Profile
Barnidipine 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). The initial dose is 5 to 10 mg once daily, increased, according to response, to a usual maintenance dose of 10 to 20 mg once daily.

◊ Reviews.

1. Malhotra HS, Plosker GL. Barnidipine. *Drugs* 2001; **61:** 989–96.
2. Liau CS. Barnidipine: a new calcium channel blocker for hypertension treatment. *Expert Rev Cardiovasc Ther* 2005; **3:** 207–13.

Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Dilacor†; ***Belg.:*** Vasexten; ***Cz.:*** Vasexten; ***Gr.:*** Vasexten; ***Ital.:*** Libradin; Osipine; Vasexten; ***Jpn:*** Hypoca; ***Neth.:*** Cyress; Libradin; Vasexten; ***Philipp.:*** Hypoca; ***Port.:*** Cyress; Libradin; Vasexten; ***Spain:*** Libradin; ***Thai.:*** Hypoca.

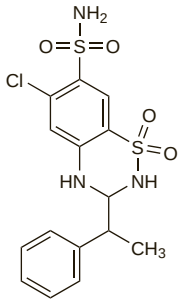
Bemetizide *(BAN, rINN)* ⊗

Bemetizida; Bémétizide; Bemetizidum; Diu-60. 6-Chloro-3,4-dihydro-3-(α-methylbenzyl)-2*H*-1,2,4-benzothiadiazine-7-sulphonamide 1,1-dioxide.

Беметизид

$C_{15}H_{16}ClN_3O_4S_2$ = 401.9.

CAS — 1824-52-8.



Profile
Bemetizide is a thiazide diuretic (see Hydrochlorothiazide, p.1307) that is used, often with triamterene, in the treatment of oedema and hypertension.

Preparations
Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Belg.:*** Diucomb†; ***Ger.:*** dehydro sanol tri; Diucomb.

Bemiparin Sodium *(BAN, rINN)*

Bemiparina sódica; Bémiparine Sodique; Bemiparinum Natricum.

Бемипарин Натрий

CAS — 9041-08-1.

ATC — B01AB12.

ATC Vet — QB01AB12.

Description. Bemiparin sodium is prepared by alkaline degradation of heparin obtained from the intestinal mucosa of pigs. The majority of the components have a 2-*O*-sulfo-4-enepyranosuronic acid structure at the non-reducing end and a 2-*N*,6-*O*-disulfo-D-glucosamine structure at the reducing end of their chain. The average relative molecular mass is about 3600 (3000 to 4200). The degree of sulfation is about 2 per disaccharide unit.

Units
As for Low-molecular-weight Heparins, p.1329.

Adverse Effects, Treatment, and Precautions
As for Low-molecular-weight Heparins, p.1329.

Severe bleeding with bemiparin sodium may be reduced by intravenous protamine sulfate; 1.4 mg of protamine sulfate is stated to inhibit the effects of 100 units of bemiparin sodium.

Interactions
As for Low-molecular-weight Heparins, p.1329.

Pharmacokinetics
Bemiparin sodium is rapidly absorbed after subcutaneous injection with a bioavailability of about 96%. Peak plasma activity is reached in about 2 to 4 hours, depending on the dose. The elimination half-life is about 5 to 6 hours.

Uses and Administration
Bemiparin sodium is a low-molecular-weight heparin (p.1329) with anticoagulant activity. It is used for the prevention and treatment of venous thromboembolism (p.1189), and to prevent clotting during extracorporeal circulation.

In the prophylaxis of **venous thromboembolism** during general surgery with moderate risk, bemiparin sodium is given subcutaneously in a dose of 2500 units once daily, with the first dose given 2 hours before or 6 hours after surgery; in patients undergoing orthopaedic surgery with high risk of thromboembolism the dose should be 3500 units initially and then once daily. Treatment should be continued for at least 7 to 10 days and until the patient is fully ambulant. For treatment of thromboembolism, a dose of 115 units/kg is given subcutaneously once daily.

In some countries bemiparin sodium is used for prophylaxis in non-surgical patients at moderate or high risk of venous thromboembolism, a dose of 2500 or 3500 units being given daily according to risk. Bemiparin sodium is also used in some countries for secondary prevention of venous thromboembolism in patients with transitory risk factors, a dose of 3500 units being given daily for up to 3 months as an alternative to oral anticoagulant therapy.

For the prevention of clotting in the extracorporeal circulation during **haemodialysis**, bemiparin sodium is given into the arterial side of the dialyser in a single dose of 2500 units for patients weighing less than 60 kg and 3500 units for patients weighing more than 60 kg.

◊ References.

1. Kakkar VV, *et al*. A comparative double-blind, randomised trial of a new second generation LMWH (bemiparin) and UFH in the prevention of post-operative venous thromboembolism. *Thromb Haemost* 2000; **83:** 523–9.
2. Chapman TM, Goa KL. Bemiparin: a review of its use in the prevention of venous thromboembolism and treatment of deep vein thrombosis. *Drugs* 2003; **63:** 2357–77.
3. Martínez-González J, *et al*. Bemiparin: second-generation, low-molecular-weight heparin for treatment and prophylaxis of venous thromboembolism. *Expert Rev Cardiovasc Ther* 2008; **6:** 793–802.

Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Badyket; ***Cz.:*** Zibor; ***Gr.:*** Ivor; Ivormax; ***Hung.:*** Zibor; ***Ital.:*** Ivor; ***Port.:*** Ivor; ***Spain:*** Hibor; ***UK:*** Zibor.

Benazepril Hydrochloride

(BANM, USAN, rINNM)

Benatsepriilihydrokloridi; Bénazépril, chlorhydrate de; Benazepril Hidroklorür; Benazeprilhydroklorid; Benazeprili hydrochloridum; Benazeprili Hydrochloridum; CGS-14824A (benazepril or benazepril hydrochloride); Hidrocloruro de benazepril. {(3*S*)-3-[(1*S*)-1-Ethoxycarbonyl-3-phenylpropylamino]-2,3,4,5-tetrahydro-2-oxo-1*H*-1-benzazepin-1-yl}acetic acid hydrochloride; 1-Carboxymethyl-3-[1-ethoxycarbonyl-3-phenyl-(1*S*)-propylamino]-2,3,4,5-tetrahydro-1*H*-1(3*S*)-benzazepin-2-one hydrochloride.

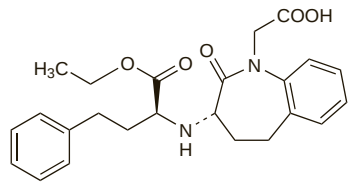
Беназеприла Гидрохлорид

$C_{24}H_{28}N_2O_5$,HCl = 461.0.

CAS — 86541-75-5 (benazepril); 86541-74-4 (benazepril hydrochloride).

ATC — C09AA07.

ATC Vet — QC09AA07.



(benazepril)

Pharmacopoeias. In *US*.

USP 31 (Benazepril Hydrochloride). A white to off-white crystalline powder. Soluble in water, in alcohol, and in methyl alcohol. Store at a temperature below 30°, preferably between 15° and 30°.

Adverse Effects, Treatment, and Precautions
As for ACE inhibitors, p.1193.

Interactions
As for ACE inhibitors, p.1196.

Pharmacokinetics
Benazepril acts as a prodrug of the diacid benazeprilat, its active metabolite. At least 37% of an oral dose of benazepril is absorbed. Benazepril is almost completely metabolised in the liver to benazeprilat. Peak plasma concentrations of benazeprilat after an oral dose of benazepril have been achieved in 1 to 2 hours in the fasting state or 2 to 4 hours in the nonfasting state. Both benazepril and benazeprilat are about 95% bound to plasma proteins. Benazeprilat is excreted mainly in the urine; about 11 to 12% is excreted in the bile. The effective half-life for accumulation of benazeprilat is 10 to 11 hours after multiple doses of benazepril. The elimination of benazeprilat is slowed in renal impairment, although biliary excretion may compensate to some extent. Small amounts of benazepril and benazeprilat are distributed into breast milk.

◊ References.

1. Kaiser G, *et al*. Pharmacokinetics of the angiotensin converting enzyme inhibitor benazepril HCl (CGS 14 824A) in healthy volunteers after single and repeated administration. *Biopharm Drug Dispos* 1989; **10:** 365–76.
2. Kaiser G, *et al*. Pharmacokinetics of a new angiotensin-converting enzyme inhibitor, benazepril hydrochloride, in special populations. *Am Heart J* 1989; **117:** 746–51.
3. Kaiser G, *et al*. Pharmacokinetics and pharmacodynamics of the ace inhibitor benazepril hydrochloride in the elderly. *Eur J Clin Pharmacol* 1990; **38:** 379–85.
4. Macdonald N-J, *et al*. A comparison in young and elderly subjects of the pharmacokinetics and pharmacodynamics of single and multiple doses of benazepril. *Br J Clin Pharmacol* 1993; **36:** 201–4.

Uses and Administration
Benazepril is an ACE inhibitor (p.1193). It is used in the treatment of hypertension (p.1171) and heart failure (p.1165).

Benazepril owes its activity to benazeprilat to which it is converted after oral dosage. The haemodynamic effects are seen within 1 hour of a single oral dose and the maximum effect occurs after about 2 to 4 hours, although the full effect may not develop for 1 to 2 weeks during chronic dosing. The haemodynamic action lasts for about 24 hours, allowing once-daily dosing. Benazepril is given orally as the hydrochloride.

In the treatment of **hypertension**, the usual initial dose of benazepril hydrochloride is 10 mg once daily. An initial dose of 5 mg once daily is suggested for patients with renal impairment (see below) or who are receiving a *diuretic*; if possible the diuretic should be withdrawn 2 or 3 days before benazepril is started and resumed later if necessary.

The usual maintenance dose is 20 to 40 mg daily, which may be given in 2 divided doses if control is inadequate with a single dose; doses of up to 80 mg daily have been used.

In the treatment of **heart failure** the usual initial dose of benazepril hydrochloride is 2.5 mg once daily, adjusted according to response to a maximum dose of 20 mg daily.

Administration in children. Experience with benazepril in children is limited. US licensed product information recommends an initial oral dose of 200 micrograms/kg once daily for hypertension in children 6 years of age and over. Maintenance doses up to 600 micrograms/kg daily (maximum 40 mg daily) have been studied. Insufficient evidence is available to recommend doses for younger children or for any children with creatinine clearance below 30 mL/minute.

Administration in renal impairment. In patients with a creatinine clearance of less than 30 mL/minute, the initial dose of benazepril hydrochloride for hypertension is 5 mg once daily and the maintenance dose should not exceed 40 mg daily.