Metabolism. Timolol appears to be metabolised[1] by the cytochrome P450 isoenzyme CYP2D6 and studies[2-4] have shown that it is influenced by genetic polymorphism.

1. Volotinen M, *et al.* Timolol metabolism in human liver microsomes is mediated principally by CYP2D6. *Drug Metab Dispos* 2007; **35:** 1135–41.
2. McGourty JC, *et al.* Pharmacokinetics and beta-blocking effects of timolol in poor and extensive metabolizers of debrisoquin. *Clin Pharmacol Ther* 1985; **38:** 409–13.
3. Lewis RV, *et al.* Timolol and atenolol: relationships between oxidation phenotype, pharmacokinetics and pharmacodynamics. *Br J Clin Pharmacol* 1985; **19:** 329–33.
4. Lennard MS, *et al.* Timolol metabolism and debrisoquine oxidation polymorphism: a population study. *Br J Clin Pharmacol* 1989; **27:** 429–34.

Uses and Administration

Timolol is a non-cardioselective beta blocker (p.1225). It is reported to lack intrinsic sympathomimetic and membrane-stabilising activity.

Timolol is used as the maleate in the management of glaucoma (p.1873), hypertension (p.1171), angina pectoris (p.1157), and myocardial infarction (p.1175). It is also used in the prophylactic treatment of migraine (p.616). The hemihydrate is also used.

Eye drops containing timolol maleate or hemihydrate equivalent to 0.25 and 0.5% of timolol are instilled twice daily to reduce **raised intra-ocular pressure** in open-angle **glaucoma** and ocular hypertension. Once-daily use may suffice when the intra-ocular pressure has been controlled. Gel-forming eye drops are also available that are instilled once daily.

For other indications timolol is given orally. In **hypertension** timolol maleate is usually given in initial doses of 10 mg daily, increased according to response at intervals of 7 or more days. Usual maintenance doses are 10 to 40 mg daily, but doses up to 60 mg daily may be required in some patients; doses above 30 mg daily should be given in 2 equally divided doses.

In **angina pectoris** the initial dose is 5 mg twice daily, increased at intervals of 3 or more days by 10 mg daily. Most patients respond to 35 to 45 mg daily in divided doses, but some patients may require up to 60 mg daily.

In patients who have had a **myocardial infarction** timolol maleate is given in initial doses of 5 mg twice daily for 2 days, starting 7 to 28 days after infarction, and increased subsequently in the absence of any contra-indicating adverse effects, to 10 mg twice daily.

Doses of 10 to 20 mg daily of timolol maleate are used in the prophylaxis of **migraine**.

Reduced doses may be required in renal or hepatic impairment.

Preparations

BP 2008: Timolol Eye Drops; Timolol Tablets;
USP 31: Timolol Maleate and Hydrochlorothiazide Tablets; Timolol Maleate Ophthalmic Solution; Timolol Maleate Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Glatim; Ingetim; Klonalol; Ofal; Plostim; Poentimol; Proflax; Protevis; Timed; Timoler; Timolpres; Timoptic; Zopirol; ***Austral.:*** Nyogel; Optimol†; Tenopt; Timoptol; Timoptol-XE; ***Austria:*** Blocadren; Dispatim; Ophtilan†; Tim-Ophtal; Timabak; Timax; Timo-COMOD; Timoftal; Timohexal; Timoptic; ***Belg.:*** Blocadren; Nyogel; Nyolol; Timabak; Timo-POS; Timoptol; Timoptolgel; ***Braz.:*** Glaucotrat; Glautimol; Nyolol; Tenoftal; Timabak; Timoptol; ***Canad.:*** Apo-Timol; Apo-Timop; Novo-Timol; Tim-Ak†; Timoptic; ***Chile:*** Glausolets; Nyolol; Timabak; Timop; Timoptol-XE; Tiof; ***Cz.:*** Arutimol; Oftan; Oftensin†; Ophthalmo-Timogal; Timo-COMOD; Timogal†; Timohexal; Timoptol; Uni Timolol; ***Denm.:*** Aquanil; Oftamolol; Optimol; Timacar; Timosan; ***Fin.:*** Aquanil†; Blocanol; Timosan; ***Fr.:*** Digaol; Nyogel; Ophtim; Timabak; Timacor; Timo-COMOD; Timoptol; ***Ger.:*** Arutimol; Chibro-Timoptol; Dispatim; Nyogel; Tim-Ophtal; Timo-COMOD; Timo-Stulln; TimoEDO; Timohexal; Timomann; Timosine†; ***Gr.:*** Flumetol†; Glafemak; Lithimole; Noval; Nyogel; Nyolol; Temserin; Thilotim; Timabak; Timodose†; Waucosin†; Yesan; ***Hong Kong:*** Apo-Timop; Glauco-Oph†; Nyolol; Oftan; Optimol; Timabak; Timoptol; ***Hung.:*** Arutimol; Cusimolol; Nyolol; Oftan Timolol; ***India:*** Glucomol; Glucotim; Ocupres; Ocutim; Timolo; ***Indon.:*** Isotic Adretor; Kentimol; Nyolol; Tim-Ophtal; Ximex Opticom; ***Irl.:*** Nyogel; Timoptol; ***Israel:*** Nyolol; Octil†; Tiloptic; V-Optic; ***Ital.:*** Blocadren; Cusimolol; Droptimol; Ialutim; Nyogel; Oftimolo; Timolabak; Timolux; Timoptol; Timosoft; ***Jpn:*** Timoptol; ***Malaysia:*** Cusimolol; Nyolol†; Timo-COMOD†; Timolast; Timoptol; ***Mex.:*** Blocadren; Horex; Imot; Jertz; Nyolol; Shemol; Timoptol; Timozzard; Tiof†; ***Mon.:*** Nyolol; ***Neth.:*** Loptomit†; Nyogel; Timo-COMOD; Timoptol; ***Norw.:*** Aquanil; Blocadren; Oftamolol; Oftan; Timosan; ***NZ:*** Apo-Timol; Apo-Timop; Gen-Timolol†; Hypermol; Nyogel†; Tilmat; Timolux; Timoptol; ***Philipp.:*** Elevex; Glocure-Opta; Nyolol; Oftan; Timabak; Timoptol; ***Pol.:*** Cusimolol; Nyolol; Oftan; Oftensin; Timo-COMOD; Timohexal; Timoptic; ***Port.:*** Blocadren†; Cusimolol†; Nyogel; Nyolol; Timabak; Timogel; Timoglau; Timolen; Timoptol; ***Rus.:*** Arutimol (Арутимол); Glymol (Глимол); Nyolol (Ниолол); Ocumed (Окумед); Ocupres-E (Окупрес-Е); Oftan Timolol (Офтан Тимолол); Optimol (Оптимол); Timohexal (Тимогексал); ***S.Afr.:*** Glaucosan; Nyogel; Timoptol; ***Singapore:*** Nyolol; Timabak; Timoptol; ***Spain:*** Cusimolol; Nyolol; Timabak; Timoftol; Timogel; ***Swed.:*** Aquanil†; Blocadren; Optimol; Timosan; ***Switz.:*** Nyolol; Oftan†; Timisol; Timo-COMOD; Timoptic; ***Thai.:*** Glauco-Oph; Nyolol; Oftan†; Timo-Optal; Timodrop; Timoptol; Timosil; ***Turk.:*** Cusimolol; Nyolol; Timo-COMOD; Timoftal; Timoptic; Timosol; ***UK:*** Betim; Glau-opt†; Nyogel; Timoptol; ***USA:*** Betimol; Blocadren; Isatol; Istalol; Timoptic; ***Venez.:*** Globitan; Imot†; Matigel; Matilol; Nyolol; Timoptol.

Multi-ingredient: ***Arg.:*** Combigan; Cosopt; Dorlamida T; Dorzoflax†; Glaucocin†; Glaucotensil; Glaucotensil TD; Louten T; Moducren†; Ocuprostim; Ofal P†; Pilotim; Timed 0.5; Timed D; Timpilo†; Xalacom; ***Austral.:*** Combigan; Cosopt; Timpilo; Xalacom; ***Austria:*** Cosopt; Fotil; Moducrin; Timpilo; Timsopt; Xalacom; ***Belg.:*** Cosopt; Xalacom; ***Braz.:*** Combigan; Cosopt; Xalacom; ***Canad.:*** Combigan; Cosopt; Timolide†; Timpilo†; Xalacom; ***Chile:*** Combigan; Cosopt; Dorsof T; Gaax T; Glaucotensil T; Glausolets Plus; Latof-T; Tiof Plus; Xalacom; ***Cz.:*** Combigan; Cosopt; DuoTrav; Fotil; Ganfort; Timpilo†; Xalacom; ***Denm.:*** Cosopt; Fotil; Timpilo†; Xalcom; ***Fin.:*** Cosopt; Fotil; Timpilo†; Xalcom; ***Fr.:*** Cosopt; Moducren; Pilobloq; Timpilo†; Xalacom; ***Ger.:*** Cosopt; Fotil; Moducrin; Timpilo†; TP-Ophtal; Xalacom; ***Gr.:*** Combigan; Cosopt; Dropiltim; DuoTrav; Fotil†; Ganfort; T+P; Tesol†; Timpilo; Xalacom; Yvano; ***Hong Kong:*** Cosopt; Moducren; Timpilo; Xalacom; ***Hung.:*** Combigan; Cosopt; DuoTrav; Fotil; Xalacom; ***Indon.:*** Xalacom; ***Irl.:*** Combigan; Cosopt; Moducren; Xalacom; ***Israel:*** Cosopt; Timpilo; Xalacom; ***Ital.:*** Cosopt; Equiton; Glautimol; Pilobloc; Timicon; Xalacom; ***Malaysia:*** Cosopt; Timpilo†; Xalacom; ***Mex.:*** Combigan-D; Cosopt; Xalacom; ***Neth.:*** Cosopt; Fotil; Xalacom; ***Norw.:*** Cosopt; Fotil; Timpilo†; Xalcom; ***NZ:*** Combigan; Cosopt; DuoTrav; Timpilo; Xalacom; ***Philipp.:*** Cosopt; Fotil; Xalacom; ***Pol.:*** Cosopt; DuoTrav; Fotil; Xalacom; ***Port.:*** Combigan; Cosopt; DuoTrav; Fotil; Ganfort; Moducren†; Tavu; Timoglau Plus; Timosopt; Xalacom; ***Rus.:*** Fotil (Фотил); Xalacom (Ксалаком); ***S.Afr.:*** Cosopt; Moducren; Servatrin; Xalacom; ***Singapore:*** Cosopt; Timpilo†; Xalacom; ***Spain:*** Xalacom; ***Swed.:*** Cosopt; Fotil; Timpilo†; Xalcom; ***Switz.:*** Combigan; Cosopt; Fotil†; Moducren; Timpilo†; Xalacom; ***Thai.:*** Cosopt; Fotil†; Xalacom; ***Turk.:*** Cosopt; ***UK:*** Combigan; Cosopt; DuoTrav; Ganfort; Moducren†; Prestim; Xalacom; ***USA:*** Combigan; Cosopt; Timolide; ***Venez.:*** Cosopt; Dobet; Glaucotensil T; Xalacom.

Tinzaparin Sodium *(BAN, USAN, rINN)*

Tintsapariininatrium; Tinzaparin sodná sůl; Tinzaparin Sodyum; Tinzaparina sódica; Tinzaparine sodique; Tinzaparinnatrium; Tinzaparin-nátrium; Tinzaparino natrio druska; Tinzaparinum natricum.

Тинзапарин Натрий

CAS — 9041-08-1.

ATC — B01AB10.

ATC Vet — QB01AB10.

Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Tinzaparin Sodium). It is prepared by enzymatic depolymerisation, using heparinase from *Flavobacterium heparinum*, of heparin obtained from the intestinal mucosa of pigs. The majority of the components have a 2-*O*-sulfo-4-enepyranosuronic acid structure at the non-reducing end and a 2-*N*,6-*O*-disulfo-D-glucosamine structure at the reducing end of their chain. The mass-average relative molecular mass ranges between 5500 and 7500, with a characteristic value of about 6500. The mass percentage of chains lower than 2000 is not more than 10%. The degree of sulfation is 1.8 to 2.5 per disaccharide unit.

The potency is not less than 70 units and not more than 120 units of anti-factor Xa activity per mg with reference to the dried substance and the ratio of anti-factor Xa activity to anti-factor IIa (antithrombin) activity is between 1.5 and 2.5.

Units

As for Low-molecular-weight Heparins, p.1329.

Adverse Effects, Treatment, and Precautions

As for Low-molecular-weight Heparins, p.1329.

Severe bleeding with tinzaparin sodium may be reduced by the slow intravenous injection of protamine sulfate; 1 mg of protamine sulfate is stated to inhibit the effects of 100 units of tinzaparin sodium.

Interactions

As for Low-molecular-weight Heparins, p.1329.

Pharmacokinetics

Tinzaparin sodium is absorbed after subcutaneous injection with a bioavailability of about 90%. Peak plasma activity is reached within 4 to 6 hours. The elimination half-life is about 90 minutes but detectable anti-factor Xa activity persists for up to 24 hours.

Uses and Administration

Tinzaparin sodium is a low-molecular-weight heparin (p.1329) with anticoagulant properties. It is used in the prevention and treatment of venous thromboembolism (p.1189) and to prevent clotting during extracorporeal circulation.

For *prophylaxis* of **venous thromboembolism** tinzaparin sodium is given by subcutaneous injection in a variety of dosage regimens.

- For patients undergoing general surgical procedures 3500 units of tinzaparin sodium are given 2 hours before the procedure, followed by 3500 units once daily for 7 to 10 days.
- In patients at high risk, such as those undergoing orthopaedic surgery, a dose of 50 units/kg has been recommended; alternatively, a dose of 4500 units may be given 12 hours before surgery, followed by 4500 units once daily.

For the *treatment* of venous thromboembolism tinzaparin sodium is given in a dose of 175 units/kg by subcutaneous injection once daily for at least 6 days and until adequate oral anticoagulation is established.

For prevention of clotting in the extracorporeal circulation during **haemodialysis**, tinzaparin sodium may be given into the arterial side of the dialyser or intravenously. The dialyser may be primed with 500 to 1000 mL sodium chloride 0.9% containing 5000 units tinzaparin sodium/litre. For dialysis sessions lasting less than 4 hours a single dose of 2000 to 2500 units tinzaparin sodium is given; for longer sessions an initial dose of 2500 units is followed by an infusion of 750 units/hour.

◊ References.

1. Friedel HA, Balfour JA. Tinzaparin: a review of its pharmacology and clinical potential in the prevention and treatment of thrombo-embolic disorders. *Drugs* 1994; **48:** 638–60.
2. Neely JL, *et al.* Tinzaparin sodium: a low-molecular-weight heparin. *Am J Health-Syst Pharm* 2002; **59:** 1426–36.
3. Nutescu EA, *et al.* Tinzaparin: considerations for use in clinical practice. *Ann Pharmacother* 2003; **37:** 1831–40.
4. Cheer SM, *et al.* Tinzaparin sodium: a review of its pharmacology and clinical use in the prophylaxis and treatment of thromboembolic disease. *Drugs* 2004; **64:** 1479–502.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Innohep†; ***Belg.:*** Innohep; ***Canad.:*** Innohep; ***Denm.:*** Innohep; ***Fin.:*** Innohep†; ***Fr.:*** Innohep; ***Ger.:*** Innohep; ***Gr.:*** Innohep; ***Hong Kong:*** Innohep; ***Irl.:*** Innohep; ***Israel:*** Innohep†; ***Malaysia:*** Innohep; ***Neth.:*** Innohep; ***Norw.:*** Innohep; ***NZ:*** Innohep; ***Philipp.:*** Innohep; ***Port.:*** Innohep; ***Singapore:*** Innohep; ***Spain:*** Innohep; ***Swed.:*** Innohep; ***Thai.:*** Innohep; ***Turk.:*** Innohep; ***UK:*** Innohep; ***USA:*** Innohep.

Tioclomarol *(rINN)*

LM-550; Tioclomarolum. 3-[5-Chloro-α-(4-chloro-β-hydroxyphenethyl)-2-thenyl]-4-hydroxycoumarin.

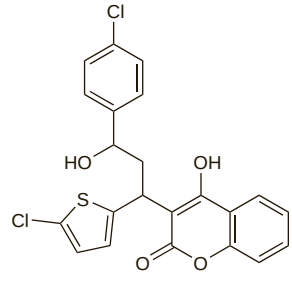
Тиокломарол

$C_{22}H_{16}Cl_2O_4S$ = 447.3.

CAS — 22619-35-8.

ATC — B01AA11.

ATC Vet — QB01AA11.



Profile

Tioclomarol is an oral coumarin anticoagulant with actions similar to those of warfarin (p.1425) that has been used in the management of thromboembolic disorders.

Preparations

Proprietary Preparations (details are given in Part 3)

Fr.: Apegmone†.

Tirilazad Mesilate *(BANM, rINNM)*

Mesilato de tirilazad; Tirilatsadiinimesilaatti; Tirilazad, Mésilate de; Tirilazad Mesylate *(USAN)*; Tirilazadi Mesilas; Tirilazadini Mesilas; Tirilazadinmesilat; U-74006F (tirilazad or tirilazad mesilate). 21-[4-(2,6-Di-1-pyrrolidinyl-4-pyrimidinyl)-1-piperazinyl]-16α-methylpregna-1,4,9(11)-triene-3,20-dione monomethanesulfonate hydrate.

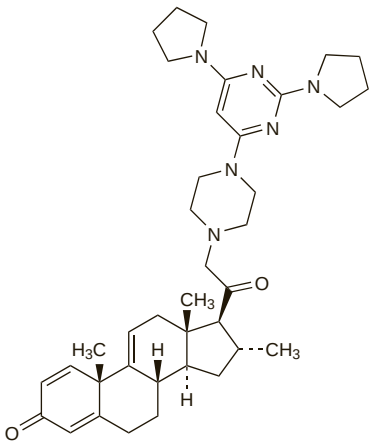
Тирилазада Мезилат

$C_{38}H_{52}N_6O_2,CH_4O_3S,xH_2O$ = 721.0 (anhydrous).

CAS — 110101-66-1 (tirilazad); 111793-42-1 (tirilazad mesilate); 149042-61-5 (tirilazad mesilate).

ATC — N07XX01.

ATC Vet — QN07XX01.



(tirilazad)

Profile

Tirilazad, a lazaroid, is an inhibitor of lipid peroxidation thought to have a cytoprotective effect against radicals produced in response to tissue trauma. It has been used in the prevention of secondary tissue damage in subarachnoid haemorrhage. It has also been investigated in spinal cord injuries, head injuries, and ischaemic stroke.

◊ References.

1. Fleishaker JC, *et al.* Evaluation of the pharmacokinetics and tolerability of tirilazad mesylate, a 21-aminosteroid free radical scavenger: multiple-dose administration. *J Clin Pharmacol* 1993; **33:** 182–90.
2. Hulst LK, *et al.* Effect of age and gender on tirilazad pharmacokinetics in humans. *Clin Pharmacol Ther* 1994; **55:** 378–84.
3. Haley EC, *et al.* Phase II trial of tirilazad in aneurysmal subarachnoid haemorrhage: a report of the Cooperative Aneurysm Study. *J Neurosurg* 1995; **82:** 786–90.
4. Clark WM, *et al.* Lazaroids: CNS pharmacology and current research. *Drugs* 1995; **50:** 971–83.
5. Marshall LF, *et al.* A multicenter trial on the efficacy of using tirilazad mesylate in cases of head injury. *J Neurosurg* 1998; **89:** 519–25.
6. Fleishaker JC, *et al.* Hormonal effects on tirilazad clearance in women: assessment of the role of CYP3A. *J Clin Pharmacol* 1999; **39:** 260–7.
7. The Tirilazad International Steering Committee. Tirilazad for acute ischaemic stroke. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2001 (accessed 24/06/05).

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Freedox†; ***Belg.:*** Freedox†; ***S.Afr.:*** Freedox†; ***Switz.:*** Freedox†.

Tirofiban Hydrochloride

(BANM, USAN, rINNM)

Hidrocloruro de tirofibán; L-700462; MK-383; MK-0383; Tirofiban, Chlorhydrate de; Tirofiban Hidroklorür; Tirofibani Hydrochloridum. *N*-(Butylsulfonyl)-4-[4-(4-piperidyl)butoxy]-L-phenylalanine hydrochloride monohydrate.

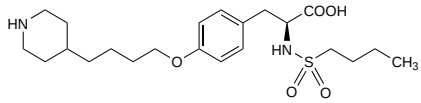
Тирофибана Гидрохлорид

$C_{22}H_{36}N_2O_5S,HCl,H_2O$ = 495.1.

CAS — 144494-65-5 (tirofiban); 142373-60-2 (anhydrous tirofiban hydrochloride); 150915-40-5 (tirofiban hydrochloride monohydrate);.

ATC — B01AC17.

ATC Vet — QB01AC17.



(tirofiban)

Adverse Effects

Bleeding is the most common adverse effect of tirofiban. Other side-effects include nausea, headache, fever, rashes and other hypersensitivity reactions, and thrombocytopenia.

Effects on the blood. References[1,2] to tirofiban-associated thrombocytopenia.

1. Mulot A, *et al.* Practical approach to the diagnosis and management of thrombocytopenia associated with tirofiban treatment. *Am J Hematol* 2004; **77:** 67–71.
2. Patel S, *et al.* Profound thrombocytopenia associated with tirofiban: case report and review of literature. *Angiology* 2005; **56:** 351–5.

Precautions

As for Abciximab, p.1192.

Pharmacokinetics

After stopping an infusion of tirofiban, the antiplatelet effect persists for about 4 to 8 hours. The plasma half-life is about 2 hours. Tirofiban is not highly bound to plasma proteins; the unbound fraction in plasma is about 35%. Tirofiban is eliminated largely unchanged in the urine, with some biliary excretion in the faeces. Tirofiban is removed by haemodialysis.

◊ Reviews.

1. Kondo K, Umemura K. Clinical pharmacokinetics of tirofiban, a nonpeptide glycoprotein IIb/IIIa receptor antagonist: comparison with the monoclonal antibody abciximab. *Clin Pharmacokinet* 2002; **41:** 187–95.

Uses and Administration

Tirofiban hydrochloride is an antiplatelet drug that reversibly inhibits binding of fibrinogen to the glycoprotein IIb/IIIa receptors of platelets. It is given with heparin and aspirin for the management of unstable angina, both in patients managed medically and in those undergoing percutaneous coronary procedures. Tirofiban is used as the hydrochloride, but the dose is expressed in terms of the base; 110 nanograms of tirofiban hydrochloride monohydrate is equivalent to 100 nanograms of tirofiban base.

Tirofiban is given intravenously, at an initial rate of 400 nanograms/kg per minute for 30 minutes, and then continued at 100 nanograms/kg per minute. The recommended duration of treatment is at least 48 hours. Tirofiban infusion may be continued during coronary angiography, and should be maintained for 12 to 24 hours after angioplasty or atherectomy. The entire duration of treatment should not exceed 108 hours.

The dose of tirofiban should be reduced in patients with renal impairment (see below).

◊ General references.

1. McClellan KJ, Goa KL. Tirofiban: a review of its use in acute coronary syndromes. *Drugs* 1998; **56:** 1067–80.
2. Menozzi A, *et al.* Tirofiban in acute coronary syndromes. *Expert Rev Cardiovasc Ther* 2005; **3:** 193–206.
3. Shanmugam G. Tirofiban and emergency coronary surgery. *Eur J Cardiothorac Surg* 2005; **28:** 546–50.
4. Bukow SC, *et al.* Tirofiban for the treatment of ischaemic stroke. *Expert Opin Pharmacother* 2006; **7:** 73–9.
5. Mukherjee D, Roffi M. Current strategies with high-dose tirofiban. *Expert Opin Drug Metab Toxicol* 2007; **3:** 275–80.
6. Winter JP, Juergens CP. The role of tirofiban in the management of coronary artery disease. *Cardiovasc Hematol Disord Drug Targets* 2008; **8:** 138–46.

Administration in renal impairment. Patients with renal impairment (creatinine clearance less than 30 mL/minute) should receive half the usual infusion dose of tirofiban.

Ischaemic heart disease. Patients with acute coronary syndromes may be treated either medically or with percutaneous coronary interventions such as angioplasty or stenting. Tirofiban, given with heparin and aspirin, has been tried as adjunctive therapy. A study[1] comparing tirofiban with heparin in the **medical management** of unstable angina (p.1157) or non-Q-wave myocardial infarction reported an initial benefit, at 2 days, of reduced risk of refractory ischaemia, myocardial infarction, or death with tirofiban. This benefit was not maintained at 7 or 30 days after treatment, although a further analysis[2] found that the risk of death or myocardial infarction at 30 days was reduced in patients with raised troponin I concentrations who received tirofiban. In another study,[3] the combination of heparin and tirofiban also reduced the risk of refractory ischaemia, myocardial infarction, or death, compared with heparin alone, and benefit was maintained at 6 months. About half of these patients also underwent revascularisation procedures or surgery if required.

Tirofiban has also been studied in patients undergoing **interventional therapy** (see Reperfusion and Revascularisation Procedures, p.1181), but results have been mixed. The RESTORE trial[4] found short-term benefit with tirofiban as an adjunct to heparin in patients undergoing angioplasty or atherectomy for acute coronary syndromes (unstable angina or myocardial infarction), but this was not maintained at 30 days and there was no effect on restenosis after 6 months. However, another study using a higher loading dose found a reduced rate of clinical events in patients given tirofiban, both early after the procedure and on longer-term follow-up,[5] and an observational study[6] in patients with acute myocardial infarction also found improved outcomes. Pretreatment with tirofiban for 24 to 48 hours before intervention was found to improve angiographic outcomes compared with periprocedural treatment,[7] but there was no difference in clinical events at 30 days. In patients undergoing planned interventions, tirofiban was found to improve outcomes compared with placebo;[8] another study found that it was less effective than abciximab at 30 days,[9] although this difference was no longer apparent after 6 months.[10]

1. The Platelet Receptor Inhibition in Ischemic Syndrome Management (PRISM) Study Investigators. A comparison of aspirin plus tirofiban with aspirin plus heparin for unstable angina. *N Engl J Med* 1998; **338:** 1498–1505.
2. Heeschen C, *et al.* Troponin concentrations for stratification of patients with acute coronary syndromes in relation to therapeutic efficacy of tirofiban. *Lancet* 1999; **354:** 1757–62.
3. The Platelet Receptor Inhibition in Ischemic Syndrome Management in Patients Limited by Unstable Signs and Symptoms (PRISM-PLUS) Study Investigators. Inhibition of the platelet glycoprotein IIb/IIIa receptor with tirofiban in unstable angina and non-Q-wave myocardial infarction. *N Engl J Med* 1998; **338:** 1488–97.
4. Gibson CM, *et al.* Six-month angiographic and clinical follow-up of patients prospectively randomized to receive either tirofiban or placebo during angioplasty in the RESTORE trial. *J Am Coll Cardiol* 1998; **32:** 28–34.
5. Valgimigli M, *et al.* The additive value of tirofiban administered with the high-dose bolus in the prevention of ischemic complications during high-risk coronary angioplasty: the ADVANCE Trial. *J Am Coll Cardiol* 2004; **44:** 14–19.
6. De Luca G, *et al.* Impact of adjunctive tirofiban administration on myocardial perfusion and mortality in patients undergoing primary angioplasty for ST-segment elevation myocardial infarction. *Thromb Haemost* 2005; **93:** 820–3.
7. van 't Hof AWJ, *et al.* A comparison of two invasive strategies in patients with non-ST elevation acute coronary syndromes: results of the Early or Late Intervention in unStable Angina (ELISA) pilot study. *Eur Heart J* 2003; **24:** 1401–5.
8. Bonz AW, *et al.* Effect of additional temporary glycoprotein IIb/IIIa receptor inhibition on troponin release in elective percutaneous coronary interventions after pretreatment with aspirin and clopidogrel (TOPSTAR trial). *J Am Coll Cardiol* 2002; **40:** 662–8.
9. Topol EJ, *et al.* Comparison of two platelet glycoprotein IIb/IIIa inhibitors, tirofiban and abciximab, for the prevention of ischemic events with percutaneous coronary revascularization. *N Engl J Med* 2001; **344:** 1888–94.
10. Moliterno DJ, *et al.* Outcomes at 6 months for the direct comparison of tirofiban and abciximab during percutaneous coronary revascularisation with stent placement: the TARGET follow-up study. *Lancet* 2002; **360:** 355–60.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Agrastat; ***Austral.:*** Agrastat; ***Austria:*** Aggrastat; ***Belg.:*** Aggrastat; ***Braz.:*** Agrastat; ***Canad.:*** Aggrastat; ***Chile:*** Agrastat; ***Cz.:*** Aggrastat; ***Denm.:*** Aggrastat; ***Fin.:*** Aggrastat; ***Fr.:*** Agrastat; ***Ger.:*** Aggrastat; ***Gr.:*** Aggrastat; Avastar†; ***Hong Kong:*** Aggrastat; ***Hung.:*** Aggrastat; ***India:*** Aggribloc; ***Irl.:*** Aggrastat; ***Israel:*** Aggrastat; ***Ital.:*** Aggrastat; ***Malaysia:*** Aggrastat; ***Mex.:*** Agrastat; ***Neth.:*** Aggrastat; ***Norw.:*** Aggrastat; ***NZ:*** Aggrastat; ***Philipp.:*** Aggrastat; ***Pol.:*** Aggrastat; ***S.Afr.:*** Aggrastat; ***Singapore:*** Aggrastat; ***Spain:*** Agrastat; ***Swed.:*** Aggrastat; ***Switz.:*** Aggrastat; ***Thai.:*** Aggrastat; ***Turk.:*** Aggrastat; ***UK:*** Aggrastat; ***USA:*** Aggrastat; ***Venez.:*** Agrastat.

Tocainide *(BAN, USAN, rINN)*

Tocainida; Tocaïnide; Tocainidum; Tokainid; Tokainidi; W-36095. 2-Aminopropiono-2',6'-xylidide.

Токаинид

$C_{11}H_{16}N_2O$ = 192.3.

CAS — 41708-72-9.

ATC — C01BB03.

ATC Vet — QC01BB03.