5. Katz LJ. Twelve-month evaluation of brimonidine-purite versus brimonidine in patients with glaucoma or ocular hypertension. *J Glaucoma* 2002; **11:** 119–26.
6. Sherwood MB, *et al.* Twice-daily 0.2% brimonidine-0.5% timolol fixed-combination therapy vs monotherapy with timolol or brimonidine in patients with glaucoma or ocular hypertension: a 12-month randomized trial. *Arch Ophthalmol* 2006; **124:** 1230–8.
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.: Alphagan; Brimo-Klonal; Brimopress; Oftalmotonil; ***Austral.:*** Alphagan; Enidin; ***Austria:*** Alphagan; ***Belg.:*** Alphagan; ***Braz.:*** Alphagan; ***Canad.:*** Alphagan; ***Chile:*** Agglad Ofteno; Alphagan; Brimopress; ***Cz.:*** Alphagan; ***Denm.:*** Alphagan; ***Fin.:*** Alphagan; ***Fr.:*** Alphagan; ***Ger.:*** Alphagan; ***Gr.:*** Alphagan; Benil; Brimodine; Brinal; Brinidin; ***Hong Kong:*** Alphagan; ***Hung.:*** Alphagan†; ***India:*** Brimodin; Iobrim; ***Irl.:*** Alphagan; ***Israel:*** Alphagan; ***Ital.:*** Alphagan; ***Malaysia:*** Alphagan; ***Mex.:*** Agglad; Alphagan; Nor-Tenz; ***Neth.:*** Alphagan; ***Norw.:*** Alphagan; ***NZ:*** Alphagan; ***Philipp.:*** Alphagan; ***Pol.:*** Alphagan; ***Port.:*** Alphagan; ***S.Afr.:*** Alphagan; ***Singapore:*** Alphagan; ***Spain:*** Alphagan; ***Swed.:*** Alphagan; ***Switz.:*** Alphagan; ***Thai.:*** Alphagan; ***Turk.:*** Alphagan; ***UK:*** Alphagan; ***USA:*** Alphagan; ***Venez.:*** Agglad Ofteno; Alphagan.

Multi-ingredient: ***Arg.:*** Combigan; ***Austral.:*** Combigan; ***Braz.:*** Combigan; ***Canad.:*** Combigan; ***Chile:*** Combigan; ***Cz.:*** Combigan; ***Gr.:*** Combigan; ***Hung.:*** Combigan; ***India:*** Brimodin P; ***Irl.:*** Combigan; ***Mex.:*** Combigan-D; ***NZ:*** Combigan; ***Port.:*** Combigan; ***Switz.:*** Combigan; ***UK:*** Combigan; ***USA:*** Combigan.

Brinzolamide *(BAN, USAN, rINN)* ⊗

AL-4862; Brintsolamidi; Brinzolamid; Brinzolamida; Brinzolamidum. (*R*)-4-(Ethylamino)-3,4-dihydro-2-(3-methoxypropyl)-2*H*-thieno[3,2-e]-1,2-thiazine-6-sulfonamide 1,1-dioxide.

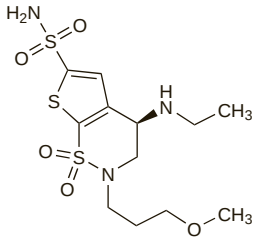
Бринзоламид

$C_{12}H_{21}N_3O_5S_3$ = 383.5.

CAS — 138890-62-7.

ATC — S01EC04.

ATC Vet — QS01EC04.



Pharmacopoeias. In *US.*
USP 31 (Brinzolamide). A white or almost white powder. Insoluble in water; slightly soluble in alcohol and in methyl alcohol.

Adverse Effects and Precautions

As for Dorzolamide, p.1880.

Effects on the eyes. Corneal oedema has been noted in the eyes of 2 patients after the long-term use of brinzolamide 1% eye drops;[1] both patients recovered after brinzolamide was stopped.

1. Zhao JC, Chen T. Brinzolamide induced reversible corneal decompensation. *Br J Ophthalmol* 2005; **89:** 389–90.

Uses and Administration

Brinzolamide is a carbonic anhydrase inhibitor with actions and uses similar to those of dorzolamide (p.1880). It is used to reduce intra-ocular pressure in the management of open-angle glaucoma and ocular hypertension (p.1873), either alone or as adjunctive therapy with a topical beta blocker. A 1% suspension is instilled into the eye two or three times daily.

Glaucoma. References.

1. Cvetkovic RS, Perry CM. Brinzolamide : a review of its use in the management of primary open-angle glaucoma and ocular hypertension. *Drugs Aging* 2003; **20:** 919–47.

Preparations

USP 31: Brinzolamide Ophthalmic Suspension.

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

Carbachol *(BAN, rINN)*

Carbach.; Carbacholi Cloridum; Carbacholine; Carbacholum; Carbacholum Chloratum; Carbacol; Choline Chloride Carbamate; Karbachol; Karbacholis; Karbakol; Karbakoli; Karbaminocholiny chlorek. *O*-Carbamoylcholine chloride; (2-Carbamoyloxyethyl)trimethylammonium chloride.

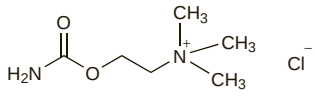
Карбахол

$C_6H_{15}ClN_2O_2$ = 182.6.

CAS — 51-83-2.

ATC — N07AB01; S01EB02.

ATC Vet — QA03AB92; QN07AB01; QS01EB02.



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

Pharmacopoeias. In *Chin., Eur.* (see p.vii), and *US.*
Ph. Eur. 6.2 (Carbachol). A white or almost white, crystalline, hygroscopic powder. Very slightly soluble in water; sparingly soluble in alcohol; practically insoluble in acetone. Store in airtight containers. Protect from light.
USP 31 (Carbachol). A white powder. Freely soluble in water; sparingly soluble in alcohol; practically insoluble in chloroform and in ether. Store in airtight containers.

Incompatibility. Chlorocresol (0.025 to 0.1%) and chlorobutanol (0.5%) were both found to be incompatible with a solution of carbachol (0.8%) and sodium chloride (0.69%), very slight precipitates forming on heating and increasing on standing.[1]

1. *PSGB Lab Report No.911* 1962.

Adverse Effects, Treatment, and Precautions

As described for choline esters under Acetylcholine Chloride, p.1877. Carbachol has substantial nicotinic activity which may be unmasked by the use of atropine to counteract muscarinic effects.

Carbachol also produces adverse effects and requires precautions similar to those of other miotics such as pilocarpine (p.1885) when used in the eye, but may produce more ciliary spasm than pilocarpine.

Effects on the gastrointestinal tract. Fatal oesophageal rupture has been reported[1] after subcutaneous injection of carbachol to relieve urinary retention.

1. Cochrane P. Spontaneous oesophageal rupture after carbachol therapy. *BMJ* 1973; **1:** 463–4.

Overdosage. Life-threatening attacks of profuse sweating, intestinal cramps, explosive defaecation, hypothermia, hypotension, and bradycardia occurred in a 36-year-old man after deliberate poisoning with 30 to 40 mg of carbachol.[1] The patient's 10-year-old son had died after poisoning with a similar dose of carbachol.

1. Sangster B, *et al.* Two cases of carbachol intoxication. *Neth J Med* 1979; **22:** 27–8.

Interactions

NSAIDs. Licensed UK product information for acetylcholine chloride ophthalmic preparations states that there have been reports that acetylcholine and carbachol were ineffective when used in patients treated with topical (ophthalmic) NSAIDs.

Uses and Administration

Carbachol, a choline ester, is a quaternary ammonium parasympathomimetic with the muscarinic and nicotinic actions of acetylcholine (p.1877). It is not inactivated by cholinesterases so its actions are more prolonged than those of acetylcholine.

Carbachol has a miotic action and is usually given intra-ocularly to produce miosis in ocular surgery and to reduce postoperative rises in intra-ocular pressure; up to 0.5 mL of a 0.01% solution is instilled into the anterior chamber of the eye (intracameral instillation). The maximum degree of miosis is usually obtained within 2 to 5 minutes of intra-ocular instillation and miosis lasts for 24 hours.

Eye drops containing up to 3% of carbachol have also been used to lower intra-ocular pressure in glaucoma, usually three times daily with other miotics (see below). Miosis occurs within 10 to 20 minutes of instillation and lasts for 4 to 8 hours; reduction in intra-ocular pressure lasts for 8 hours.

Carbachol has been used for the treatment of urinary retention including postoperative urinary retention. It has also been used in some countries for the treatment of decreased gastrointestinal motility.

Dry mouth. Carbachol has been used as an alternative to pilocarpine in the treatment of radiation-induced xerostomia.[1] The overall treatment of dry mouth is discussed on p.2140.

1. Joensuu H. Treatment for post-irradiation xerostomia. *N Engl J Med* 1994; **330:** 141–2.

Glaucoma and ocular hypertension. Carbachol is sometimes used as an alternative to pilocarpine in the management of glaucoma (p.1873) when resistance or intolerance to pilocarpine develops. It is also instilled into the anterior chamber of the eye (intracameral instillation) to minimise postoperative rises in intra-ocular pressure associated with ocular surgery, and some[1,2] have found it to be more effective than acetylcholine.

1. Ruiz RS, *et al.* Effects of carbachol and acetylcholine on intramuscular pressure after cataract extraction. *Am J Ophthalmol* 1989; **107:** 7–10.
2. Hollands RH, *et al.* Control of intraocular pressure after cataract extraction. *Can J Ophthalmol* 1990; **25:** 128–32.

Preparations

USP 31: Carbachol Intraocular Solution; Carbachol Ophthalmic Solution.

Proprietary Preparations (details are given in Part 3)
Arg.: Miostat; ***Austral.:*** Miostat; ***Belg.:*** Miostat; ***Braz.:*** Miostat†; ***Canad.:*** Carbastat†; Miostat; ***Cz.:*** Jestryl†; Miostat; ***Fin.:*** Doryl†; ***Ger.:*** Carbamann; Doryl†; Jestryl†; ***Hong Kong:*** Miostat†; ***Hung.:*** Miostat; ***Israel:*** Miostat; ***Ital.:*** Mioticol; ***Malaysia:*** Miostat; ***Neth.:*** Miostat; ***Philipp.:*** Miostat; ***Pol.:*** Miostat; ***S.Afr.:*** Miosys†; ***Singapore:*** Miostat; ***Swed.:*** Isopto Karbakolin; Miostat; ***Switz.:*** Doryl†; Miostat; ***Thai.:*** Miostat; ***Turk.:*** Miostat; ***USA:*** Carbastat; Miostat; ***Venez.:*** Miostat†.

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

Cyclopentolate Hydrochloride

(BANM, rINNM)

Ciklopentolát-hidroklorid; Ciklopentolato hidrochloridas; Cloridrato de Ciclopentolato; Cyclopentolate, chlorhydrate de; Cyclopentolati hydrochloridum; Cyklopentolát hydrochlorid; Cyklopentolathydroklorid; Hidrocloruro de ciclopentolato; Siklopentolat Hidroklorür; Syklopentolaattihydrokloridi. 2-Dimethylaminoethyl 2-(1-hydroxycyclopentyl)-2-phenylacetate hydrochloride.

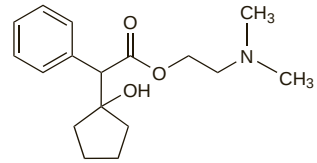
Циклопентолата Гидрохлорид

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

CAS — 512-15-2 (cyclopentolate); 5870-29-1 (cyclopentolate hydrochloride).

ATC — S01FA04.

ATC Vet — QS01FA04.



(cyclopentolate)

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

Pharmacopoeias. In *Eur.* (see p.vii), *Jpn*, and *US.*
Ph. Eur. 6.2 (Cyclopentolate Hydrochloride). A white or almost white, crystalline powder. Very soluble in water; freely soluble in alcohol. A 1% solution in water has a pH of 4.5 to 5.5.
USP 31 (Cyclopentolate Hydrochloride). A white crystalline powder, which develops a characteristic odour on standing. Very soluble in water; freely soluble in alcohol; insoluble in ether. pH of a 1% solution in water is between 4.5 and 5.5. Store at a temperature not exceeding 8° in airtight containers.

Adverse Effects, Treatment, and Precautions

As for Atropine Sulfate, p.1219.

Eye drops of cyclopentolate hydrochloride may cause temporary irritation.

Abuse. Cyclopentolate eye drops have been abused.[1] One of 2 patients who did so had been instilling 200 to 400 drops of cyclopentolate into both eyes daily for about 4 months, presumably for its CNS effects, and experienced intense nausea, vomiting, weakness, and tremors on withdrawal.

1. Sato EH, *et al.* Abuse of cyclopentolate hydrochloride (Cyclogyl) drops. *N Engl J Med* 1992; **326:** 1363–4.

Hypersensitivity. Two children developed hypersensitivity reactions shortly after the instillation of 1% cyclopentolate hydrochloride eye drops into each eye.[1] Both children initially had a facial rash but in one of them the rash later spread to include the arms and legs and was accompanied by mild breathlessness.

1. Jones LWJ, Hodes DT. Possible allergic reactions to cyclopentolate hydrochloride: case reports with literature review of uses and adverse reactions. *Ophthalmic Physiol Opt* 1991; **11:** 16–21.