Tetanus. Autonomic overactivity, usually due to excessive catecholamine release, may occur as a complication of tetanus and is usually controlled with sedation (see p.1901). Beta blockers have also been used but may produce severe hypertension and are therefore not usually recommended. Labetalol has both alpha- and beta-blocking properties and intravenous labetalol has been used successfully to control the cardiovascular effects of tetanus,[1] although it has not been shown to offer any advantage over propranolol in this situation. Esmolol, a short-acting beta blocker, has also been used.[2]

1. Domenighetti GM, *et al.* Hyperadrenergic syndrome in severe tetanus: extreme rise in catecholamines responsive to labetalol. *BMJ* 1984; **288:** 1483–4.
2. King WW, Cave DR. Use of esmolol to control autonomic instability of tetanus. *Am J Med* 1991; **91:** 425–8.

Tetralogy of Fallot. For the use of beta blockers in the management of tetralogy of Fallot, see under Uses of Propranolol, p.1381.

Tremor. Tremor is a rhythmical oscillation of part of the body caused by involuntary contraction of opposing muscles. It may occur during action, maintenance of posture, or at rest, and varies in frequency and amplitude. Resting tremor is associated mainly with parkinsonism (p.791), whereas action tremor, which includes postural tremor and kinetic tremor, occurs in a wide variety of disorders. Treatment of the underlying disorder may remove the tremor. Drugs such as bronchodilators, tricyclic antidepressants, lithium, and caffeine may induce tremor; withdrawal of the causative drug usually alleviates the tremor. However, tremor often has no known underlying cause. Such tremor is referred to as **essential tremor** or benign essential tremor; it is usually postural and tends to affect the hands, head, voice, and sometimes the legs and trunk. It is exacerbated by emotional stress and anxiety. Essential tremor may appear at any age and is a lifelong condition that may progress with increasing age. In many cases there is a family history of the disorder (familial essential tremor).

Mild cases of essential tremor may not require regular drug treatment. Single doses of a beta blocker or a benzodiazepine may be useful in acute circumstances to control exacerbations provoked by stress. A single dose of propranolol usually produces a maximum effect after 1 to 2 hours and the effect may persist for several hours. Small amounts of alcohol may also provide effective temporary relief of essential tremor, although its regular use is obviously discouraged.

For more severe cases of essential tremor long-term drug treatment may be required (and may also be tried in other forms of tremor).[1-5] A beta blocker (usually a non-cardioselective beta blocker such as propranolol) is often the first drug used. Up to 70% of people have been reported to respond, although the average tremor reduction is only about 50 to 60%. The beneficial effect appears to be mainly due to blockade of peripheral $beta_2$ receptors on extrafusal muscle fibres and muscle spindles, although there may also be a CNS effect. Adverse effects may be troublesome on long-term use. Primidone may also be tried[6] although there may be a high incidence of acute adverse reactions after initial doses. Concern has been expressed that patients may become tolerant to these drugs given long-term. However, 3 small studies found a reduced response on long-term therapy in only a few patients.[7-9] Local injection of botulinum A toxin has been tried in refractory essential tremor. Benzodiazepines, and antimuscarinic or dopaminergic antiparkinsonian drugs may be effective in some forms of tremor.[1] Other drugs that have shown some benefit include gabapentin and topiramate.[1-4,10] Many other drugs have been tried, but there is little evidence to support their use.[10] In very severe disabling cases, surgery (thalamotomy or deep brain stimulation) may have to be considered.

1. Habib-ur-Rehman. Diagnosis and management of tremor. *Arch Intern Med* 2000; **160:** 2438–44.
2. Louis ED. Essential tremor. *N Engl J Med* 2001; **345:** 887–91.
3. Lyons K, *et al.* Benefits and risks of pharmacological treatments for essential tremor. *Drug Safety* 2003; **26:** 461–81.
4. Pahwa R, Lyons KE. Essential tremor: differential diagnosis and current therapy. *Am J Med* 2003; **115:** 134–42.
5. Benito-León J, Louis ED. Clinical update: diagnosis and treatment of essential tremor. *Lancet* 2007; **369:** 1152–4.
6. Koller WC, Royse VL. Efficacy of primidone in essential tremor. *Neurology* 1986; **36:** 121–4.
7. Koller WC, Vetere-Overfield B. Acute and chronic effects of propranolol and primidone in essential tremor. *Neurology* 1989; **39:** 1587–8.
8. Calzetti S, *et al.* Clinical and computer-based assessment of long-term therapeutic efficacy of propranolol in essential tremor. *Acta Neurol Scand* 1990; **81:** 392–6.
9. Sasso E, *et al.* Primidone in the long-term treatment of essential tremor: a prospective study with computerized quantitative analysis. *Clin Neuropharmacol* 1990; **13:** 67–76.
10. Zesiewicz TA, *et al.* Practice parameter: therapies for essential tremor: report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2005; **64:** 2008–20. Also available at: http://www.neurology.org/cgi/reprint/64/12/2008.pdf (accessed 10/01/08)

Betaxolol Hydrochloride

(BANM, USAN, rINNM) ⊗

ALO-1401-02; Betaksolol Hidroklorür; Betaksololihydrokloridi; Betaksololio hidrochloridas; Bétaxolol, chlorhydrate de; Betaxolol-hidroklorid; Betaxolol-hydrochlorid; Betaxololhydroklorid; Betaxololi hydrochloridum; Hidrocloruro de betaxolol; SL-75212-10. 1-{4-[2-(Cyclopropylmethoxy)ethyl]phenoxy}-3-isopropylaminopropan-2-ol hydrochloride.

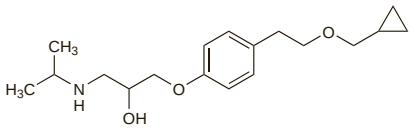
Бетаксолола Гидрохлорид

$C_{18}H_{29}NO_3$,HCl = 343.9.

CAS — 63659-18-7 (betaxolol); 63659-19-8 (betaxolol hydrochloride).

ATC — C07AB05; S01ED02.

ATC Vet — QC07AB05; QS01ED02.



(betaxolol)

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

Ph. Eur. 6.2 (Betaxolol Hydrochloride). A white or almost white crystalline powder. Very soluble in water; freely soluble in alcohol; soluble in dichloromethane. Protect from light.

USP 31 (Betaxolol Hydrochloride). A white crystalline powder. Freely soluble in water, in alcohol, in chloroform, and in methyl alcohol. pH of a 2% solution in water is between 4.5 and 6.5. Store in airtight containers.

Adverse Effects, Treatment, and Precautions

As for Beta Blockers, p.1226.

Interactions

The interactions associated with beta blockers are discussed on p.1228.

Pharmacokinetics

Betaxolol is completely absorbed from the gastrointestinal tract and undergoes only minimal first-pass metabolism, resulting in a high oral bioavailability of about 90%. It has high lipid solubility. Betaxolol is about 50% bound to plasma proteins. It crosses the placenta and is distributed into breast milk where higher concentrations have been achieved than in maternal blood. The plasma elimination half-life of betaxolol ranges from 14 to 22 hours. The primary route of elimination is via hepatic metabolism and urinary excretion; only about 15% is excreted in the urine as unchanged drug.

Pregnancy and breast feeding. The pharmacokinetics of betaxolol were investigated in the perinatal period in 28 pregnant hypertensive patients receiving doses of 10 to 40 mg daily.[1] Pharmacokinetic values were similar to those seen in non-pregnant patients. Umbilical-cord concentrations were similar to maternal blood concentrations and showed a negative correlation between concentration in cord blood and timing of the last dose of betaxolol. Thus the betaxolol concentration in neonates can be considerably reduced by stopping maternal drug use 16 to 18 hours before birth. The blood-betaxolol half-life in the neonates ranged from 14.8 to 38.5 hours. The mean apparent half-life in infants with gestational age less than 36 weeks was about 32% higher than in full-term neonates. Betaxolol concentrations in milk and/or colostrum were determined in 3 mothers. In all samples the milk-to-blood ratio was greater than 2.

1. Morselli PL, *et al.* Placental transfer and perinatal pharmacokinetics of betaxolol. *Eur J Clin Pharmacol* 1990; **38:** 477–83.

Uses and Administration

Betaxolol is a cardioselective beta blocker (p.1225). It is reported to lack intrinsic sympathomimetic activity and to have little membrane-stabilising activity.

Betaxolol is used as the hydrochloride in the management of hypertension (p.1171), angina pectoris (p.1157), and glaucoma (p.1873).

In **hypertension** betaxolol hydrochloride is given in an initial oral dose of 10 mg once daily, which may be doubled if necessary after 1 to 2 weeks. Doses above 20 mg daily do not usually give additional benefit, but up to 40 mg daily has been tolerated. Similar doses are used in **angina pectoris**.

An initial dose of 5 mg daily is suggested for elderly patients. Reduced dosages should also be used in patients with severe renal impairment (see below).

Eye drops containing the equivalent of 0.25 or 0.5% betaxolol as the hydrochloride are instilled twice daily to reduce raised intra-ocular pressure in ocular hypertension and open-angle **glaucoma**.

◊ General references.

1. Buckley MM-T, *et al.* Ocular betaxolol: a review of its pharmacological properties, and therapeutic efficacy in glaucoma and ocular hypertension. *Drugs* 1990; **40:** 75–90.

Administration in renal impairment. The clearance of betaxolol is reduced in patients with renal impairment and the dose may therefore need to be reduced. Licensed US product information recommends an initial dose of betaxolol hydrochloride 5 mg daily in patients with severe renal impairment or on dialysis; the dose may be increased by 5 mg every 2 weeks, to a maximum of 20 mg daily.

Speech disorders. A 50-year-old man who had stuttered since childhood obtained striking improvement in his stuttering when he was given betaxolol 20 mg daily for essential hypertension.[1]

1. Burris JF, *et al.* Betaxolol and stuttering. *Lancet* 1990; **335:** 223.

Preparations

BP 2008: Betaxolol Eye Drops, Solution; Betaxolol Eye Drops, Suspension; ***USP 31:*** Betaxolol Ophthalmic Solution; Betaxolol Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Betasel; Tonobexol; ***Austral.:*** Betoptic; Betoquin; ***Austria:*** Betoptic; Kerlone; ***Belg.:*** Betoptic; Kerlone; ***Braz.:*** Betoptic; Presmin; ***Canad.:*** Betoptic; ***Chile:*** Bemaz; Beof; Betoptic; ***Cz.:*** Betalmic; Betaxa; Betoptic; Lokren; ***Denm.:*** Betoptic; Kerlon†; ***Fin.:*** Betoptic; Kerlon; ***Fr.:*** Betoptic; Kerlone; ***Ger.:*** Betoptima; Kerlone; ***Gr.:*** Armament; Betoptic; Eifel; Kerlone; Pertaxol†; ***Hong Kong:*** Betoptic; ***Hung.:*** Betoptic; Lokren; ***India:*** Optipres; ***Indon.:*** Betoptima; Optibet; ***Irl.:*** Betoptic; ***Israel:*** Betoptic; Kerlone; ***Ital.:*** Betoptic; Kerlon; ***Jpn:*** Kerlong; ***Malaysia:*** Betac; Betoptic; Kerlone; ***Mex.:*** Beofta†; Betoptic; BTX-HA Ofteno; ***Neth.:*** Betoptic; Kerlon; ***Norw.:*** Betoptic; ***NZ:*** Betoptic; ***Philipp.:*** Betoptic; Kerlone; ***Pol.:*** Betabion; Betoptic; Lokren; Optibetol; ***Port.:*** Bertocil; Betaglau; Betoptic; Davixolol; ***Rus.:*** Betac (Бетак); Betoptic (Бетоптик); Lokren (Локрен); ***S.Afr.:*** Betoptic; ***Singapore:*** Betac; Betoptic; Kerlone; ***Spain:*** Betoptic; ***Swed.:*** Betoptic; Kerlon†; ***Switz.:*** Betoptic; Kerlon†; ***Thai.:*** Betoptic; ***Turk.:*** Betoptic; ***UK:*** Betoptic; ***USA:*** Betoptic; Kerlone; ***Venez.:*** Betaxol; Betoptic.

Bevantolol Hydrochloride *(BANM, USAN, rINNM)* ⊗

Bévantolol, Chlorhydrate de; Bevantololhydroklorid; Bevantololi Hydrochloridum; Bevantololihydrokloridi; CI-775; Hidrocloruro de bevantolol; NC-1400. 1-(3,4-Dimethoxyphenethylamino)-3-*m*-tolyloxypropan-2-ol hydrochloride.

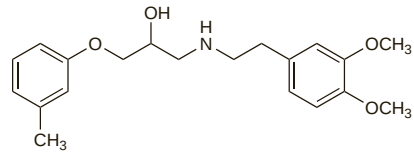
Бевантолола Гидрохлорид

$C_{20}H_{27}NO_4$,HCl = 381.9.

CAS — 59170-23-9 (bevantolol); 42864-78-8 (bevantolol hydrochloride).

ATC — C07AB06.

ATC Vet — QC07AB06.



(bevantolol)

Profile

Bevantolol is a cardioselective beta blocker (p.1225). It is reported to lack significant intrinsic sympathomimetic activity but has weak membrane-stabilising properties and also has vasodilator activity. It has been given orally as the hydrochloride in the management of hypertension and angina pectoris.

◊ References.

1. Frishman WH, *et al.* Bevantolol: a preliminary review of its pharmacodynamic and pharmacokinetic properties, and therapeutic efficacy in hypertension and angina pectoris. *Drugs* 1988; **35:** 1–21.