Rotavirus diarrhoea. A randomised double-blind placebo-controlled study[1] in 38 young children (median age 11 months) with confirmed rotavirus diarrhoea found that oral nitazoxanide 7.5 mg/kg twice daily for 3 days significantly reduced the duration of rotavirus disease. The median time to resolution of illness after the first dose was 31 hours for those given nitazoxanide compared with 75 hours for those in the placebo group.

1. Rossignol J-F, *et al.* Effect of nitazoxanide for treatment of severe rotavirus diarrhoea: randomised double-blind placebo-controlled trial. *Lancet* 2006; **368:** 124–9.

Worm infections. Nitazoxanide has been used in various helminthiases, including ascariasis (p.134), hymenolepiasis (p.136), the liver fluke infection fascioliasis (p.137), and trichuriasis (p.139).

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Heliton†; Nixoran; ***Braz.:*** Annita; ***Mex.:*** Bionit; Daxon; Kidonax; Mitafar; NTZ†; Padovan Ton; Paramix; Rosanil; ***USA:*** Alinia; ***Venez.:*** Celectan.

Multi-ingredient: ***Mex.:*** Heliton.

Ornidazole *(USAN, rINN)*

Ornidatsoli; Ornidazol; Ornidazolum; Ro-7-0207. 1-Chloro-3-(2-methyl-5-nitroimidazol-1-yl)propan-2-ol.

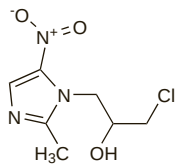
Орнидазол

$C_7H_{10}ClN_3O_3$ = 219.6.

CAS — 16773-42-5.

ATC — G01AF06; J01XD03; P01AB03.

ATC Vet — QG01AF06; QJ01XD03; QP51AA03.



Adverse Effects and Precautions

As for Metronidazole, p.837.

Pharmacokinetics

Ornidazole is readily absorbed from the gastrointestinal tract and peak plasma concentrations are reached within 3 hours. After repeated oral doses of 500 mg every 12 hours, steady-state peak and trough concentrations are 14 and 6 micrograms/mL respectively.

The plasma elimination half-life of ornidazole is 12 to 14 hours. Less than 15% is bound to plasma proteins. It is widely distributed in body tissues and fluids, including the CSF.

Ornidazole is metabolised in the liver and is excreted in the urine, mainly as conjugates and metabolites, and to a lesser extent in the faeces. Biliary excretion may be important in the elimination of ornidazole and its metabolites.

◊ References.

1. Schwartz DE, Jeunet F. Comparative pharmacokinetic studies of ornidazole and metronidazole in man. *Chemotherapy* 1976; **22:** 19–29.
2. Matheson I, *et al.* Plasma levels after a single oral dose of 1.5 g ornidazole. *Br J Vener Dis* 1977; **53:** 236–9.
3. Schwartz DE, *et al.* Metabolic studies of ornidazole in the rat, in the dog and in man. *Xenobiotica* 1979; **9:** 571–81.
4. Turcant A, *et al.* Pharmacokinetics of ornidazole in neonates and infants after a single intravenous infusion. *Eur J Clin Pharmacol* 1987; **32:** 111–13.
5. Martin C, *et al.* Pharmacokinetics and tissue penetration of a single dose of ornidazole (1,000 milligrams intravenously) for antibiotic prophylaxis in colorectal surgery. *Antimicrob Agents Chemother* 1990; **34:** 1921–4.
6. Bourget P, *et al.* Disposition of ornidazole and its metabolites during pregnancy. *J Antimicrob Chemother* 1995; **35:** 691–6.

Hepatic impairment. The elimination of ornidazole after a single intravenous dose of 500 mg was impaired in 10 patients with severe liver cirrhosis when compared with 10 healthy subjects; mean half-lives were 21.9 hours and 14.1 hours respectively.[1] These results suggested that the interval between doses of ornidazole should be doubled in patients with marked hepatic impairment. The need for dose adjustment was confirmed in further studies of patients with other forms of liver disease.[2,3]

1. Taburet AM, *et al.* Pharmacokinetics of ornidazole in patients with severe liver cirrhosis. *Clin Pharmacol Ther* 1986; **40:** 359–64.
2. Bourget P, *et al.* Ornidazole pharmacokinetics in several hepatic diseases. *J Pharmacol Clin* 1988; **7:** 25–32.
3. Taburet AM, *et al.* Pharmacokinetics of ornidazole in patients with acute viral hepatitis, alcoholic cirrhosis, and extrahepatic cholestasis. *Clin Pharmacol Ther* 1989; **45:** 373–9.

Renal impairment. The half-life of intravenous ornidazole was not prolonged in a study in patients with advanced chronic renal failure, including those on continuous ambulatory peritoneal dialysis, although total plasma clearance was halved; modification of the usual dosage is not necessary in such patients. However, the drug was removed by haemodialysis and ornidazole should be given after the dialysis session rather than before.[1] In another study[2] the systemic availability and total body clearance of ornidazole were unaffected in chronic renal failure; it was considered that an additional dose should be given before haemodialysis to compensate for removal during that procedure.

1. Merdjan H, *et al.* Pharmacokinetics of ornidazole in patients with renal insufficiency; influence of haemodialysis and peritoneal dialysis. *Br J Clin Pharmacol* 1985; **19:** 211–17.
2. Horber FF, *et al.* High haemodialysis clearance of ornidazole in the presence of a negligible renal clearance. *Eur J Clin Pharmacol* 1989; **36:** 389–93.

Uses and Administration

Ornidazole is a 5-nitroimidazole derivative. It has the antimicrobial actions of metronidazole and is used similarly (see p.839) in the treatment of susceptible protozoal infections and also in the treatment and prophylaxis of anaerobic bacterial infections.

It is given orally after food, or intravenously. Intravenous solutions of ornidazole should be diluted to 5 mg or less per mL and 100 or 200 mL infused over 15 to 30 minutes.

In **amoebiasis**, 500 mg of ornidazole is given orally twice daily for 5 to 10 days; children are given 25 mg/kg as a single daily dose for 5 to 10 days. Patients with amoebic dysentery may be given 1.5 g as a single daily dose for 3 days; the children's dose is 40 mg/kg daily. An alternative regimen for adults over 60 kg is 1 g twice daily for 3 days. In severe amoebic dysentery and amoebic liver abscess, ornidazole may be given by intravenous infusion in a dose of 0.5 to 1 g initially, followed by 500 mg every 12 hours for 3 to 6 days; the children's dose is 20 to 30 mg/kg daily.

In **giardiasis**, 1 or 1.5 g of ornidazole is given orally as a single daily dose for 1 or 2 days; the children's dose is 30 or 40 mg/kg daily.

In **trichomoniasis**, a single oral dose of 1.5 g is given; alternatively, a 5-day oral course of ornidazole 500 mg twice daily may be used. Sexual partners should also be treated. The children's dose is 25 mg/kg as a single dose by mouth.

For the treatment of **anaerobic bacterial infections,** ornidazole is given by intravenous infusion in an initial dose of 0.5 to 1 g, followed by 1 g daily as a single dose or in two divided doses for 5 to 10 days; oral therapy with 500 mg every 12 hours should be substituted as soon as possible. Children may be given 10 mg/kg intravenously every 12 hours for 5 to 10 days.

For the prevention of postoperative anaerobic bacterial infections, 1 g is given by intravenous infusion about 30 minutes before surgery.

Administration in hepatic impairment. In view of the prolonged half-life and reduced clearance of ornidazole reported in patients with hepatic dysfunction (see above), the interval between doses should be doubled in patients with severe hepatic impairment.

Administration in renal impairment. The elimination of ornidazole is reported to be largely unaltered in patients with impaired renal function (see under Pharmacokinetics, above). Dosage adjustment is therefore usually unnecessary, although patients receiving haemodialysis should be given a supplemental dose of ornidazole before dialysis; a supplemental dose of 500 mg should be given if the daily dose is 2 g daily or 250 mg should be given if the daily dose is 1 g daily.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Mebaxol; ***Belg.:*** Tiberal; ***Chile:*** Invigan; ***Cz.:*** Avrazor; ***Fr.:*** Tiberal; ***Gr.:*** Betiral†; ***India:*** Giro; Oniz; Ornida; Zil; ***Mex.:*** Danubial†; ***NZ:*** Tiberal; ***Rus.:*** Dazolic (Дазолик); Ornisid (Орнисид); ***Spain:*** Tinerol†; ***Switz.:*** Tiberal; ***Turk.:*** Biteral; Borneral; Ornidone; Ornisid; Ornitop; ***Venez.:*** Tiberal†.

Multi-ingredient: ***India:*** Bidoflox-Oz†; Gatiquin Oz Kit; Levoflox Oz Kit; Ocimix; Orflaz Kit; Ornof; Tariflox Plus.

Paromomycin Sulfate *(rINNM)*

Aminosidin Sulphate; Aminosidine Sulphate; Catenulin Sulphate; Crestomycin Sulphate; Estomycin Sulphate; Hydroxymycin Sulphate; Monomycin A Sulphate; Neomycin E Sulphate; Paromomycin Sulphate *(BANM)*; Paromomycine, Sulfate de; Paromomycini Sulfas; Paucimycin Sulphate; Sulfato de paromomicina. *O*-2,6-Diamino-2,6-dideoxy-β-L-idopyranosyl-(1→3)-*O*-β-D-ribofuranosyl-(1→5)-*O*-[2-amino-2-deoxy-α-D-glucopyranosyl-(1→4)]-2-deoxystreptamine sulphate.

Паромомицина Сульфат

$C_{23}H_{45}N_5O_{14}.xH_2SO_4$.

CAS — 59-04-1 (paromomycin); 7542-37-2 (paromomycin); 1263-89-4 (paromomycin sulfate).

ATC — A07AA06.

ATC Vet — QA07AA06.

Pharmacopoeias. In *Chin.*, *Int.*, *It.*, and *US*.
USP 31 (Paromomycin Sulfate). The sulfate salt of an antibiotic substance produced by the growth of *Streptomyces rimosus* var. *paromomycinus*, or a mixture of two or more such salts.
A creamy-white to light yellow, odourless or practically odourless, very hygroscopic powder. It loses not more than 5% of its weight on drying. Very soluble in water; insoluble in alcohol, in chloroform, and in ether. pH of a 3% solution in water is between 5.0 and 7.5. Store in airtight containers.

Adverse Effects, Treatment, and Precautions

As for Neomycin, p.305.

Effects on the pancreas. Pancreatitis was associated with use of paromomycin during treatment of cryptosporidiosis in a patient with HIV infection.[1]

1. Tan WW, *et al.* Paromomycin-associated pancreatitis in HIV-related cryptosporidiosis. *Ann Pharmacother* 1995; **29:** 22–4.

Interactions

As for Neomycin, p.305.

Antimicrobial Action

Paromomycin is active against various protozoa including *Leishmania* spp., *Entamoeba histolytica*, and *Cryptosporidium* spp. In addition, it has an antibacterial spectrum similar to that of neomycin (p.305). There is cross-resistance between paromomycin and kanamycin, framycetin, neomycin, and streptomycin.

Paromomycin also has anthelmintic properties against tapeworms.

Antimycobacterial activity. References.

1. Kanyok TP, *et al.* Activity of aminosidine (paromomycin) for Mycobacterium tuberculosis and Mycobacterium avium. *J Antimicrob Chemother* 1994; **33:** 323–7.
2. Piersimoni C, *et al.* Bacteriostatic and bactericidal activities of paromomycin against Mycobacterium avium complex isolates. *J Antimicrob Chemother* 1994; **34:** 421–4.
3. Kanyok TP, *et al.* In vivo activity of paromomycin against susceptible and multidrug-resistant Mycobacterium tuberculosis and M. avium complex strains. *Antimicrob Agents Chemother* 1994; **38:** 170–3.

Pharmacokinetics

Paromomycin is poorly absorbed from the gastrointestinal tract and most of the dose is eliminated unchanged in the faeces.

Parenteral administration. References.

1. Kanyok TP, *et al.* Pharmacokinetics of intramuscularly administered aminosidine in healthy subjects. *Antimicrob Agents Chemother* 1997; **41:** 982–6.

Uses and Administration

Paromomycin is an aminoglycoside antibiotic that has been given orally in the treatment of intestinal protozoal infections, including amoebiasis, cryptosporidiosis, and giardiasis. It has also been tried parenterally for visceral, and topically for cutaneous, leishmaniasis. For details of these infections and their treatment, see under Choice of Antiprotozoal, p.822. It has been used in the treatment of tapeworm infection, but it is not the treatment of choice. Like neomycin (p.305), it has been used in the suppression of intestinal flora both pre-operatively and in the management of hepatic encephalopathy.

Paromomycin is given as the sulfate although doses are expressed in terms of the base. In intestinal amoebiasis, the dose for both adults and children is the equivalent of paromomycin 25 to 35 mg/kg daily in 3 divided oral doses with meals for 5 to 10 days. Similar doses have been tried in cryptosporidiosis.

In taeniasis and other tapeworm infections, a dose of 4 g is given orally as a single dose or in divided doses over the course of one hour.

For hepatic coma, 4 g is given daily in divided oral doses at regular intervals for 5 to 6 days.

Leishmaniasis. Topical treatment with paromomycin 15% plus methylbenzethonium chloride 5 or 12% has produced promising results[1-3] in *cutaneous leishmaniasis* (p.824); paromomycin 12 to 15% with urea 10% was better tolerated.[4] However, benefit has not been seen in all studies.[5,6] Treatment with topical paromomycin plus systemic meglumine antimonate was initially promising in patients with New World cutaneous leishmaniasis;[7] however, a subsequent study[8] found no clear advantage over treatment with meglumine antimonate alone. Good responses to parenteral paromomycin 14 mg/kg daily, with sodium stibogluconate 10 mg/kg daily, in cases of *diffuse cutaneous leishmaniasis* have also been reported.[9]

Paromomycin has also been used intramuscularly, either alone[10] or with sodium stibogluconate,[11] in the treatment of *visceral leishmaniasis* in an area of India with increasing resistance to pentavalent antimony compounds. The authors of one study[10] found paromomycin 16 or 20 mg/kg daily for 21 days to be significantly more effective than sodium stibogluconate 20 mg/kg daily for 30 days and suggested that paromomycin be considered as first-line treatment for visceral leishmaniasis in this region. Oral paromomycin plus intravenous pentamidine was reported to be effective in the treatment of amphotericin-resistant visceral leishmaniasis in an HIV-infected patient.[12]

1. El-On J, *et al.* Topical treatment of Old World cutaneous leishmaniasis caused by Leishmania major: a double-blind control study. *J Am Acad Dermatol* 1992; **27:** 227–31.
2. Krause G, Kroeger A. Topical treatment of American cutaneous leishmaniasis with paromomycin and methylbenzethonium chloride: a clinical study under field conditions in Ecuador. *Trans R Soc Trop Med Hyg* 1994; **88:** 92–4.
3. Arana BA, *et al.* Randomized, controlled, double-blind trial of topical treatment of cutaneous leishmaniasis with paromomycin plus methylbenzethonium chloride ointment in Guatemala. *Am J Trop Med Hyg* 2001; **65:** 466–70.
4. Bryceson ADM, *et al.* Treatment of Old World cutaneous leishmaniasis with aminosidine ointment: results of an open study in London. *Trans R Soc Trop Med Hyg* 1994; **88:** 226–8.
5. Ben Salah A, *et al.* A randomized, placebo-controlled trial in Tunisia treating cutaneous leishmaniasis with paromomycin ointment. *Am J Trop Med Hyg* 1995; **53:** 162–6.
6. Asilian A, *et al.* A randomized, placebo-controlled trial of a two week regimen of aminosidine (paromomycin) ointment for treatment of cutaneous leishmaniasis in Iran. *Am J Trop Med Hyg* 1995; **53:** 648–51.
7. Soto J, *et al.* Successful treatment of New World cutaneous leishmaniasis with a combination of topical paromomycin/methylbenzethonium chloride and injectable meglumine antimonate. *Clin Infect Dis* 1995; **20:** 47–51.
8. Soto J, *et al.* Topical paromomycin/methylbenzethonium chloride plus parenteral meglumine antimonate as treatment for American cutaneous leishmaniasis: controlled study. *Clin Infect Dis* 1998; **26:** 56–8.
9. Teklemariam S, *et al.* Aminosidine and its combination with sodium stibogluconate in the treatment of diffuse cutaneous leishmaniasis caused by Leishmania aethiopica. *Trans R Soc Trop Med Hyg* 1994; **88:** 334–9.
10. Jha TK, *et al.* Randomised controlled trial of aminosidine (paromomycin) v sodium stibogluconate for treating visceral leishmaniasis in North Bihar, India. *BMJ* 1998; **316:** 1200–5.
11. Thakur CP, *et al.* A prospective randomized, comparative, open-label trial of the safety and efficacy of paromomycin (aminosidine) plus sodium stibogluconate versus sodium stibogluconate alone for the treatment of visceral leishmaniasis. *Trans R Soc Trop Med Hyg* 2000; **94:** 429–31.
12. Manfredi R, *et al.* Diffuse cutaneous dissemination of visceral leishmaniasis during human immunodeficiency virus (HIV) infection, despite negligible immunodeficiency: repeated failure of liposomal amphotericin B administration, followed by successful long-term pentamidine and paromomycin administration. *Int J Antimicrob Agents* 2008; **31:** 590–2.

Trichomoniasis. Local application of a paromomycin cream has been tried in a small number of patients with metronidazole-resistant vaginal trichomoniasis (p.827) with moderate success.[1]

1. Nyirjesy P, *et al.* Difficult-to-treat trichomoniasis: results with paromomycin cream. *Clin Infect Dis* 1998; **26:** 986–8.

Preparations

USP 31: Paromomycin Sulfate Capsules; Paromomycin Sulfate Syrup.

Proprietary Preparations (details are given in Part 3)

Austria: Humatin; ***Belg.:*** Gabbroral; ***Canad.:*** Humatin; ***Ger.:*** Humatin; ***Indon.:*** Gabbryl; ***Ital.:*** Gabbroral; Humatin; Kaman; ***Spain:*** Humatin; ***Switz.:*** Humatin; ***USA:*** Humatin.

Multi-ingredient: ***Israel:*** Leshcutan.

Pentamidine Isetionate *(BANM, rINNM)*

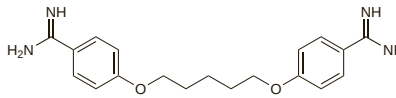
Isetionato de pentamidina; M&B-800; Pentamidiinidi-isetionaatti; Pentamidin Izetiyonat; Pentamidindiisetionat; Pentamidin-diisetionát; Pentamidin-diizetionát; Pentamidine Diisetionate; Pentamidine, diisétionate de; Pentamidine Isethionate *(USAN)*; Pentamidine, Isétionate de; Pentamidini diisetionas; Pentamidini Isethionas; Pentamidini Isetionas; Pentamidino diizetionatas; Pentamidyny diizetionian. 4,4′-(Pentamethylenedioxy)dibenzamidine bis(2-hydroxyethanesulphonate).

Пентамидина Изетионат

$C_{19}H_{24}N_4O_2.2C_2H_6O_4S$ = 592.7.

CAS — 100-33-4 (pentamidine); 140-64-7 (pentamidine isetionate).

ATC — P01CX01.



(pentamidine)

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

Ph. Eur. 6.2 (Pentamidine Diisetionate; Pentamidine Isetionate BP 2008). A white or almost white powder or colourless crystals; it is hygroscopic. Freely soluble in water; sparingly soluble in alcohol; practically insoluble in dichloromethane. A 5% solution in water has a pH of 4.5 to 6.5. Store in airtight containers.

Incompatibility. Immediate precipitation occurred when a solution of pentamidine isetionate 3 mg/mL in glucose 5% was mixed with each of 5 cephalosporin and 1 cephamycin injections.[1]

Pentamidine isetionate is reported to be incompatible with foscarnet.

1. Lewis JD, El-Gendy A. Cephalosporin-pentamidine isethionate incompatibilities. *Am J Health-Syst Pharm* 1996; **53:** 1461–2.

Pentamidine Mesilate *(BANM, rINNM)*

Mesilato de pentamidina; Pentamidine Dimethylsulphonate; Pentamidine, Mésilate de; Pentamidine Mesylate; Pentamidine Methanesulphonate; Pentamidini Mesilas; RP-2512. Pentamidine dimethanesulphonate.

Пентамидина Мезилат

$C_{19}H_{24}N_4O_2.2CH_3SO_3H$ = 532.6.

CAS — 6823-79-6.

Pharmacopoeias. In *Int.*

Adverse Effects

Pentamidine is a toxic drug and adverse effects are frequent and sometimes severe when given parenterally; fatalities have been reported. Renal impairment is common, usually manifesting as mild and reversible raised blood urea nitrogen and serum creatinine concentrations, but acute renal failure can occur. Raised liver enzyme values and haematological disturbances such as leucopenia, anaemia, and occasionally thrombocytopenia, may develop. Hypoglycaemia, sometimes followed by hyperglycaemia and type 1 diabetes mellitus, is well documented; there have been occasional reports of acute pancreatitis.

The rapid intravenous injection of pentamidine has resulted in sudden hypotension and immediate reactions such as dizziness, headache, vomiting, breathlessness, tachycardia, and fainting. Hypotension may also occur when pentamidine is given intramuscularly or by slow intravenous infusion. Intramuscular pentamidine often causes pain, swelling, sterile abscess formation, and tissue necrosis at the site of injection. Similar damage can follow extravasation during intravenous dosage.

Other adverse effects reported include hypocalcaemia, hyperkalaemia, skin rashes, the Stevens-Johnson syndrome, fever, flushing, gastrointestinal effects such as nausea, vomiting, and taste disturbances, confusion, hallucinations, and cardiac arrhythmias.

Pentamidine is not as toxic when given by inhalation for the prophylaxis of pneumocystis pneumonia. The commonest adverse effects with this route are cough and bronchoconstriction and may be controlled by a bronchodilator. Inhalation may leave a bitter taste. Pneumothorax has been reported, but may be associated with the disease. There have been rare reports of adverse effects such as those seen when pentamidine is given by injection.

Incidence of adverse effects. Adverse effects were seen in 46.8% of 404 patients given pentamidine parenterally for the treatment of pneumocystis pneumonia, according to an analysis from the CDC in the USA.[1] The reactions included impaired renal function (23.5% of patients), abnormal liver function (9.6%), hypoglycaemia (6.2%), haematological disturbances (4.2%), skin rashes (1.5%), and hypocalcaemia (1.2%). Local reactions at injection sites such as pain and abscess occurred in 18.3% and immediate adverse effects such as hypotension in 9.6%.

Retrospective studies[2-4] suggest that adverse reactions occur more commonly in patients with AIDS.

An evaluation of pentamidine in the treatment of 82 patients with visceral leishmaniasis further illustrates its toxicity.[5] Cardiotoxicity (tachycardia, hypotension, and ECG changes of non-specific myocarditis), occurred in about 23% of patients. No hypoglycaemic reaction was noted, but 4 patients developed diabetes mellitus and 3 of them were found to be insulin-dependent. Other adverse reactions included gastrointestinal effects (anorexia, nausea, vomiting, abdominal pain, or diarrhoea) in about 78%, CNS effects (headache associated with flushing, delirium, or sensory disturbances resembling pins and needles) in about 24%, mild reversible albuminuria in about 7%, and allergic manifestations (generalised urticaria, itching, and conjunctival congestion) in about 5%. One patient had severe anaphylaxis.

1. Walzer PD, *et al.* Pneumocystis carinii pneumonia in the United States: epidemiologic, diagnostic and clinical features. *Ann Intern Med* 1974; **80:** 83–93.
2. Lachaal M, Venuto RC. Nephrotoxicity and hyperkalemia in patients with acquired immunodeficiency syndrome treated with pentamidine. *Am J Med* 1989; **87:** 260–3.
3. Briceland LL, Bailie GR. Pentamidine-associated nephrotoxicity and hyperkalemia in patients with AIDS. *DICP Ann Pharmacother* 1991; **25:** 1171–4.
4. O'Brien JG, *et al.* A 5-year retrospective review of adverse drug reactions and their risk factors in human immunodeficiency virus-infected patients who were receiving intravenous pentamidine therapy for Pneumocystis carinii pneumonia. *Clin Infect Dis* 1997; **24:** 854–9.
5. Jha TK. Evaluation of diamidine compound (pentamidine isethionate) in the treatment of resistant cases of kala-azar occurring in North Bihar, India. *Trans R Soc Trop Med Hyg* 1983; **77:** 167–70.

Effects on the blood. Haemolytic anaemia has been reported in a 55-year-old man with AIDS being treated with intravenous pentamidine for pneumocystis pneumonia. Symptoms developed after a cumulative dose of 3740 mg of pentamidine had been given and resolved several days after stopping the pentamidine.[1]

1. Taguchi H, *et al.* Pentamidine-induced hemolytic anemia in an AIDS patient. *Ann Pharmacother* 1999; **33:** 503.

Effects on carbohydrate metabolism. As reported under Incidence of Adverse Effects, above, pentamidine can have a range of effects on carbohydrate metabolism. Four patients receiving pentamidine for pneumocystis pneumonia developed severe fasting hypoglycaemia followed later by hyperglycaemia and type 1 diabetes mellitus.[1] It has been suggested that pentamidine has a toxic effect on the β-cells of the pancreatic islets and can induce an early cytolytic release of insulin and hypoglycaemia, followed by β-cell destruction, insulin deficiency, and diabetes mellitus.[1,2] AIDS patients appear to be highly susceptible and have a higher incidence of hypoglycaemia due to pentamidine.[3] The action on the pancreas has led to fatal acute *pancreatitis*;[4-6] fatal hypoglycaemia has also been reported.[7] These reports[1-5,7] involved pentamidine given by injection; pancreatitis[8,9] and diabetes mellitus[10,11] have also been reported in patients given pentamidine by aerosol inhalation.

1. Bouchard P, *et al.* Diabetes mellitus following pentamidine-induced hypoglycemia in humans. *Diabetes* 1982; **31:** 40–5.
2. Osei K, *et al.* Diabetogenic effect of pentamidine: in vitro and in vivo studies in a patient with malignant insulinoma. *Am J Med* 1984; **77:** 41–6.
3. Stahl-Bayliss CM, *et al.* Pentamidine-induced hypoglycemia in patients with the acquired immune deficiency syndrome. *Clin Pharmacol Ther* 1986; **39:** 271–5.
4. Salmeron S, *et al.* Pentamidine and pancreatitis. *Ann Intern Med* 1986; **105:** 140–1.
5. Zuger A, *et al.* Pentamidine-associated fatal acute pancreatitis. *JAMA* 1986; **256:** 2383–5.
6. Sauleda J, *et al.* Probable pentamidine-induced acute pancreatitis. *Ann Pharmacother* 1994; **28:** 52–3.
7. Sattler FR, Waskin H. Pentamidine and fatal hypoglycemia. *Ann Intern Med* 1987; **107:** 789–90.
8. Herer B, *et al.* Pancreatitis associated with pentamidine by aerosol. *BMJ* 1989; **298:** 605.
9. Hart CC. Aerosolized pentamidine and pancreatitis. *Ann Intern Med* 1989; **111:** 691.
10. Fisch A. Diabetes mellitus in a patient with AIDS after treatment with pentamidine aerosol. *BMJ* 1990; **301:** 875.
11. Chen JP, *et al.* Diabetes after aerosolized pentamidine. *Ann Intern Med* 1991; **114:** 913–14.

Effects on the cardiovascular system. *Hypotension* is a problem with intravenous pentamidine, but can be reduced by infusing the dose over 60 minutes, when the incidence of hypotension appears to be similar to that with the intramuscular route.[1,2] Intravenous pentamidine has also been associated with *torsade de pointes*.[3-5]

1. Navin TR, Fontaine RE. Intravenous versus intramuscular administration of pentamidine. *N Engl J Med* 1984; **311:** 1701.