Pharmacopoeias. In *Jpn* and *Pol*.

Profile
Lanatoside C is a cardiac glycoside with positive inotropic activity. It is obtained from digitalis lanata leaf (p.1258). It has general properties similar to those of digoxin (p.1259) and has been used in the treatment of some cardiac arrhythmias and in heart failure.

Mixtures of lanatosides A, B, and C have also been used.

Preparations
Proprietary Preparations (details are given in Part 3)
Arg.: Develanid†; ***Mex.:*** Cedilanid.

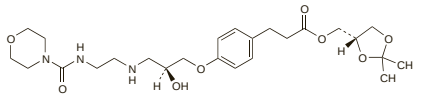
Landiolol Hydrochloride *(rINNM)* ⊗

Hidrocloruro de landiolol; Landiolol, Chlorhydrate de; Landiololi Hydrochloridum; ONO-1101. (–)-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]methyl *p*-((*S*)-2-hydroxy-3-{[2-(4-morpholinecarboxamido)ethyl]amino}propoxy)hydrocinnamate hydrochloride.

Ландиолола Гидрохлорид

$C_{25}H_{39}N_3O_8$,HCl = 546.1.

CAS — 133242-30-5 (landiolol); 144481-98-1 (landiolol hydrochloride).



(landiolol)

Profile
Landiolol is a short-acting, cardioselective beta blocker given intravenously as the hydrochloride in the management of intra- and postoperative cardiac arrhythmias.

◊ References.

1. Kitamura A, *et al.* Efficacy of an ultrashort-acting beta-adrenoceptor blocker (ONO-1101) in attenuating cardiovascular responses to endotracheal intubation. *Eur J Clin Pharmacol* 1997; **51:** 467–71.
2. Atarashi H, *et al.* Pharmacokinetics of landiolol hydrochloride, a new ultra-short-acting beta-blocker, in patients with cardiac arrhythmias. *Clin Pharmacol Ther* 2000; **68:** 143–50.
3. Mizuno J, *et al.* Age and sex-related differences in dose-dependent hemodynamic response to landiolol hydrochloride during general anesthesia. *Eur J Clin Pharmacol* 2007; **63:** 243–52.

Preparations
Proprietary Preparations (details are given in Part 3)
Jpn: Onoact.

Lanoteplase *(USAN, rINN)*

BMS-200980; Lanoteplasa; Lanotéplase; Lanoteplasum; Sun-9216. *N*-[N^2-(*N*-Glycyl-L-alanyl)-L-arginyl]-117-L-glutamine-245-L-methionine-(1-5)-(87-527)-plasminogen activator (human tissue-type protein moiety).

Ланотеплаза

$C_{2184}H_{3323}N_{633}O_{666}S_{29}$ = 50032.5.

CAS — 171870-23-8.

Profile
Lanoteplase is a thrombolytic that has been investigated in acute myocardial infarction; development was stopped after an unacceptable rate of intracranial haemorrhage was found.

◊ References.

1. The InTIME-II Investigators. Intravenous NPA for the treatment of infarcting myocardium early: InTIME-II, a double-blind comparison of single-bolus lanoteplase vs accelerated alteplase for the treatment of patients with acute myocardial infarction. *Eur Heart J* 2000; **21:** 2005–13.

Lappaconitine Hydrobromide

(1α,14α,16β)-20-Ethyl-1,14,16-trimethoxyaconitane-4,8,9-triol 4-[2-(acetylamino)benzoate] hydrobromide.

Лаппаконитина Гидробромид

$C_{32}H_{44}N_2O_8$,HBr = 665.6.

CAS — 32854-75-4 (lappaconitine); 97792-45-5 (lappaconitine hydrobromide).

Profile
Lappaconitine hydrobromide is an antiarrhythmic drug given orally in a usual dose of 25 mg three times daily.

Preparations
Proprietary Preparations (details are given in Part 3)
Rus.: Allapinin (Аллапинин).

Leech

Blutegel; Hirudo; Sangsue; Sanguessugas; Sanguijuela; Sanguisuga.

Description. *Hirudo medicinalis* is the leech commonly used in medicine and is a fresh-water annelid.

NOTE. The substance described in the *Chin. P.* as Hirudo (Leech) is the dried body of *Whitmania pigra*, *Hirudo nipponica*, or *Whitmania acranulata*.

Profile
Leeches are used for withdrawing blood from congested areas and have been found to be of value in plastic surgery. The buccal secretion of the leech contains the anticoagulant hirudin (p.1305). Once used a leech should not be applied to another patient.

There have been reports of wound infection from *Aeromonas hydrophila* transmitted by leeches. Prolonged bleeding for up to 10 hours may occur from the site of attachment after removal of the leech.

◊ Leeches are commonly used in plastic surgery and this has been reviewed.[1]

Wound infection by *Aeromonas hydrophila*, an organism normally found in the gut of the leech, is a recognised complication of the use of leeches for decongestion after plastic surgery. Other infecting organisms include *Aeromonas sobria* and *Serratia marcescens*. Infections have caused minor wound drainage, cellulitis, abscess, tissue loss, and sepsis, and a case of meningitis secondary to *Aeromonas* infection has been reported.[2] The following protocol has been suggested:[1] the site of application should first be cleaned with heparinised saline, and antibacterial prophylaxis with a quinolone and an aminoglycoside given for the duration of application. Patients discharged with open wounds should continue with oral antibacterials until wound closure.

In addition to its anticoagulant properties the buccal secretion of the leech contains anti-inflammatory substances, and leeches have been reported to provide subjective relief of symptoms[3,4] in osteoarthritis.

1. Whitaker IS, *et al.* Hirudo medicinalis and the plastic surgeon. *Br J Plast Surg* 2004; **57:** 348–53.
2. Ouderkirk JP, *et al.* Aeromonas meningitis complicating medicinal leech therapy. Abstract: *Clin Infect Dis* 2004; **38**: 603. Full version: http://www.journals.uchicago.edu/doi/full/10.1086/381438 (accessed 19/08/08)
3. Michalsen A, *et al.* Effect of leeches therapy (Hirudo medicinalis) in painful osteoarthritis of the knee: a pilot study. *Ann Rheum Dis* 2001; **60:** 986.
4. Michalsen A, *et al.* Effectiveness of leech therapy in osteoarthritis of the knee: a randomized, controlled trial. *Ann Intern Med* 2003; **139:** 724–30.

Lepirudin *(BAN, rINN)*

HBW-023; Lepirudiini; Lepirudina; Lépirudine; Lepirudinum. L-Leucine-2-L-threonine-63-desulfohirudin (*Hirudo medicinalis* isoform HV1).

Лепирудин

$C_{287}H_{440}N_{80}O_{111}S_6$ = 6979.4.

CAS — 138068-37-8.

ATC — B01AE02.

ATC Vet — QB01AE02.

Adverse Effects and Precautions
The most frequent adverse effect of the direct thrombin inhibitors is bleeding. Hypersensitivity reactions have been reported. There have been reports of severe anaphylactic reactions, including death, with many occurring on re-exposure. There may be cross-reactivity with other hirudins or hirudin analogues.

Intramuscular injection should be avoided as it may cause local haematoma.

Direct thrombin inhibitors should be used with caution or avoided in patients with hepatic or renal impairment, and in those who are bleeding or at serious risk of bleeding, including those with haemorrhagic blood disorders, recent major bleeding, cerebrovascular disorders, bacterial endocarditis, severe hypertension, or patients who have recently undergone major surgery or puncture of large vessels or organ biopsy.

Hypersensitivity. The EMEA reported[1] in October 2002 that they were aware of 7 cases of severe anaphylactic reactions in patients given lepirudin; in 6 cases this followed re-exposure to the drug, and in 5 cases the patient died. A review[2] of the manufacturer's safety database identified 9 patients with severe anaphylactic reactions associated with lepirudin; 4 patients died, all of whom had received lepirudin within the previous 1 to 12 weeks. Although the risk of severe anaphylaxis was estimated to be low (0.015% on first exposure and 0.16% on re-exposure),[2] alternative treatment should be considered before re-exposure to lepirudin and it should only be used where treatment for an anaphylactic reaction is available.[1,2]

1. EMEA. EMEA public statement on Refludan (lepirudin)—fatal anaphylactic reactions (issued October 2002). Available at: http://www.emea.europa.eu/pdfs/human/press/pus/2771702en.pdf (accessed 16/05/08)
2. Greinacher A, *et al.* Anaphylactic and anaphylactoid reactions associated with lepirudin in patients with heparin-induced thrombocytopenia. *Circulation* 2003; **108:** 2062–5.

Interactions
Use of direct thrombin inhibitors with thrombolytics, oral anticoagulants, or drugs that affect platelet function may increase the risk of bleeding.

Pharmacokinetics
Lepirudin is metabolised and excreted by the kidney. About 45% of an intravenous dose is detected in the urine and about 35% is excreted unchanged. The terminal elimination half-life of lepirudin is about 1.3 hours. In patients with severe renal impairment the half-life may be prolonged to about 2 days.

Breast feeding. Three hours after injection, plasma concentrations of hirudin in a woman receiving lepirudin 50 mg subcutaneously twice daily were 0.5 to 1 microgram/mL, but no hirudin was detected in the breast milk.

1. Lindhoff-Last E, *et al.* Hirudin treatment in a breastfeeding woman. *Lancet* 2000; **355:** 467–8.

Uses and Administration
Lepirudin is a recombinant hirudin (p.1305) that is a direct inhibitor of thrombin. It is used as an anticoagulant in the management of thromboembolic disorders (p.1187) in patients with heparin-induced thrombocytopenia. It has been investigated in arterial thromboembolic disorders such as myocardial infarction and unstable angina.

In the management of thromboembolism in patients with heparin-induced thrombocytopenia lepirudin is given in an initial dose of 400 micrograms/kg by slow intravenous injection. This is followed by a maintenance dose of 150 micrograms/kg per hour by continuous intravenous infusion, adjusted according to response, usually for 2 to 10 days. Response should be monitored according to the activated partial thromboplastin time (APTT) ratio to achieve a target of 1.5 to 2.5. Doses must not exceed those based on a patient weight of 110 kg and in general an infusion rate of 210 micrograms/kg per hour should not be exceeded.

Doses of lepirudin should be reduced in patients with renal impairment, and infusions should be avoided in those on haemodialysis (see below).

Administration in renal impairment. Doses of lepirudin should be reduced in patients with renal impairment. The initial dose is reduced to 200 micrograms/kg, and the maintenance infusion rate is reduced according to creatinine clearance (CC):
- CC 45 to 60 mL/minute: infusion rate 50% of normal rate
- CC 30 to 44 mL/minute: 30% of normal rate
- CC 15 to 29 mL/minute: 15% of normal rate
- CC below 15 mL/minute: infusion of lepirudin should be avoided, although in haemodialysis patients or cases of acute renal failure further intravenous bolus doses of 100 micrograms/kg may be used on alternate days, according to response

Heparin-induced thrombocytopenia. Lepirudin is effective for the management of thromboembolism in patients with heparin-induced thrombocytopenia[1] (see Effects on the Blood under Adverse Effects of Heparin p.1302). Bleeding is the main complication during treatment, particularly with usual doses (see Uses and Administration, above) and in patients with renal impairment,[2] and use of lower doses has been suggested.[1,2]

1. Lubenow N, *et al.* HIT Investigators Group. Lepirudin in patients with heparin-induced thrombocytopenia—results of the third prospective study (HAT-3) and a combined analysis of HAT-1, HAT-2, and HAT-3. *J Thromb Haemost* 2005; **3:** 2428–36.
2. Tardy B, *et al.* GEHT-HIT Study Group. Predictive factors for thrombosis and major bleeding in an observational study in 181 patients with heparin-induced thrombocytopenia treated with lepirudin. *Blood* 2006; **108:** 1492–6.

Ischaemic heart disease. Recombinant hirudins have been investigated as alternatives to heparin in the management of acute ST-elevation myocardial infarction (p.1175) and in non-ST elevation myocardial infarction and unstable angina (see Angina Pectoris, p.1157), and have been used as adjuncts to medical or interventional treatment. Overall they appear to have some benefit over heparin,[1] but their precise role in each situation remains to be confirmed.

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.

1. Direct Thrombin Inhibitor Trialists' Collaborative Group. Direct thrombin inhibitors in acute coronary syndromes: principal results of a meta-analysis based on individual patients' data. *Lancet* 2002; **359:** 294–302.
2. The Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) IIa Investigators. Randomized trial of intravenous heparin versus recombinant hirudin for acute coronary syndromes. *Circulation* 1994; **90:** 1631–7.
3. Antman EM, *et al*. Hirudin in acute myocardial infarction: safety report from the Thrombolysis and Thrombin Inhibition in Myocardial Infarction (TIMI) 9A trial. *Circulation* 1994; **90:** 1624–30.
4. Neuhaus K-L, *et al*. Safety observations from the pilot phase of the randomized r-Hirudin for Improvement of Thrombolysis (HIT-III) study: a study of the Arbeitsgemeinschaft Leitender Kardiologischer Krankenhausärzte (ALKK). *Circulation* 1994; **90:** 1638–42.
5. Zeymer U, Neuhaus K-L. Hirudin and excess bleeding: implications for future use. *Drug Safety* 1995; **12:** 234–9.
6. Conrad KA. Clinical pharmacology and drug safety: lessons from hirudin. *Clin Pharmacol Ther* 1995; **58:** 123–6.
7. The Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) IIb Investigators. A comparison of recombinant hirudin with heparin for the treatment of acute coronary syndromes. *N Engl J Med* 1996; **335:** 775–82.
8. Antman EM. Hirudin in acute myocardial infarction: thrombolysis and thrombin inhibition in myocardial infarction (TIMI) 9B trial. *Circulation* 1996; **94:** 911–21.
9. Neuhaus K-L, *et al.* Recombinant hirudin (lepirudin) for the improvement of thrombolysis with streptokinase in patients with acute myocardial infarction: results of the HIT-4 trial. *J Am Coll Cardiol* 1999; **34:** 966–73.
10. The Hirulog and Early Reperfusion or Occlusion (HERO)-2 Trial Investigators. Thrombin-specific anticoagulation with bivalirudin versus heparin in patients receiving fibrinolytic therapy for acute myocardial infarction: the HERO-2 randomised trial. *Lancet* 2001; **358:** 1855–63.
11. Organization to Assess Strategies for Ischemic Syndromes (OASIS) Investigators. Comparison of the effects of two doses of recombinant hirudin compared with heparin in patients with acute myocardial ischemia without ST elevation: a pilot study. *Circulation* 1997; **96:** 769–77.
12. Organisation to Assess Strategies for Ischemic Syndromes (OASIS-2) Investigators. Effects of recombinant hirudin (lepirudin) compared with heparin on death, myocardial infarction, refractory angina, and revascularisation procedures in patients with acute myocardial ischaemia without ST elevation: a randomised trial. *Lancet* 1999; **353:** 429–38.
13. Topol EJ, *et al.* Recombinant hirudin for unstable angina pectoris: a multicenter, randomized angiographic trial. *Circulation* 1994; **89:** 1557–66.
14. Kong DF, *et al.* Clinical outcomes of bivalirudin for ischemic heart disease. *Circulation* 1999; **100:** 2049–53.
15. Stone GW, *et al.* The ACUITY Investigators. Bivalirudin for patients with acute coronary syndromes. *N Engl J Med* 2006; **355:** 2203–16.
16. van den Bos AA, *et al.* Safety and efficacy of recombinant hirudin (CGP 39 393) versus heparin in patients with stable angina undergoing coronary angioplasty. *Circulation* 1993; **88:** 2058–66.
17. Serruys PW, *et al.* A comparison of hirudin with heparin in the prevention of restenosis after coronary angioplasty. *N Engl J Med* 1995; **333:** 757–63.
18. Manfredi JA, *et al.* Lepirudin as a safe alternative for effective anticoagulation in patients with known heparin-induced thrombocytopenia undergoing percutaneous coronary intervention: case reports. *Catheter Cardiovasc Interv* 2001; **52:** 468–72.
19. Pinto DS, *et al.* Combination platelet glycoprotein IIb/IIIa receptor and lepirudin administration during percutaneous coronary intervention in patients with heparin-induced thrombocytopenia. *Catheter Cardiovasc Interv* 2003; **58:** 65–8.
20. Cochran K, *et al.* Use of lepirudin during percutaneous vascular interventions in patients with heparin-induced thrombocytopenia. *J Invasive Cardiol* 2003; **15:** 617–21.
21. Lincoff AM, *et al.* Bivalirudin and provisional glycoprotein IIb/IIIa blockade compared with heparin and planned glycoprotein IIb/IIIa blockade during percutaneous coronary intervention: REPLACE-2 randomized trial. *JAMA* 2003; **289:** 853–63. Correction. *ibid.*; 1638.
22. Lincoff AM, *et al.* Long-term efficacy of bivalirudin and provisional glycoprotein IIb/IIIa blockade vs heparin and planned glycoprotein IIb/IIIa blockade during percutaneous coronary revascularization: REPLACE-2 randomized trial. *JAMA* 2004; **292:** 696–703. Correction. *ibid*. 2006; **296:** 46.
23. Stone GW, *et al.* Bivalirudin in patients with acute coronary syndromes undergoing percutaneous coronary intervention: a subgroup analysis from the Acute Catheterization and Urgent Intervention Triage strategy (ACUITY) trial. *Lancet* 2007; **369:** 907–19.
24. Dyke CM, *et al.* A comparison of bivalirudin to heparin with protamine reversal in patients undergoing cardiac surgery with cardiopulmonary bypass: the EVOLUTION-ON study. *J Thorac Cardiovasc Surg* 2006; **131:** 533 –9.
25. Riess F-C, *et al.* Recombinant hirudin for cardiopulmonary bypass anticoagulation: a randomized, prospective, and heparin-controlled pilot study. *Thorac Cardiovasc Surg* 2007; **55:** 233–8.

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.

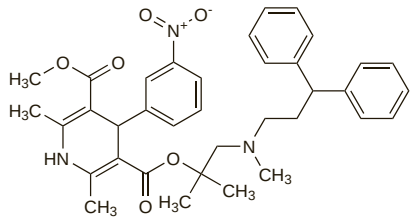
Лерканидипина Гидрохлорид

$C_{36}H_{41}N_3O_6$,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.

1. McClellan KJ, Jarvis B. Lercanidipine: a review of its use in hypertension. *Drugs* 2000; **60:** 1123–40.
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.

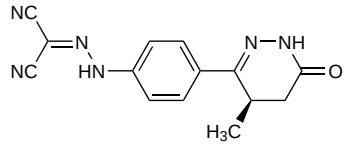
Левосимендан

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

1. Figgitt DP, *et al*. Levosimendan. *Drugs* 2001; **61:** 613–27.
2. Follath F, *et al.* Efficacy and safety of intravenous levosimendan compared with dobutamine in severe low-output heart failure (the LIDO study): a randomised double-blind trial. *Lancet* 2002; **360:** 196–202.
3. McBride BF, White CM. Levosimendan: implications for clinicians. *J Clin Pharmacol* 2003; **43:** 1071–81.
4. Innes CA, Wagstaff AJ. Levosimendan: a review of its use in the management of acute decompensated heart failure. *Drugs* 2003; **63:** 2651–71.
5. Earl GL, Fitzpatrick JT. Levosimendan: a novel inotropic agent for treatment of acute, decompensated heart failure. *Ann Pharmacother* 2005; **39:** 1888–96.
6. De Luca L, *et al.* Evidence-based use of levosimendan in different clinical settings. *Eur Heart J* 2006; **27:** 1908–20.
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.