2. Oguchi H, *et al.* Pharmacokinetics of temocapril and enalapril in patients with various degrees of renal insufficiency. *Clin Pharmacokinet* 1993; **24:** 421–7.
3. Furuta S, *et al.* Pharmacokinetics of temocapril, an ACE inhibitor with preferential biliary excretion, in patients with impaired liver function. *Eur J Clin Pharmacol* 1993; **44:** 383–5.
4. Arakawa M, *et al.* Pharmacokinetics and pharmacodynamics of temocapril during repeated dosing in elderly hypertensive patients. *Eur J Clin Pharmacol* 2001; **56:** 775–9.
5. Song JC, White CM. Clinical pharmacokinetics and selective pharmacodynamics of new angiotensin converting enzyme inhibitors: an update. *Clin Pharmacokinet* 2002; **41:** 207–24.
6. Yasunari K, *et al.* Pharmacological and clinical studies with temocapril, an angiotensin converting enzyme inhibitor that is excreted in the bile. *Cardiovasc Drug Rev* 2004; **22:** 189–98.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Acecol.

Tenecteplase *(BAN, USAN, rINN)*

Tenecteplasa; Ténectéplase; Tenecteplasum; TNK-tPA. [103-L-Asparagine-117-L-glutamine-296-L-alanine-297-L-alanine-298-L-alanine-299-L-alanine]plasminogen activator (human tissue-type).

Тенектеплас

CAS — 191588-94-0.
ATC — B01AD11.
ATC Vet — QB01AD11.

Description. Tenecteplase is a 527 amino acid glycoprotein produced by recombinant DNA technology. It is a modified form of human tissue plasminogen activator.

Adverse Effects, Treatment, and Precautions

As for Streptokinase, p.1402

Interactions

As for Streptokinase, p.1404

Pharmacokinetics

After intravenous injection in patients with acute myocardial infarction, tenecteplase has a biphasic clearance from plasma with an initial half-life of 20 to 24 minutes and a terminal phase half-life of 90 to 130 minutes. It is cleared mainly by hepatic metabolism.

◊ Reviews.

1. Tanswell P, *et al.* Pharmacokinetics and pharmacodynamics of tenecteplase in fibrinolytic therapy of acute myocardial infarction. *Clin Pharmacokinet* 2002; **41:** 1229–45.

Uses and Administration

Tenecteplase is a thrombolytic drug. It converts plasminogen to plasmin, a proteolytic enzyme that has fibrinolytic effects. The mechanisms of fibrinolysis are discussed further under Haemostasis and Fibrinolysis on p.1045. Tenecteplase is a fibrin-specific thrombolytic (see p.1156).

Tenecteplase is used similarly to streptokinase (p.1404) in acute myocardial infarction (p.1175). It is given intravenously as a single bolus dose over 5 to 10 seconds as soon as possible after the onset of symptoms. The dose is based on body-weight and ranges from 30 mg in patients less than 60 kg to a maximum of 50 mg in those 90 kg or above.

◊ References.

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2. Assessment of the Safety and Efficacy of a New Thrombolytic (ASSENT-2) Investigators. Single-bolus tenecteplase compared with front-loaded alteplase in acute myocardial infarction: the ASSENT-2 double-blind randomised trial. *Lancet* 1999; **354:** 716–22.
3. Llevadot J, *et al.* Bolus fibrinolytic therapy in acute myocardial infarction. *JAMA* 2001; **286:** 442–9.
4. The Assessment of the Safety and Efficacy of a New Thrombolytic Regimen (ASSENT)-3 Investigators. Efficacy and safety of tenecteplase in combination with enoxaparin, abciximab, or unfractionated heparin: the ASSENT-3 randomised trial in acute myocardial infarction. *Lancet* 2001; **358:** 605–13.
5. Turcasso NM, Nappi JM. Tenecteplase for treatment of acute myocardial infarction. *Ann Pharmacother* 2001; **35:** 1233–40.
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7. Melzer C, *et al.* Fibrinolysis of acute peripheral arterial occlusion with tenecteplase—a new weight-optimized treatment regimen. *J Thromb Thrombolysis* 2004; **18:** 43–6.
8. Spöhr F, *et al.* International multicentre trial protocol to assess the efficacy and safety of tenecteplase during cardiopulmonary resuscitation in patients with out-of-hospital cardiac arrest: the Thrombolysis in Cardiac Arrest (TROICA) Study. *Eur J Clin Invest* 2005; **35:** 315–23.
9. Kelly RV, *et al.* Safety of adjunctive intracoronary thrombolytic therapy during complex percutaneous coronary intervention: initial experience with intracoronary tenecteplase. *Catheter Cardiovasc Interv* 2005; **66:** 327–32.
10. Assessment of the Safety and Efficacy of a New Treatment Strategy with Percutaneous Coronary Intervention (ASSENT-4 PCI) investigators. Primary versus tenecteplase-facilitated percutaneous coronary intervention in patients with ST-segment elevation acute myocardial infarction (ASSENT-4 PCI): randomised trial. *Lancet* 2006; **367:** 569–78.
11. Kline JA, *et al.* Tenecteplase to treat pulmonary embolism in the emergency department. *J Thromb Thrombolysis* 2007; **23:** 101–5.

Preparations

Proprietary Preparations (details are given in Part 3)
Austral.: Metalyse; ***Austria:*** Metalyse; ***Belg.:*** Metalyse; ***Braz.:*** Metalyse; ***Canad.:*** TNKase; ***Chile:*** Metalyse; ***Cz.:*** Metalyse; ***Denm.:*** Metalyse; ***Fin.:*** Metalyse; ***Fr.:*** Metalyse; ***Ger.:*** Metalyse; ***Gr.:*** Metalyse; ***Hong Kong:*** Metalyse; ***Hung.:*** Metalyse; ***Irl.:*** Metalyse; ***Ital.:*** Metalyse; ***Malaysia:*** Metalyse; ***Mex.:*** Metalyse; ***Neth.:*** Metalyse; ***Norw.:*** Metalyse; ***NZ:*** Metalyse; ***Pol.:*** Metalyse; ***Port.:*** Metalyse; ***Rus.:*** Metalyse (Метализе); ***S.Afr.:*** Metalyse; ***Spain:*** Metalyse; ***Swed.:*** Metalyse; ***Switz.:*** Metalyse; ***Thai.:*** Metalyse; ***UK:*** Metalyse; ***USA:*** TNKase.

Tenitramine

Tenitramina. *NNN′N′*-Tetrakis(2-hydroxyethyl)ethylenediamine tetranitrate.

$C_{10}H_{20}N_6O_{12}$ = 416.3.
CAS — 21946-79-2.
ATC — C01DA38.
ATC Vet — QC01DA38.

Profile

Tenitramine is a vasodilator with general properties similar to those of glyceryl trinitrate (p.1296) that has been used in angina pectoris (p.1157).

Preparations

Proprietary Preparations (details are given in Part 3)
Ital.: Tenitran†.

Teprotide *(BAN, USAN, rINN)*

BPF_{9a}; L-Pyroglutamyl-L-tryptophyl-L-prolyl-L-arginyl-L-prolyl-L-glutaminyl-L-isoleucyl-L-prolyl-L-proline; SQ-20881; Teprotida; Téprotide; Teprotidum; 2-L-Tryptophan-3-de-L-leucine-4-de-L-proline-8-L-glutaminebradykinin potentiator B. 5-oxo-Pro-Trp-Pro-Arg-Pro-Gln-Ile-Pro-Pro.

Тепротид

$C_{53}H_{76}N_{14}O_{12}$ = 1101.3.
CAS — 35115-60-7.

Profile

Teprotide is a nonapeptide originally found in the venom of *Bothrops jararaca*, a South American pit-viper. It is an ACE inhibitor with a short duration of action and has been given parenterally as an investigational tool.

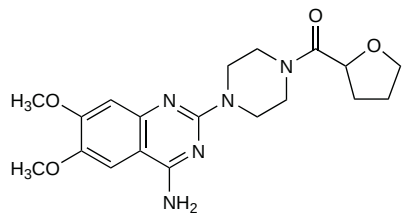
Terazosin Hydrochloride

(BANM, USAN, rINNM)

Abbott-45975; Hidrocloruro de terazosina; Teratsosiinihydrokloridi; Terazosin Hidroklorür; Térazosine, chlorhydrate de; Terazosinhydroklorid; Terazosini hydrochloridum. 1-(4-Amino-6,7-dimethoxyquinazolin-2-yl)-4-(tetrahydro-2-furoyl)piperazine hydrochloride dihydrate; 6,7-Dimethoxy-2-[4-(tetrahydrofuran-2-carbonyl)piperazin-1-yl]quinazolin-4-ylamine hydrochloride dihydrate.

Теразозина Гидрохлорид

$C_{19}H_{25}N_5O_4$,HCl,$2H_2O$ = 459.9.
CAS — 63590-64-7 (terazosin); 63074-08-8 (anhydrous terazosin hydrochloride); 70024-40-7 (terazosin hydrochloride dihydrate).
ATC — G04CA03.
ATC Vet — QG04CA03.



(terazosin)

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

Ph. Eur. 6.2 (Terazosin Hydrochloride Dihydrate). White or slightly yellow, crystalline powder. Sparingly soluble in water; very slightly soluble in alcohol; slightly soluble in methyl alcohol; practically insoluble in acetone. A 2% solution in water has a pH of 3.0 to 5.0. Protect from light.

USP 31 (Terazosin Hydrochloride). A white to pale yellow, crystalline powder. soluble in water and in methyl alcohol; freely soluble in isotonic saline solution; slightly soluble in alcohol and in 0.1N hydrochloric acid; practically insoluble in acetone and in hexanes; very slightly soluble in chloroform. Store in airtight containers at a temperature between 20° and 25°.

Adverse Effects, Treatment, and Precautions

As for Prazosin Hydrochloride, p.1375.

Urinary incontinence. For reference to urinary incontinence associated with terazosin, see under Adverse Effects of Prazosin Hydrochloride, p.1375.

Interactions

As for Prazosin Hydrochloride, p.1376.

Pharmacokinetics

Terazosin is rapidly and almost completely absorbed from the gastrointestinal tract after oral doses; the bioavailability is reported to be about 90%. Peak plasma concentrations are achieved in about 1 hour. Terazosin is 90 to 94% protein bound. It is metabolised in the liver; one of the metabolites is reported to possess antihypertensive activity. The half-life in plasma is about 12 hours. Terazosin is excreted in faeces via the bile, and in the urine, as unchanged drug and metabolites.

Uses and Administration

Terazosin is an $alpha_1$-adrenoceptor blocker (p.1153) with actions similar to those of prazosin (p.1376), but a longer duration of action.

It is used in the management of hypertension (p.1171) and in benign prostatic hyperplasia (p.2178) to relieve symptoms of urinary obstruction.

Terazosin is given orally as the hydrochloride, but doses are usually expressed in terms of the base. Terazosin hydrochloride 1.2 mg is equivalent to about 1 mg of terazosin. After oral doses its hypotensive effects are seen within 15 minutes and may last for up to 24 hours, permitting once daily dosage.

To avoid the risk of collapse which may occur in some patients after the first dose the initial dose for both hypertension and benign prostatic hyperplasia is 1 mg of terazosin at bedtime, increasing gradually at intervals of 7 days according to the patient's response. For **hypertension** the usual maintenance dose is 2 to 10 mg once daily and the usual maximum dose is 20 mg daily in a single dose or two divided doses. For **benign prostatic hyperplasia** the usual maintenance dose is 5 to 10 mg once daily.

◊ Reviews.

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2. Achari R, Laddu A. Terazosin: a new alpha adrenoceptor blocking drug. *J Clin Pharmacol* 1992; **32:** 520–3.
3. Wilt TJ, *et al.* Terazosin for benign prostatic hyperplasia. Available in the Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2000 (accessed 01/02/06).

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Andrin; Benaprost; Blavin; Eglidon; Flumarc; Fosfomik; Geriprost; Isontyn; Panaprost; Proxatan; Rotiaz; ***Austral.:*** Hytrin; ***Austria:*** Urocard; Uroflo; Vicard; ***Belg.:*** Hytrin; Terazosabb; Uro-Hytrin; ***Braz.:*** Hytrin; ***Canad.:*** Hytrin; ***Chile:*** Adecur; Hytrin; ***Cz.:*** Hytrin; Kornam; ***Denm.:*** Sinalfa; ***Fr.:*** Dysalfa; Hytrine; ***Ger.:*** Flotrin; Heitrin; Tera; Terablock; Teranar; Terazid; Terazoflo; ***Gr.:*** Hytrin; Vlanodrin; ***Hong Kong:*** Hytrin; ***Hung.:*** Hyron†; Hytrin; Kornam†; Setegis; ***India:*** Hytrin; Olyster; Zytrin; ***Indon.:*** Hytrin; ***Irl.:*** Benph; Hytrin; ***Israel:*** Hytrin; ***Ital.:*** Ezosina; Ibiprovir†; Itrin; Prostatil; Terafluss; Teraprost; Unoprost; Urodie; ***Malaysia:*** Hytrin; Terasin; ***Mex.:*** Adecur; Hytrin; Romaken; ***Neth.:*** Hytrin; ***Norw.:*** Sinalfa; ***NZ:*** Hytrin; ***Philipp.:*** Conmy; Hytrin; Lotencin; ***Pol.:*** Hytrin; Kornam; Setegis; Tesin; ***Port.:*** Hytrin; ***Rus.:*** Hytrin (Хитрин)†; Kornam (Корнам); Setegis (Сетегис); ***S.Afr.:*** Hytrin; ***Singapore:*** Hytrin; ***Spain:*** Alfaprost; Deflox; Magnurol; Mayul; Sutif; Tazusin†; Teraumon; Zayasel; ***Swed.:*** Hytrinex; Sinalfa; ***Switz.:*** Hytrin BPH; ***Thai.:*** Hytrin; ***Turk.:*** Hytrin; ***UK:*** Hytrin; ***USA:*** Hytrin; ***Venez.:*** Adecur; Hytrin.