Labetalol is used as the hydrochloride in the management of hypertension (p.1171). It is also used to induce hypotension during surgery. Labetalol decreases blood pressure more rapidly than other beta blockers; the full antihypertensive effect may be seen within 1 to 3 hours of an oral dose.

In **hypertension** labetalol hydrochloride is usually given in an initial oral dose of 100 mg twice daily with food, gradually increased if necessary according to response and standing blood pressure, to 200 to 400 mg twice daily; total daily doses of 2.4 g, in two to four divided doses, have occasionally been required. Lower doses may be adequate in elderly patients; an initial dose of 50 to 100 mg twice daily has been recommended, and the usual maintenance dose is 100 to 200 mg twice daily.

For the emergency treatment of hypertension labetalol hydrochloride may be given by slow intravenous injection. In the UK a dose of 50 mg is recommended, given over a period of at least 1 minute; if necessary this dose may be repeated at intervals of 5 minutes until a total of 200 mg has been given. In the USA an initial dose of 20 mg is recommended, given over 2 minutes; subsequent doses of 40 to 80 mg may be given every 10 minutes, if necessary, up to a maximum of 300 mg. Blood pressure should be monitored, and the patient should remain supine during the injection and for 3 hours afterwards, to avoid excessive orthostatic hypotension. After bolus intravenous injection a maximum effect is usually obtained within 5 minutes and usually lasts up to 6 hours, although it may extend as long as 18 hours.

Labetalol hydrochloride has also been given by intravenous infusion in usual doses of 2 mg/minute. Suggested concentrations for intravenous infusions are 1 mg/mL or 2 mg/3 mL of suitable diluent. In hypertension in pregnancy, labetalol infusion may be started at the rate of 20 mg/hour, then doubled every 30 minutes until a satisfactory response is obtained or a dose of 160 mg/hour is reached. In hypertension after myocardial infarction, labetalol infusion may be started at the rate of 15 mg/hour and gradually increased until a satisfactory response is obtained or a dose of 120 mg/hour is reached.

The initial dose in **hypotensive anaesthesia** is 10 to 20 mg intravenously, with increments of 5 to 10 mg if satisfactory hypotension is not achieved after 5 minutes. A higher initial dose may be required in patients who do not receive halothane anaesthesia.

For the use of labetalol in children, see below.

Action. Labetalol has 2 optical centres; it is used as the racemic mixture of the 4 stereoisomers. The *R,R*- isomer is responsible for the beta-blocking activity and has limited alpha-blocking activity; it also has beta-adrenergic mediated peripheral vasodilating activity. The *S,R*-isomer has the most potent alpha-blocking activity. The *S,S*-isomer has some alpha-blocking activity and the *R,S*-isomer does not appear to have either alpha- or beta-adrenergic blocking effect.[1] The pure *R,R*-isomer, dilevalol, was withdrawn from the market because of hepatotoxicity.

1. Gold EH, *et al*. Synthesis and comparison of some cardiovascular properties of the stereoisomers of labetalol. *J Med Chem* 1982; **25:** 1363–70.

Administration in children. Labetalol has been used in the management of hypertension in children,[1] although experience is limited. The *BNFC* suggests the following doses:

for **hypertensive emergencies**, labetalol hydrochloride may be given by intravenous infusion as follows:

- neonates: 500 micrograms/kg per hour adjusted at intervals of at least 15 minutes according to response, to a maximum of 4 mg/kg per hour
- 1 month to 12 years: 0.5 to 1 mg/kg per hour adjusted at intervals of at least 15 minutes according to response, to a maximum of 3 mg/kg per hour
- 12 to 18 years: 30 to 120 mg/hour adjusted at intervals of at least 15 minutes according to response

for **hypertension**, labetalol hydrochloride may be given as follows:

- 1 month to 12 years: 1 to 2 mg/kg three or four times daily by mouth or a single intravenous injection in a dose of 250 to 500 micrograms/kg to a maximum of 20 mg
- 12 to 18 years: similar doses to adults (see above) although a lower initial oral dose of 50 to 100 mg twice daily is recommended

1. Bunchman TE, *et al*. Intravenously administered labetalol for treatment of hypertension in children. *J Pediatr* 1992; **120:** 140–4.

Preparations

BP 2008: Labetalol Injection; Labetalol Tablets;
USP 31: Labetalol Hydrochloride Injection; Labetalol Hydrochloride Oral Suspension; Labetalol Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Biascor; ***Austral.:*** Presolol; Trandate; ***Austria:*** Trandate; ***Belg.:*** Trandate; ***Canad.:*** Trandate; ***Chile:*** Trandate; ***Cz.:*** Coreton†; Trandate; ***Denm.:*** Trandate; ***Fin.:*** Albetol; ***Fr.:*** Trandate; ***Gr.:*** Trandate; ***Hong Kong:*** Trandate; ***Irl.:*** Trandate; ***Israel:*** Trandate; ***Ital.:*** Ipolab; Trandate; ***Malaysia:*** Tolbetol†; Trandate; ***Neth.:*** Trandate; ***Norw.:*** Trandate; ***NZ:*** Hybloc; Trandate; ***Port.:*** Trandate†; ***S.Afr.:*** Trandate; ***Singapore:*** Trandate; ***Spain:*** Trandate; ***Swed.:*** Trandate; ***Switz.:*** Trandate; ***UK:*** Trandate; ***USA:*** Normodyne†; Trandate; ***Venez.:*** Trandate†.

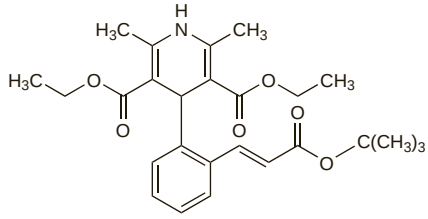
Multi-ingredient: ***Ital.:*** Trandiur.

Lacidipine *(BAN, USAN, rINN)*

GR-43659X; GX-1048; Lacidipin; Lacidipino; Lacidipinum; Lasidipiini; Lasidipin. Diethyl 4-{2-[(*tert*-butoxycarbonyl)vinyl]phenyl}-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate.

Лацидипин

$C_{26}H_{33}NO_6$ = 455.5.
CAS — 103890-78-4.
ATC — C08CA09.
ATC Vet — QC08CA09.



Pharmacopoeias. In *Br.*
BP 2008 (Lacidipine). A white to pale yellow crystalline powder. Practically insoluble in water; sparingly soluble in dehydrated alcohol; freely soluble in acetone and in dichloromethane.

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

Lacidipine is rapidly but poorly absorbed from the gastrointestinal tract after oral doses and undergoes extensive first-pass metabolism; the bioavailability has been reported to be 2 to 9%, or 18.5% (range 4 to 52%) using a more sensitive assay method. It is more than 95% bound to plasma proteins. Lacidipine is eliminated by metabolism in the liver and metabolites are excreted mainly by the biliary route. About 70% of an oral dose is eliminated in the faeces, the remainder in the urine. The average steady-state terminal elimination half-life of lacidipine is 13 to 19 hours.

Uses and Administration

Lacidipine 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).

The usual initial dose of lacidipine is 2 mg once daily by mouth increased if necessary after 3 to 4 weeks or more to 4 mg daily; a further increase in dose to 6 mg daily may be necessary in some patients.

◊ Reviews.

1. Lee CR, Bryson HM. Lacidipine: a review of its pharmacodynamic and pharmacokinetic properties and therapeutic potential in the treatment of hypertension. *Drugs* 1994; **48:** 274–96.
2. Zanchetti A, ed. Cardiovascular advantages of a third generation calcium antagonist: symposium on lacidipine. *Drugs* 1999; **57** (suppl 1): 1–29.
3. McCormack PL, Wagstaff AJ. Lacidipine: a review of its use in the management of hypertension. *Drugs* 2003; **63:** 2327–56.

Preparations

BP 2008: Lacidipine Tablets.

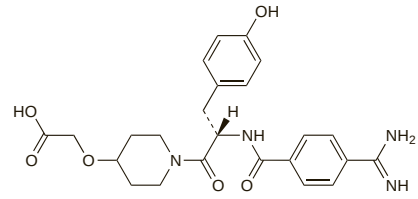
Proprietary Preparations (details are given in Part 3)
Arg.: Lacipil†; Midotens†; ***Belg.:*** Motens; ***Braz.:*** Lacipil; Midotens; ***Cz.:*** Lacipil; ***Denm.:*** Midotens; ***Fr.:*** Caldine; ***Ger.:*** Motens; ***Gr.:*** Balnox; Lacipil; Lacitens; Motens; ***Hong Kong:*** Lacipil; ***Hung.:*** Lacipil; ***India:*** Sinopil; ***Indon.:*** Lacipil; ***Ital.:*** Aponil; Lacipil; Lacirex; Ladip; Viapres; ***Malaysia:*** Lacipil; ***Mex.:*** Lacipil; Midotens; ***Neth.:*** Motens; ***Philipp.:*** Lacipil; ***Pol.:*** Lacipil; ***Port.:*** Lacipil; Tens; ***Rus.:*** Lacipil (Лаципил); ***Singapore:*** Lacipil; ***Spain:*** Lacimen; Lacipil; Motens; ***Switz.:*** Motens; ***Thai.:*** Motens; ***Turk.:*** Lacipil; ***UK:*** Motens; ***Venez.:*** Lacipil; Tens†.

Lamifiban *(USAN, rINN)*

Lamifibán; Lamifibanum; Ro-44-9883; Ro-44-9883/000. ({1-[*N*-(*p*-Amidinobenzoyl)-L-tyrosyl]-4-piperidyl}oxy)acetic acid.

Ламифибан

$C_{24}H_{28}N_4O_6$ = 468.5.
CAS — 144412-49-7 (lamifiban); 243835-65-6 (lamifiban hydrochloride).



Profile

Lamifiban is a glycoprotein IIb/IIIa-receptor antagonist. It has been investigated as an antiplatelet drug given intravenously for the management of thromboembolic disorders, such as unstable angina and myocardial infarction.

◊ References.

1. Théroux P, *et al*. Platelet membrane receptor glycoprotein IIb/IIIa antagonism in unstable angina: the Canadian Lamifiban Study. *Circulation* 1996; **94:** 899–905.
2. The PARAGON Investigators. International, randomized, controlled trial of lamifiban (a platelet glycoprotein IIb/IIIa inhibitor), heparin, or both in unstable angina. *Circulation* 1998; **97:** 2386–95.
3. The PARADIGM Investigators. Combining thrombolysis with the platelet glycoprotein IIb/IIIa inhibitor lamifiban: results of the Platelet Aggregation Receptor Antagonist Dose Investigation and Reperfusion Gain in Myocardial Infarction (PARADIGM) trial. *J Am Coll Cardiol* 1998; **32:** 2003–10.
4. Global Organization Network (PARAGON)-B Investigators. Randomized, placebo-controlled trial of titrated intravenous lamifiban for acute coronary syndromes. *Circulation* 2002; **105:** 316–21.

Lanatoside C *(BAN, rINN)*

Celanide; Celanidum; Lanatosid C; Lanatosidi C; Lanatósido C; Lanatosidum C; Lanatozyd c. 3-[(*O*-β-D-Glucopyranosyl-(1→4)-*O*-3-acetyl-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-*O*-2,6-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-*O*-2,6-dideoxy-β-D-*ribo*-hexopyranosyl)oxy]-12,14-dihydroxy-3β,5β,12β-card-20(22)-enolide.

Ланатозид С

$C_{49}H_{76}O_{20}$ = 985.1.
CAS — 17575-22-3.
ATC — C01AA06.
ATC Vet — QC01AA06.