

Tirilazad Mesilate (BANM, rINN)

Mesilate 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]-1,6- α -methylpregna-1,4,9(11)-triene-3,20-dione monomethanesulfonate hydrate.

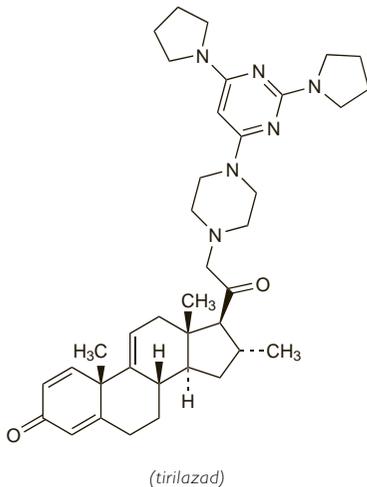
Тирилазада Мезилат

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

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

ATC — N07XX01.

ATC Vet — QN07XX01.

**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, rINN)

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

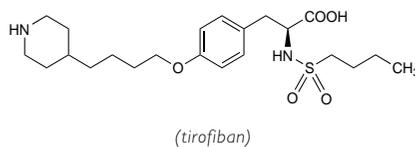
Тирофибана Гидрохлорид

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

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

ATC — B01AC17.

ATC Vet — QB01AC17.

**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 Pharmacokinetics* 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. Shannugam 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 study¹ 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 analysis² 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 trial⁴ 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 study⁶ 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. Heesch 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. *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:** Agrastat; **Belg.:** Agrastat; **Brez.:** Agrastat; **Canad.:** Agrastat; **Chile:** Agrastat; **Cz.:** Agrastat; **Denm.:** Agrastat; **Fin.:** Agrastat; **Fr.:** Agrastat; **Ger.:** Agrastat; **Gr.:** Agrastat; **Avastar†;** **Hong Kong:** Agrastat; **Hung.:** Agrastat; **India:** Agrastat; **Int.:** Agrastat; **Israel:** Agrastat; **Ital.:** Agrastat; **Malaysia:** Agrastat; **Mex.:** Agrastat; **Neth.:** Agrastat; **Norw.:** Agrastat; **NZ:** Agrastat; **Philipp.:** Agrastat; **Pol.:** Agrastat; **S.Afr.:** Agrastat; **Singapore:** Agrastat; **Spain:** Agrastat; **Swed.:** Agrastat; **Switz.:** Agrastat; **Thai.:** Agrastat; **Turk.:** Agrastat; **UK:** Agrastat; **USA:** Agrastat; **Venez.:** Agrastat.

Tocainide (BAN, USAN, rINN)

Tocainida; Tocainide; Tocainidum; Tokainid; Tokainidi; W-36095. 2-Aminopropiono-2',6'-xylylidide.

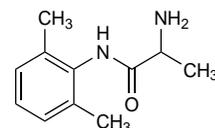
Токаинид

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

CAS — 41708-72-9.

ATC — C01BB03.

ATC Vet — QC01BB03.



Tocainide Hydrochloride (BANM, rINNM)

Hidrocloruro de tocaína; Tocaínaide, Chlorhydrate de; Tocainidi Hydrochloridum.

Токаинида Гидрохлорид
 $C_{11}H_{16}N_2O \cdot HCl = 228.7$.
 CAS — 35891-93-1.
 ATC — C01BB03.
 ATC Vet — QC01BB03.

Pharmacopoeias. In *Chin.* and *US*.

USP 31 (Tocainide Hydrochloride). A fine, white, odourless powder. Freely soluble in water and in alcohol; practically insoluble in chloroform and in ether.

Profile

Tocainide is a class Ib antiarrhythmic (p.1153) with similar properties to mexiletine (p.1339); like mexiletine it is structurally related to lidocaine (p.1862). Tocainide hydrochloride has been given orally and intravenously in the management of ventricular arrhythmias but severe haematological and pulmonary toxicity limit its use.

◇ General references.

1. Holmes B, *et al.* Tocainide: a review of its pharmacological properties and therapeutic efficacy. *Drugs* 1983; **26**: 93–123.

Preparations

USP 31: Tocainide Hydrochloride Tablets.

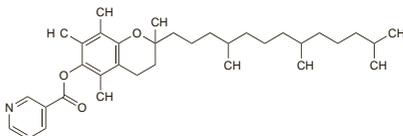
Proprietary Preparations (details are given in Part 3)

Ger.: Xylotocant; **USA:** Tonocard†.

Tocopherol Nicotinate

Tocoferilo, nicotinato de; Tocopheryl Nicotinate; Vitamin E Nicotinate. (±)- α -Tocopherol nicotinate.

Токоферола Никотинат
 $C_{35}H_{53}NO_3 = 535.8$.
 CAS — 51898-34-1; 16676-75-8.



Pharmacopoeias. In *Jpn.*

Profile

Tocopherol nicotinate is a lipid regulating drug and a vasodilator. It is used in the treatment of hyperlipidaemias (p.1169), and in peripheral (p.1178) and cerebral vascular disorders (p.1165). The usual oral dose is 100 to 200 mg three times daily.

Preparations

Proprietary Preparations (details are given in Part 3)

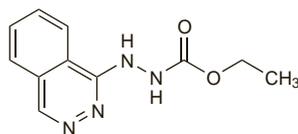
Hong Kong: Hijuven; **Indon.:** Enico; **Jpn:** Juvela; **Malaysia:** Hijuven; **Philipp.:** Hijuven; **Port.:** Nicotjuvel†; Reoferol.

Multi-ingredient: **Arg.:** Anaphase; **Fr.:** Anaphase; **Ital.:** Evitex; **Spain:** Evitex A E Fuerte.

Todalazine Hydrochloride (BANM, pINNM)

BT-621; CEPH; Ecarazine Hydrochloride; Hidrocloruro de todalazina; Todalazine, Chlorhydrate de; Todalazini Hydrochloridum; Todalaziny chlorowodorek. Ethyl 3-(phthalazin-1-yl)carbazate hydrochloride monohydrate.

Тодалазина Гидрохлорид
 $C_{11}H_{12}N_4O_2 \cdot HCl \cdot H_2O = 286.7$.
 CAS — 14679-73-3 (todalazine); 3778-76-5 (anhydrous todalazine hydrochloride).



(todalazine)

Pharmacopoeias. In *Jpn* and *Pol*.

Profile

Todalazine hydrochloride is an antihypertensive structurally related to hydralazine (p.1305) and with similar properties.

Preparations

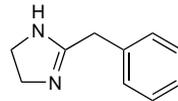
Proprietary Preparations (details are given in Part 3)

Pol.: Binazin.

Tolazoline Hydrochloride (BANM, rINNM)

Benzazoline Hydrochloride; Hidrocloruro de tolazolina; Tolazol. Hydrochlor.; Tolazoline, Chlorhydrate de; Tolazolini Hydrochloridum; Tolazolium Chloratum. 2-Benzyl-2-imidazoline hydrochloride.

Толазолина Гидрохлорид
 $C_{10}H_{12}N_2 \cdot HCl = 196.7$.
 CAS — 59-98-3 (tolazoline); 59-97-2 (tolazoline hydrochloride).
 ATC — C04AB02; M02AX02.
 ATC Vet — QC04AB02; QM02AX02.



(tolazoline)

NOTE. Do not confuse with benazoline (see Metizoline, p.1565), which is a sympathomimetic vasoconstrictor, or with benzolizol, which is a herbicide.

Pharmacopoeias. In *Chin.* and *US*.

USP 31 (Tolazoline Hydrochloride). A white to off-white, crystalline powder. Its solutions are slightly acid to litmus. Soluble 1 in less than 1 of water, 1 in 2 of alcohol, 1 in 3 of chloroform, and 1 in 10 000 of ether. Store at a temperature of 25°, excursions permitted between 15° and 30°.

Adverse Effects

Adverse effects of tolazoline include piloerection, headache, flushing, tachycardia, cardiac arrhythmias, tingling, chilliness, shivering, sweating, nausea, vomiting, diarrhoea, and epigastric pain. Orthostatic hypotension or marked hypertension may occur, especially with large doses. Tolazoline stimulates gastric acid and may exacerbate peptic ulcer disease. Oliguria, haematuria, myocardial infarction, gastrointestinal haemorrhage, thrombocytopenia and other blood dyscrasias have been reported.

Intra-arterial injection has been followed by a burning sensation in the limb.

Effects in the neonate. Hypochloreaemic metabolic alkalosis,¹ acute renal failure,² and duodenal perforation³ have been reported in neonates given tolazoline.

- Adams JM, *et al.* Hypochloreaemic metabolic alkalosis following tolazoline-induced gastric hypersecretion. *Pediatrics* 1980; **65**: 298–300.
- Trompeter RS, *et al.* Tolazoline and acute renal failure in the newborn. *Lancet* 1981; **i**: 1219.
- Wilson RG, *et al.* Duodenal perforation associated with tolazoline. *Arch Dis Child* 1985; **60**: 878–9.

Treatment of Adverse Effects

In the event of overdosage hypotension is best treated by keeping the patient recumbent with the head lowered. If necessary the circulation may be maintained by infusion of suitable electrolyte solutions. Hypotension may be treated with ephedrine. Adrenaline is not suitable for the reversal of hypotension induced by alpha blockers since it may exacerbate the hypotension by stimulating beta receptors.

Precautions

Tolazoline should not be given to patients with hypotension and when used for peripheral vascular disease should be avoided in ischaemic heart disease or after a cerebrovascular accident. Since tolazoline stimulates gastric secretion of hydrochloric acid it may activate stress ulcers and may cause significant hypochloreaemic alkalosis. Pretreatment of infants with antacids may prevent gastrointestinal bleeding, although use of intravenous ranitidine is not recommended (see below under Interactions). Tolazoline should not be used in the presence of peptic ulcer disease and should be used with caution in patients with mitral stenosis.

Interactions

Tolazoline should not be used with sympathomimetics such as adrenaline since the hypotensive effect may be potentiated due to unopposed beta-adrenoceptor stimulation. Tolazoline may cause a disulfiram-like reaction if given with alcohol.

Ranitidine. Intravenous ranitidine reversed the falls in pulmonary and systemic vascular resistances in 12 children who had been given tolazoline as a pulmonary vasodilator.¹

- Bush A, *et al.* Cardiovascular effects of tolazoline and ranitidine. *Arch Dis Child* 1987; **62**: 241–6.

Sympathomimetics. For a report of fatal hypotension associated with the use of tolazoline with *dopamine*, see Vasodilators under the Interactions of Sympathomimetics, p.1408.

Pharmacokinetics

Tolazoline is absorbed from the gastrointestinal tract. It is more rapidly absorbed after intramuscular injection. An elimination half-life in neonates of 3 to 13 hours has been reported after intravenous use, although it may be as high as about 40 hours and is inversely related to urine output. Tolazoline is rapidly excreted in the urine, largely unchanged.

Uses and Administration

Tolazoline hydrochloride is a vasodilator that has a direct dilator action on the peripheral blood vessels. It has some alpha-adrenoceptor blocking activity and also stimulates smooth muscle in the gastrointestinal tract, increases gastrointestinal secretion, can cause mydriasis, and has a stimulant effect on the heart.

Tolazoline hydrochloride is used intravenously to reduce pulmonary artery pressure in persistent pulmonary hypertension in neonates with persistent fetal circulation (see below). It has been used orally and by subcutaneous, intramuscular, intravenous, or slow intra-arterial injection in the treatment of peripheral vascular disease. It has also been given in some ophthalmic conditions.

Pulmonary hypertension. Tolazoline and other vasodilators have been tried in persistent pulmonary hypertension in the newborn (p.1179) in an attempt to induce selective pulmonary vasodilation and improve gas exchange. The response is variable and often unsuccessful due to concomitant systemic hypotension, a failure to achieve or sustain pulmonary vasodilation, and adverse effects, and other therapies such as high-frequency oscillatory ventilation, extracorporeal membrane oxygenation, and inhaled nitric oxide are now more widely used.

The loading dose for pulmonary hypertension in neonates that has been recommended by licensed product information is 1 to 2 mg/kg over 5 to 10 minutes by intravenous infusion; this is then followed by doses of up to 1 to 2 mg/kg per hour. Infants with reduced urine output may require lower maintenance doses. The high incidence of adverse effects has, however, led to several studies investigating the use of lower doses. One group suggested that a loading dose of 500 micrograms/kg given intravenously followed by a continuous infusion of 500 micrograms/kg per hour was more appropriate and safer than standard doses.¹ In a retrospective study² of extremely preterm infants (mean gestational age 24 weeks) with severe hypoxaemia (possibly attributable to persistent pulmonary hypertension), tolazoline was given as a slow bolus infusion, with most patients receiving a dose of 0.5 to 1 mg/kg; some required further doses.

Tolazoline has also been given via the endotracheal route,^{3,4} although as it is acid in solution it may contribute to alveolar injury. In a study⁴ of 12 neonates with gestational age ranging from 25 to 42 weeks, endotracheal tolazoline at doses from 1 to 2.5 mg/kg was found to cause no adverse systemic effects.

The *BNFC* gives a dose of 1 mg/kg by slow intravenous injection, followed by 200 micrograms/kg per hour by infusion if necessary. It warns that doses in excess of 300 micrograms/kg per hour are associated with cardiotoxicity and renal failure. A suggested dose for endotracheal use is 200 micrograms/kg diluted in 0.5 to 1 mL of sodium chloride 0.9%.

- Monin P, *et al.* Treatment of persistent fetal circulation syndrome of the newborn: comparison of different doses of tolazoline. *Eur J Clin Pharmacol* 1987; **31**: 569–73.
- Nuntarumit P, *et al.* Efficacy and safety of tolazoline for treatment of severe hypoxemia in extremely preterm infants. *Pediatrics* 2002; **109**: 852–6.
- Welch JC, *et al.* Endotracheal tolazoline for severe persistent pulmonary hypertension of the newborn. *Br Heart J* 1995; **73**: 99–100.
- Parida SK, *et al.* Endotracheal tolazoline administration in neonates with persistent pulmonary hypertension. *J Perinatol* 1997; **17**: 461–4.

Preparations

USP 31: Tolazoline Hydrochloride Injection.

Proprietary Preparations (details are given in Part 3)

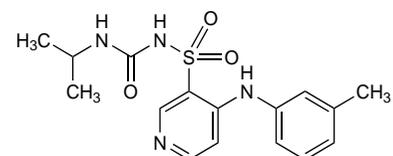
Cz.: Divascal; **Gr.:** Prisco†; Priscoline†.

Multi-ingredient: **Switz.:** Lunadon.

Torazemide (BAN, rINN) ⊗

AC-4464; BM-02015; Torasemid; Torasemid bezvodý; Torasemid, vattenfri; Torasemida; Torasemide; Torasemide anhydre; Torasemidi; Torasemidi, vedetön; Torasemidum; Torasemidum anhydricum; Torasemidas, bevandenis; Torsemide (USAN). 1-Isopropyl-3-(4-*m*-toluidinopyridine-3-sulphonyl)urea.

Торасемид
 $C_{16}H_{20}N_4O_3S = 348.4$.
 CAS — 56211-40-6 (torasemide); 72810-59-4 (torasemide sodium).
 ATC — C03CA04.
 ATC Vet — QC03CA04.



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

Ph. Eur. 6.2 (Torasemide, Anhydrous). A white or almost white powder. It exhibits polymorphism. Practically insoluble in water; slightly soluble in alcohol. It is sparingly soluble in dilute water-