Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Frigol; ***Cz.:*** Xanidil; ***Ger.:*** Complamin spezial; ***Hung.:*** Xavin; ***India:*** Complamina; ***Ital.:*** Complamin; Vedrin†; ***Neth.:*** Complamin; ***Pol.:*** Sadamin; ***Switz.:*** Complamin.

Multi-ingredient: ***Spain:*** Rulun.

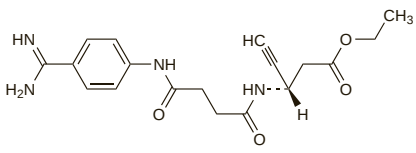
Xemilofiban Hydrochloride *(USAN, rINNM)*

Hidrocloruro de xemilofibán; SC-54684A; Xémilofiban, Chlorhydrate de; Xemilofibani Hydrochloridum. Ethyl (3*S*)-3-{3-[(*p*-amidinophenyl)carbamoyl]propionamido}-4-pentynoate monohydrochloride.

Ксемилофибана Гидрохлорид

$C_{18}H_{22}N_4O_4,HCl$ = 394.9.

CAS — 149820-74-6 (xemilofiban); 156586-91-3 (xemilofiban hydrochloride).



(xemilofiban)

Profile

Xemilofiban is a glycoprotein IIb/IIIa-receptor antagonist. It has been investigated as an oral antiplatelet drug for the management of thromboembolic disorders such as unstable angina, and after angioplasty, but results have been disappointing.

◊ References.

1. O'Neill WW, *et al.* Long-term treatment with a platelet glycoprotein-receptor antagonist after percutaneous coronary revascularization. *N Engl J Med* 2000; **342:** 1316–24.

Xipamide *(BAN, USAN, rINN)* ⊗

Be-1293; Ksipamidi; MJF-10938; Xipamid; Xipamida; Xipamidum. 4-Chloro-5-sulphamoylsalicylo-2′,6′-xylidide; 5-(Aminosulphonyl)-4-chloro-*N*-(2,6-dimethylphenyl)-2-hydroxy-benzamide.

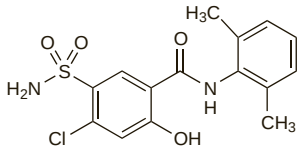
Ксипамид

$C_{15}H_{15}ClN_2O_4S$ = 354.8.

CAS — 14293-44-8.

ATC — C03BA10.

ATC Vet — QC03BA10.



Adverse Effects, Treatment, and Precautions

As for Hydrochlorothiazide, p.1307.

Effects on electrolyte balance. Although reductions in plasma-potassium concentrations with xipamide have been shown to be on average comparable with those produced by thiazide and loop diuretics at equipotent doses,[1] there have been several reports of marked hypokalaemia in individual patients. Asymptomatic hypokalaemia was reported in 4 of 5 patients[2] (serum-potassium concentrations of less than 3.4 mmol/litre) and in 3 of 13 patients[3] (serum-potassium concentrations of less than 3.0 mmol/litre). Severe hypokalaemia resulting in ventricular arrhythmias has been reported after xipamide used alone[4] or with indapamide.[5] Profound electrolyte disturbances with altered consciousness and ventricular extrasystoles occurred in a patient taking digoxin after the addition of xipamide for 10 days.[6] A case of hypokalaemic periodic paralysis associated with xipamide use has also been reported.[7]

1. Prichard BNC, Brogden RN. Xipamide: a review of its pharmacodynamic and pharmacokinetic properties and therapeutic efficacy. *Drugs* 1985; **30:** 313–32.
2. Weissberg P, Kendall MJ. Hypokalaemia and xipamide. *BMJ* 1982; **284:** 975.
3. Raftery EB, *et al.* A study of the antihypertensive action of xipamide using ambulatory intra-arterial monitoring. *Br J Clin Pharmacol* 1981; **12:** 381–5.
4. Altmann P, Hamblin JJ. Ventricular fibrillation induced by xipamide. *BMJ* 1982; **284:** 494.
5. Boulton AJM, Hardisty CA. Ventricular arrhythmias precipitated by treatment with non-thiazide diuretics. *Practitioner* 1982; **226:** 125–8.
6. Bentley J. Hypokalaemia and xipamide. *BMJ* 1982; **284:** 975.
7. Boulton AJM, Hardisty CA. Hypokalaemic periodic paralysis precipitated by diuretic therapy and minor surgery. *Postgrad Med J* 1982; **58:** 106–7.

Hepatic impairment. For a recommendation that xipamide should be given with caution to patients with liver disease, see under Pharmacokinetics, below.

Interactions

As for Hydrochlorothiazide, p.1309.

Pharmacokinetics

Xipamide has been reported to be well absorbed from the gastrointestinal tract. Absorption is fairly rapid with peak plasma concentrations occurring within 1 or 2 hours of oral doses. It is 99% bound to plasma proteins, and is excreted in the urine, partly unchanged and partly in the form of the glucuronide metabolite. It is reported to have a plasma half-life of about 5 to 8 hours. In patients with renal impairment excretion in the bile becomes more prominent.

◊ References.

1. Beermann B, Grind M. Clinical pharmacokinetics of some newer diuretics. *Clin Pharmacokinet* 1987; **13:** 254–66.

Hepatic impairment. Xipamide was present in the plasma and in ascitic fluid in patients with liver cirrhosis in proportion to the protein content of the respective compartments.[1] The amount of drug excreted into the urine was much greater in patients with liver disease than in healthy control subjects. This was attributed to a diminution in hepatic elimination, which could result in significant effects on the clinical response to xipamide. Thus patients with cholestasis could have an enhanced response to xipamide. On the other hand cirrhotic patients with the hepatorenal syndrome may be resistant to diuretics. Xipamide should be used with caution in patients with liver disease.

1. Knauf H, *et al.* Xipamide disposition in liver cirrhosis. *Clin Pharmacol Ther* 1990; **48:** 628–32.

Renal impairment. After single oral and intravenous doses of xipamide 20 mg the drug appeared to be completely absorbed from the gastrointestinal tract.[1] The mean elimination half-life in healthy subjects was 7 hours and two-thirds of the clearance was by extrarenal routes. There was some accumulation in patients with chronic renal failure, with a calculated elimination half-life of 9 hours in end-stage renal disease.

1. Knauf H, Mutschler E. Pharmacodynamics and pharmacokinetics of xipamide in patients with normal and impaired kidney function. *Eur J Clin Pharmacol* 1984; **26:** 513–20.

Uses and Administration

Xipamide is a diuretic, structurally related to indapamide, with actions and uses similar to those of the thiazide diuretics (see Hydrochlorothiazide, p.1310). It is given orally for hypertension (p.1171), and for oedema, including that associated with heart failure (p.1165).

Diuresis begins about 1 or 2 hours after an oral dose, reaches a peak at 4 to 6 hours, and lasts for about 12 hours.

In the treatment of **hypertension** the usual dose is 20 mg daily as a single morning dose, either alone, or with other antihypertensives. In some patients a dose of 10 mg daily may be adequate. In the treatment of **oedema** the usual initial dose is 40 mg daily, subsequently reduced to 20 mg daily, according to response; in resistant cases 80 mg daily may be required.

◊ References.

1. Prichard BNC, Brogden RN. Xipamide: a review of its pharmacodynamic and pharmacokinetic properties and therapeutic efficacy. *Drugs* 1985; **30:** 313–32.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Aquaphoril; ***Fr.:*** Lumitens†; ***Ger.:*** Aquaphor; Aquex; Xipa; Xipalsis; Xipagamma; ***India:*** Xipamid; ***Ital.:*** Aquafor†; ***Port.:*** Diurexan; ***S.Afr.:*** Diurexan†; ***Spain:*** Demiax†; Diurex; ***UK:*** Diurexan.

Multi-ingredient: ***Ger.:*** Durotan†; Neotri.

Zofenopril Calcium *(BANM, USAN, rINNM)*

Calcii Zofenoprilum; SQ-26991; Zofenopril cálcico; Zofénopril Calcique. Calcium salt of (4*S*)-1-[(2*S*)-3-(Benzylthio)-2-methylpropionyl]-4-(phenylthio)-L-proline.

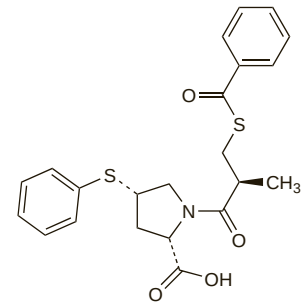
Кальций Зофеноприл

$C_{44}H_{44}CaN_2O_8S_4$ = 897.2.

CAS — 81872-10-8 (zofenopril); 81938-43-4 (zofenopril calcium).

ATC — C09AA15.

ATC Vet — QC09AA15.



(zofenopril)

Profile

Zofenopril is an ACE inhibitor (p.1193) that is used in the management of hypertension (p.1171) and myocardial infarction (p.1175). It owes its activity to the active metabolite zofenoprilat (SQ-26333) to which it is converted after oral doses. It is given orally in a usual daily maintenance dose of 30 to 60 mg of the calcium salt, as a single dose or in two divided doses.

◊ References.

1. Ambrosioni E, *et al.* The effect of the angiotensin-converting-enzyme inhibitor zofenopril on mortality and morbidity after anterior myocardial infarction. *N Engl J Med* 1995; **332:** 80–5.
2. Borghi C, *et al.* Effects of the administration of an angiotensin-converting enzyme inhibitor during the acute phase of myocardial infarction in patients with arterial hypertension: SMILE study investigators: Survival of Myocardial Infarction Long-term Evaluation. *Am J Hypertens* 1999; **12:** 665–72.
3. Borghi C, *et al.* A review of the angiotensin-converting enzyme inhibitor, zofenopril, in the treatment of cardiovascular diseases. *Expert Opin Pharmacother* 2004; **5:** 1965–77.
4. Buikema H. Use of the ACE inhibitor zofenopril in the treatment of ischemic heart disease. *Expert Rev Cardiovasc Ther* 2006; **4:** 631–47.
5. Ambrosioni E. Defining the role of zofenopril in the management of hypertension and ischemic heart disorders. *Am J Cardiovasc Drugs* 2007; **7:** 17–24.

Preparations

Proprietary Preparations (details are given in Part 3)
Chile: Bifril; ***Fr.:*** Zofenil; ***Gr.:*** Zofepril; Zopranol; ***Irl.:*** Zofenil; ***Ital.:*** Bifril; Zantipres; Zopranol; ***Neth.:*** Zofil; Zopranol; ***Port.:*** Zofenil; Zopranol; ***Rus.:*** Zocardis (Зокардис); ***Spain:*** Zofenil; Zopranol; ***Swed.:*** Bifril†; ***Switz.:*** Zofenil; ***Turk.:*** Zoprotec.

Multi-ingredient: ***Fr.:*** Zofenilduo; ***Gr.:*** Zofepril Plus; Zopranol Plus; ***Ital.:*** Bifrizide; Zantipride; Zoprazide; ***Port.:*** Zofenil Plus.