Preparations

USP 31: Benazepril Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Boncordin†; ***Belg.:*** Cibacen; ***Braz.:*** Lotensin; ***Canad.:*** Lotensin; ***Denm.:*** Cibacen; ***Fr.:*** Briem; Cibacene; ***Ger.:*** Cibacen; ***Gr.:*** Cibacen; ***Hung.:*** Lotensin; ***India:*** Benace; ***Indon.:*** Cibacen; ***Irl.:*** Cibacen; ***Israel:*** Cibacen; ***Ital.:*** Cibacen; Tensanil; Zinadril; ***Mex.:*** Lotensin; ***Neth.:*** Cibacen; ***Philipp.:*** Cibacen; ***Pol.:*** Lisonid; Lotensin; ***Rus.:*** Lotensin (Лотензин); ***S.Afr.:*** Cibace; ***Spain:*** Cibacen; Labopal; ***Switz.:*** Cibacen; ***Turk.:*** Cibacen; ***USA:*** Lotensin; ***Venez.:*** Lotensin†.

Multi-ingredient: ***Arg.:*** Adrebloc†; Amlopril; Amzepril†; Arteriosan Plus; Coroval B; Ilduc Duo; Pelmec Duo; Terloc Duo; ***Braz.:*** Lotensin H; ***Fr.:*** Briazide; Cibadrex; ***Ger.:*** Benazeplus; Benazepril comp; Benazepril HCT; Cibadrex; ***Gr.:*** Cibadrex; ***Hung.:*** Lotensin HCT; ***India:*** Amace-BP; ***Ital.:*** Cibadrex; Tensadiur; Zinadiur; ***Neth.:*** Cibadrex; ***Pol.:*** Lotensin HCT; ***S.Afr.:*** Cibadrex; ***Spain:*** Cibadrex; Labodrex; ***Switz.:*** Cibadrex; ***Turk.:*** Cibadrex; ***USA:*** Lotensin HCT; Lotrel; ***Venez.:*** Amlibon B.

Bencyclane Fumarate *(rINNM)*

Bencyclane, Fumarate de; Bencyclane Hydrogen Fumarate; Bencyclani Fumaras; Bensiklan Hidrojen Fumarat; Fumarato de benciclano. 3-(1-Benzylcycloheptyloxy)-*NN*-dimethylpropylamine hydrogen fumarate.

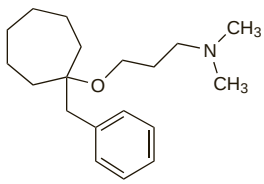
Бенциклана Фумарат

$C_{19}H_{31}NO,C_4H_4O_4$ = 405.5.

CAS — 2179-37-5 (bencyclane); 14286-84-1 (bencyclane fumarate).

ATC — C04AX11.

ATC Vet — QC04AX11.



(bencyclane)

Profile

Bencyclane fumarate is a vasodilator used in the management of peripheral (p.1178) and cerebral vascular disorders (p.1165) in usual oral doses of 100 to 200 mg three times daily. It has also been given intravenously.

Bencyclane acefyllinate has also been used.

Preparations

Proprietary Preparations (details are given in Part 3)

Austria: Ludilat; ***Braz.:*** Fludilat; ***Ger.:*** Fludilat; ***Hung.:*** Halidor; ***Indon.:*** Fludilat; ***Pol.:*** Halidor; ***Port.:*** Fludilat†; Fluxema†; ***Rus.:*** Halidor (Галидор); ***Thai.:*** Fludilat; ***Turk.:*** Angiodel; ***Venez.:*** Dantifar†; Fludilat.

Bendroflumethiazide *(BAN, rINN)* ⊗

Bendrofluaz.; Bendrofluazide; Bendroflumethiazid; Bendroflumétháizide; Bendroflumethiazidum; Bendroflumetiatsidi; Bendroflumetiazid; Bendroflumetiazida; Bendroflumetiazidas; Benzydroflumethiazide; FT-81. 3-Benzyl-3,4-dihydro-6-trifluoromethyl-2*H*-1,2,4-benzothiadiazine-7-sulphonamide 1,1-dioxide.

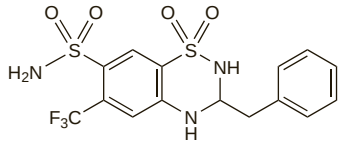
Бендрофлуметиазид

$C_{15}H_{14}F_3N_3O_4S_2$ = 421.4.

CAS — 73-48-3.

ATC — C03AA01.

ATC Vet — QC03AA01.



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

Ph. Eur. 6.2 (Bendroflumethiazide). A white or almost white crystalline powder. Practically insoluble in water; soluble in alcohol; freely soluble in acetone.

USP 31 (Bendroflumethiazide). A white to cream-coloured, finely divided, crystalline powder. Is odourless or has a slight odour. Practically insoluble in water; soluble 1 in 23 of alcohol and 1 in 200 of ether; freely soluble in acetone. Store in airtight containers.

Adverse Effects, Treatment, and Precautions

As for Hydrochlorothiazide, p.1307.

Breast feeding. Bendroflumethiazide is used to suppress lactation (see Uses below). However, the American Academy of Pediatrics considers[1] that it is usually compatible with breast feeding.

1. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 06/07/04)

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

Overdosage. Tonic-clonic convulsions occurred in a previously healthy 14-year-old girl after ingestion of bendroflumethiazide 150 to 200 mg.[1] The convulsions were not associated with any measurable disturbance of serum electrolytes.

1. Hine KR, *et al.* Bendrofluazide convulsions. *Lancet* 1982; **i:** 564.

Interactions

As for Hydrochlorothiazide, p.1309.

Pharmacokinetics

Bendroflumethiazide has been reported to be completely absorbed from the gastrointestinal tract and to have a plasma half-life of about 3 or 4 hours. It is highly bound to plasma proteins. There are indications that bendroflumethiazide is fairly extensively metabolised; about 30% is excreted unchanged in the urine.

◊ References.

1. Beermann B, *et al.* Pharmacokinetics of bendroflumethiazide. *Clin Pharmacol Ther* 1977; **22:** 385–8.
2. Beermann B, *et al.* Pharmacokinetics of bendroflumethiazide in hypertensive patients. *Eur J Clin Pharmacol* 1978; **13:** 119–24.

Uses and Administration

Bendroflumethiazide is a thiazide diuretic with actions and uses similar to those of hydrochlorothiazide (p.1310). It is used for hypertension (p.1171), either alone or with other antihypertensives such as ACE inhibitors and beta blockers. It is also used for oedema, including that associated with heart failure (p.1165), and with renal or hepatic disorders. Other indications have included the suppression of lactation.

Bendroflumethiazide is given orally; diuresis starts in about 2 hours after a dose, peaks after about 3 to 6 hours, and lasts for 12 to 18 hours or longer.

In the treatment of **hypertension** bendroflumethiazide 2.5 mg daily, either alone or with other antihypertensives, is usually adequate although doses of up to 20 mg daily have sometimes been suggested.

In the treatment of **oedema** the usual initial dose is 5 to 10 mg daily or on alternate days; in some cases initial doses of up to 20 mg may be necessary. Maintenance dosage schedules have varied from 2.5 to 10 mg once to three times weekly in the UK to 2.5 to 5 mg daily or intermittently in the USA.

An initial dose for children is up to 400 micrograms/kg daily, reduced to 50 to 100 micrograms/kg for maintenance.

Doses of 5 mg twice daily for about 5 days have been used to **suppress lactation**.

In the management of **idiopathic hypercalciuria** (see Renal Calculi, p.2181) the *BNF* considers that, with increased fluid intake, a sufficient dose is 2.5 mg daily.

Preparations

BP 2008: Bendroflumethiazide Tablets;
USP 31: Bendroflumethiazide Tablets; Nadolol and Bendroflumethiazide Tablets.

Proprietary Preparations (details are given in Part 3)

Austral.: Aprinox; ***Denm.:*** Centyl; ***Irl.:*** Centyl; ***Norw.:*** Centyl; ***NZ:*** Neo-NaClex; ***Swed.:*** Salures; ***UK:*** Aprinox; Neo-NaClex; ***USA:*** Naturetin†.

Multi-ingredient: ***Arg.:*** Hidromens†; Pertenso; Sumal; ***Austria:*** Inderetic†; Sali-Aldopur; ***Belg.:*** Inderetic†; ***Braz.:*** Diserim; ***Denm.:*** Centyl med Kaliumklorid; ***Fr.:*** Precyclan; Tensionorme; ***Ger.:*** Docidrazin†; Dociretic; Pertenso N; Sali-Aldopur†; Sotaziden N; Spirostada comp†; Tensoflux; ***Irl.:*** Centyl K; Low Centyl K; ***Mex.:*** Corgaretic; ***Neth.:*** Inderetic; ***Norw.:*** Centyl med Kaliumklorid; ***S.Afr.:*** Corgaretic; Inderetic†; ***Spain:*** Betadipresan Diu†; Neatenol Diu; Neatenol Diuvas; Spiromeston; ***Swed.:*** Centyl K; Salures-K; ***Switz.:*** Inderetic†; ***UK:*** Centyl K; Corgaretic†; Inderetic†; Inderex†; Neo-NaClex-K; Prestim; ***USA:*** Corzide; Rauzide†.

Benfluorex Hydrochloride *(BANM, pINNM)*

Benfluoreksihydrokloridi; Benfluorekso hidrochloridas; Benfluorex, chlorhydrate de; Benfluorex-hidroklorid; Benfluorex-hydrochlorid; Benfluorexhydroklorid; Benfluorexi hydrochloridum; Hidrocloruro de benfluorex; JP-992; SE-780. 2-[α-Methyl-3-(trifluoromethyl)phenethylamino]ethyl benzoate hydrochloride.

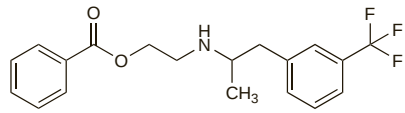
Бенфлуорекса Гидрохлорид

$C_{19}H_{20}F_3NO_2$,HCl = 387.8.

CAS — 23602-78-0 (benfluorex); 35976-51-3 (± benfluorex); 23642-66-2 (benfluorex hydrochloride).

ATC — C10AX04.

ATC Vet — QC10AX04.



(benfluorex)

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

Ph. Eur. 6.2 (Benfluorex Hydrochloride). A white or almost white powder. It exhibits polymorphism. Slightly soluble in water; sparingly soluble or soluble in alcohol; soluble in dichloromethane; freely soluble in methyl alcohol.

Profile

Benfluorex hydrochloride is a lipid regulating drug used in the treatment of hyperlipidaemias (p.1169). It has also been used as an adjunct in the management of type 2 diabetes mellitus (p.431).

Benfluorex hydrochloride is given orally in usual doses of 150 mg three times daily with meals.

Preparations

Proprietary Preparations (details are given in Part 3)

Fr.: Mediator; ***Gr.:*** Lipophoral; ***Hong Kong:*** Mediaxal; ***Ital.:*** Mediaxal†; ***Malaysia:*** Axal; Mediaxal; ***Port.:*** Mediator; ***Singapore:*** Mediaxal; ***Spain:*** Modulator†; ***Venez.:*** Lipascor.

Benidipine Hydrochloride *(rINNM)*

Bénidipine, Chlorhydrate de; Benidipini Hydrochloridum; Hidrocloruro de benidipino; KW-3049; Nakadipine Hydrochloride. (±)-(*R**)-3-[(*R**)-1-Benzyl-3-piperidyl]methyl 1,4-dihydro-2,6-dimethyl-4-(*m*-nitrophenyl)-3,5-pyridinedicarboxylate hydrochloride.

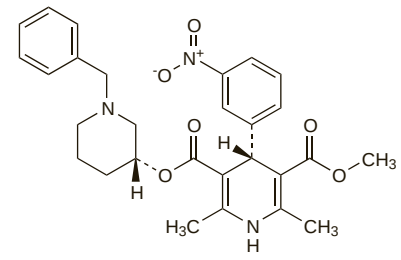
Бенидипина Гидрохлорид

$C_{28}H_{31}N_3O_6$,HCl = 542.0.

CAS — 105979-17-7 (benidipine); 91599-74-5 (benidipine hydrochloride).

ATC — C08CA15.

ATC Vet — QC08CA15.



(benidipine)

Pharmacopoeias. In *Jpn.*

Profile

Benidipine is a dihydropyridine calcium-channel blocker with general properties similar to those of nifedipine (p.1350). It is given orally as the hydrochloride in the management of hypertension (p.1171) and angina pectoris (p.1157). In hypertension, the usual dose is 2 to 4 mg once daily, increased to 8 mg once daily if necessary. In angina pectoris, the usual dose is 4 mg twice daily.

Preparations

Proprietary Preparations (details are given in Part 3)

India: Caritec; ***Jpn:*** Coniel; ***Philipp.:*** Coniel.

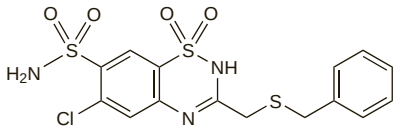
Benzthiazide *(BAN, rINN)* ⊗

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.

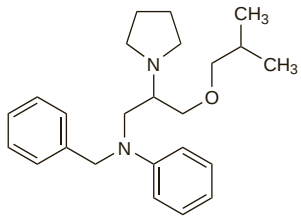
Бепридила Гидрохлорид

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

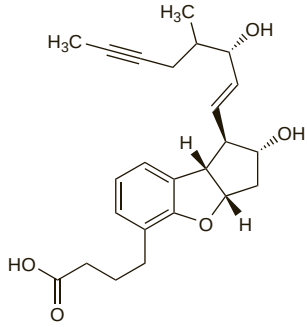
Натрий Берапрост

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