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

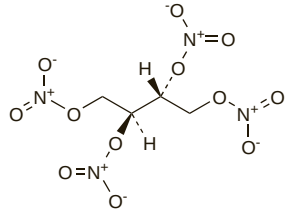
Proprietary Preparations (details are given in Part 3)
Austral.: Integrilin; ***Belg.:*** Integrilin; ***Canad.:*** Integrilin; ***Chile:*** Integrilin†; ***Cz.:*** Integrilin; ***Denm.:*** Integrilin; ***Fin.:*** Integrilin; ***Fr.:*** Integrilin; ***Ger.:*** Integrilin; ***Gr.:*** Integrilin; ***Hong 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.

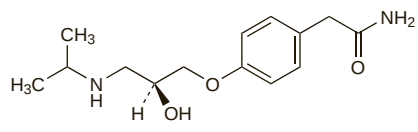
Handling. Undiluted eritrityl tetranitrate can be exploded by percussion or excessive heat.

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.

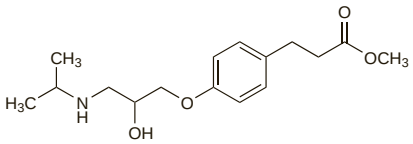
Esmolol Hydrochloride

(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.