for more than 60 days were affected (7 severely). Since the associated bone changes may persist for months after stopping alprostadil, caution should be exercised to avoid misdiagnosis.

1. Ueda K, *et al.* Cortical hyperostosis following long-term administration of prostaglandin E in infants with cyanotic congenital heart disease. *J Pediatr* 1980; **97:** 834–6.
2. Ringel RE, *et al.* Periosteal changes secondary to prostaglandin administration. *J Pediatr* 1983; **103:** 251–3.
3. Williams JL. Periosteal hyperostosis resulting from prostaglandin therapy. *Eur J Radiol* 1986; **6:** 231–2.
4. Kalloghlian AK, *et al.* Cortical hyperostosis simulating osteomyelitis after short-term prostaglandin E infusion. *Eur J Pediatr* 1996; **155:** 173–4.
5. Woo K, *et al.* Cortical hyperostosis: a complication of prolonged prostaglandin infusion in infants awaiting cardiac transplantation. *Pediatrics* 1994; **93:** 417–20.

Effects on the gastrointestinal tract. Hyperplasia of the gastric mucosa, resulting in gastric outlet obstruction, has been reported in several neonates receiving alprostadil infusion.[1-3] It was suggested that this effect was dose-dependent.[1] Regression of the obstruction usually occurred after cessation of therapy.

For a report of necrotising enterocolitis in infants receiving alprostadil for congenital heart disease, see Dinoprostone, p.2007.

1. Peled N, *et al.* Gastric-outlet obstruction induced by prostaglandin therapy in neonates. *N Engl J Med* 1992; **327:** 505–10.
2. Merkus PJFM, *et al.* Prostaglandin E1 and gastric outlet obstruction in infants. *Lancet* 1993; **342:** 747.
3. Kobayashi N, *et al.* Acute gastric outlet obstruction following the administration of prostaglandin: an additional case. *Pediatr Radiol* 1997; **27:** 57–9.

Effects on the metabolism. Severe hyperglycaemia with apparent ketoacidosis occurred during postoperative infusion of alprostadil in the infant of a diabetic mother.[1] The manufacturers had received reports of hyperglycaemia associated with alprostadil in 5 infants, one of whom had a diabetic mother. Hypoglycaemia has also been reported in a few infants.[2]

1. Cohen MH, Nihill MR. Postoperative ketotic hyperglycaemia during prostaglandin E infusion in infancy. *Pediatrics* 1983; **71:** 842–4.
2. Lewis AB, *et al.* Side effects of therapy with prostaglandin E in infants with critical congenital heart disease. *Circulation* 1981; **64:** 893–8.

Effects on the skin. A 63-year-old man with Peyronie's disease[1] developed toxic pustuloderma (acute generalised exanthematous pustulosis) 6 days after receiving a single intracavernosal injection of alprostadil to define the penile morphology. He was treated with antihistamines and topical corticosteroids and the condition resolved completely within a week.

1. Gallego I, *et al.* Toxic pustuloderma induced by intracavernous prostaglandin E . *Br J Dermatol* 1997; **136:** 975–6.

Priapism. If priapism (p.1333) occurs after the use of alprostadil for erectile dysfunction, its treatment should not be delayed more than 6 hours. Initial therapy is by penile aspiration. If aspiration is unsuccessful a sympathomimetic with action on alpha-adrenergic receptors is given by cautious intracavernosal injection, with continuous monitoring of blood pressure and pulse. Extreme caution is necessary in patients with coronary heart disease, hypertension, cerebral ischaemia, or if taking an antidepressant. Low doses and dilute solutions are recommended as follows:

- intracavernosal injection of phenylephrine 100 to 200 micrograms (0.5 to 1 mL of a 200 micrograms/mL solution) every 5 to 10 minutes; maximum total dose 1 mg

alternatively

- intracavernosal injection of adrenaline 10 to 20 micrograms (0.5 to 1 mL of a 20 micrograms/mL solution) every 5 to 10 minutes; maximum total dose 100 micrograms

alternatively

- intracavernosal injection of metaraminol may be used, but it should be noted that fatal hypertensive crises have been reported; metaraminol 100 micrograms (5 mL of a 20 micrograms/mL solution) may be given by careful slow injection every 15 minutes; a maximum total dose of up to 1 mg has been suggested

If necessary the sympathomimetic injections can be followed by further penile aspiration. If sympathomimetics are unsuccessful, urgent surgical referral is required.

Pharmacokinetics

On infusion alprostadil is rapidly metabolised by oxidation during passage through the pulmonary circulation. It is excreted in the urine as metabolites within about 24 hours. Systemic absorption of alprostadil occurs after intracavernosal injection.

◊ References.

1. Cox JW, *et al.* Pulmonary extraction and pharmacokinetics of prostaglandin E during continuous intravenous infusion in patients with adult respiratory distress syndrome. *Am Rev Respir Dis* 1988; **137:** 5–12.
2. Cawello W, *et al.* Dose proportional pharmacokinetics of alprostadil (prostaglandin E) in healthy volunteers following intravenous infusion. *Br J Clin Pharmacol* 1995; **40:** 273–6.
3. Lea AP, *et al.* Intracavernous alprostadil: a review of its pharmacodynamic and pharmacokinetic properties and therapeutic potential in erectile dysfunction. *Drugs Aging* 1996; **8:** 56–74.

Uses and Administration

Alprostadil is a prostaglandin (p.2374) that causes vasodilatation and prevents platelet aggregation. The endogenous substance is termed prostaglandin E_1. Alprostadil is used mainly in congenital heart disease and in erectile dysfunction (p.2179).

In the management of **erectile dysfunction**, alprostadil is given by intracavernosal injection; preparations may contain alprostadil or alprostadil alfadex, but the dose is expressed in terms of the base. Alprostadil may also be given as an intra-urethral application.

By *intracavernosal injection*, the initial dose should be low, for example 2.5 micrograms, and is increased incrementally until a suitable dose is established. Normally, the second dose should be 5 micrograms if some response to the first dose is observed, or 7.5 micrograms if there is no response; increments should then be of 5 to 10 micrograms until an effective dose is reached. The usual dose range is 5 to 20 micrograms and the maximum recommended dose is 60 micrograms. In cases of erectile dysfunction of neurogenic origin secondary to spinal cord injury an initial dose of 1.25 micrograms has been given, with a second dose of 2.5 micrograms, a third dose of 5 micrograms, and subsequent increments of 5 micrograms. While finding a suitable dose, the interval between doses should be at least 1 day if there has been a partial response. If there is no response however, the next, higher dose may be given within 1 hour. Once established, the optimal dose should be given not more than once daily and not more than three times per week.

Alprostadil may also be injected intracavernosally in the diagnosis of erectile dysfunction in doses ranging from 5 to 20 micrograms.

By *intra-urethral (transurethral) application*, the initial dose is 250 micrograms. The dose may be increased incrementally to 500 or 1000 micrograms or decreased to 125 micrograms according to response. The optimal dose should be given not more than twice daily or seven times per week. A dose of 500 micrograms may be used diagnostically.

Alprostadil is also available in some countries as a *topical* formulation for the treatment of erectile dysfunction. There is also ongoing investigation of the use of topical formulations for female sexual dysfunction.

Alprostadil is used to maintain the patency of the ductus arteriosus in neonates with **congenital heart disease** until surgery is possible. It is given by continuous intravenous infusion beginning with doses of 50 to 100 nanograms/kg per minute; doses should be reduced as soon as possible to the minimum necessary to maintain response. Lower starting doses may be effective in some patients. The dose can be increased to 400 nanograms/kg per minute but, in general, higher infusion rates do not improve effect. Alprostadil may also be given by continuous infusion through an umbilical artery catheter placed at the ductal opening.

Ergotamine poisoning. Alprostadil[1,2] is one of many drugs that have been used to treat the circulatory disturbances in ergotamine poisoning (p.620).

1. Levy JM, *et al.* Prostaglandin E for alleviating symptoms of ergot intoxication: a case report. *Cardiovasc Intervent Radiol* 1984; **7:** 28–30.
2. Horstmann R, *et al.* Kritische Extremitätenischämie durch Ergotismus. *Dtsch Med Wochenschr* 1993; **118:** 1067–71.

Haemorrhagic cystitis. Bladder irrigation with alprostadil produced resolution of severe haemorrhagic cystitis in 5 of 6 children who had undergone bone marrow transplantation.[1] Alprostadil was given via a catheter and retained for 1 hour each day for at least 7 consecutive days.

1. Trigg ME, *et al.* Prostaglandin E bladder instillations to control severe hemorrhagic cystitis. *J Urol (Baltimore)* 1990; **143:** 92–4.

Hepatic disorders. Benefit has been reported in patients with *viral hepatitis* (p.851) given intravenous alprostadil alone or followed by oral dinoprostone or misoprostol.[1,2] Prostaglandins were studied because they had previously been shown to have a cytoprotective effect in experimentally induced hepatitis or in isolated hepatocytes, but the mechanism by which they exerted a beneficial effect was uncertain.

Combined intravenous therapy with glucagon, insulin, and alprostadil formulated in lipid microspheres has also been found effective in preventing *acute fulminant hepatic failure* after hepatic arterial infusion of antineoplastic chemotherapy.[3]

1. Sinclair SB, *et al.* Biochemical and clinical response of fulminant viral hepatitis to administration of prostaglandin E: a preliminary report. *J Clin Invest* 1989; **84:** 1063–9.
2. Flowers M, *et al.* Prostaglandin E in the treatment of recurrent hepatitis B infection after orthotopic liver transplantation. *Transplantation* 1994; **58:** 183–92.
3. Ikegami T, *et al.* Randomized control trial of lipo-prostaglandin E in patients with acute liver injury induced by Lipiodol-targeted chemotherapy. *Clin Pharmacol Ther* 1995; **57:** 582–9.

Organ and tissue transplantation. Alprostadil and other prostaglandin analogues have been investigated in regimens for the management of solid organ transplantation, with variable results. For reference to the use of alprostadil in intestinal grafts see p.1813.

References.

1. Merion RM. Prostaglandins in liver transplantation. *Adv Exp Med Biol* 1997; **433:** 13–18.
2. Iberer F, *et al.* Prostaglandins in heart transplantation. *Adv Exp Med Biol* 1997; **433:** 19–22.
3. Ray JG. Prostaglandin E1 analogs do not improve renal function among either transplant or nontransplant patients: no further trials required. *Transplantation* 1998; **66:** 476–83.

Peripheral vascular disease. Various prostaglandins, including alprostadil,[1-7] have been used in the treatment of peripheral vascular disease (p.1178), particularly in severe Raynaud's syndrome, but do not constitute mainline therapy.

1. Clifford PC, *et al.* Treatment of vasospastic disease with prostaglandin E . *BMJ* 1980; **281:** 1031–4.
2. Telles GS, *et al.* Prostaglandin E in severe lower limb ischaemia: a double-blind controlled trial. *Br J Surg* 1984; **71:** 506–8.
3. Mohrland JS, *et al.* A multiclinic, placebo-controlled, double-blind study of prostaglandin E in Raynaud's syndrome. *Ann Rheum Dis* 1985; **44:** 754–60.
4. Sethi GK, *et al.* Intravenous infusion of prostaglandin E (PGE) in management of limb ischemia. *Am Surg* 1986; **52:** 474–8.
5. Langevitz P, *et al.* Treatment of refractory ischemic skin ulcers in patients with Raynaud's phenomenon with PGE infusions. *J Rheumatol* 1989; **16:** 1433–5.
6. The ICAI Study Group. Prostanoids for chronic critical leg ischemia: a randomized, controlled, open-label trial with prostaglandin E . *Ann Intern Med* 1999; **130:** 412–21.
7. Bartolone S, *et al.* Efficacy evaluation of prostaglandin E1 against placebo in patients with progressive systemic sclerosis and significant Raynaud's phenomenon. *Minerva Cardioangiol* 1999; **47:** 137–43.

Preparations

USP 31: Alprostadil Injection.

Proprietary Preparations (details are given in Part 3)

Arg.: Cardiobron; Caverject†; Prolisina VR; Prostavasin; ***Austral.:*** Caverject; Muse†; Prostin VR; ***Austria:*** Alprostapint; Caverject; Minprog; Muse; Prostavasin; Virilan; ***Belg.:*** Caverject; Prostin VR; ***Braz.:*** Apilcav†; Aplicav; Caverject; Muse†; Prostavasin; ***Canad.:*** Caverject; Muse; Prostin VR; ***Chile:*** Caverject; Prostin Pediatrico; ***Cz.:*** Alprostan; Alprostapint; Caverject; Edex†; Karon; Muse; Prostavasin; Prostin VR†; ***Denm.:*** Caverject; Muse; Prostivas; ***Fin.:*** Caverject; Muse; Prostivas; ***Fr.:*** Caverject; Edex; Muse; Prostine VR; ***Ger.:*** Caverject; Minprog; Muse; Prostavasin; Viridal; ***Gr.:*** Caverject; Edex†; Prostin VR; ***Hong Kong:*** Befar; Caverject; Prostavasin; Prostin VR; ***Hung.:*** Alprostapint; Caverject; Prostavasin; Prostin VR; ***India:*** Prostin VR; ***Irl.:*** Caverject; Muse; Viridal; ***Israel:*** Alprostapint; Caverject; Muse†; Prostin VR; ***Ital.:*** Alprostar; Caverject; Prostavasin; Prostin VR; Viridal; ***Jpn:*** Liple; Palux; Prostandin; ***Malaysia:*** Caverject; Prostin VR; ***Mex.:*** Caverject; Muse†; ***Neth.:*** Caverject; Muse; Prostin VR; ***Norw.:*** Bondil; Caverject; Prostivas; ***NZ:*** Caverject; Muse†; Prostin VR; ***Pol.:*** Caverject; Prostavasin; Prostin VR; ***Port.:*** Caverject; Muse; Prostin VR; Vasoprost; ***Rus.:*** Alprostan (Алпростан); Caverject (Каверджект); Vasaprostan (Вазапростан); Vazaprostan (Вазапростан); ***S.Afr.:*** Caverject; Muse; Prostin VR; ***Singapore:*** Caverject; Eglandin†; ***Spain:*** Caverject; Sugiran; ***Swed.:*** Bondil; Caverject; Prostivas; ***Switz.:*** Caverject; Muse; Prostin VR; ***Thai.:*** Caverject†; Muse†; Prostin VR; ***UK:*** Caverject; Muse; Prostin VR; Viridal; ***USA:*** Caverject; Edex; Muse; Prostin VR; ***Venez.:*** Caverject.

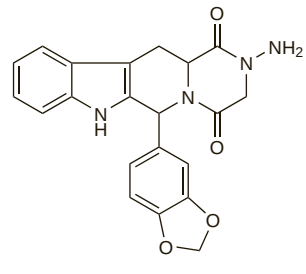
Multi-ingredient: ***USA:*** Tri-Mix.

Aminotadalafil

6-(1,3-Benzodioxol-5-yl)-2,3,6,7,12,12a-hexahydro-2-aminopyrazino[1′,2′:1,6]pyrido[3,4-b]indole-1,4-dione.

Аминотадалафил

$C_{21}H_{18}N_4O_4$ = 390.4.



Profile
Aminotadalafil is an analogue of tadalafil (p.2196) that has been used in various preparations or dietary supplements and illegally promoted in some countries for the management of erectile dysfunction.

Dapoxetine Hydrochloride *(USAN, rINNM)*

Dapoxétine, Chlorhydrate de; Dapoxetini Hydrochloridum; Hidrocloruro de dapoxetina; LY-210448 (dapoxetine). (+)-(*S*)-*N*,*N*-Dimethyl-alpha-[2-(1-naphthyloxy)ethyl]benzylamine hydrochloride.

Дапоксетина Гидрохлорид

$C_{21}H_{23}NO, HCl = 341.9$.

CAS — 119356-77-3 (dapoxetine); 129938-20-1 (dapoxetine hydrochloride).

Profile
Dapoxetine hydrochloride is a rapidly absorbed short-acting SSRI being investigated specifically for on-demand treatment of premature ejaculation (p.2181).

◊ References.

1. Pryor JL, *et al.* Efficacy and tolerability of dapoxetine in treatment of premature ejaculation: an integrated analysis of two double-blind, randomised controlled trials. *Lancet* 2006; **368:** 929–37.
2. Modi NB, *et al.* Single- and multiple-dose pharmacokinetics of dapoxetine hydrochloride, a novel agent for the treatment of premature ejaculation. *J Clin Pharmacol* 2006; **46:** 301–9.
3. Andersson KE, *et al.* Pharmacokinetic and pharmacodynamic features of dapoxetine, a novel drug for 'on-demand' treatment of premature ejaculation. *BJU Int* 2006; **97:** 311–15.
4. Dresser MJ, *et al.* Pharmacokinetics of dapoxetine, a new treatment for premature ejaculation: impact of age and effects of a high-fat meal. *J Clin Pharmacol* 2006; **46:** 1023–9.

Darifenacin *(BAN, USAN, rINN)*

Darifenacina; Darifénacine; Darifenacinum; UK-88525. (*S*)-1-[2-(2,3-Dihydro-5-benzofuranyl)ethyl]-α,α-diphenyl-3-pyrrolidineacetamide.

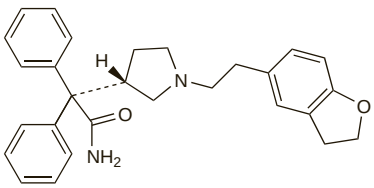
Дарифенацин

$C_{28}H_{30}N_2O_2 = 426.6$.

CAS — 133099-04-4.

ATC — G04BD10.

ATC Vet — QG04BD10.



Darifenacin Hydrobromide *(BANM, USAN, rINNM)*

Darifénacine, Bromhydrate de; Darifenacini Hydrobromidum; Hidrobromuro de darifenacina; UK-88525-04. (*S*)-2-{1-[2-(2,3-Dihydrobenzofuran-5-yl)ethyl]-3-pyrrolidnyl}-2,2-diphenylacetamide hydrobromide.

Дарифенацина Гидробромид

$C_{28}H_{30}N_2O_2,HBr = 507.5$.

CAS — 133099-07-7.

ATC — G04BD10.

ATC Vet — QG04BD10.

Adverse Effects, Treatment, and Precautions

As for Atropine Sulfate, p.1219. Darifenacin should be used with caution in patients also receiving inhibitors of cytochrome P450 isoenzymes (see Interactions and Uses and Administration, below). It should also be used with caution in hepatic impairment (see Administration in Hepatic Impairment, below).

Interactions

As for antimuscarinics in general (see Atropine Sulfate, p.1220). Exposure to darifenacin may be increased by drugs that inhibit the cytochrome P450 isoenzymes CYP2D6 and CYP3A4. Inducers of CYP3A4 may reduce plasma concentrations of darifenacin. Dosage adjustment for darifenacin may be necessary (see Uses and Administration, below). Darifenacin itself is also a moderate inhibitor of CYP2D6.

Pharmacokinetics

After an oral dose, darifenacin is subject to extensive first-pass metabolism and has a bioavailability of about 15 to 19%. It is about 98% bound to plasma proteins. Darifenacin is metabolised in the liver by the cytochrome P450 isoenzymes CYP2D6 and CYP3A4. The pharmacokinetics of darifenacin at steady state are dose-dependent because of the saturation of CYP2D6 metabolism. Most of a dose is excreted as metabolites in the urine and faeces.

◊ References.

1. Kerbusch T, *et al.* Population pharmacokinetic modelling of darifenacin and its hydroxylated metabolite using pooled data, incorporating saturable first-pass metabolism, CYP2D6 genotype and formulation-dependent bioavailability. *Br J Clin Pharmacol* 2003; **56:** 639–52.
2. Devineni D, *et al.* Pharmacokinetics of darifenacin, an M selective receptor antagonist: effects of renal or hepatic impairment. *Br J Clin Pharmacol* 2005; **59:** 632–3.
3. Skerjanec A. The clinical pharmacokinetics of darifenacin. *Clin Pharmacokinet* 2006; **45:** 325–50.

Uses and Administration

Darifenacin is a selective M_3 antimuscarinic with actions similar to those of atropine (p.1220); it is claimed to have a greater selectivity for the muscarinic receptors of the bladder.

Darifenacin is used in the management of urinary frequency, urgency, and incontinence in detrusor instability (p.2180). It is given orally as the hydrobromide but doses are described in terms of the base: darifenacin hydrobromide 8.9 mg is equivalent to about 7.5 mg of darifenacin. The usual initial dose is the equivalent of darifenacin 7.5 mg once daily; after 2 weeks of treatment this may be increased to 15 mg once daily if necessary.

The starting dose of 7.5 mg should only be increased with caution in patients also receiving potent inhibitors of the cytochrome P450 isoenzyme CYP2D6, such as paroxetine and terbinafine. Darifenacin should be avoided, or a dose of 7.5 mg daily not exceeded, in patients also receiving potent inhibitors of CYP3A4, such as HIV-protease inhibitors, ketoconazole, and itraconazole. The dose of darifenacin should be increased with caution in the presence of moderate inhibitors of CYP3A4, such as macrolide antibacterials, fluconazole, and grapefruit juice.

Darifenacin should be used with caution in hepatic impairment, see below.

Darifenacin is being studied in irritable bowel syndrome.

◊ References.

1. Haab F, *et al.* Darifenacin, an M selective receptor antagonist, is an effective and well-tolerated once-daily treatment for overactive bladder. *Eur Urol* 2004; **45:** 420–9.
2. Chapple C, *et al.* A pooled analysis of three phase III studies to investigate the efficacy, tolerability and safety of darifenacin, a muscarinic M selective receptor antagonist, in the treatment of overactive bladder. *BJU Int* 2005; **95:** 993–1001.
3. Foote J, *et al.* Treatment of overactive bladder in the older patient: pooled analysis of three phase III studies of darifenacin, an M selective receptor antagonist. *Eur Urol* 2005; **48:** 471–7.
4. Parsons M, *et al.* Darifenacin in the treatment of overactive bladder. *Int J Clin Pract* 2005; **59:** 831–8.

Administration in hepatic impairment. Licensed product information states that the dose of darifenacin should not exceed 7.5 mg once daily in patients with moderate hepatic impairment (Child-Pugh category B), and its use should be avoided in severe impairment (Child-Pugh category C).

Preparations

Proprietary Preparations (details are given in Part 3)
Cz.: Emselex; ***Ger.:*** Emselex; ***Gr.:*** Emselex; ***Hung.:*** Emselex; ***Neth.:*** Emselex; ***S.Afr.:*** Enablex; ***Swed.:*** Emselex; ***UK:*** Emselex; ***USA:*** Enablex.

Desmopressin *(BAN, rINN)*

DDAVP; Desmopresina; Desmopresinas; Desmopressiini; Desmopressine; Desmopressinum; Dezmopresszin. 1-(3-Mercaptopropionic acid)-8-D-arginine-vasopressin; [1-Deamino,8-D-arginine]vasopressin.

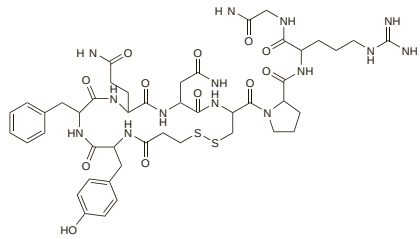
Дезмопрессин

$C_{46}H_{64}N_{14}O_{12}S_2 = 1069.2$.

CAS — 16679-58-6.

ATC — H01BA02.

ATC Vet — QH01BA02.



Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Desmopressin). A synthetic cyclic nonapeptide, available as an acetate. A white or almost white, fluffy powder. Soluble in water, in alcohol, and in glacial acetic acid. Store in airtight containers at 2° to 8°. Protect from light.

Desmopressin Acetate *(BANM, USAN, rINNM)*

Acetato de desmopresina; Desmopresin Asetat; Desmopressine, Acétate de; Desmopressini Acetas.

Дезмопрессина Ацетат

$C_{46}H_{64}N_{14}O_{12}S_2,C_2H_4O_2,3H_2O = 1183.3$.

CAS — 62288-83-9 (anhydrous desmopressin acetate); 62357-86-2 (desmopressin acetate trihydrate).

ATC — H01BA02.

ATC Vet — QH01BA02.

Pharmacopoeias. In *US*.
USP 31 (Desmopressin Acetate). A white, fluffy powder. Soluble in water, in alcohol, and in acetic acid. Store in airtight containers at a temperature not exceeding 25°, but preferably between 2° and 8°. Protect from light.

Units

27 units of desmopressin are contained in about 27 micrograms of desmopressin (with 5 mg of human albumin and citric acid) in one ampoule of the first International Standard (1980).

Adverse Effects and Precautions

Adverse effects of desmopressin include headache, nausea, and mild abdominal cramps; there may be pain and swelling at the site of injection. With large intravenous doses hypotension, with tachycardia and facial flushing, may occur; some patients may experience an increase in blood pressure. Occasionally there may be cerebral or coronary thrombosis. Hypersensitivity reactions have also occurred. The antidiuretic action of desmopressin can produce water intoxication and hyponatraemia, occasionally leading to convulsions. The incidence of hyponatraemia may be higher with nasal formulations than with oral formulations. Nasal doses may cause local irritation, congestion, and epistaxis.

Precautions to be observed with desmopressin are similar to those for vasopressin (see p.2412). It should not be given to patients with type IIB von Willebrand's disease, in whom the release of clotting factors may lead to platelet aggregation and thrombocytopenia. When desmopressin is used diagnostically, or for the treatment of enuresis, the fluid intake should be limited to a minimum and only to satisfy thirst from 1 hour before to 8 hours after use (see also Effects on Electrolytes, below).

Effects on the cardiovascular system. Facial flushing and warmth after intravenous desmopressin reflect a vasodilator action[1] or may be due to an opioid mechanism in the CNS.[2] A drop in diastolic blood pressure of about 14 mmHg and an increase in heart rate of 20 beats/minute are the rule during intravenous infusion of desmopressin in doses of 400 nanograms/kg or more.[1] The hypotensive effects of desmopressin were responsible for a serious reaction, involving cyanosis and dyspnoea, in a 21-month-old child with cyanotic heart disease.[3] Thrombosis (including myocardial infarction)[4-6] and cerebral infarction[7] have been associated rarely with the use of intravenous desmopressin. An analysis[8] of events in patients undergoing major surgery suggested, however, that co-existing conditions in elderly patients and the surgical procedures themselves were associated with a high risk of thrombosis, and that desmopressin did not increase the incidence of thrombotic events.

Licensed product information also warns of the possibility of an increase in blood pressure.

1. Brommer EJP, *et al.* Desmopressin and hypotension. *Ann Intern Med* 1985; **103:** 962.