have reduced the metabolism of dopamine in this patient. Caution may be necessary if dopamine is given to patients who have been receiving selegiline within the previous 2 weeks.

1. Rose LM, *et al.* A hypertensive reaction induced by concurrent use of selegiline and dopamine. *Ann Pharmacother* 2000; **34:** 1020–4.

Pharmacokinetics

The vasoconstrictor properties of dopamine preclude its use by the subcutaneous or intramuscular route. Like adrenaline (p.1204) it is inactive when given orally, and it is rapidly inactivated in the body by similar processes, with a half-life of about 2 minutes. Dopamine is a metabolic precursor of noradrenaline and a proportion is excreted as the metabolites of noradrenaline. Nevertheless, the majority appears to be directly metabolised into dopamine-related metabolites.

◊ References.

1. Steinberg C, Notterman DA. Pharmacokinetics of cardiovascular drugs in children: inotropes and vasopressors. *Clin Pharmacokinet* 1994; **27:** 345–67.
2. Juste RN, *et al.* Dopamine clearance in critically ill patients. *Intensive Care Med* 1998; **24:** 1217–20.
3. MacGregor DA, *et al.* Pharmacokinetics of dopamine in healthy male subjects. *Anesthesiology* 2000; **92:** 338–46.
4. Johnston AJ, *et al.* Pharmacokinetics and pharmacodynamics of dopamine and norepinephrine in critically ill head-injured patients. *Intensive Care Med* 2004; **30:** 45–50.

Uses and Administration

Dopamine is a catecholamine sympathomimetic (p.1408) with both direct and indirect effects. It is formed in the body by the decarboxylation of levodopa, and is both a neurotransmitter in its own right (notably in the brain) and a precursor of noradrenaline. Dopamine differs from adrenaline and noradrenaline in dilating renal and mesenteric blood vessels and increasing urine output, apparently by a specific dopaminergic mechanism. This effect is predominant at low infusion rates (about 2 micrograms/kg per minute); at slightly higher infusion rates (around 2 to 10 micrograms/kg per minute) it also stimulates $beta_1$-adrenergic receptors in the myocardium, and at 10 to 20 micrograms/kg per minute the effects of alpha-adrenergic stimulation, such as vasoconstriction, predominate. The inotropic action of dopamine on the heart is associated with less cardiac-accelerating effect, and a lower incidence of arrhythmias, than that of isoprenaline.

Dopamine also inhibits release of prolactin from the anterior pituitary.

Dopamine is used in acute heart failure, as occurs in cardiogenic shock (p.1183) and myocardial infarction (p.1175); it is also used in renal failure (but see below, under Surgery and Intensive Care), in cardiac surgery, and in septic shock.

Dopamine is given as the hydrochloride by intravenous infusion as a dilute solution (usually 1.6 or 3.2 mg/mL, although more dilute solutions may be used where fluid expansion is not a problem), in glucose 5%, sodium chloride 0.9%, or other suitable diluents; many fluids are suitable and licensed product information should be consulted. The initial rate is 1 to 5 micrograms/kg per minute, gradually increased by up to 5 to 10 micrograms/kg per minute according to the patient's blood pressure, cardiac output, and urine output. Up to 20 to 50 micrograms/kg per minute may be required in seriously ill patients; higher doses have been given. A reduction in urine flow, without hypotension, may indicate a need to reduce the dose. To avoid tissue necrosis dopamine is best given via a large vein high up in a limb, preferably the arm. When gradually stopping dopamine it is advised that care be taken to avoid undue hypotension associated with very low dosage levels, where vasodilatation could predominate.

Surgery and intensive care. Dopamine has an established role as an inotrope in cardiogenic shock and in cardiac surgery; it has also been used as a **renal protectant,** due to the apparently beneficial effects of lower doses on renal function. Studies in healthy *animals* and human subjects have shown that low-dose dopamine increases renal blood flow, natriuresis, diuresis, and possibly glomerular filtration rate. Low doses of dopamine (sometimes termed 'renal-dose' dopamine) have therefore been widely used in patients at risk of renal failure, such as those undergoing major surgery or in intensive care, as well as for the treatment of acute renal failure. However, clinical studies have failed to convincingly demonstrate that low-dose dopamine is effective in either preventing acute renal failure in patients at high risk, or in improving renal function or outcome in patients with established acute renal failure. A placebo-controlled, randomised study[1] in critically-ill patients with early renal dysfunction and meta-analyses[2,3] including studies of varying design, failed to show any clinical benefit in those receiving dopamine. It is now generally considered[2,4,5] that low-dose dopamine has no place as a renal protectant in the routine management of critically ill patients.

Dopexamine, which like dopamine acts as a peripheral dopamine agonist, has been used similarly but evidence of benefit is limited and it is generally not recommended (see Critical Care under Dopexamine, p.1274).

1. Australian and New Zealand Intensive Care Society (ANZICS) Clinical Trials Group. Low-dose dopamine in patients with early renal dysfunction: a placebo-controlled randomised trial. *Lancet* 2000; **356:** 2139–43.
2. Kellum JA, Decker JM. Use of dopamine in acute renal failure: a meta-analysis. *Crit Care Med* 2001; **29:** 1526–31.
3. Friedrich JO, *et al.* Meta-analysis: low-dose dopamine increases urine output but does not prevent renal dysfunction or death. *Ann Intern Med* 2005; **142:** 510–24.
4. Galley HF. Renal-dose dopamine: will the message now get through? *Lancet* 2000; **356:** 2112–13. Correction. *ibid.* 2001; **357:** 890.
5. Holmes CL, Walley KR. Bad medicine: low-dose dopamine in the ICU. *Chest* 2003; **123:** 1266–75.

Preparations

BP 2008: Dopamine Intravenous Infusion;
USP 31: Dopamine Hydrochloride and Dextrose Injection; Dopamine Hydrochloride Injection.

Proprietary Preparations (details are given in Part 3)

Arg.: Dopatropin; Hettytropin†; Inotropin; Megadose; ***Belg.:*** Dynatra; ***Braz.:*** Constriction; Dopabane; Dopacris; Revimine; Revivan; Vasomine†; ***Canad.:*** Intropin†; ***Cz.:*** Tensamin; ***Denm.:*** Abbodop; Dopmin; Giludop; ***Fin.:*** Abbodop; Dopmin; ***Gr.:*** Giludop; ***Hong Kong:*** Intropin†; ***India:*** Dopinga; ***Indon.:*** Cetadop; Dopac; Indop; ***Israel:*** Docard; ***Ital.:*** Revivan; ***Jpn:*** Inovan; Pre Dopa; ***Malaysia:*** Dopmin; ***Mex.:*** Clorpamina†; Drynalken; Flemina†; Inotropisa; Miocina; Zetarina; ***Neth.:*** Dynatra; ***Norw.:*** Abbodop; ***Philipp.:*** Docard; Myocard; ***Port.:*** Cordodopa; Medopa; ***S.Afr.:*** Dynos; Intropin; ***Singapore:*** Dopmin†; ***Swed.:*** Abbodop; Giludop; Intropin†; ***Thai.:*** Dopamex; Dopaminex; Dopmin; Inopin; ***Turk.:*** Dopmin; ***USA:*** Intropin†; ***Venez.:*** Dopina; Rascordin†.

Dopexamine Hydrochloride

(BANM, USAN, rINNM) ⊗

Dopeksamiinihydrokloridi; Dopeksamin Hidroklorür; Dopéxamine, Chlorhydrate de; Dopexamine, dichlorhydrate de; Dopexamine dihydrochloride; Dopexaminhydroklorid; Dopexamini dihydrochloridum; Dopexamini Hydrochloridum; FPL-60278 (dopexamine); FPL-60278AR; Hidrocloruro de dopexamina. 4-{2-[6-(Phenethylamino)hexylamino]ethyl}pyrocatechol dihydrochloride.

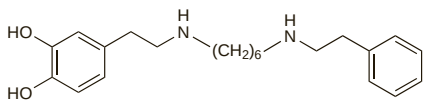
Допексамина Гидрохлорид

$C_{22}H_{32}N_2O_2,2HCl$ = 429.4.

CAS — 86197-47-9 (dopexamine); 86484-91-5 (dopexamine dihydrochloride).

ATC — C01CA14.

ATC Vet — QC01CA14.



(dopexamine)

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Dopexamine Dihydrochloride). A white or almost white, crystalline powder. Soluble in water; sparingly soluble in alcohol and in methyl alcohol; practically insoluble in acetone. A 1% solution in water has a pH of 3.7 to 5.7. Protect from light.

Incompatibility. Dopexamine is inactivated in alkaline solutions such as sodium bicarbonate 5%.

Adverse Effects and Precautions

As for Sympathomimetics, p.1407. Dopexamine has mainly beta-agonist and dopaminergic actions; its most common adverse effect is tachycardia, and transient hypotension may also occur. Dopexamine may cause a small reduction in platelet counts and should not be given to thrombocytopenic patients.

Interactions

As for Sympathomimetics, p.1407. The interactions of dopexamine are mainly due to its beta-agonist and dopaminergic actions; it may also potentiate the effects of noradrenaline and some other sympathomimetics by inhibiting neuronal uptake of noradrenaline.

Pharmacokinetics

Dopexamine has a short half-life in blood of about 6 to 7 minutes. It is excreted as metabolites in bile and in urine.

Uses and Administration

Dopexamine is a sympathomimetic (p.1408) with direct and indirect effects. It stimulates $beta_2$ adrenoceptors and peripheral dopamine receptors and also inhibits the neuronal reuptake of noradrenaline. These actions result in an increased cardiac output, peripheral vasodilatation, and an increase in renal and mesenteric blood flow.

Dopexamine hydrochloride is used to provide short-term haemodynamic support, for example after cardiac surgery or in exacerbations of chronic heart failure. It is given as an intravenous infusion of either 400 or 800 micrograms/mL in glucose 5%, sodium chloride 0.9%, or other suitable diluents, through a central or large peripheral vein; more concentrated solutions may be given via a central vein but concentrations should not exceed 4 mg/mL. The initial dose is generally 0.5 micrograms/kg per minute and is then increased to 1 microgram/kg per minute; further increases, in increments of 0.5 to 1 microgram/kg per minute at intervals of not less than 15 minutes, may be made up to a total of 6 micrograms/kg per minute if necessary. Heart rate, blood pressure, urine output, and cardiac output should be monitored. On withdrawal, the dose should be reduced gradually.

◊ References.

1. Fitton A, Benfield P. Dopexamine hydrochloride. *Drugs* 1990; **39:** 308–30.
2. Anonymous. Dopexamine after cardiac surgery. *Drug Ther Bull* 1995; **33:** 30–2.

Critical care. Dopexamine has been reported to increase splanchnic blood flow and it has been used with the aim of preventing renal and gastrointestinal dysfunction in critically-ill patients.[1] Although there may be a reduction in ischaemic damage to the gut,[2] a study[3] in critically-ill patients failed to show any improvement in outcome with the use of dopexamine. Studies[4,5] using dopexamine to increase oxygen delivery in high-risk surgical patients have also failed to show any benefit in terms of postoperative mortality or organ function, and a systematic review[6] found insufficient evidence to recommend the use of dopexamine in either patient group. A later meta-analysis[7] found that overall, perioperative dopexamine infusion reduced the length of hospital stay in patients having major surgery, but showed no survival benefit; however, at low doses (up to 1 microgram/kg per minute) dopexamine infusion seemed also to be associated with improved survival.

Use of low-dose dopamine for renal protection is not recommended (see Surgery and Intensive Care, p.1274).

1. Lisbon A. Dopexamine, dobutamine, and dopamine increase splanchnic blood flow: what is the evidence? *Chest* 2003; **123** (suppl): 460S–463S.
2. Baguneid MS, *et al.* A randomized study to evaluate the effect of a perioperative infusion of dopexamine on colonic mucosal ischemia after aortic surgery. *J Vasc Surg* 2001; **33:** 758–63.
3. Ralph CJ, *et al.* A randomised controlled trial investigating the effects of dopexamine on gastrointestinal function and organ dysfunction in the critically ill. *Intensive Care Med* 2002; **28:** 884–90. Correction. *ibid*; 1001. [dose]
4. Takala J, *et al.* Effect of dopexamine on outcome after major abdominal surgery: a prospective, randomized, controlled multicenter study. *Crit Care Med* 2000; **28:** 3417–23.
5. Stone MD, *et al.* Effect of adding dopexamine to intraoperative volume expansion in patients undergoing major elective abdominal surgery. *Br J Anaesth* 2003; **91:** 619–24.
6. Renton MC, Snowden CP. Dopexamine and its role in the protection of hepatosplanchnic and renal perfusion in high-risk surgical and critically ill patients. *Br J Anaesth* 2005; **94:** 459–67.
7. Pearse RM, *et al.* Effect of dopexamine infusion on mortality following major surgery: individual patient data meta-regression analysis of published clinical trials. *Crit Care Med* 2008; **36:** 1323–9.

Preparations

Proprietary Preparations (details are given in Part 3)
Cz.: Dopacard†; ***Denm.:*** Dopacard; ***Fin.:*** Dopacard; ***Fr.:*** Dopacard; ***Ger.:*** Dopacard; ***Irl.:*** Dopacard; ***NZ:*** Dopacard†; ***Swed.:*** Dopacard†; ***Switz.:*** Dopacard†; ***UK:*** Dopacard.

Doxazosin Mesilate *(BANM, rINNM)*

Doksazosyny mezylan; Doxazosin Mesylate *(USAN)*; Doxazosin Methanesulphonate; Doxazosine, mésilate de; Doxazosini mesilas; Doxazosin-mesylát; Mesilato de doxazosina; UK-33274-27. 1-(4-Amino-6,7-dimethoxyquinazolin-2-yl)-4-(1,4-benzodioxan-2-ylcarbonyl)piperazine methanesulphonate.

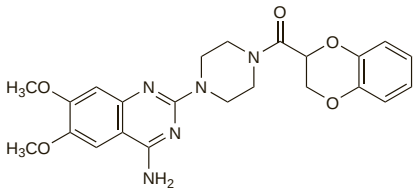
Доксазозина Мезилат

$C_{23}H_{25}N_5O_5,CH_3SO_3H$ = 547.6.

CAS — 74191-85-8 (doxazosin); 77883-43-3 (doxazosin mesilate).

ATC — C02CA04.

ATC Vet — QC02CA04.



(doxazosin)

Pharmacopoeias. In *Eur.* (see p.vii) and *US.*.
Ph. Eur. 6.2 (Doxazosin Mesilate). A white or almost white crystalline powder. It exhibits polymorphism and some forms may be hygroscopic. Slightly soluble in water and in methyl alcohol; soluble in a mixture of 15 volumes of water and 35 volumes of tetrahydrofuran; practically insoluble in acetone. Store in airtight containers.
USP 31 (Doxazosin Mesylate). A white to tan-coloured powder. Very slightly soluble in water and in methyl alcohol; freely soluble in formic acid. Store at a temperature below 30°.

Adverse Effects, Treatment, and Precautions

As for Prazosin Hydrochloride, p.1375.

Effects on mental function. For a report of acute psychosis associated with doxazosin use, see under Adverse Effects of Prazosin Hydrochloride, p.1375.

Hypotension. Six of 18 hypertensive patients had first-dose orthostatic hypotension after receiving doxazosin 1 mg; three others had substantial but asymptomatic reductions in supine systolic blood pressure after the first dose.[1] The effect might have been exacerbated since all these patients were also receiving beta blockers or diuretics, or both. A further patient, who was also taking methyldopa, withdrew from the study with persistent orthostatic hypotension.

1. Oliver RM, *et al.* The pharmacokinetics of doxazosin in patients with hypertension and renal impairment. *Br J Clin Pharmacol* 1990; **29:** 417–22.

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

Pharmacokinetics

Doxazosin is well absorbed after oral doses, peak plasma concentrations occurring 2 to 3 hours after a dose. Oral bioavailability is about 65%. It is extensively metabolised in the liver, and excreted in faeces as metabolites and a small amount of unchanged drug. Elimination from plasma is biphasic, with a mean terminal half-life of about 22 hours. The pharmacokinetics are not altered in patients with renal impairment. Doxazosin is about 98% bound to plasma proteins and is not removed by dialysis.

◊ Reviews.

1. Elliott HL, *et al.* Pharmacokinetic overview of doxazosin. *Am J Cardiol* 1987; **59:** 78G–81G.

Uses and Administration

Doxazosin is an alpha$_1$-adrenoceptor blocker (p.1153) with actions and uses similar to those of prazosin (p.1376), but a longer duration of action. It is used in the management of hypertension and in benign prostatic hyperplasia to relieve symptoms of urinary obstruction (below).

Doxazosin is given orally as the mesilate, but doses are usually expressed in terms of the base. Doxazosin mesilate 1.2 mg is equivalent to about 1 mg of doxazosin. After an oral dose maximum reduction in blood pressure is reported to occur in 2 to 6 hours and the effects are maintained for 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 is 1 mg, preferably at bedtime. Dosage may be increased after 1 or 2 weeks according to response. Usual maintenance doses for **hypertension** are up to 4 mg once daily; doses of 16 mg daily should not be exceeded. For **benign prostatic hyperplasia** the usual maintenance dose is 2 to 4 mg daily; doses of 8 mg daily should not be exceeded.

Doxazosin may also be given as a modified-release preparation.

◊ Reviews.

1. Fulton B, *et al.* Doxazosin: an update of its clinical pharmacology and therapeutic applications in hypertension and benign prostatic hyperplasia. *Drugs* 1995; **49:** 295–320.

Benign prostatic hyperplasia. References to the use of doxazosin in patients with benign prostatic hyperplasia (p.2178).

1. Doggrell SA. After ALLHAT: doxazosin for the treatment of benign prostatic hyperplasia. *Expert Opin Pharmacother* 2004; **5:** 1957–64.
2. MacDonald R, *et al.* Doxazosin for treating lower urinary tract symptoms compatible with benign prostatic obstruction: a systematic review of efficacy and adverse effects. *BJU Int* 2004; **94:** 1263–70.
3. Goldsmith DR, Plosker GL. Doxazosin gastrointestinal therapeutic system: a review of its use in benign prostatic hyperplasia. *Drugs* 2005; **65:** 2037–47.
4. Wilt TJ, MacDonald R. Doxazosin in the treatment of benign prostatic hypertrophy: an update. *Clin Interv Aging* 2006; **1:** 389–401.
5. Bhardwa J, *et al.* Finasteride and doxazosin alone or in combination for the treatment of benign prostatic hyperplasia. *Expert Opin Pharmacother* 2007; **8:** 1337–44.

Hypertension. Alpha blockers are among the drug groups that have been used as first-line therapy for hypertension (p.1171). However, in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)[1] the doxazosin arm of the study was terminated early due to an increased incidence of heart failure in patients receiving doxazosin compared with those receiving chlortalidone and alpha blockers are now only recommended for third-line therapy unless indicated for another reason.

1. The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. Major cardiovascular events in hypertensive patients randomized to doxazosin vs chlorthalidone: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA* 2000; **283:** 1967–75. Correction. *ibid.* 2002; **288**: 2976.

Pain. For reference to the use of doxazosin in pain, see under Uses of Phentolamine Mesilate, p.1371.

Preparations

USP 31: Doxazosin Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Cardura; Doxasin; Doxolbran; Lafedoxin; Prostazosina; Vazosin; ***Austria:*** Adoxa; Ascalan; Doxano†; Doxapress; Hibadren; Prostadilat; Supressin; ***Braz.:*** Carduran; Doxsol; Euprostatin; Prodil†; Unoprost; Zoflux; ***Canad.:*** Cardura; ***Chile:*** Alfadoxin; Angicon; Cardura; Dorbantil; ***Cz.:*** Cardura; Dosano; Dozone; Kamiren; Windoxa; Zoxon; ***Denm.:*** Biozosin; Cardosin; Carduran; Doxacar†; ***Fr.:*** Zoxan; ***Ger.:*** Alfamedin; Cardular; Diblocin; Doxa-Puren; Doxacor; Doxagamma; Doxamax†; DoxaUro†; Doxazoflo; Doxazomerck†; Jutalar; Uriduct; ***Gr.:*** Cardura; Maguran; Protectura; ***Hong Kong:*** Cardura; Doxasyn; ***Hung.:*** Cardura; Doxagal; Doxicard; ***India:*** Doxacard; ***Indon.:*** Cardura; ***Irl.:*** Cardura; Doxatan; ***Israel:*** Cadex; Cardoral; Doxaloc; ***Ital.:*** Benur; Cardura; Dedralen; Normothen; ***Jpn:*** Cardenalin†; ***Malaysia:*** Cardura; Magurol; Pencor; ***Mex.:*** Cardura; ***Neth.:*** Cardura; Progandol; Zoxan; ***Norw.:*** Carduran; ***NZ:*** Cardoxan; Dosan; ***Pol.:*** Apo-Doxan; Cardura; Doxanorm; Doxar; Doxaratio; Doxonex; Kamiren; Prostatic; Vaxosin; Zoxon; ***Port.:*** Cardura; ***Rus.:*** Artezine (Артезин); Cardura (Кардура); Kamiren (Камирен); Magurol (Магурол); Tonocardin (Тонокардин); Zoxon (Зоксон); ***S.Afr.:*** Cardugen; Cardura; ***Singapore:*** Cardura; Pencor; ***Spain:*** Carduran; Doxatensa; Doximax Neo; Progandol; ***Swed.:*** Alfadil; ***Switz.:*** Cardura; ***Thai.:*** Cardura; Carxasin; Cazosin; Dezcard; Dozozin; Duracard; Genzosin; Pencor; ***Turk.:*** Cardura; Doksura; Doxacor; ***UK:*** Cardura; Doxadura; ***USA:*** Cardura; ***Venez.:*** Cardura.

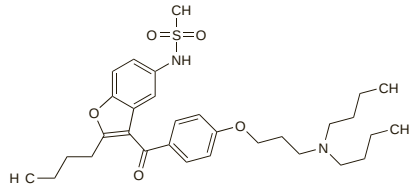
Dronedarone *(rINN)*

Dronedarona; Dronédarone; Dronedaronum; SR-33589. *N*-(2-Butyl-3-{*p*-[3-(dibutylamino)propoxy]benzoyl}-5-benzofuranyl)methanesulfonamide.

Дронедарон

$C_{31}H_{44}N_2O_5S$ = 556.8.

CAS — 141626-36-0.



Profile

Dronedarone is structurally related to amiodarone and is under investigation as an antiarrhythmic.

◊ References.

1. Touboul P, *et al.* Dronedarone for prevention of atrial fibrillation: a dose-ranging study. *Eur Heart J* 2003; **24:** 1481–7.
2. Dale KM, White CM. Dronedarone: an amiodarone analog for the treatment of atrial fibrillation and atrial flutter. *Ann Pharmacother* 2007; **41:** 599–605.
3. Singh BN, *et al.* EURIDIS and ADONIS Investigators. Dronedarone for maintenance of sinus rhythm in atrial fibrillation or flutter. *N Engl J Med* 2007; **357:** 987–99.

Duteplase *(rINN)*

Duteplasa; Dutéplase; Duteplasum; 245-L-Methionine Plasminogen Activator; SM-9527.

Дутеплаза

$C_{2736}H_{4174}N_{914}O_{824}S_{46}$ = 64529.0.

CAS — 120608-46-0.

Profile

Duteplase is a thrombolytic drug. It is a biosynthetic derivative of endogenous tissue plasminogen activator and has been used similarly to alteplase (p.1207) in the treatment of thromboembolic disorders, particularly acute myocardial infarction.

◊ References.

1. Hayashi H, *et al.* Effects of intravenous SM-9527 (double-chain tissue plasminogen activator) on left ventricular function in the chronic stage of acute myocardial infarction. *Clin Cardiol* 1993; **16:** 409–14.
2. Malcolm AD, *et al.* ESPRIT: a European study of the prevention of reocclusion after initial thrombolysis with duteplase in acute myocardial infarction. *Eur Heart J* 1996; **17:** 1522–31.

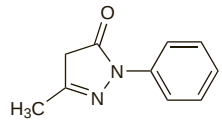
Edaravone *(rINN)*

Edaravona; Édaravone; Edaravonum; MCI-186; Norphenazone. 3-Methyl-1-phenyl-2-pyrazolin-5-one.

Эдаравон

$C_{10}H_{10}N_2O$ = 174.2.

CAS — 89-25-8.



Profile

Edaravone is a free-radical scavenger used in the management of acute ischaemic stroke (p.1185). It is given by intravenous infusion in a dose of 30 mg twice daily, infused over 30 minutes, beginning within 24 hours of stroke onset and continued for up to 14 days.

◊ References.

1. Edaravone Acute Infarction Study Group. Effect of a novel free radical scavenger, edaravone (MCI-186), on acute brain infarction: randomized, placebo-controlled, double-blind study at multicenters. *Cerebrovasc Dis* 2003; **15:** 222–9.
2. Tsujita K, *et al.* Effects of edaravone on reperfusion injury in patients with acute myocardial infarction. *Am J Cardiol* 2004; **94:** 481–4.
3. Tsujita K, *et al.* Long-term efficacy of edaravone in patients with acute myocardial infarction. *Circ J* 2006; **70:** 832–7.
4. Hishida A. Clinical analysis of 207 patients who developed renal disorders during or after treatment with edaravone reported during post-marketing surveillance. *Clin Exp Nephrol* 2007; **11:** 292–6.
5. Watanabe T, *et al.* The novel antioxidant edaravone: from bench to bedside. *Cardiovasc Ther* 2008; **26:** 101–14.