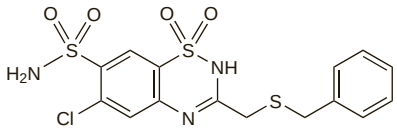
Benzthiazide *(BAN, rINN)* ⊗

Benzthiazidum; Benztiazida; P-1393. 3-Benzylthiomethyl-6-chloro-2*H*-1,2,4-benzothiadiazine-7-sulphonamide 1,1-dioxide.

Бензтиазид

$C_{15}H_{14}ClN_3O_4S_3$ = 431.9.

CAS — 91-33-8.



Profile

Benzthiazide is a thiazide diuretic with properties similar to those of hydrochlorothiazide (p.1307). It is used for oedema, including that associated with heart failure (p.1165), and has also been used for hypertension (p.1171). It has been given alone but is often given with triamterene. The usual initial oral dose for oedema is 75 mg daily, although higher doses have been given. The dose is reduced for maintenance; intermittent dosing may be adequate.

Preparations

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

Multi-ingredient: ***India:*** Ditide; ***Switz.:*** Dyrenium compositum; ***UK:*** Dytide.

Bepridil Hydrochloride *(BANM, USAN, rINNM)*

Bepridiilihydrokloridi; Bépridil, Chlorhydrate de; Bepridilhydroklorid; Bepridili Hydrochloridum; CERM-1978; Hidrocloruro de bepridil; Org-5730. *N*-Benzyl-*N*-(3-isobutoxy-2-pyrrolidin-1-ylpropyl)aniline hydrochloride monohydrate.

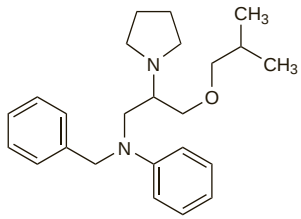
Бепридила Гидрохлорид

$C_{24}H_{34}N_2O,HCl,H_2O$ = 421.0.

CAS — 64706-54-3 (bepridil); 49571-04-2 (bepridil); 64616-81-5 (anhydrous bepridil hydrochloride); 74764-40-2 (bepridil hydrochloride monohydrate).

ATC — C08EA02.

ATC Vet — QC08EA02.



(bepridil)

Profile

Bepridil is a calcium-channel blocker (p.1154). It has similar properties to nifedipine (p.1350) but reduces the heart rate and does not usually cause reflex tachycardia. It also has antiarrhythmic activity. It is not related chemically to other calcium-channel blockers such as diltiazem, nifedipine, or verapamil.

Bepridil is used as the hydrochloride in the management of angina pectoris (p.1157). Ventricular arrhythmias, including torsade de pointes, and agranulocytosis have been associated with bepridil and, as a result, it is usually reserved for patients who have not responded adequately to other anti-anginal drugs. The usual initial dose is 200 mg of bepridil hydrochloride orally once daily. Provided that prolongation of the QT interval has not occurred after 2 to 4 weeks, the dose may be increased, if necessary, to a maximum of 300 mg once daily. Elderly patients and those with hepatic or renal impairment may be given an initial dose of 100 mg once daily; in exceptional circumstances this may be increased to a maximum of 200 mg once daily.

◊ References.

1. Hollingshead LM, *et al.* Bepridil: a review of its pharmacological properties and therapeutic use in stable angina pectoris. *Drugs* 1992; **44:** 835–57.
2. Awni WM, *et al.* Pharmacokinetics of bepridil and two of its metabolites in patients with end-stage renal disease. *J Clin Pharmacol* 1995; **35:** 379–83.

Porphyria. Bepridil is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *in-vitro* systems.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Unicordium; ***USA:*** Vascor†.

Beraprost Sodium *(USAN, rINNM)*

Beraprost sódico; Béraprost Sodique; ML-1129; ML-1229 (beraprost); Natrii Beraprostum; TRK-100. Sodium (±)-(1*R*,2*R*,3a*S*,8b*S*)-2,3,3a,8b-tetrahydro-2-hydroxy-1-[(*E*)-(3*S*,4*RS*)-3-hydroxy-4-methyl-1-octen-6-ynyl]-1*H*-cyclopenta[*b*]benzofuran-5-butyrate.

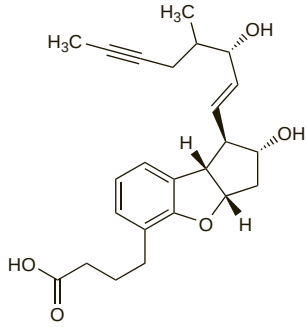
Натрий Берапрост

$C_{24}H_{29}NaO_5$ = 420.5.

CAS — 88430-50-6 (beraprost); 88475-69-8 (beraprost sodium).

ATC — B01AC19.

ATC Vet — QB01AC19.



(beraprost)

Profile

Beraprost is a synthetic analogue of epoprostenol (prostacyclin) that causes vasodilatation and prevents platelet aggregation. It is given orally as the sodium salt in the management of pulmonary hypertension (p.1179) and peripheral vascular disease (p.1178).

In primary pulmonary hypertension, beraprost sodium is given in an initial dose of 60 micrograms daily in three divided doses; this may be increased gradually if necessary to 180 micrograms daily in three or four divided doses. For peripheral vascular disease a dose of 120 micrograms daily in three divided doses is used.

Adverse effects of beraprost include headache, flushing, nausea, diarrhoea, and increased liver enzyme, bilirubin, and triglyceride concentrations.

Cardiovascular disorders. References to the use of beraprost for pulmonary hypertension or intermittent claudication;[1-7] results of studies for the latter indication have been conflicting. It has been tried with sildenafil in patients with pulmonary hypertension.[8]

1. Nagaya N, *et al.* Effect of orally active prostacyclin analogue on survival of outpatients with primary pulmonary hypertension. *J Am Coll Cardiol* 1999; **34:** 1188–92.
2. Lievre M, *et al.* Oral beraprost sodium, a prostaglandin I analogue, for intermittent claudication: a double-blind, randomized, multicenter controlled trial. *Circulation* 2000; **102:** 426–31.
3. Melian EB, Goa KL. Beraprost: a review of its pharmacology and therapeutic efficacy in the treatment of peripheral arterial disease and pulmonary arterial hypertension. *Drugs* 2002; **62:** 107–33.
4. Galiè N, *et al.* Effects of beraprost sodium, an oral prostacyclin analogue, in patients with pulmonary arterial hypertension: a randomized, double-blind, placebo-controlled trial. *J Am Coll Cardiol* 2002; **39:** 1496–1502.
5. Mohler ER, *et al.* Treatment of intermittent claudication with beraprost sodium, an orally active prostaglandin I analogue: a double-blinded, randomized, controlled trial. *J Am Coll Cardiol* 2003; **41:** 1679–86.
6. Barst RJ, *et al.* Beraprost therapy for pulmonary arterial hypertension. *J Am Coll Cardiol* 2003; **41:** 2119–25.
7. Hashiguchi M, *et al.* Studies on the effectiveness and safety of cilostazol, beraprost sodium, prostaglandin E1 for the treatment of intermittent claudication. *Yakugaku Zasshi* 2004; **124:** 321–32.
8. Ikeda D, *et al.* Addition of oral sildenafil to beraprost is a safe and effective therapeutic option for patients with pulmonary hypertension. *J Cardiovasc Pharmacol* 2005; **45:** 286–9.

Preparations

Proprietary Preparations (details are given in Part 3)
Indon.: Dorner; ***Jpn:*** Dorner; ***Philipp.:*** Dorner; ***Thai.:*** Dorner.

Beta Blockers ⊗

β-Bloqueantes.

Бета-блокаторы

Beta blockers (beta-adrenoceptor blocking drugs or antagonists) are competitive antagonists of catecholamines at beta-adrenergic receptors in a wide range of tissues. Although they have broadly similar properties they differ in their affinity for $beta_1$ or $beta_2$ receptor subtypes, intrinsic sympathomimetic activity, membrane-stabilising activity, blockade of alpha-adrenergic receptors, and pharmacokinetic properties including differences in lipid solubility (see Table 4, below, for some of these characteristics). These differences may affect the choice of drug in specific situations.

Table 4. Characteristics of beta blockers.

Beta blocker	$Beta_1$ selectivity	ISA*	MSA**	Vasodilator activity
Acebutolol	+	+	+	0
Alprenolol	0	+	0	0
Atenolol	+	0	0	0
Betaxolol	+	0	0	0
Bisoprolol	+	0	0	0
Carteolol	0	+	0	0
Carvedilol	0	0	0	+
Celiprolol	+	+	–	+
Esmolol	+	0	0	0
Labetalol	0	0	0	+
Levobunolol	0	0	0	0
Metipranolol	0	0	0	0
Metoprolol	+	0	0	0
Nadolol	0	0	0	0
Nebivolol	+	0	0	+
Oxprenolol	0	+	+	0
Penbutolol	0	0	0	0
Pindolol	0	++	0	0
Propranolol	0	0	++	0
Sotalol	0	0	0	0
Timolol	0	0	0	0

0 = absent or low; + = moderate; ++ = high; – = no information

* ISA = Intrinsic sympathomimetic activity

** MSA = Membrane-stabilising activity