Inositol Nicotinate *(BAN, rINN)*

Inositol Niacinate *(USAN)*; Inositol, Nicotinate d'; Inositoli Nicotinas; Inositolinikotinaatti; Inositolnikotinat; Nicotinato de inositol; NSC-49506; Win-9154. *meso*-Inositol hexanicotinate; *myo*-Inositol hexanicotinate.

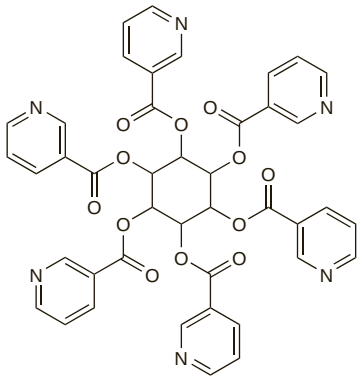
Инозитола Никотинат

$C_{42}H_{30}N_6O_{12}$ = 810.7.

CAS — 6556-11-2.

ATC — C04AC03.

ATC Vet — QC04AC03.



Pharmacopoeias. In *Br.*

BP 2008 (Inositol Nicotinate). A white or almost white, odourless or almost odourless powder. Practically insoluble in water, in alcohol, in acetone, and in ether; sparingly soluble in chloroform. It dissolves in dilute mineral acids.

Profile

Inositol nicotinate is a vasodilator and is believed to be slowly hydrolysed to nicotinic acid (p.1957). It is given orally in the management of peripheral vascular disease (p.1178). The usual dose is 3 g daily given in divided doses. The dose may be increased to 4 g daily if necessary.

Inositol nicotinate has been used in hyperlipidaemias.

Preparations

BP 2008: Inositol Nicotinate Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Evicyl†; ***Ger.:*** Hamovannad†; Nicolip; ***Irl.:*** Hexogen†; Hexopal; ***Neth.:*** Palohex; ***UK:*** Hexopal.

Multi-ingredient: ***Ger.:*** Zellaforte N Plus†; ***S.Afr.:*** Geratar.

Irbesartan *(BAN, USAN, rINN)*

BMS-186295; Irbesartaani; Irbésartan; Irbesartán; Irbesartanum; SR-47436. 2-Butyl-3-[*p*-(*o*-1*H*-tetrazol-5-ylphenyl)benzyl]-1,3-diazaspiro[4.4]non-1-en-4-one.

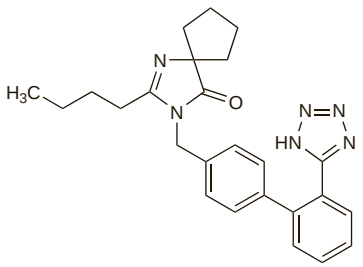
Ирбесартан

$C_{25}H_{28}N_6O$ = 428.5.

CAS — 138402-11-6.

ATC — C09CA04.

ATC Vet — QC09CA04.



Pharmacopoeias. In *US.*

USP 31 (Irbesartan). A white to off-white, crystalline powder. Practically insoluble in water; slightly soluble in alcohol and in dichloromethane. Store in airtight containers at a temperature below 30°.

Adverse Effects and Precautions

As for Losartan Potassium, p.1326.

Interactions

As for Losartan Potassium, p.1327.

Pharmacokinetics

Irbesartan is rapidly absorbed from the gastrointestinal tract with an oral bioavailability of 60 to 80%. Peak plasma concentrations of irbesartan occur 1.5 to 2 hours after an oral dose. Irbesartan is about 96% bound to plasma proteins. It undergoes some metabolism in the liver, primarily by the cytochrome P450 isoenzyme CYP2C9, to inactive metabolites. It is excreted as unchanged drug and metabolites in the bile and in urine; about 20% of an oral or intravenous dose is excreted in the urine, with less than 2% as unchanged drug. The terminal elimination half-life is about 11 to 15 hours.

◊ References.

1. Sica DA, *et al.* The pharmacokinetics of irbesartan in renal failure and maintenance hemodialysis. *Clin Pharmacol Ther* 1997; **62:** 610–18.
2. Marino MR, *et al.* Pharmacokinetics and pharmacodynamics of irbesartan in healthy subjects. *J Clin Pharmacol* 1998; **38:** 246–55.
3. Marino MR, *et al.* Pharmacokinetics and pharmacodynamics of irbesartan in patients with hepatic cirrhosis. *J Clin Pharmacol* 1998; **38:** 347–56.
4. Vachharajani NN, *et al.* Oral bioavailability and disposition characteristics of irbesartan, an angiotensin antagonist, in healthy volunteers. *J Clin Pharmacol* 1998; **38:** 702–7.
5. Vachharajani NN, *et al.* The effects of age and gender on the pharmacokinetics of irbesartan. *Br J Clin Pharmacol* 1998; **46:** 611–13.
6. Sakarcan A, *et al.* The pharmacokinetics of irbesartan in hypertensive children and adolescents. *J Clin Pharmacol* 2001; **41:** 742–9.

Uses and Administration

Irbesartan is an angiotensin II receptor antagonist with actions similar to those of losartan (p.1327). It is used in the management of hypertension (p.1171) including the treatment of renal disease in hypertensive diabetic patients (see Kidney Disorders, under Uses of Losartan, p.1328). Irbesartan is also under investigation in heart failure.

Irbesartan is given orally. After a dose the hypotensive effect peaks within 3 to 6 hours and persists for at least 24 hours. The maximum hypotensive effect is achieved within 4 to 6 weeks after starting therapy.

In **hypertension**, irbesartan is given in a dose of 150 mg once daily increased, if necessary, to 300 mg once daily. A lower initial dose of 75 mg once daily may be considered in elderly patients over 75 years, for patients with intravascular volume depletion, and for those receiving haemodialysis.

For the treatment of **renal disease** in hypertensive type 2 diabetics, irbesartan should be given in an initial dose of 150 mg once daily, increased to 300 mg once daily for maintenance.

◊ Reviews.

1. Gillis JC, Markham A. Irbesartan: a review of its pharmacodynamic and pharmacokinetic properties and therapeutic use in the management of hypertension. *Drugs* 1997; **54:** 885–902.
2. Brown MJ. Irbesartan treatment in hypertension. *Hosp Med* 1998; **59:** 808–11.
3. Markham A, *et al.* Irbesartan: an updated review of its use in cardiovascular disorders. *Drugs* 2000; **59:** 1187–1206.
4. Croom KF, *et al.* Irbesartan: a review of its use in hypertension and in the management of diabetic nephropathy. *Drugs* 2004; **64:** 999–1028.
5. Ravera M, *et al.* Prevention and treatment of diabetic nephropathy: the program for irbesartan mortality and morbidity evaluation. *J Am Soc Nephrol* 2005; **16** (suppl 1): S48–S52.
6. Palmer AJ, *et al.* Irbesartan treatment of patients with type 2 diabetes, hypertension and renal disease: a UK health economics analysis. *Int J Clin Pract* 2007; **61:** 1626–33.
7. Flack JM. Maximising antihypertensive effects of angiotensin II receptor blockers with thiazide diuretic combination therapy: focus on irbesartan/hydrochlorothiazide. *Int J Clin Pract* 2007; **61:** 2093–1102.

Administration in children. Although irbesartan appears to be well-tolerated in children with hypertension and has been shown to reduce blood pressure in small studies,[1] US licensed product information notes that doses of up to 4.5 mg/kg once daily were ineffective in children aged 6 to 16 years and no longer recommends use in such patients.

In children with chronic kidney diseases, irbesartan has been reported to reduce blood pressure and proteinuria.[2,3] The initial dose was 37.5 mg once daily for children weighing 10 to 20 kg, 75 mg once daily for those weighing 21 to 40 kg, and 150 mg once daily for those weighing more than 40 kg; doses could be doubled if the blood pressure response was inadequate.

1. Sakarcan A, *et al.* The pharmacokinetics of irbesartan in hypertensive children and adolescents. *J Clin Pharmacol* 2001; **41:** 742–9.
2. Franscini LMD, *et al.* Effectiveness and safety of the angiotensin II antagonist irbesartan in children with chronic kidney diseases. *Am J Hypertens* 2002; **15:** 1057–63.
3. Gartenmann AC, *et al.* Better renoprotective effect of angiotensin II antagonist compared to dihydropyridine calcium channel blocker in childhood. *Kidney Int* 2003; **64:** 1450–4.

Preparations

USP 31: Irbesartan and Hydrochlorothiazide Tablets; Irbesartan Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Adana; Aprovel; Avapro; ***Austral.:*** Avapro; Karvea; ***Belg.:*** Aprovel; ***Braz.:*** Aprovel; Avapro; ***Canad.:*** Avapro; ***Chile:*** Aprovel; ***Cz.:*** Aprovel; Karvea; ***Denm.:*** Aprovel; ***Fin.:*** Aprovel; ***Fr.:*** Aprovel; ***Ger.:*** Aprovel; Karvea; ***Gr.:*** Aprovel; Karvea; ***Hong Kong:*** Aprovel; ***Hung.:*** Aprovel; ***India:*** Iroveł; Xarb; ***Indon.:*** Aprovel; Fristens; Iretensa; Irvell; ***Irl.:*** Aprovel; ***Israel:*** Irban†; ***Ital.:*** Aprovel; Karvea; ***Malaysia:*** Aprovel; ***Mex.:*** Aprovel; Avapro; ***Neth.:*** Aprovel; Karvea; ***Norw.:*** Aprovel; ***NZ:*** Karvea; ***Philipp.:*** Aprovel; ***Pol.:*** Aprovel; ***Port.:*** Aprovel; Karvea; ***Rus.:*** Aprovel (Апровель); ***S.Afr.:*** Aprovel; ***Singapore:*** Aprovel; ***Spain:*** Aprovel; Karvea; ***Swed.:*** Aprovel; ***Switz.:*** Aprovel; ***Thai.:*** Aprovel; ***Turk.:*** Karvea; ***UK:*** Aprovel; ***USA:*** Avapro; ***Venez.:*** Aprovel.

Multi-ingredient: ***Arg.:*** Adana Plus; Avapro HCT; CoAprovel; ***Austral.:*** Avapro HCT; Karvezide; ***Belg.:*** CoAprovel; ***Braz.:*** Aprozide; ***Canad.:*** Avalide; ***Chile:*** CoAprovel; ***Cz.:*** CoAprovel; Karvezide; ***Denm.:*** CoAprovel; ***Fr.:*** CoAprovel; ***Ger.:*** CoAprovel; Karvezide; ***Gr.:*** CoAprovel; Karvezide; ***Hong Kong:*** Aprovel HCT†; CoAprovel; ***Hung.:*** CoAprovel; ***India:*** Xarb-H; ***Indon.:*** CoAprovel; Irtan Plus; ***Irl.:*** CoAprovel; ***Israel:*** Irban Plus†; ***Ital.:*** CoAprovel; Karvezide; ***Malaysia:*** CoAprovel; ***Mex.:*** Avalide; CoAprovel; ***Neth.:*** CoAprovel; Karvezide; ***Norw.:*** CoAprovel; ***NZ:*** Karvezide; ***Philipp.:*** CoAprovel; ***Port.:*** CoAprovel; Karvezide; ***S.Afr.:*** CoAprovel; ***Singapore:*** CoAprovel; ***Spain:*** CoAprovel; Karvezide; ***Swed.:*** CoAprovel; ***Switz.:*** CoAprovel; ***Thai.:*** Aprovel HCT†; CoAprovel; ***Turk.:*** Karvezide; ***UK:*** CoAprovel; ***USA:*** Avalide; ***Venez.:*** CoAprovel.

Isoprenaline *(BAN, rINN)* ⊗

Isoprenaliini; Isoprenalin; Isoprenalina; Isoprénaline; Isoprenalinum; Isopropylarterenol; Isopropylnoradrenaline; Isoproterenol. 1-(3,4-Dihydroxyphenyl)-2-isopropylaminoethanol.

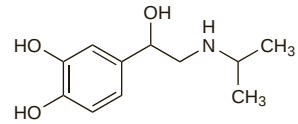
Изопреналин

$C_{11}H_{17}NO_3$ = 211.3.

CAS — 7683-59-2.

ATC — C01CA02; R03AB02; R03CB01.

ATC Vet — QC01CA02; QR03AB02; QR03CB01.



Isoprenaline Hydrochloride *(BANM, rINNM)* ⊗

Hidrocloruro de isoprenalina; Isoprenaliinihydrokloridi; Isoprénaline, chlorhydrate d'; Isoprenalin-hydrochlorid; Isoprenalinhydroklorid; Isoprenalini hydrochloridum; Isopropylarterenol Hydrochloride; Isopropylnoradrenaline Hydrochloride; Isoproterenol Hydrochloride; Izoprenalin Hidroklorür; Izoprenalin-hidroklorid; Izoprenalino hidrochloridas.

Изопреналина Гидрохлорид

$C_{11}H_{17}NO_3$,HCl = 247.7.

CAS — 51-30-9.

ATC — C01CA02; R03AB02; R03CB01.

ATC Vet — QC01CA02; QR03AB02; QR03CB01.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US.*

Ph. Eur. 6.2 (Isoprenaline Hydrochloride). A white or almost white crystalline powder. Freely soluble in water; sparingly soluble in alcohol; practically insoluble in dichloromethane. A 5% solution in water has a pH of 4.3 to 5.5. Store in airtight containers. Protect from light.

USP 31 (Isoproterenol Hydrochloride). A white to practically white, odourless, crystalline powder. It gradually darkens on exposure to air and light. Soluble 1 in 3 of water and 1 in 50 of alcohol; less soluble in dehydrated alcohol; insoluble in chloroform and in ether. A 1% solution in water has a pH of about 5. Solutions become pink to brownish-pink on standing exposed to air and almost immediately so when made alkaline. Store in airtight containers. Protect from light.

Isoprenaline Sulfate *(rINNM)* ⊗

Isoprenaliinisulfaatti; Isoprenalin sulfát dihydrát; Isoprénaline, sulfate d'; Isoprenaline Sulphate *(BANM)*; Isoprenalini sulfas; Isoprenalini Sulfas Dihydricus; Isoprenalinsulfat; Isopropylarterenol Sulphate; Isopropylnoradrenaline Sulphate; Isoproterenol Sulfate; Izoprenalino sulfatas; Izoprenalin-szulfát; Izoprenaliny siarczan; Sulfato de isoprenalina.

Изопреналина Сульфат

$(C_{11}H_{17}NO_3)_2,H_2SO_4,2H_2O$ = 556.6.

CAS — 299-95-6 (anhydrous isoprenaline sulfate); 6700-39-6 (isoprenaline sulfate dihydrate).

ATC — C01CA02; R03AB02; R03CB01.

ATC Vet — QC01CA02; QR03AB02; QR03CB01.

Pharmacopoeias. In *Eur.* (see p.vii), *Int.*, and *US*.
Ph. Eur. 6.2 (Isoprenaline Sulphate). A white or almost white crystalline powder. Freely soluble in water; very slightly soluble in alcohol. A 5% solution in water has a pH of 4.3 to 5.5. Store in airtight containers. Protect from light.
USP 31 (Isoproterenol Sulfate). A white to practically white, odourless, crystalline powder. It gradually darkens on exposure to light and air. Soluble 1 in 4 of water; very slightly soluble in alcohol, in chloroform, in ether, and in benzene. A 1% solution in water has a pH of about 5. Solutions become pink to brownish-pink on standing exposed to air, and almost immediately so when made alkaline. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

As for Sympathomimetics, p.1407. Isoprenaline has almost exclusively beta-agonist properties but also stimulates the CNS; its main adverse effects include tachycardia and cardiac arrhythmias, palpitations, hypotension, tremor, headache, sweating, and facial flushing. Prolonged use of isoprenaline has been associated with swelling of the parotid glands.

Prolonged use of sublingual tablets may also cause severe damage to the teeth due to the acidic nature of the drug. Sublingual use or inhalation may colour the saliva or sputum red.

Increased mortality. For a discussion of the increased mortality and morbidity that has sometimes been observed in asthmatic patients using beta agonists and reference to an early epidemic associated with isoprenaline inhalers, see Fenoterol, p.1121.

Interactions

As for Sympathomimetics, p.1407. Due to the risk of arrhythmias, isoprenaline should not be used with other potent beta$_1$ agonists such as adrenaline.

Theophylline. For reports of increased theophylline clearance following use of isoprenaline, see p.1145.

Pharmacokinetics

As a result of sulfate conjugation in the gut, isoprenaline is considerably less active orally than after parenteral doses. It is absorbed through the oral mucosa and has accordingly been given sublingually, but absorption by this route remains very erratic. Isoprenaline in the body is resistant to metabolism by monoamine oxidase, but is metabolised by catechol-*O*-methyltransferase in the liver, lungs, and other tissues, the metabolite then being conjugated before excretion in the urine. Whereas the sulfate conjugate of isoprenaline is inactive the methylated metabolite exhibits weak activity.

After intravenous injection isoprenaline has a plasma half-life of about one to several minutes according to whether the rate of injection is rapid or slow; it is almost entirely excreted in the urine as unchanged drug and metabolites within 24 hours. A much slower onset of action and a more extended initial half-life has been found after oral dosage. Isoprenaline is reported to have a duration of action of up to about 2 hours after inhalation; it has been shown that a large proportion of an inhaled dose is swallowed.

◊ References.

1. Blackwell EW, *et al.* The fate of isoprenaline administered by pressurized aerosols. *Br J Pharmacol* 1970; **39:** 194P–195P.
2. Conolly ME, *et al.* Metabolism of isoprenaline in dog and man. *Br J Pharmacol* 1972; **46:** 458–72.
3. Blackwell EW, *et al.* Metabolism of isoprenaline after aerosol and direct intrabronchial administration in man and dog. *Br J Pharmacol* 1974; **50:** 587–91.
4. Reyes G, *et al.* The pharmacokinetics of isoproterenol in critically ill pediatric patients. *J Clin Pharmacol* 1993; **33:** 29–34.

Uses and Administration

Isoprenaline is a sympathomimetic (p.1408) that acts almost exclusively on beta-adrenergic receptors. It has a powerful stimulating action on the heart and increases cardiac output, excitability, and rate; it also causes peripheral vasodilatation and produces a fall in diastolic blood pressure and usually maintains or slightly increases systolic blood pressure. In addition, isoprenaline has bronchodilating properties. It also stimulates the CNS.

Isoprenaline has been used in a variety of cardiac disorders. It may be used for the temporary prevention or control of Stokes-Adams attacks and in severe bradycardia unresponsive to atropine, but use of a pacemaker is preferred. It has also been advocated as an adjunct for other cardiac disorders including shock (p.1183) and torsade de pointes (see Cardiac Arrhythmias, p.1160). It has been used in the diagnosis of congenital heart defects.

In the management of **cardiac disorders**, isoprenaline is usually given as the hydrochloride by slow intravenous infusion under ECG control. Infusion rates may range from 0.5 to 10 micrograms/minute depending on the clinical condition of the patient; 1 to 4 micrograms/minute may be adequate to correct bradycardia but rates of 4 to 8 micrograms/minute may be required for acute Stokes-Adams attacks. Isoprenaline hydrochloride can be given by intracardiac injection in extreme cases. It has also been given subcutaneously or intramuscularly in initial doses of 200 micrograms (as 1 mL of a 0.02% solution) and by slow intravenous injection in initial doses of 20 to 60 micrograms (as 1 to 3 mL of a 0.002% solution); doses are subsequently adjusted according to ventricular rate. Tablets of isoprenaline hydrochloride have been given orally or sublingually.

Isoprenaline has been used as a bronchodilator in the management of **reversible airways obstruction** but sympathomimetics with a selective action on beta$_2$ receptors, such as salbutamol, are now preferred (see Asthma, p.1108). It has been given as the sulfate or hydrochloride, usually by inhalation; sublingual tablets and intravenous injections have also been used.

Preparations

BP 2008: Isoprenaline Injection;
USP 31: Acetylcysteine and Isoproterenol Hydrochloride Inhalation Solution; Isoproterenol Hydrochloride and Phenylephrine Bitartrate Inhalation Aerosol; Isoproterenol Hydrochloride Inhalation Aerosol; Isoproterenol Hydrochloride Injection; Isoproterenol Hydrochloride Tablets; Isoproterenol Inhalation Solution; Isoproterenol Sulfate Inhalation Aerosol; Isoproterenol Sulfate Inhalation Solution.

Proprietary Preparations (details are given in Part 3)
Arg.: Ciapar†; Proterenal†; ***Austral.:*** Isuprel; ***Austria:*** Ingelan; ***Belg.:*** Isuprel; ***Cz.:*** Isuprel; ***Fr.:*** Isuprel; ***Ger.:*** Ingelan†; ***Gr.:*** Isuprel†; Saventrine†; ***Hung.:*** Isuprel†; ***India:*** Autohaler†; Isolin; ***Indon.:*** Isuprel; ***Irl.:*** Saventrine†; ***Israel:*** Isuprel; ***NZ:*** Isuprel; ***S.Afr.:*** Imuprel; Lenoprel†; ***Singapore:*** Isuprel†; Saventrine†; ***Spain:*** Aleudrina; ***Thai.:*** Isuprel; ***USA:*** Isuprel; Medihaler-Iso.

Multi-ingredient: ***Arg.:*** Zantril†; ***Austria:*** Ingelan; ***Ger.:*** Ingelan†; ***Mex.:*** Isobutil†; ***Port.:*** Prelus†; ***Spain:*** Aldo Asma; Frenal Compositum; ***USA:*** Norisodrine with Calcium Iodide.

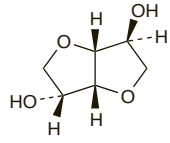
Isosorbide *(BAN, USAN, rINN)* ⊗

AT-101; Isosorbida; Isosorbidum; NSC-40725. 1,4:3,6-Dianhydro-D-glucitol.

Изосорбид

$C_6H_{10}O_4$ = 146.1.

CAS — 652-67-5.



Pharmacopoeias. In *Jpn.*
US includes Isosorbide Concentrate.
USP 31 (Isosorbide Concentrate). An aqueous solution containing 70.0 to 80.0% w/w of isosorbide. A colourless to slightly yellow liquid. Soluble in water and in alcohol. Store in airtight containers. Protect from light.

Profile

Isosorbide is an osmotic diuretic with properties similar to those of mannitol (p.1330). It is reported to cause less nausea and vomiting than other oral osmotic diuretics.

Isosorbide is used for short-term reduction of intra-ocular pressure in acute glaucoma or prior to surgery (p.1873). The usual oral dose is 1 to 3 g/kg 2 to 4 times daily. The onset of action is usually within 30 minutes and lasts for up to 5 or 6 hours.

Preparations

USP 31: Isosorbide Concentrate; Isosorbide Oral Solution.

Proprietary Preparations (details are given in Part 3)
Mex.: Biordyn; ***USA:*** Ismotic.

Isosorbide Dinitrate *(BAN, USAN, rINN)*

Dinitrato de isosorbida; ISDN; Isosorbid dinitrát; Isosorbiddinitrat; Isosorbide, dinitrate d'; Isosorbidi dinitras; Isosorbididinitraatti; Izosorbid Dinitrat; Izosorbido dinitratas; Izosorbidu diazotan; Izoszorbid-dinitrát; Sorbide Nitrate. 1,4:3,6-Dianhydro-D-glucitol 2,5-dinitrate.

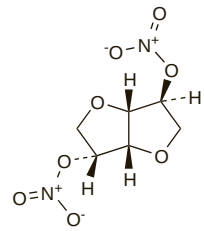
Изосорбида Динитрат

$C_6H_8N_2O_8$ = 236.1.

CAS — 87-33-2.

ATC — C01DA08; C05AE02.

ATC Vet — QC01DA08; QC05AE02.



Pharmacopoeias. In *Chin.* and *Jpn.*
Eur. (see p.vii), *Int.*, and *US* include diluted isosorbide dinitrate.
Ph. Eur. 6.2 (Isosorbide Dinitrate, Diluted). A dry mixture of isosorbide dinitrate and lactose monohydrate or mannitol. The solubility of the diluted product depends on the diluent and its concentration. Protect from light.
Undiluted isosorbide dinitrate is a fine, white or almost white, crystalline powder. Very slightly soluble in water; sparingly soluble in alcohol; very soluble in acetone.
USP 31 (Diluted Isosorbide Dinitrate). A dry mixture of isosorbide dinitrate (usually about 25%) with lactose, mannitol, or other suitable inert excipients, the latter being added to minimise the risk of explosion. It may contain up to 1% of a suitable stabiliser such as ammonium phosphate. It is an ivory-white, odourless powder. Store in airtight containers.
Undiluted isosorbide dinitrate occurs as white crystalline rosettes. Very slightly soluble in water; sparingly soluble in alcohol; very soluble in acetone; freely soluble in chloroform.

Handling. Undiluted isosorbide dinitrate may explode if subjected to percussion or excessive heat.

Stability. The loss of isosorbide dinitrate from solution during infusion was found to be 30% with PVC plastic intravenous infusion sets but negligible when polyolefin or glass delivery systems were used.[1] Another study reported a 23% decrease in isosorbide dinitrate concentration after 24 hours of storage at 21° in PVC containers; most of the loss occurred in the first 6 hours. Loss of potency was not noted when isosorbide dinitrate was stored under similar conditions in glass bottles or polyethylene, nylon, and polypropylene laminated bags.[2]

1. Kowaluk EA, *et al.* Drug loss in polyolefin infusion systems. *Am J Hosp Pharm* 1983; **40:** 118–19.
2. Martens HJ, *et al.* Sorption of various drugs in polyvinyl chloride, glass, and polyethylene-lined infusion containers. *Am J Hosp Pharm* 1990; **47:** 369–73.

Adverse Effects, Treatment, and Precautions

As for Glyceryl Trinitrate, p.1296.

Effects on the blood. Haemolysis occurred in 2 patients with G6PD deficiency during treatment with isosorbide dinitrate.[1]

1. Aderka D, *et al.* Isosorbide dinitrate-induced hemolysis in G6PD-deficient subjects. *Acta Haematol (Basel)* 1983; **69:** 63–4.

Headache. The most common adverse effect of nitrate therapy is headache which usually decreases after a few days. There has been a report[1] of a severe continuous unilateral headache with an oculosympathetic paresis on the same side associated with isosorbide dinitrate therapy.

1. Mueller RA, Meienberg O. Hemicrania with oculosympathetic paresis from isosorbide dinitrate. *N Engl J Med* 1983; **308:** 458–9.

Hypersensitivity. Laryngeal oedema developed on two occasions in a woman after the use of isosorbide dinitrate spray;[1] nifedipine was also given sublingually which on the second occasion caused a noticeable increase in the laryngeal swelling induced by the nitrate.

1. Silfvast T, *et al.* Laryngeal oedema after isosorbide dinitrate spray and sublingual nifedipine. *BMJ* 1995; **311:** 232.

Nitrate tolerance. Continuous use of organic nitrates is associated with tolerance to their haemodynamic effects; for an overview of nitrate tolerance, see under Precautions for Glyceryl Trinitrate, p.1297.