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.

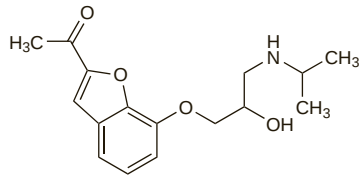
There is a loss of effect over time (tachyphylaxis) with apraclonidine and the benefit in most patients lasts for less than a month.

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.



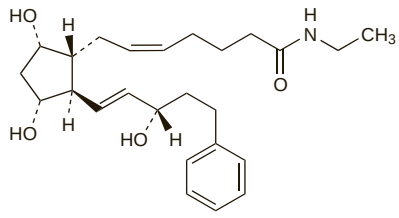
(befunolol)

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.

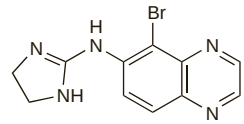
1. Sherwood M, *et al.* Six-month comparison of bimatoprost once-daily and twice-daily with timolol twice-daily in patients with elevated intraocular pressure. *Surv Ophthalmol* 2001; **45** (suppl 4): S361–S368.
2. Brandt JD, *et al.* Comparison of once- or twice-daily bimatoprost with twice-daily timolol 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.