Bezalex; Bezalip; Bifaren; Bionolip; Colser; Fazebit; Klestran†; Lesbest; Lipocin; Neptalip; Nivetril; Redalip; Solibay†; Zaf; ***Neth.:*** Bezalip; ***NZ:*** Bezalip; Fibalip; ***Philipp.:*** Bezastad; ***Pol.:*** Bezamidin; ***Port.:*** Bezalip; ***S.Afr.:*** Bezalip; ***Singapore:*** Bezalip; Zafibral; ***Spain:*** Difaterol; Eulitop; Reductero†; ***Swed.:*** Bezalip; ***Switz.:*** Cedur; ***Thai.:*** Bezalip; Bezamil; Polyzalip; Raset†; ***UAE:*** Lipitrol; ***UK:*** Bezagen; Bezalip; Bezalip Mono; Fibrazate; Zimbacol; ***Venez.:*** Bezalip; Detrex†.

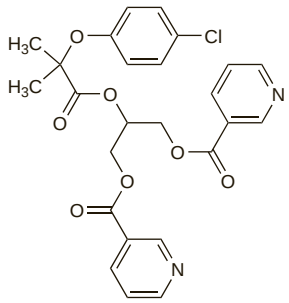
Binifibrate *(rINN)*

Binifibrato; Binifibratum. 2-(4-Chlorophenoxy)-2-methylpropionic acid ester with 1,3-dinicotinoyloxypropan-2-ol.

Бинифибрат

$C_{25}H_{23}ClN_2O_7$ = 498.9.

CAS — 69047-39-8.



Profile

Binifibrate, a derivative of clofibrate (p.1246) and nicotinic acid (p.1957), is a lipid regulating drug that has been used in the treatment of hyperlipidaemias.

Preparations

Proprietary Preparations (details are given in Part 3)
Spain: Antopal†; Biniwas†.

Bisoprolol Fumarate

(BANM, USAN, rINNM) ⊗

Bisoprolol Fumarat; Bisoprolol, Fumarate de; Bisoprolol Hemifumarate; Bisoprolol, hémifumarate de; Bisoprololfumarat; Bisoprololi Fumaras; Bisoprololi hemifumaras; Bisoprololifumaraatti; CL-297939; EMD-33512 (bisoprolol or bisoprolol fumarate); Fumarato de bisoprolol. 1-[4-(2-Isopropoxyethoxymethyl)phenoxy]-3-isopropylaminopropan-2-ol fumarate.

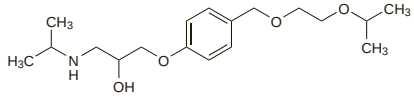
Бизопролола Фумарат

$(C_{18}H_{31}NO_4)_2,C_4H_4O_4$ = 767.0.

CAS — 66722-44-9 (bisoprolol); 66722-45-0 (bisoprolol fumarate); 104344-23-2 (bisoprolol fumarate).

ATC — C07AB07.

ATC Vet — QC07AB07.



(bisoprolol)

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

Ph. Eur. 6.2 (Bisoprolol Fumarate). A white or almost white, slightly hygroscopic powder. It exhibits polymorphism. Very soluble in water; freely soluble in methyl alcohol. Store in airtight containers. Protect from light.

USP 31 (Bisoprolol Fumarate). A white crystalline powder. Very soluble in water and in methyl alcohol; freely soluble in alcohol, in chloroform, and in glacial acetic acid; slightly soluble in acetone and in ethyl acetate. Store in airtight containers. Protect from light.

Adverse Effects, Treatment, and Precautions

As for Beta Blockers, p.1226.

Interactions

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

Pharmacokinetics

Bisoprolol is almost completely absorbed from the gastrointestinal tract and undergoes only minimal first-pass metabolism resulting in an oral bioavailability of about 90%. Peak plasma concentrations are reached 2 to 4 hours after oral doses. Bisoprolol is about 30% bound to plasma proteins. It has a plasma elimination half-life of 10 to 12 hours. Bisoprolol is moderately lipid-soluble. It is metabolised in the liver and excreted in urine, about 50% as unchanged drug and 50% as metabolites.

Uses and Administration

Bisoprolol is a cardioselective beta blocker (p.1225). It is reported to be devoid of intrinsic sympathomimetic and membrane-stabilising properties.

Bisoprolol is given as the fumarate in the management of hypertension (p.1171) and angina pectoris (p.1157). It is also used as an adjunct to standard therapy in patients with stable chronic heart failure (p.1165).

In **hypertension** or **angina pectoris** the usual dose of bisoprolol fumarate is 5 to 10 mg orally as a single daily dose; the maximum recommended dose is 20 mg daily. A reduction in dose may be necessary in patients with hepatic or renal impairment (see below).

In **heart failure** the initial oral dose of bisoprolol fumarate is 1.25 mg once daily. If tolerated, the dose should be doubled after 1 week, and then increased gradually at 1 to 4 week intervals to the maximum dose tolerated; this should not exceed 10 mg once daily.

◊ References.

1. Johns TE, Lopez LM. Bisoprolol: is this just another beta-blocker for hypertension or angina? *Ann Pharmacother* 1995; **29:** 403–14.
2. CIBIS-II Investigators and Committees. The Cardiac Insufficiency Bisoprolol Study II (CIBIS-II): a randomised trial. *Lancet* 1999; **353:** 9–13.
3. McGavin JK, Keating GM. Bisoprolol: a review of its use in chronic heart failure. *Drugs* 2002; **62:** 2677–96.

Administration in hepatic or renal impairment. US licensed product information recommends that the initial dose of bisoprolol fumarate for hypertension should be 2.5 mg daily and that the dose should be increased cautiously in patients with severe hepatic impairment or renal impairment (creatinine clearance less than 40 mL/minute). UK licensed product information recommends a maximum dose of 10 mg daily for both angina pectoris and hypertension in patients with severe hepatic impairment or with a creatinine clearance of less than 20 mL/minute.

Bisoprolol is not dialysable.

Preparations

USP 31: Bisoprolol Fumarate and Hydrochlorothiazide Tablets; Bisoprolol Fumarate Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Concor; Corbis; Lostaprolol; ***Austral.:*** Bicor; ***Austria:*** Bisocor; Bisostad; Bisotyrol†; Cardiocor; Concor; Darbalan; Nanalan; Rivacor; ***Belg.:*** Bisoprotop; Docbisopro; Emconcor; Isoten; ***Braz.:*** Concor; ***Canad.:*** Monocor; ***Chile:*** Concor; ***Cz.:*** Bisoblock; Bisocard; Bisogamma; Bivaxol; Concor; Concor Cor; Kordobis; Rivocor; ***Denm.:*** Bisocor; Cardicor; Emconcor; ***Fin.:*** Bisomerck; Bisopral; Emconcor; Orloc; ***Fr.:*** Cardensiel; Cardiocor; Detensiel; Soprol†; ***Ger.:*** Biso; Biso Lich; Biso-Puren; BisoAPS; Bisobeta; Bisobloc†; Bisogamma; Bisohexal; Bisomerck; Concor; Cordalin†; Fondril; Jutabis; ***Gr.:*** Abitrol; Blocatens; Pactens; Speridol; ***Hong Kong:*** Concor; ***Hung.:*** Bisoblock; Bisocard; Bisogamma; Bisogen; Concor; Concor Cor; Coviogal; ***India:*** Concor; ***Indon.:*** B-Beta; Concor; Hapsen; Lodoz; Maintate; ***Irl.:*** Bisocor; Bisopine; Cardicor; Emcolol; Emcor; Soprol; ***Israel:*** Bisolol; Cardiloc; Concor; ***Ital.:*** Cardicor; Concor; Congescor; Pluscor; Sequacor; ***Jpn:*** Maintate; ***Malaysia:*** Concor; ***Mex.:*** Concor; ***Neth.:*** Bisobloc†; Bisoblock; Cardicor†; Emcor; ***Norw.:*** Emconcor; ***Philipp.:*** Concore; ***Pol.:*** Bisocard; Bisohexal; Bisopromerck; Bisoratio; Concor; Corectin; ***Port.:*** Concor; Libracor; ***Rus.:*** Biprol (Бипрол); Bisocard (Бисокард); Bisogamma (Бисогамма); Concor (Конкор); Corbis (Корбис); ***S.Afr.:*** Adco-Bisocor; Bilocor; Bisohexal; Cardicor; Concor; ***Singapore:*** Concor; ***Spain:*** Emconcor; Euradal; Godal; ***Swed.:*** Bisomerck; Emconcor; ***Switz.:*** Bilol; Concor; ***Thai.:*** Concor; Novacor; ***Turk.:*** Concor; ***UK:*** Bipranix†; Cardicor; Emcor; Monocor†; Soloc†; Vivacor; ***USA:*** Zebeta; ***Venez.:*** Concor.

Multi-ingredient: ***Arg.:*** Corbis D; Ziac; ***Austria:*** Bisocombin; Bisoprolol comp; Bisoprolol-HCT; Bisostad plus; Concor Plus; Darbalan Plus; Nanalan Plus; Rivacor Plus; ***Belg.:*** Co-Bisoprolol; Emcoretic; Lodoz; Maxsoten; Merck-Co-Bisoprolol; ***Braz.:*** Biconcor; ***Chile:*** Ziac; ***Cz.:*** Concor Plus†; Lodoz; Tebis Plus H; ***Fin.:*** Bisoprolol Comp; Emconcor Comp; Orloc Comp; ***Fr.:*** Lodoz; Wytens; ***Ger.:*** Biso comp; Biso-Puren comp; Bisobeta comp; Bisohexal plus; BisoLich comp; Bisomerck Plus; Bisoplus; Bisoprolol Comp; Bisoprolol HCT; Bisoprolol Plus; Concor Plus; Fondril HCT; ***Hong Kong:*** Lodoz; ***Hung.:*** Concor Plus; Lodoz; ***India:*** Lodoz; ***Ital.:*** Lodoz; ***Mex.:*** Biconcor; ***Neth.:*** Emcoretic; ***Norw.:*** Lodoz; ***Philipp.:*** Ziac; ***Port.:*** Concor Plus; ***S.Afr.:*** Ziak; ***Singapore:*** Lodoz; ***Spain:*** Emcoretic; ***Switz.:*** Concor Plus; Lodoz; ***Thai.:*** Lodoz; ***USA:*** Ziac; ***Venez.:*** Biconcor; Ziac.

Bivalirudin *(BAN, USAN, rINN)*

BG-8967; Bivalirudina; Bivalirudine; Bivalirudinum; Hirulog.

Бивалирудин

$C_{98}H_{138}N_{24}O_{33}$ = 2180.3.

CAS — 128270-60-0.

ATC — B01AE06.

ATC Vet — QB01AE06.

Incompatibility. The manufacturer of bivalirudin states that it is incompatible with: alteplase, amiodarone hydrochloride, amphotericin B, chlorpromazine hydrochloride, diazepam, prochlorperazine edisilate, reteplase, streptokinase, and vancomycin hydrochloride.

Adverse Effects and Precautions

As for Lepirudin, p.1323.

Interactions

As for Lepirudin, p.1323.

Pharmacokinetics

Bivalirudin is partly metabolised and partly excreted by the kidney. When given intravenously the plasma half-life is about 25 minutes in patients with normal renal function but is prolonged in renal impairment. Bivalirudin does not bind to plasma proteins and is removed by haemodialysis.

◊ References.

1. Robson R, *et al.* Bivalirudin pharmacokinetics and pharmacodynamics: effect of renal function, dose, and gender. *Clin Pharmacol Ther* 2002; **71:** 433–9.

Uses and Administration

Bivalirudin, an analogue of the peptide hirudin (p.1305), is a direct thrombin inhibitor with actions similar to Lepirudin, p.1323. It is used as an anticoagulant in patients undergoing percutaneous coronary interventions, including those with, or at risk of, heparin-induced thrombocytopenia. It is also used in patients with acute coronary syndromes in whom early intervention is planned, and has been investigated in patients with acute coronary syndromes treated medically (see Ischaemic Heart Disease, under Uses and Administration of Lepirudin, p.1323).

Some preparations state that bivalirudin is present as the hydrate of the trifluoroacetate salt but doses are given in terms of bivalirudin.

In the management of patients undergoing **planned percutaneous coronary intervention** (PCI), the initial dose of bivalirudin is 750 micrograms/kg by intravenous injection followed immediately by an intravenous infusion of 1.75 mg/kg per hour; the activated clotting time should be measured 5 minutes after the initial injection and a second injection of 300 micrograms/kg should be given if anticoagulation is inadequate. The infusion should be given for the duration of the procedure and may be continued for up to 4 hours afterwards; licensed prescribing information in the USA allows the infusion to then be continued at a lower dose of 200 micrograms/kg per hour for up to 20 hours if required.

As part of the management of patients with **acute coronary syndromes**, the initial dose of bivalirudin is 100 micrograms/kg by intravenous injection, followed by an intravenous infusion of 250 micrograms/kg per hour. In patients managed *medically*, the infusion may be continued for up to 72 hours. For those who proceed to *PCI or coronary artery bypass surgery without cardiopulmonary bypass*, a further intravenous injection of 500 micrograms/kg should be given, and the infusion should be increased to 1.75 mg/kg per hour for the duration of the procedure; after PCI, the infusion may be continued at a dose of 250 micrograms/kg per hour for a further 4 to 12 hours if required. For those who proceed to *coronary artery bypass surgery with cardiopulmonary bypass*, the infusion should be stopped 1 hour before the procedure and the patient should be treated with unfractionated heparin.

The dose of bivalirudin should be reduced in patients with renal impairment (see below).

◊ References.

1. Carswell CI, Plosker GL. Bivalirudin: a review of its potential place in the management of acute coronary syndromes. *Drugs* 2002; **62:** 841–70.
2. Sciulli TM, Mauro VF. Pharmacology and clinical use of bivalirudin. *Ann Pharmacother* 2002; **36:** 1028–41.
3. Moen MD, *et al.* Bivalirudin: a review of its use in patients undergoing percutaneous coronary intervention. *Drugs* 2005; **65:** 1869–91.