daily.

Glaucoma. References to the use of brimonidine in glaucoma and raised intra-ocular pressure.

1. Adkins JC, Balfour JA. Brimonidine: a review of its pharmacological properties and clinical potential in the management of open-angle glaucoma and ocular hypertension. *Drugs Aging* 1998; **12:** 225–41.
2. Cantor LB. The evolving pharmacotherapeutic profile of brimonidine, an alpha 2-adrenergic agonist, after four years of continuous use. *Expert Opin Pharmacother* 2000; **1:** 815–34.
3. David R. Brimonidine (Alphagan): a clinical profile four years after launch. *Eur J Ophthalmol* 2001; **11** (suppl 2): S72–S77.
4. Lee DA, Gornbein JA. Effectiveness and safety of brimonidine as adjunctive therapy for patients with elevated intraocular pressure in a large, open-label community trial. *J Glaucoma* 2001; **10:** 220–6.