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.

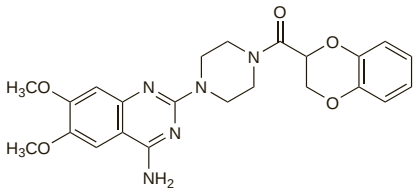
Доксазозина Мезилат

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

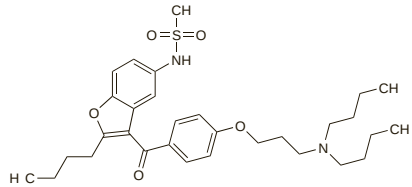
Dronedarone *(rINN)*

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.

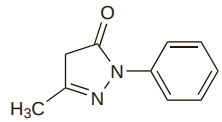
Edaravone *(rINN)*

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.