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.

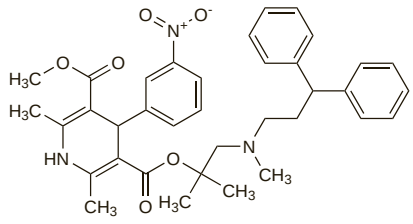
Лерканидипина Гидрохлорид

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

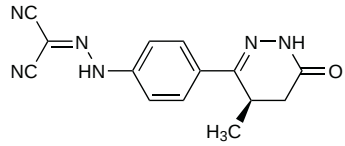
Левосимендан

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

Lidoflazine *(BAN, USAN, rINN)*

Lidoflazina; Lidoflazinum; McN-JR-7904; Ordiflazine; R-7904. 4-[3-(4,4′-Difluorobenzhydryl)propyl]piperazin-1-ylaceto-2′,6′-xylidide.

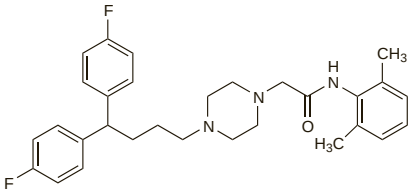
Лидофлазин

$C_{30}H_{35}F_2N_3O$ = 491.6.

CAS — 3416-26-0.

ATC — C08EX01.

ATC Vet — QC08EX01.



Profile

Lidoflazine is a calcium-channel blocker (p.1154) that reduces AV conduction. It has been used in angina pectoris.

Preparations

Proprietary Preparations (details are given in Part 3)
India: Clinium; ***S.Afr.:*** Clinium.

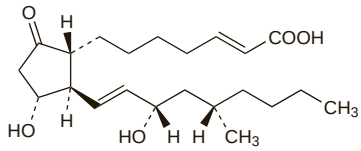
Limaprost *(rINN)*

Limaprostum; ONO-1206; OP-1206. (*E*)-7-{(1*R*,2*R*,3*R*)-3-Hydroxy-2-[(*E*)-(3*S*,5*S*)-3-hydroxy-5-methyl-1-nonenyl]-5-oxocyclopentyl}-2-heptenoic acid.

Лимапрост

$C_{22}H_{36}O_5$ = 380.5.

CAS — 74397-12-9 (limaprost); 88852-12-4 (limaprost alfadex).



Pharmacopoeias. *Jpn* includes limaprost alfadex.

Profile

Limaprost is a synthetic analogue of alprostadil (prostaglandin E_1) used in the management of peripheral vascular disease (p.1178). It is given orally as limaprost alfadex, in a dose equivalent to limaprost 15 to 30 micrograms daily in three divided doses.

◊ References.

1. Shono T, Ikeda K. Rapid effect of oral limaprost in Raynaud's disease in childhood. *Lancet* 1989; **i:** 908.
2. Murai C, *et al.* Oral limaprost for Raynaud's phenomenon. *Lancet* 1989; **ii:** 1218.
3. Aoki Y, *et al.* Possible participation of a prostaglandin E1 analogue in the aggravation of diabetic nephropathy. *Diabetes Res Clin Pract* 1992; **16:** 233–8.
4. Sato Y, *et al.* Effect of oral administration of prostaglandin E1 on erectile dysfunction. *Br J Urol* 1997; **80:** 772–5.
5. Swainston Harrison T, Plosker GL. Limaprost. *Drugs* 2007; **67:** 109–18.

Preparations

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

Linsidomine Hydrochloride *(rINNM)*

Hidrocloruro de linsidomina; Linsidomine, Chlorhydrate de; Linsidomini Hydrochloridum. 3-Morpholinosydnonimine hydrochloride.

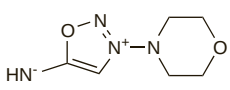
Линсидомина Гидрохлорид

$C_6H_{10}N_4O_2$,HCl = 206.6.

CAS — 33876-97-0 (linsidomine); 16142-27-1 (linsidomine hydrochloride).

ATC — C01DX18.

ATC Vet — QC01DX18.



(linsidomine)

Profile

Linsidomine is a nitrovasodilator and a metabolite of molsidomine (p.1343) and has been given intravenously or via the intracoronary route for coronary vasodilatation.

◊ References.

1. Delonca J, *et al.* Comparative efficacy of the intravenous administration of linsidomine, a direct nitric oxide donor, and isosorbide dinitrate in severe unstable angina: a French multicentre study. *Eur Heart J* 1997; **18:** 1300–6.

Preparations

Proprietary Preparations (details are given in Part 3)
Fr.: Corvasal†.

Lisinopril *(BAN, USAN, rINN)*

L-154826; Lisinopriili; Lisinoprilum; Lizinopril; Lizinoprilis; MK-521. *N*-{*N*-[(*S*)-1-Carboxy-3-phenylpropyl]-L-lysyl}-L-proline dihydrate.

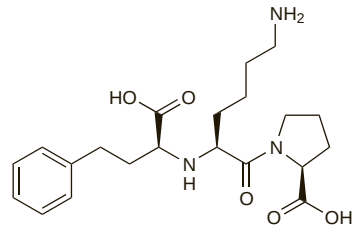
Лизиноприл

$C_{21}H_{31}N_3O_5$,$2H_2O$ = 441.5.

CAS — 76547-98-3 (anhydrous lisinopril); 83915-83-7 (lisinopril dihydrate).

ATC — C09AA03.

ATC Vet — QC09AA03.



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

Ph. Eur. 6.2 (Lisinopril Dihydrate). A white or almost white crystalline powder. Soluble in water; practically insoluble in dehydrated alcohol and in acetone; sparingly soluble in methyl alcohol.

USP 31 (Lisinopril). A white crystalline powder. Soluble 1 in 10 of water and 1 in 70 of methyl alcohol; practically insoluble in alcohol, in acetone, in acetonitrile, in chloroform, and in ether.

Suspension. The US licensed prescribing information provides the following method for making 200 mL of a suspension containing lisinopril 1 mg/mL. Add 10 mL of purified water to a polyethylene terephthalate bottle containing ten 20-mg tablets (*Prinivil, Merck* or *Zestril, AstraZeneca*) and shake for at least 1 minute. Add 30 mL of *Bicitra* (*Alza, USA*) and 160 mL of *Ora-Sweet SF* (*Paddock, USA*) to the bottle and gently shake for several seconds. The suspension should be stored at or below 25° and can be stored for up to 4 weeks. Studies of the characteristics of this and other liquid dosage forms of lisinopril have been published.[1,2]

1. Thompson KC, *et al.* Characterization of an extemporaneous liquid formulation of lisinopril. *Am J Health-Syst Pharm* 2003; **60:** 69–74.
2. Nahata MC, Morosco RS. Stability of lisinopril in two liquid dosage forms. *Ann Pharmacother* 2004; **38:** 396–9.

Adverse Effects, Treatment, and Precautions

As for ACE inhibitors, p.1193.

Porphyria. Lisinopril has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Interactions

As for ACE inhibitors, p.1196.

Pharmacokinetics

Lisinopril is slowly and incompletely absorbed after oral doses. About 25% of a dose is absorbed on average, but the absorption varies considerably between individuals, ranging from about 6 to 60%. It is already an active diacid and does not need to be metabolised *in vivo*. Peak concentrations in plasma are reported to occur after about 7 hours. Lisinopril is reported not to be significantly bound to plasma proteins. It is excreted unchanged in the urine. The effective half-life for accumulation after multiple doses is 12 hours in patients with normal renal function. Lisinopril is removed by haemodialysis.

◊ References.

1. Till AE, *et al.* The pharmacokinetics of lisinopril in hospitalized patients with congestive heart failure. *Br J Clin Pharmacol* 1989; **27:** 199–204.
2. Neubeck M, *et al.* Pharmacokinetics and pharmacodynamics of lisinopril in advanced renal failure: consequence of dose adjustment. *Eur J Clin Pharmacol* 1994; **46:** 537–43.

Uses and Administration

Lisinopril is an ACE inhibitor (p.1193). It is used in the treatment of hypertension (p.1171) and heart failure (p.1165), prophylactically after myocardial infarction (p.1175), and in diabetic nephropathy (see Kidney Disorders, p.1199).

The haemodynamic effects of lisinopril are seen within 1 to 2 hours of a single oral dose and the maximum effect occurs after about 6 hours, although the full effect may not develop for several weeks during chronic dosing. The haemodynamic action lasts for about 24 hours after once-daily dosing. Lisinopril is given orally as the dihydrate, but doses are expressed in terms of the anhydrous substance. Lisinopril 2.72 mg as the dihydrate is equivalent to about 2.5 mg of anhydrous lisinopril. The dose of lisinopril should be reduced in patients with renal impairment (see below).

In the treatment of **hypertension**, the usual initial dose is 10 mg daily. Since there may be a precipitous fall in blood pressure in some patients when starting therapy with an ACE inhibitor, the first dose should preferably be given at bedtime. Hypotension is particularly likely in patients with renovascular hypertension, volume depletion, heart failure, or severe hypertension and such patients should be given a lower initial dose of 2.5 to 5 mg once daily. Patients taking diuretics should have the diuretic withdrawn 2 or 3 days before lisinopril is started and resumed later if required; if this is not possible, an initial dose of 5 mg once daily should be given. The usual maintenance dose is 20 mg given once daily, though up to 80 mg daily may be given if necessary.

In the management of **heart failure**, severe first-dose hypotension on introduction of an ACE inhibitor is common in patients on loop diuretics, but their temporary withdrawal may cause rebound pulmonary oedema. Thus treatment should be started with a low dose under close medical supervision. Lisinopril is given in an initial dose of 2.5 mg daily. In the USA an initial dose of 5 mg daily is suggested. Usual maintenance doses range from 5 to 40 mg daily.

After **myocardial infarction**, treatment with lisinopril may be started within 24 hours of the onset of symptoms in an initial dose of 5 mg once daily for two days, then increased to 10 mg once daily. An initial dose of 2.5 mg once daily is recommended for patients with a low systolic blood pressure.

In the management of **diabetic nephropathy**, hypertensive type 2 diabetics with microalbuminuria may be given a dose of 10 mg once daily, increased if necessary to 20 mg once daily to achieve a sitting diastolic blood pressure below 90 mmHg.

◊ Reviews.

1. Lancaster SG, Todd PA. Lisinopril: a preliminary review of its pharmacodynamic and pharmacokinetic properties, and therapeutic use in hypertension and congestive heart failure. *Drugs* 1988; **35:** 646–69.
2. Goa KL, *et al.* Lisinopril: a review of its pharmacology and clinical efficacy in the early management of acute myocardial infarction. *Drugs* 1996; **52:** 564–88.
3. Goa KL, *et al.* Lisinopril: a review of its pharmacology and use in the management of the complications of diabetes mellitus. *Drugs* 1997; **53:** 1081–1105.
4. Simpson K, Jarvis B. Lisinopril: a review of its use in congestive heart failure. *Drugs* 2000; **59:** 1149–67.

Administration in children. Lisinopril has been reported to be an effective and well-tolerated antihypertensive in children 6 years of age and older,[1] although it has been used successfully in younger children.[2] US licensed product information recommends an oral starting dose for lisinopril of 70 micrograms/kg (up to 5 mg) once daily for children 6 years of age and older (but see also Administration in Renal Impairment, below). The *BNFC* recommends similar doses for children aged 6 to 12 years and states that this dose may be increased at intervals of 1 to 2 weeks to a maximum of 600 micrograms/kg or 40 mg once daily. For children between 12 and 18 years of age the *BNFC* recom-