Initial studies comparing heparin with the recombinant hirudins desirudin[2,3] (p.1257) or lepirudin[4] in patients with acute ST-elevation **myocardial infarction** treated with thrombolytics had to be stopped because of higher than expected haemorrhagic stroke rates,[5,6] and subsequent studies using lower doses of desirudin[7,8] or lepirudin[9] failed to show a clear benefit over heparin. A study[10] with bivalirudin, a synthetic analogue of hirudin, in similar patients also found no mortality benefit; there were fewer reinfarctions in the bivalirudin group, but the risk of bleeding was increased. The role of hirudins is therefore not established, although they may be useful in patients with heparin-induced thrombocytopenia.

Studies in patients with **acute coronary syndromes** (non-ST elevation myocardial infarction and unstable angina) suggest that lepirudin is superior to heparin in preventing cardiovascular death, myocardial infarction, and refractory angina.[11,12] A study[13] comparing desirudin with heparin in unstable angina found that angiographic outcomes were better with desirudin, but another study[7] found little benefit in terms of mortality or recurrent ischaemia. Bivalirudin appears to be as effective as heparin in patients with acute coronary syndromes, but unlike the other hirudins the risk of major bleeding may be reduced.[14,15]

Hirudins have also been studied in patients undergoing **percutaneous coronary interventions** (see Reperfusion and Revascularisation Procedures, p.1181). Desirudin has been used in patients undergoing angioplasty[16,17] and appears to be safe, although no benefit has been shown over heparin. Lepirudin has been used as an alternative to heparin in patients with heparin-induced thrombocytopenia.[18-20] Bivalirudin is effective in patients with stable coronary artery disease[21,22] or acute coronary syndromes[21-23] undergoing percutaneous coronary interventions, and may reduce the need for adjunctive glycoprotein IIb/IIIa inhibitors.[21-23]

In patients undergoing **coronary artery bypass grafting**, hirudins may be an alternative to unfractionated heparin, and positive results have been reported with bivalirudin[24] and with lepirudin;[25] however, postoperative bleeding is increased and it was suggested[25] that hirudins should be reserved for patients with contra-indications to heparin, such as those with heparin-induced thrombocytopenia.

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Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Refludan; ***Austria:*** Refludan; ***Belg.:*** Refludan; ***Canad.:*** Refludan; ***Cz.:*** Refludan; ***Denm.:*** Refludan†; ***Fin.:*** Refludan†; ***Fr.:*** Refludan; ***Ger.:*** Refludan; ***Gr.:*** Refludan†; ***Hung.:*** Refludan; ***Irl.:*** Refludan; ***Ital.:*** Refludan; ***Neth.:*** Refludan; ***Norw.:*** Refludan; ***NZ:*** Refludan; ***Port.:*** Refludan; ***S.Afr.:*** Refludin; ***Spain:*** Refludin; ***Swed.:*** Refludan†; ***Switz.:*** Refludan; ***UK:*** Refludan; ***USA:*** Refludan.

Lercanidipine Hydrochloride

(BANM, USAN, rINNM)

Hidrocloruro de lercanidipino; Lercanidipine, Chlorhydrate de; Lercanidipini Hydrochloridum; Lerkanidipin Hidroklorür; Masnidipine Hydrochloride; R-75; Rec-15-2375. (±)-2-[(3,3-Diphenylpropyl)methylamino]-1,1-dimethylethyl methyl 1,4-dihydro-2,6-dimethyl-4-(*m*-nitrophenyl)-3,5-pyridinedicarboxylate hydrochloride.

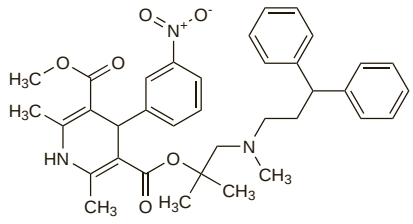
Лерканидипина Гидрохлорид

$C_{36}H_{41}N_3O_6$,HCl = 648.2.

CAS — 100427-26-7 (lercanidipine); 132866-11-6 (lercanidipine hydrochloride).

ATC — C08CA13.

ATC Vet — QC08CA13.



(lercanidipine)

Adverse Effects, Treatment, and Precautions

As for dihydropyridine calcium-channel blockers (see Nifedipine, p.1350).

Interactions

As for dihydropyridine calcium-channel blockers (see Nifedipine, p.1352).

Pharmacokinetics

Lercanidipine is completely absorbed from the gastrointestinal tract after oral doses but undergoes extensive saturable first-pass metabolism. Bioavailability is low but is increased in the presence of food. Peak plasma concentrations occur about 1.5 to 3 hours after oral dosage. Lercanidipine is rapidly and widely distributed. It is more than 98% bound to plasma proteins. Lercanidipine is extensively metabolised, primarily by the cytochrome P450 isoenzyme CYP3A4, mainly to inactive metabolites; about 50% of an oral dose is excreted in the urine. A terminal elimination half-life of about 2 to 5 hours has been reported, but studies using a more sensitive assay have suggested a value of 8 to 10 hours.

Uses and Administration

Lercanidipine is a dihydropyridine calcium-channel blocker with actions similar to those of nifedipine (p.1354). It is used in the treatment of hypertension (p.1171).

Lercanidipine is given by mouth as the hydrochloride in a usual initial dose of 10 mg once daily before food, increased if necessary, after at least 2 weeks, to 20 mg daily.

◊ Reviews.

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2. Bang LM, *et al.* Lercanidipine : a review of its efficacy in the management of hypertension. *Drugs* 2003; **63:** 2449–72.
3. Beckey C, *et al.* Lercanidipine in the treatment of hypertension. *Ann Pharmacother* 2007; **41:** 465–74.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Lercadip; ***Austral.:*** Zanidip; ***Austria:*** Zanidip; ***Belg.:*** Zanidip; ***Braz.:*** Zanidip; ***Chile:*** Zanidip; ***Cz.:*** Lerpin; ***Denm.:*** Zanidip; ***Fin.:*** Zanidip; ***Fr.:*** Lercan; Zanidip; ***Ger.:*** Carmen; Corifeo; ***Gr.:*** Lercadip; Zanidip; ***Hong Kong:*** Zanidip; ***Hung.:*** Lercaton; Zanidip; ***India:*** Lerez; ***Indon.:*** Zanidip; ***Irl.:*** Zanidip; ***Israel:*** Vasodip; ***Ital.:*** Cardiovasc; Lercadip; Zanedip; ***Malaysia:*** Zanidip; ***Mex.:*** Evipress; Zanidip; ***Neth.:*** Lerdip; ***Norw.:*** Zanidip; ***NZ:*** Zanidip; ***Philipp.:*** Zanidip; ***Port.:*** Zanicor; Zanidip; ***S.Afr.:*** Zanidip; ***Singapore:*** Zanidip†; ***Spain:*** Lercadip; Lerzam; Zanidip; ***Swed.:*** Zanidip; ***Switz.:*** Zanidip; ***Thai.:*** Zanidip; ***Turk.:*** Lercadip; ***UK:*** Zanidip; ***Venez.:*** Lercadip; Zanidip.

Multi-ingredient: ***India:*** Lerez-AT†.

Levosimendan *(USAN, rINN)*

Lévosimendan; Levosimendán; Levosimendanum; (–)-OR-1259. Mesoxalonitrile (–)-{*p*-[(*R*)-1,4,5,6-tetrahydro-4-methyl-6-oxo-3-pyridazinyl]phenyl}hydrazone.

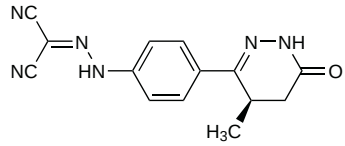
Левосимендан

$C_{14}H_{12}N_6O$ = 280.3.

CAS — 141505-33-1.

ATC — C01CX08.

ATC Vet — QC01CX08.



Profile

Levosimendan is a cardiac inotrope and vasodilator with calcium-sensitising properties, used in the management of acute heart failure (p.1165). It is given intravenously in a loading dose of 6 to 24 micrograms/kg over 10 minutes followed by a continuous infusion of 50 to 200 nanograms/kg per minute, adjusted according to response.

◊ References.

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7. Antila S, *et al.* Clinical pharmacology of levosimendan. *Clin Pharmacokinet* 2007; **46:** 535–52.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Simdax; ***Austria:*** Simdax; ***Chile:*** Daxim; ***Cz.:*** Simdax; ***Fin.:*** Simdax; ***Gr.:*** Simdax; ***Hong Kong:*** Simdax; ***Hung.:*** Simdax; ***Israel:*** Simdax; ***Ital.:*** Simdax; ***Mex.:*** Simdax; ***Norw.:*** Simdax; ***NZ:*** Simdax; ***Port.:*** Simdax; ***Rus.:*** Simdax (Симдакс); ***Spain:*** Simdax; ***Swed.:*** Simdax; ***Turk.:*** Simdax; ***Venez.:*** Daxim.