7. Kingma K, *et al.* Double-blind, placebo-controlled study of intravenous prostacyclin on hemodynamics in severe Raynaud's phenomenon: the acute vasodilatory effect is not sustained. *J Cardiovasc Pharmacol* 1995; **26:** 388–93.
8. Denton CP, Black CM. Raynaud's phenomenon and scleroderma. In: Snaith ML, ed. *ABC of rheumatology.* 3rd ed. London: BMJ Publishing Group, 2004: 87–91.

Pulmonary hypertension. Epoprostenol was originally introduced into the management of end-stage pulmonary hypertension (p.1179) to sustain patients long enough for them to have heart-lung transplantation. However, long-term therapy may also have a role as an alternative to transplantation; sustained clinical improvement and improved survival have been reported[1-4] in some patients with idiopathic pulmonary arterial hypertension given long-term intravenous therapy using portable infusion pumps, as well as in patients with pulmonary arterial hypertension associated with other diseases.[4-7]

Inhaled epoprostenol, a route that may overcome some of the adverse effects associated with parenteral use, has had some success in adults[8,9] with pulmonary hypertension and in neonates[10,11] with persistent pulmonary hypertension.

1. Higenbottam T, *et al.* Long term intravenous prostaglandin (epoprostenol or iloprost) for treatment of severe pulmonary hypertension. *Heart* 1998; **80:** 151–5.
2. Herner SJ, Mauro LS. Epoprostenol in primary pulmonary hypertension. *Ann Pharmacother* 1999; **33:** 340–7.
3. McLaughlin VV, *et al.* Survival in primary pulmonary hypertension: the impact of epoprostenol therapy. *Circulation* 2002; **106:** 1477–82.
4. Kuhn KP, *et al.* Outcome in 91 consecutive patients with pulmonary arterial hypertension receiving epoprostenol. *Am J Respir Crit Care Med* 2003; **167:** 580–6.
5. McLaughlin VV, *et al.* Compassionate use of continuous prostacyclin in the management of secondary pulmonary hypertension: a case series. *Ann Intern Med* 1999; **130:** 740–3.
6. Badesch DB, *et al.* Continuous intravenous epoprostenol for pulmonary hypertension due to the scleroderma spectrum of disease: a randomized, controlled trial. *Ann Intern Med* 2000; **132:** 425–34.
7. Fisher KA, *et al.* Sarcoidosis-associated pulmonary hypertension: outcome with long-term epoprostenol treatment. *Chest* 2006; **130:** 1481–8.
8. Olschewski H, *et al.* Aerosolized prostacyclin and iloprost in severe pulmonary hypertension. *Ann Intern Med* 1996; **124:** 820–4.
9. Mikhail G, *et al.* An evaluation of nebulized prostacyclin in patients with primary and secondary pulmonary hypertension. *Eur Heart J* 1997; **18:** 1499–1504.
10. Bindl L, *et al.* Aerosolised prostacyclin for pulmonary hypertension in neonates. *Arch Dis Child Fetal Neonatal Ed* 1994; **71:** F214–F216.
11. Kelly LK, *et al.* Inhaled prostacyclin for term infants with persistent pulmonary hypertension refractory to inhaled nitric oxide. *J Pediatr* 2002; **141:** 830–2.

Stroke. Results with epoprostenol in patients with acute stroke have been inconclusive and a systematic review of randomised studies concluded that too few patients had been studied for the effect of epoprostenol on survival to be determined.[1]

1. Bath PMW. Prostacyclin and analogues for acute ischaemic stroke. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2004 (accessed 04/07/05).

Thrombotic microangiopathies. Platelet aggregation has a major role in the pathogenesis of thrombotic thrombocytopenic purpura and the related disorder, haemolytic-uraemic syndrome (p.1076). Prostacyclin deficiency has been demonstrated in both conditions, but case reports of epoprostenol[1,2] or iloprost[3,4] treatment have indicated variable results.

1. Bobbio-Pallavicini E, *et al.* Intravenous prostacyclin (as epoprostenol) infusion in thrombotic thrombocytopenic purpura: four case reports and review of the literature. *Haematologica* 1994; **79:** 429–37.
2. Series C, *et al.* Interet de la prostacycline dans le traitement du syndrome hémolytique et urémique: à propos d'un cas. *Rev Med Interne* 1996; **17:** 76–8.
3. Sagripanti A, *et al.* Iloprost in the treatment of thrombotic microangiopathy: report of thirteen cases. *Biomed Pharmacother* 1996; **50:** 350–6.
4. Salvi F, *et al.* Unsuccessful treatment of resistant thrombotic thrombocytopenic purpura with prostacyclin. *Haematologica* 2000; **85:** 1329–30.

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Flolan; ***Austria:*** Epoallen; Flolan; Glaxoprost; ***Belg.:*** Flolan; ***Canad.:*** Flolan; ***Cz.:*** Flolan; ***Denm.:*** Flolan; ***Fr.:*** Flolan; ***Gr.:*** Flolan; ***Irl.:*** Flolan; ***Israel:*** Flolan; ***Ital.:*** Flolan; ***Neth.:*** Flolan; ***Norw.:*** Flolan; ***Singapore:*** Flolan; ***Spain:*** Flolan; ***Switz.:*** Flolan; ***UK:*** Flolan; ***USA:*** Flolan.

Eprosartan Mesilate *(BANM, rINNM)*

Éprosartan, Mésilate d'; Eprosartan Mesylate *(USAN)*; Eprosartani Mesilas; Mesilato de eprosartán; SKF-108566-J. (*E*)-2-Butyl-1-(*p*-carboxybenzyl)-α-2-thenylimidazole-5-acrylic acid methanesulfonate.

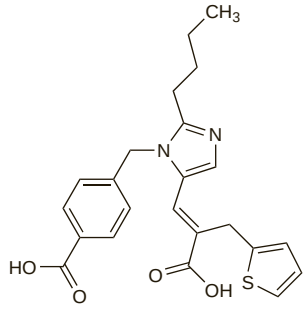
Эпрозартана Мезилат

$C_{23}H_{24}N_2O_4S,CH_4O_3S$ = 520.6.

CAS — 133040-01-4 (eprosartan); 144143-96-4 (eprosartan mesilate).

ATC — C09CA02.

ATC Vet — QC09CA02.



(eprosartan)

Adverse Effects and Precautions

As for Losartan Potassium, p.1326.

Interactions

As for Losartan Potassium, p.1327.

Pharmacokinetics

Eprosartan is absorbed from the gastrointestinal tract with an absolute oral bioavailability of about 13%. Peak plasma concentrations occur about 1 to 2 hours after an oral dose in the fasted state; giving doses with food delays absorption but this is not clinically significant. Eprosartan is about 98% bound to plasma proteins. It is excreted in the bile and in the urine, primarily as the unchanged drug; after oral doses approximately 7% of the drug is excreted in the urine, with about 2% as the acyl glucuronide. The terminal elimination half-life is about 5 to 9 hours.

◊ References.

1. Martin DE, *et al.* Pharmacokinetics and protein binding of eprosartan in healthy volunteers and in patients with varying degrees of renal impairment. *J Clin Pharmacol* 1998; **38:** 129–37.
2. Tenero DM, *et al.* Effect of age and gender on the pharmacokinetics of eprosartan. *Br J Clin Pharmacol* 1998; **46:** 267–70.

Uses and Administration

Eprosartan is an angiotensin II receptor antagonist with actions similar to those of losartan (p.1327). It is used in the management of hypertension (p.1171).

Eprosartan is given orally as the mesilate but doses are expressed in terms of the base; eprosartan mesilate 1.2 mg is equivalent to about 1 mg of eprosartan. The onset of antihypertensive effect occurs about 1 to 2 hours after administration and the maximum effect is achieved within 2 to 3 weeks after initiating therapy.

In the management of hypertension, eprosartan is given in an initial dose of 600 mg once daily. A lower initial dose of 300 mg once daily may be used in elderly patients over 75 years and has been recommended in renal or hepatic impairment (but see below). The dose should be adjusted according to response; the usual maintenance dose is 400 to 800 mg daily in a single dose or in two divided doses.

◊ Reviews.

1. McClellan KJ, Balfour JA. Eprosartan. *Drugs* 1998; **55:** 713–18.
2. Plosker GL, Foster RH. Eprosartan: a review of its use in the management of hypertension. *Drugs* 2000; **60:** 177–201.
3. Robins GW, Scott LJ. Eprosartan: a review of its use in the management of hypertension. *Drugs* 2005; **65:** 2355–77.
4. Ram CV, Rudmann MA. Unique dual mechanism of action of eprosartan: effects on systolic blood pressure, pulse pressure, risk of stroke and cognitive decline. *Expert Rev Cardiovasc Ther* 2007; **5:** 1003–11.

Administration in hepatic or renal impairment. In the UK a lower initial dose of 300 mg daily of eprosartan is recommended in patients with renal impairment (creatinine clearance less than 60 mL/minute) or mild to moderate hepatic impairment; this seems to be due to lack of clinical experience in such patients. In the USA, however, no reduction in the initial dose is considered necessary in hepatic or renal impairment, but a maximum dose of 600 mg daily is recommended for patients with moderate or severe renal impairment.

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Teveten; ***Austria:*** Teveten; ***Belg.:*** Teveten; ***Canad.:*** Teveten; ***Cz.:*** Teveten; ***Denm.:*** Teveten; ***Fin.:*** Teveten; ***Fr.:*** Teveten; ***Ger.:*** Emestar Mono; Teveten; ***Gr.:*** Epratenz†; Teveten; ***Hong Kong:*** Teveten; ***Hung.:*** Teveten; ***Irl.:*** Teveten; ***Ital.:*** Tevetenz; ***Neth.:*** Teveten; ***Norw.:*** Teveten; ***Philipp.:*** Teveten; ***Pol.:*** Teveten; ***Port.:*** Teveten; ***Rus.:*** Teveten (Теветен); ***S.Afr.:*** Teveten; ***Spain:*** Futuran; Navixen; Regulaten; Tevetens; ***Swed.:*** Teveten; ***Switz.:*** Teveten; ***Thai.:*** Teveten; ***UK:*** Teveten; ***USA:*** Teveten.

Multi-ingredient: ***Austral.:*** Teveten Plus; ***Austria:*** Teveten Plus; ***Belg.:*** Teveten Plus; ***Canad.:*** Teveten Plus; ***Cz.:*** Teveten Plus H; ***Denm.:*** Teveten Comp; ***Fin.:*** Teveten Comp; ***Fr.:*** Coteveten; ***Ger.:*** Emestar plus; Teveten Plus; ***Gr.:*** Teveten Plus; ***Hong Kong:*** Teveten Plus; ***Irl.:*** Teveten Plus; ***Neth.:*** Teveten Plus; ***Norw.:*** Teveten Comp; ***Philipp.:*** Teveten Plus; ***Port.:*** Medinor; Tensival; Teveten Plus; ***Rus.:*** Teveten Plus (Теветен Плюс); ***Spain:*** Futuran Plus; Navixen Plus; Regulaten Plus; Tevetens Plus; ***Swed.:*** Teveten Comp; ***Switz.:*** Teveten Plus; ***USA:*** Teveten HCT.

Eptifibatide *(BAN, rINN)*

C68-22; Eptifibatid; Eptifibatida; Eptifibatidi; Eptifibatidum; Integrelin; SB-1; Sch-60936. N^6-Amidino-N^2-(3-mercaptopropionyl)-L-lysylglycyl-L-α-aspartyl-L-tryptophyl-L-prolyl-L-cysteinamide, cyclic (1→6)-disulfide; S^1,S^6-Cyclo[N^6-carbamimidoyl-N^2-(3-sulfanylpropanoyl)-L-lysylglycyl-L-α-aspartyl-L-tryptophyl-L-prolyl-L-cysteinamide].

Эптифибатид

$C_{35}H_{49}N_{11}O_9S_2$ = 832.0.

CAS — 148031-34-9; 157630-07-4.

ATC — B01AC16.

ATC Vet — QB01AC16.

Adverse Effects

Bleeding is the most common adverse effect of eptifibatide. Hypotension has been reported. Antibodies to eptifibatide have not been detected.

Effects on the blood. Thrombocytopenia is an established adverse effect of the glycoprotein IIb/IIIa-receptor antagonist abciximab (see p.1192) but appears to be less common with eptifibatide. However, there have been several reports[1-5] of severe thrombocytopenia associated with eptifibatide.

1. Paradiso-Hardy FL, *et al.* Severe thrombocytopenia possibly related to readministration of eptifibatide. *Catheter Cardiovasc Interv* 2001; **54:** 63–7.
2. Hongo RH, Brent BN. Association of eptifibatide and acute profound thrombocytopenia. *Am J Cardiol* 2001; **88:** 428–31.
3. Yoder M, Edwards RF. Reversible thrombocytopenia associated with eptifibatide. *Ann Pharmacother* 2002; **36:** 628–30.
4. Coons JC, *et al.* Eptifibatide-associated acute, profound thrombocytopenia. *Ann Pharmacother* 2005; **39:** 368–72.
5. Refaat M, *et al.* Eptifibatide-induced thrombocytopenia. *J Thromb Thrombolysis* 2008; **25:** 204–6.

Precautions

As for Abciximab, p.1192.

Pharmacokinetics

Antiplatelet effects of eptifibatide persist for about 4 hours after stopping a continuous infusion. Plasma elimination half-life is about 2.5 hours. Eptifibatide is about 25% bound to plasma proteins. Renal clearance, as eptifibatide and metabolites excreted in the urine, accounts for about 50% of total body clearance.

Uses and Administration

Eptifibatide is an antiplatelet drug that reversibly inhibits its binding of fibrinogen, von Willebrand factor, and other adhesive molecules to the glycoprotein IIb/IIIa receptor of platelets. It is used, usually in combination with aspirin and heparin, in the management of unstable angina and in patients undergoing coronary angioplasty and stenting procedures.

In the management of **unstable angina**, eptifibatide is given in an initial dose of 180 micrograms/kg by intravenous injection, followed by 2 micrograms/kg per minute by intravenous infusion, for up to 72 hours. If percutaneous coronary intervention is performed during eptifibatide therapy, the infusion should be continued for 18 to 24 hours after the procedure, to a maximum total duration of 96 hours of therapy.

In patients undergoing **angioplasty**, though not presenting with unstable angina, eptifibatide is given in an initial dose of 180 micrograms/kg by intravenous injection immediately before the procedure, followed by 2 micrograms/kg per minute by intravenous infusion, with a second 180 micrograms/kg intravenous injection given 10 minutes after the first. The infusion should be continued until hospital discharge or for up to 18 to 24 hours; a minimum of 12 hours is recommended.

The dose of eptifibatide may need to be reduced in patients with renal impairment (see below).

◊ General references.

1. Gilchrist IC. Platelet glycoprotein IIb/IIIa inhibitors in percutaneous coronary intervention: focus on the pharmacokinetic-pharmacodynamic relationships of eptifibatide. *Clin Pharmacokinet* 2003; **42:** 703–20.
2. Curran MP, Keating GM. Eptifibatide: a review of its use in patients with acute coronary syndromes and/or undergoing percutaneous coronary intervention. *Drugs* 2005; **65:** 2009–35.
3. Tricoci P, *et al.* Present and evolving role of eptifibatide in the treatment of acute coronary syndromes. *Expert Rev Cardiovasc Ther* 2007; **5:** 401–12.
4. Zeymer U. The role of eptifibatide in patients undergoing percutaneous coronary intervention. *Expert Opin Pharmacother* 2007; **8:** 1147–54.
5. Zeymer U, Wienbergen H. A review of clinical trials with eptifibatide in cardiology. *Cardiovasc Drug Rev* 2007; **25:** 301–15.

Administration in renal impairment. The clearance of eptifibatide is reduced in renal impairment and plasma-eptifibatide concentrations are about doubled in patients with a creatinine clearance (CC) below 50 mL/minute.[1] Eptifibatide should not be used in severe renal impairment; it is contra-indicated in patients with CC below 30 mL/minute in the UK, and in dialysis-dependent patients in the USA. In patients with moderate renal impairment (CC below 50 mL/minute), the same bolus doses may be given as in those with normal renal function but the infusion dose should be reduced to 1 microgram/kg per minute.

1. Gretler DD, *et al.* Pharmacokinetic and pharmacodynamic properties of eptifibatide in subjects with normal or impaired renal function. *Clin Ther* 2004; **26:** 390–398.

Ischaemic heart disease. Patients with acute coronary syndromes may be treated either medically or with percutaneous coronary interventions such as angioplasty or stenting. In patients with *unstable angina* (p.1157), eptifibatide has been used as an adjunct to both medical and interventional therapy. In the PURSUIT study,[1] which compared eptifibatide with placebo in over 10 000 patients with ischaemic chest pain, the incidence of death and non-fatal myocardial infarction up to 30 days after treatment was reduced in those receiving eptifibatide; most patients also received aspirin and heparin and the number of percutaneous interventions was similar in each group.

Eptifibatide has also been of benefit as an adjunct to standard therapy in patients undergoing *elective percutaneous interventions* (see Reperfusion and Revascularisation Procedures, p.1181). In the IMPACT-II study[2] of over 4000 patients undergoing elective or emergency percutaneous coronary revascularisation, the incidence of death, myocardial infarction, and further unplanned coronary intervention was reduced in those receiving eptifibatide compared with placebo. Similar results were also obtained in a further study (ESPRIT)[3] in patients who were undergoing percutaneous coronary revascularisation with stent implantation, and benefit was maintained at 6-month follow-up.[4] Although most studies have given eptifibatide with unfractionated heparin, use with low-molecular-weight heparin also appears to be safe.[5]

In patients with *acute myocardial infarction* (p.1175), eptifibatide has been tried as an adjunct to thrombolysis or percutaneous intervention. In a study (INTRO AMI)[6] comparing eptifibatide and thrombolysis with thrombolysis alone, early patency rates were improved in those receiving eptifibatide but there was no significant difference in outcomes at 30 days. In patients undergoing interventional therapy, an observational study[7] found that eptifibatide was less effective than abciximab, but other studies[8,9] have reported similar outcomes in patients treated with abciximab or eptifibatide. Positive results have also been seen[10] with eptifibatide given in addition to thrombolytics before percutaneous intervention.

There have been reports of successful intracoronary use[11] of eptifibatide, and also prolonged intravenous use[12] in a patient unable to take oral antiplatelet drugs.

1. The PURSUIT Trial Investigators. Inhibition of platelet glycoprotein IIb/IIIa with eptifibatide in patients with acute coronary syndromes. *N Engl J Med* 1998; **339:** 436–43.
2. The IMPACT-II Investigators. Randomised placebo-controlled trial of effect of eptifibatide on complications of percutaneous coronary intervention: IMPACT-II. *Lancet* 1997; **349:** 1422–8.
3. The ESPRIT Investigators. Novel dosing regimen of eptifibatide in planned coronary stent implantation (ESPRIT): a randomised, placebo-controlled trial. *Lancet* 2000; **356:** 2037–44. Correction. *ibid.* 2001; **357:** 1370.
4. O'Shea JC, *et al.* Platelet glycoprotein IIb/IIIa integrin blockade with eptifibatide in coronary stent intervention: the ESPRIT Trial: a randomized controlled trial. *JAMA* 2001; **285:** 2468–73.
5. Bhatt DL, *et al.* Safety of concomitant therapy with eptifibatide and enoxaparin in patients undergoing percutaneous coronary intervention: results of the Coronary Revascularization Using Integrilin and Single bolus Enoxaparin Study. *J Am Coll Cardiol* 2003; **41:** 20–5.
6. Brener SJ, *et al.* Eptifibatide and low-dose tissue plasminogen activator in acute myocardial infarction: the integrilin and low-dose thrombolysis in acute myocardial infarction (INTRO AMI) trial. *J Am Coll Cardiol* 2002; **39:** 377–86.
7. Deliargyris EN, *et al.* Superior in-hospital and 30-day outcomes with abciximab versus eptifibatide: a contemporary analysis of 495 consecutive percutaneous coronary interventions. *J Invasive Cardiol* 2004; **16:** 611–16.
8. Suleiman M, *et al.* Comparison of two platelet glycoprotein IIb/IIIa inhibitors, eptifibatide and abciximab: outcomes, complications and thrombocytopenia during percutaneous coronary intervention. *J Invasive Cardiol* 2003; **15:** 319–23.
9. Raveendran G, *et al.* Eptifibatide vs abciximab as adjunctive therapy during primary percutaneous coronary intervention for acute myocardial infarction. *Mayo Clin Proc* 2007; **82:** 196–202.
10. ADVANCE MI Investigators. Facilitated percutaneous coronary intervention for acute ST-segment elevation myocardial infarction: results from the prematurely terminated ADdressing the Value of facilitated ANgioplasty after Combination therapy or Eptifibatide monotherapy in acute Myocardial Infarction (ADVANCE MI) trial. *Am Heart J* 2005; **150:** 116–22. Correction. *ibid.*; 391.
11. Deibele AJ, *et al.* Intracoronary bolus administration of eptifibatide during percutaneous coronary stenting for non ST elevation myocardial infarction and unstable angina. *J Thromb Thrombolysis* 2006; **22:** 47–50.
12. Jaffe R, *et al.* Prolonged intravenous eptifibatide infusion for prevention of coronary stent thrombosis. *Int J Cardiol* 2007; **114:** 409–11.

Preparations

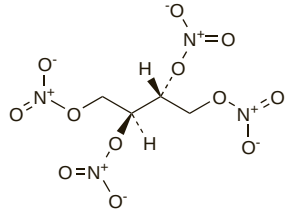
Proprietary Preparations (details are given in Part 3)
Austral.: Integrilin; ***Belg.:*** Integrilin; ***Canad.:*** Integrilin; ***Chile:*** Integrilin†; ***Cz.:*** Integrilin; ***Denm.:*** Integrilin; ***Fin.:*** Integrilin; ***Fr.:*** Integrilin; ***Ger.:*** Integrilin; ***Gr.:*** Integrilin; ***Hong Kong:*** Integrilin; ***Hung.:*** Integrilin; ***Irl.:*** Integrilin; ***Israel:*** Integrilin; ***Ital.:*** Integrilin; ***Malaysia:*** Integrilin; ***Neth.:*** Integrilin; ***Norw.:*** Integrilin; ***NZ:*** Integrilin; ***Philipp.:*** Integrilin; ***Pol.:*** Integrilin; ***Port.:*** Integrilin; ***Rus.:*** Integrilin (Интегрилин); ***S.Afr.:*** Integrilin; ***Singapore:*** Integrilin; ***Spain:*** Integrilin; ***Swed.:*** Integrilin; ***Switz.:*** Integrilin; ***Thai.:*** Integrilin; ***UK:*** Integrilin; ***USA:*** Integrilin.

Eritrityl Tetranitrate *(rINN)*

Éritrityle, Tétranitrate d'; Erithrityl Tetranitras; Erythrityltetranitrat; Eritrityylitetranitraatti; Erythritol Tetranitrate; Erythrityl Tetranitrate *(USAN)*; Erythrol Nitrate; Erythrol Tetranitrate; Nitroerythrite; Nitroerythrol; NSC-106566; Tetranitrato de eritritilo; Tetranitrol. Butane-1,2,3,4-tetrol tetranitrate.

Эритритила Тетранитрат

$C_4H_6(NO_3)_4$ = 302.1.
CAS — 7297-25-8.
ATC — C01DA13.
ATC Vet — QC01DA13.



Profile

Eritrityl tetranitrate is a vasodilator with general properties similar to those of glyceryl trinitrate (p.1296). It has been used in angina pectoris.

Diluted eritrityl tetranitrate is a mixture of eritrityl tetranitrate and lactose or other suitable inert excipients, the excipients being added to minimise the risk of explosion.

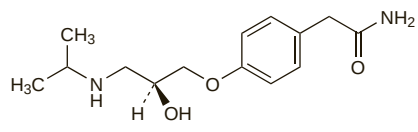
Handling. Undiluted eritrityl tetranitrate can be exploded by percussion or excessive heat.

Esatenolol *(rINN)* ⊗

(–)-Atenolol; S-Atenolol; Ésaténolol; Esatenololum. 2-{*p*-[(2*S*)-2-Hydroxy-3-(isopropylamino)propoxy]phenyl}acetamide.

Эзатенолол

$C_{14}H_{22}N_2O_3$ = 266.3.
CAS — 93379-54-5.
ATC — C07AB11.
ATC Vet — QC07AB11.



Profile

Esatenolol, the *S*(–)-isomer of atenolol, has been used similarly to atenolol (p.1217) in the treatment of cardiovascular disorders in usual oral doses of 25 to 100 mg daily.

◊ References.

1. McCoy RA, *et al.* Pharmacodynamics of racemic and S(-)-atenolol in humans. *J Clin Pharmacol* 1994; **34:** 816–22.
2. Clementi WA, *et al.* Single dose pharmacokinetics of (S)-atenolol administered orally as a single enantiomer formulation and as a racemic mixture (Tenormin). *Chirality* 1994; **6:** 169–74.

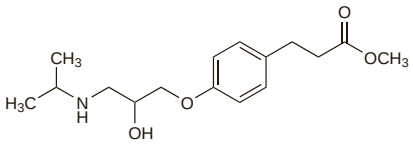
Esmolol Hydrochloride

(BANM, USAN, rINNM) ⊗

ASL-8052; Esmolol, Chlorhydrate d'; Esmolol Hidroklorür; Esmololi Hydrochloridum; Hidrocloruro de esmolol. Methyl 3-[4-(2-hydroxy-3-isopropylaminopropoxy)phenyl]propionate hydrochloride.

Эсмолола Гидрохлорид

$C_{16}H_{25}NO_4$,HCl = 331.8.
CAS — 81147-92-4 (esmolol); 84057-94-3 (esmolol); 103598-03-4 (esmolol); 81161-17-3 (esmolol hydrochloride).
ATC — C07AB09.
ATC Vet — QC07AB09.



(esmolol)

Incompatibility. Licensed product information advises against admixture of esmolol hydrochloride with sodium bicarbonate because of incompatibility. There has also been a report[1] of immediate haze formation after admixture of esmolol hydrochloride with warfarin sodium.

1. Bahal SM, *et al.* Visual compatibility of warfarin sodium injection with selected medications and solutions. *Am J Health-Syst Pharm* 1997; **54:** 2599–2600.

Adverse Effects, Treatment, and Precautions

As for Beta Blockers, p.1226.

Hypotension is the most frequently reported adverse effect associated with the infusion of esmolol hydrochloride; it generally resolves within 30 minutes once the dosage is reduced or the infusion is stopped. Local irritation at the site of infusion, inflammation, induration, and thrombophlebitis have occurred and necrosis is a hazard of extravasation. These local effects have occurred with concentrations of 20 mg/mL and it is recommended that concentrations of standard formulations should not normally exceed 10 mg/mL, particularly if given peripherally, and that the infusion should not be made into a small vein.

Effects on the CNS. Generalised tonic-clonic seizures occurred in an elderly patient given esmolol hydrochloride.[1]

1. Das G, Ferris JC. Generalized convulsions in a patient receiving ultra short-acting beta-blocker infusion. *Drug Intell Clin Pharm* 1988; **22:** 484–5.

Interactions

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

Pharmacokinetics

After intravenous doses esmolol is rapidly hydrolysed by esterases in the red blood cells. Steady-state blood concentrations are reached within 30 minutes with doses of 50 to 300 micrograms/kg per minute. The time to steady state may be reduced to 5 minutes by giving an appropriate loading dose. Blood concentrations decline in a biphasic manner with a distribution half-life of about 2 minutes and an elimination half-life of about 9 minutes. Esmolol has low lipid solubility and is about 55% bound to plasma proteins. It is excreted in urine, primarily as the de-esterified metabolite.

Uses and Administration

Esmolol is a cardioselective short-acting beta blocker (p.1225). It is reported to be lacking in intrinsic sympathomimetic and membrane-stabilising properties.

Esmolol is used as the hydrochloride in the management of supraventricular arrhythmias (p.1160). It is also used for the control of hypertension (p.1171) and tachycardia during the perioperative period.

Esmolol hydrochloride is given intravenously at a concentration usually not exceeding 10 mg/mL.