Saizen; Umatrope; Zomacton; ***Ger.:*** Genotropin; Humatrope; Norditropin; NutropinAq; Saizen; Zomacton; ***Gr.:*** Genotropin; Humatrope; Norditropin; Nutropin; Saizen; Zomacton; ***Hong Kong:*** Genotropin; Humatrope; Norditropin; Saizen; Scitropin; Serostim; ***Hung.:*** Genotropin; Humatrope; Norditropin; Nutropin; Saizen†; Zomacton†; ***India:*** Saizen; ***Indon.:*** Eutropin; Genotropin; Norditropin; Saizen; ***Irl.:*** Genotropin; Norditropin; Saizen; Zomacton; ***Israel:*** Bio-Tropin; Genotropin; Norditropin; ***Ital.:*** Genotropin; Humatrope; Norditropin; Nutropin; Saizen; Zomacton; ***Jpn:*** Growject; Norditropin; ***Malaysia:*** Genotropin; Norditropin; Saizen; ***Mex.:*** Cryo-Tropin; Genotropin; HHT; Humatrope; Norditropin; Saizen; Serostim; ***Neth.:*** Genotropin; Humatrope; Norditropin; Nutropin; Zomacton; ***Norw.:*** Genotropin; Humatrope; Norditropin; NutropinAq; Saizen; Zomacton; ***NZ:*** Genotropin; Norditropin; Saizen; ***Philipp.:*** GenHeal; Humatrope; Norditropin; Saizen; SciTropin; ***Pol.:*** Genotropin; ***Port.:*** Genotropin; Humatrope; Norditropin; NutropinAq; Omnitrope; Saizen; Valtropin; Zomacton; ***Rus.:*** Genotropin (Генотропин); Humatrope (Хуматрон); Norditropin (Нордитропин); Saizen (Сайзен); ***S.Afr.:*** Genotropin; Humatrope; Norditropin; Saizen†; ***Singapore:*** Genotropin; Humatrope†; Norditropin; Saizen; Scitropin†; ***Spain:*** Genotonorm; Humatrope; Norditropin; Nutropin; Saizen; Zomacton; ***Swed.:*** Genotropin; Humatrope; Norditropin; NutropinAq; Saizen; Zomacton; ***Switz.:*** Genotropin; Humatrope; Norditropine; Saizen; ***Thai.:*** Saizen; ***Turk.:*** Genotropin; Humatrope; Norditropin; Saizen; Zomacton; ***UK:*** Genotropin; Humatrope; Norditropin; Nutropin; Saizen; Zomacton; ***USA:*** Genotropin; Humatrope; Norditropin; Nutropin; Omnitrope; Protropin†; Saizen; Serostim; Tev-Tropin; Zorbtive; ***Venez.:*** Genotropin; Humatrope; Norditropin†; Saizen.

Lanreotide *(BAN, rINN)*

Angiopeptin; BIM-23014; BN-52030; DC-13-116; Lanreotid; Lanreotida; Lanréotide; Lanreotidi; Lanreotidum. 3-(2-Naphthyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-L-threoninamide cyclic (2→7)-disulfide.

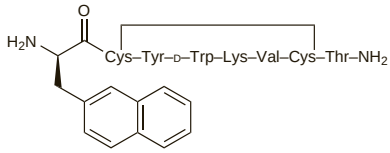
Ланреотид

$C_{54}H_{69}N_{11}O_{10}S_2$ = 1096.3.

CAS — 108736-35-2.

ATC — H01CB03.

ATC Vet — QH01CB03.



Lanreotide Acetate *(BANM, USAN, rINNM)*

Acetato de lanreotida; BIM-23014C; Lanréotide, Acétate de; Lanreotidi Acetas.

Ланреотида Ацетат

$C_{54}H_{69}N_{11}O_{10}S_2.x(C_2H_4O_2)$.

CAS — 127984-74-1.

ATC — H01CB03.

ATC Vet — QH01CB03.

Adverse Effects and Precautions

As for Octreotide Acetate, p.1803.

Interactions

As for Octreotide Acetate, p.1804.

Pharmacokinetics

After intravenous injection lanreotide has a terminal half-life of about 2.5 hours. Lanreotide is available as injectable depot preparations, and after subcutaneous or intramuscular use of these an initial rapid liberation of the drug is followed by more prolonged release with an apparent half-life of about 5 to 30 days. The absolute bioavailability is stated to range from about 50 to 80%, depending on the product.

Uses and Administration

Lanreotide is a somatostatin analogue with similar properties to those of octreotide (p.1804). It is given, as a long-acting depot injection, in the treatment of acromegaly (p.1798) and thyrotrophic adenoma, as well as in the symptomatic management of carcinoid syndrome (p.643).

Lanreotide is given as the acetate, but doses are usually expressed in terms of the base. The usual starting dose is equivalent to lanreotide 30 mg by intramuscular depot injection every 14 days. In acromegaly and carcinoid syndrome, this may be increased if necessary to 30 mg every 7 to 10 days; in thyrotrophic adenoma it may be increased to 30 mg every 10 days. An alternative preparation for acromegaly and carcinoid syndrome, given by deep subcutaneous injection every 28 days, delivers doses equivalent to 60, 90, or 120 mg of lanreotide. In patients with acromegaly who respond to treatment, lanreotide may be gradually reduced to maintenance doses of 120 mg given at intervals of up to 56 days. In those who are not adequately controlled, a maximum dose of 120 mg once every 28 days may be used.

Lanreotide has been tried for the prevention of restenosis in coronary blood vessels following angioplasty (see Reperfusion and Revascularisation Procedures, p.1181).

◊ References.

1. Wymenga ANM, *et al.* Efficacy and safety of prolonged-release lanreotide in patients with gastrointestinal neuroendocrine tumors and hormone-related symptoms. *J Clin Oncol* 1999; **17:** 1111–17.
2. Kuhn JM, *et al.* Evaluation of the treatment of thyrotropin-secreting pituitary adenomas with a slow release formulation of the somatostatin analog lanreotide. *J Clin Endocrinol Metab* 2000; **85:** 1487–91.
3. Ayuk J, *et al.* Long-term safety and efficacy of depot long-acting somatostatin analogs for the treatment of acromegaly. *J Clin Endocrinol Metab* 2002; **87:** 4142–6.
4. Caron P, *et al.* One-year follow-up of patients with acromegaly treated with fixed or titrated doses of lanreotide Autogel. *Clin Endocrinol (Oxf)* 2004; **60:** 734–40.
5. Ruszniewski P, *et al.* Rapid and sustained relief from the symptoms of carcinoid syndrome: results from an open 6-month study of the 28-day prolonged-release formulation of lanreotide. *Neuroendocrinology* 2004; **80:** 244–51.
6. Freda PU, *et al.* Long-acting somatostatin analog therapy of acromegaly: a meta-analysis. *J Clin Endocrinol Metab* 2005; **90:** 4465–73.
7. Croxtall JD, Scott LJ. Lanreotide Autogel : a review of its use in the management of acromegaly. *Drugs* 2008; **68:** 711–23.

Administration in hepatic and renal impairment. The clearance of lanreotide, given by intravenous bolus, was significantly reduced in patients with severe chronic renal impairment requiring haemodialysis.[1] However, the authors of this study suggested that considering the wide therapeutic window of lanreotide, depot formulations may be given at the usual initial dose, with further doses adjusted according to response. Clearance of lanreotide was only slightly reduced in patients with moderate to severe hepatic impairment (Child-Pugh category B and C).[2] The UK licensed product information for one depot formulation (*Somatuline Autogel; Ipsen, UK*) given every 28 days recommends that dose adjustment is not necessary in renal or hepatic impairment. Another preparation (*Somatuline LA; Ipsen, UK*) usually given every 14 days suggests that renal and hepatic function should be monitored and the dosage interval adjusted as needed.

1. Barbanoj M, *et al.* Pharmacokinetics of the somatostatin analog lanreotide in patients with severe chronic renal insufficiency. *Clin Pharmacol Ther* 1999; **66:** 485–91.
2. Tomlinson B, *et al.* Pharmacokinetic profile of the somatostatin analogue lanreotide in individuals with chronic hepatic insufficiency. *Clin Pharmacokinet* 2006; **45:** 1003–11.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Somatuline; ***Austral.:*** Somatuline; ***Austria:*** Somatuline; ***Belg.:*** Somatuline; ***Braz.:*** Somatuline†; ***Cz.:*** Somatuline; ***Denm.:*** Ipstyl; ***Fin.:*** Somatuline; ***Fr.:*** Somatuline; ***Ger.:*** Somatuline; ***Gr.:*** Somatuline; ***Hong Kong:*** Somatuline; ***Hung.:*** Somatuline; ***Irl.:*** Somatuline; ***Israel:*** Somatuline; ***Ital.:*** Ipstyl; ***Neth.:*** Somatuline; ***Norw.:*** Ipstyl; ***Pol.:*** Somatuline; ***Port.:*** Somatulina; ***Rus.:*** Somatuline (Соматулин); ***Singapore:*** Somatuline; ***Spain:*** Somatulina; ***Swed.:*** Somatuline; ***Switz.:*** Somatuline; ***UK:*** Somatuline; ***USA:*** Somatuline.

Octreotide Acetate *(BANM, USAN, rINNM)*

Acetato de octreotida; Octréotide, Acétate d'; Octreotidi Acetas; SMS-201-995 (octreotide). 2-(D-Phenylalanyl-L-cystyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-L-cystyl)-(2*R*,3*R*)-butane-1,3-diol acetate; D-Phenylalanyl-L-cysteinyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-*N*-[(1*R*,2*R*)-2-hydroxy-1-(hydroxymethyl)propyl]-L-cysteinamide cyclic (2→7) disulphide acetate.

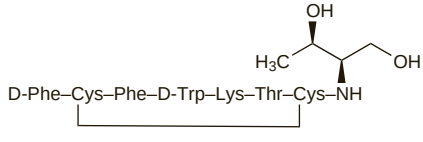
Октреотида Ацетат

$C_{49}H_{66}N_{10}O_{10}S_2.xC_2H_4O_2$ = 1019.2 (octreotide).

CAS — 83150-76-9 (octreotide); 79517-01-4 (octreotide acetate).

ATC — H01CB02.

ATC Vet — QH01CB02.



(octreotide)

Incompatibility. Apparent loss of insulin has been reported from a total parenteral nutrient solution containing octreotide; there may be an incompatibility.[1] Also the manufacturers had suggested that octreotide might be adsorbed onto plastics. However, a solution containing octreotide 200 micrograms/mL as the acetate was reported to be stable at 5° or −20° for up to 60 days when stored in polypropylene syringes.[2]

1. Rosen GH. Potential incompatibility of insulin and octreotide in total parenteral nutrient solutions. *Am J Hosp Pharm* 1989; **46:** 1128.
2. Ripley RG, *et al.* Stability of octreotide acetate in polypropylene syringes at 5 and −20°C. *Am J Health-Syst Pharm* 1995; **52:** 1910–11.

Adverse Effects and Precautions

There may be a transient local reaction at the site of injection of octreotide. Systemic adverse effects are mainly gastrointestinal and may include anorexia, nausea, vomiting, diarrhoea and steatorrhoea, abdominal discomfort, and flatulence. Use between meals or at bedtime may reduce these gastrointestinal effects. Hypersensitivity reactions and hair loss have been reported rarely.

Gallstones may develop on long-term therapy; there have been isolated reports of hepatic dysfunction and of biliary colic associated with drug withdrawal. Checks should be made for gallstones before prolonged therapy and at 6- to 12-month intervals during treatment. There have also been isolated reports of pancreatitis and of hepatic dysfunction without cholestasis. Hypoglycaemia may occur, especially in patients with insulinomas, but there is also a risk of hyperglycaemia or impaired glucose tolerance. Thyroid function should be monitored during octreotide therapy because of the possibility of hypothyroidism. Pituitary tumours that secrete growth hormone can expand during treatment, causing serious complications; patients should be monitored for signs of tumour expansion, such as visual field defects. Cardiac rhythm should be monitored during intravenous use of octreotide. Doses may need to be adjusted in patients with end-stage renal failure, in whom the clearance of octreotide is reduced.

Effects on the biliary tract. Octreotide has an inhibitory effect on gallbladder motility and bile secretion, accounting for the development of gallstones and biliary colic.[1-5]

1. Redfern JS, Fortuner WJ. Octreotide-associated biliary tract dysfunction and gallstone formation: pathophysiology and management. *Am J Gastroenterol* 1995; **90:** 1042–52.
2. Tauber JP, *et al.* The impact of continuous subcutaneous infusion of octreotide on gallstone formation in acromegalic patients. *J Clin Endocrinol Metab* 1995; **80:** 3262–6.
3. Hussaini SH, *et al.* Roles of gall bladder emptying and intestinal transit in the pathogenesis of octreotide induced gall bladder stones. *Gut* 1996; **38:** 775–83.
4. Trendle MC, *et al.* Incidence and morbidity of cholelithiasis in patients receiving chronic octreotide for metastatic carcinoid and malignant islet cell tumors. *Cancer* 1997; **79:** 830–4.
5. Moschetta A, *et al.* Severe impairment of postprandial cholecystokinin release and gall-bladder emptying and high risk of gallstone formation in acromegalic patients during Sandostatin LAR. *Aliment Pharmacol Ther* 2001; **15:** 181–5.

Effects on carbohydrate metabolism. Changes in glucose tolerance may occur in patients with acromegaly who are treated with somatostatin analogues. In a study[1] of 90 patients treated with octreotide for 6 months, impaired glucose tolerance or frank diabetes developed in half of the 55 who initially had normal glucose tolerance. There was initial impaired glucose tolerance in 24 patients, which deteriorated in 4, remained stable in 10, and normalised in 10. Of the 11 patients who were diabetic before octreotide treatment, 8 remained diabetic but 1 improved to having impaired glucose tolerance and 2 to being normal. A later study[2] of 24 patients treated with either octreotide or lanreotide also found that glucose tolerance could remain stable, deteriorate, or improve. Overall, however, there was an improvement in insulin resistance but an impairment of insulin secretion, and a deterioration in glucose homoeostasis in nondiabetic patients.

There has been a report of deterioration in glucose tolerance leading to death from diabetic ketoacidosis when octreotide treatment was stopped in a patient with acromegaly and insulin-resistant diabetes mellitus.[3]

See also Diabetes Mellitus and Hyperinsulinism under Uses and Administration, below.

1. Koop BL, *et al.* Effect of octreotide on glucose tolerance in acromegaly. *Eur J Endocrinol* 1994; **130:** 581–6.
2. Baldelli R, *et al.* Glucose homeostasis in acromegaly: effects of long-acting somatostatin analogues treatment. *Clin Endocrinol (Oxf)* 2003; **59:** 492–9.
3. Abrahamson MJ. Death from diabetic ketoacidosis after cessation of octreotide in acromegaly. *Lancet* 1990; **336:** 318–19.

Effects on the hair. Diffuse loss of scalp hair has been reported in 4 of 7 women who received octreotide; after withdrawal of octreotide in 3 of the women there was a complete recovery of scalp hair.[1] Other similar cases have also been reported. In one case, diffuse alopecia in a male patient was completely reversed when octreotide was replaced with lanreotide.[2]

1. Jönsson A, Manhem P. Octreotide and loss of scalp hair. *Ann Intern Med* 1991; **115:** 913.
2. Lami M-C, *et al.* Hair loss in three patients with acromegaly treated with octreotide. *Br J Dermatol* 2003; **149:** 655–6.

Effects on the liver. Hepatitis occurred in 2 acromegalic patients treated with octreotide 300 micrograms daily subcutaneously.[1,2] In both cases liver enzyme values returned to normal within 1 to 2 months of withdrawing octreotide, and recurred on rechallenge.

1. Arosio M, *et al.* Acute hepatitis after treatment of acromegaly with octreotide. *Lancet* 1988; **ii:** 1498.
2. González-Martín JA, *et al.* Acute liver injury and octreotide. *Am J Gastroenterol* 1996; **91:** 2434–5.

Effects on mental function. A woman with acromegaly developed manic symptoms on 2 separate occasions 2 months after starting treatment with octreotide.[1]

1. Fernández-Real J-M, *et al.* Octreotide-induced manic episodes in a patient with acromegaly. *Ann Intern Med* 2006; **144:** 704.

Effects on the pancreas. There have been reports of pancreatitis associated with octreotide[1-4] and lanreotide.[4] It has been suggested that octreotide-induced pancreatitis may result from spasm of the sphincter of Oddi, resulting in retention of activated pancreatic enzymes due to outflow obstruction.[3]

1. Fredenrich A, *et al.* Acute pancreatitis after short-term octreotide. *Lancet* 1991; **338:** 52–3.
2. Sadoul J-L, *et al.* Acute pancreatitis following octreotide withdrawal. *Am J Med* 1991; **90:** 763–4.
3. Bodemar G, Hjortswang H. Octreotide-induced pancreatitis: an effect of increased contractility of Oddi sphincter. *Lancet* 1996; **348:** 1668–9.
4. Cannavò S, *et al.* Octreotide and lanreotide treatment in active acromegaly. *J Clin Endocrinol Metab* 1997; **82:** 2376–7.

Pregnancy. There have been reports of women who have received lanreotide[1] or octreotide[2-5] during pregnancy. Most were receiving the drug for the treatment of acromegaly, although there is also a report[5] of octreotide use during pregnancy in a woman treated for nesidioblastosis. In most cases, the somatostatin analogue was stopped early in the pregnancy, but in some cases octreotide was continued to term. No maternal complications or congenital anomalies were described.

1. de Menis E, *et al.* Uneventful pregnancy in an acromegalic patient treated with slow-release lanreotide: a case report. *J Clin Endocrinol Metab* 1999; **84:** 1489.
2. Neal JM. Successful pregnancy in a woman with acromegaly treated with octreotide. *Endocr Pract* 2000; **6:** 148–50.
3. Fassnacht M, *et al.* Octreotide LAR treatment throughout pregnancy in an acromegalic woman. *Clin Endocrinol (Oxf)* 2001; **55:** 411–15.
4. Mikhail N. Octreotide treatment of acromegaly during pregnancy. *Mayo Clin Proc* 2002; **77:** 297–8.
5. Boulanger C, *et al.* Normal pregnancy in a woman with nesidioblastosis treated with somatostatin analog octreotide. *J Endocrinol Invest* 2004; **27:** 465–70.

Interactions

Octreotide has been associated with alterations in nutrient absorption and there is a theoretical possibility that it may affect the oral absorption of other drugs. Patients receiving insulin or oral hypoglycaemics may require dose adjustments of these drugs if octreotide is also used. The bioavailability of bromocriptine is increased by octreotide. It has been suggested that dosage of beta blockers, calcium-channel blockers, or drugs to control fluid and electrolyte balance may also need to be adjusted.

Ciclosporin. For a reference to octreotide reducing serum concentrations of ciclosporin, see p.1828.

Pharmacokinetics

Octreotide is rapidly absorbed after subcutaneous injection, with peak plasma concentrations reached about 25 to 40 minutes after a dose, and is distributed to body tissues. About 40 to 65% of the octreotide in the circulation is bound to plasma proteins. It is said to exhibit non-linear pharmacokinetics, with reduced clearance at high doses. Octreotide is removed from the body with a plasma elimination half-life of about 1.5 hours; half-life is prolonged in elderly patients, renal impairment, and liver cirrhosis. About a third of a dose is excreted unchanged in the urine. Octreotide diffuses across the placenta.

Uses and Administration

Octreotide is an octapeptide analogue of somatostatin (p.1809) with similar properties but a longer duration of action.

It is used as the acetate in the symptomatic management of carcinoid tumours and other secretory neoplasms such as VIPomas and glucagonomas. Octreotide acetate is also used in the treatment of acromegaly and the prevention of complications after pancreatic surgery, and may be used in the treatment of other disorders including variceal haemorrhage and HIV-associated diarrhoea. It has also been investigated in a variety of other disorders including the dumping syndrome.

In the management of **secretory neoplasms** octreotide acetate is given subcutaneously in an initial dose equivalent to 50 micrograms of octreotide once or twice daily gradually increased, according to response, to up to 600 micrograms daily in 2 to 4 divided doses. Higher doses have been used. If there is no benefit within a week of starting treatment for carcinoid tumour, continued therapy is not recommended.

Where a rapid response is required, the initial dose may be given by the intravenous route. In the UK licensed product information states that it should be diluted not less than 1 in 1 or not more than 1 in 9 in sodium chloride 0.9%, but in the USA product information permits the use of the undiluted solution as an intravenous bolus in emergencies; alternatively the dose may be given by intermittent infusion over 15 to 30 minutes, diluted in 50 to 200 mL of sodium chloride 0.9% or glucose 5%.

Once control has been established maintenance therapy with a depot preparation may be possible; initially 20 mg by intramuscular injection every 4 weeks is suggested. Subcutaneous injection with a rapid-acting preparation should be continued for 2 weeks after the first depot injection to provide symptomatic cover, and may be added to therapy when necessary thereafter. Maintenance doses of the depot preparation may be adjusted after 2 or 3 months to between 10 and 30 mg every 4 weeks, as necessary.

In **acromegaly**, the usual dose is the equivalent of 100 to 200 micrograms of octreotide three times daily by subcutaneous injection. In the USA it is suggested that dosage begin with 50 micrograms three times daily in order to minimise gastrointestinal disturbance. If there is no relevant reduction in growth hormone concentrations and no improvement in clinical symptoms within 3 months of starting treatment, octreotide should be stopped. Once control has been established maintenance therapy with a depot preparation is possible; an initial dose equivalent to 20 mg of octreotide given intramuscularly once every 4 weeks has been recommended for patients with acromegaly, adjusted after 3 months to between 10 and 30 mg every 4 weeks. For patients who are not adequately controlled on 30 mg, the dose may be further increased to 40 mg every 4 weeks. The depot preparation may also be used for short-term treatment before pituitary surgery, but the last dose should be given at least 3 to 4 weeks before surgery to ensure successful endocrine testing for tumour removal 5 to 6 weeks after surgery.

For the prevention of complications after **pancreatic surgery** the equivalent of 100 micrograms of octreotide may be given three times daily by subcutaneous injection of a rapid-acting preparation; treatment is given for 7 consecutive days, beginning at least 1 hour before laparotomy on the day of operation.

In the management of **variceal haemorrhage** in patients with cirrhosis, octreotide is given as a continuous intravenous infusion at a dose equivalent to octreotide 25 micrograms/hour for 48 hours. Doses up to 50 micrograms/hour have been used. Patients at high risk of re-bleeding may continue treatment for up to 5 days. Although not licensed for use in children in the UK, the *BNFC* includes a dose of 1 microgram/kg per hour by continuous intravenous infusion for children from 1 month to 18 years of age; higher doses may be needed initially, to a maximum dose of 50 micrograms/hour, and the dose should be reduced gradually over 24 hours once there is no active bleeding.

HIV-associated diarrhoea may be treated with an initial dose of octreotide 100 micrograms three times daily, given subcutaneously. If the diarrhoea is not controlled after a week, the dose may be increased to 250 micrograms three times daily, but if this is not effective after one week then octreotide therapy should be stopped.

◊ General reviews of octreotide.

1. Bloom SR, O'Shea D. Octreotide. *Prescribers' J* 1996; **36:** 120–4.
2. Lamberts SWJ, *et al.* Octreotide. *N Engl J Med* 1996; **334:** 246–54.

Acromegaly. Although surgery remains the most important method of treatment, octreotide has a useful role in the management of acromegaly (p.1798). It can reduce growth hormone concentrations, normalise IGF-I concentrations, reduce tumour size, and improve signs and symptoms.[1-4] There is also some evidence that it may improve cardiac function, which is usually compromised in these patients.[5-7] Octreotide can be given subcutaneously and this route is generally used initially to determine patient response and tolerance, but it must be given three times daily making it unattractive for long-term use. Intramuscular sustained-release octreotide is effective for maintenance therapy.[4,7,8] There is also increasing interest in the role of octreotide for primary therapy of acromegaly, instead of surgery[8,9] and a recent meta-analysis[10] concluded that tumour shrinkage was greatest when somatostatin analogues were given as primary rather than secondary therapy.

1. Vance ML, Harris AG. Long-term treatment of 189 acromegalic patients with the somatostatin analog octreotide: results of the International Multicenter Acromegaly Study Group. *Arch Intern Med* 1991; **151:** 1573–8.
2. Ezzat S, *et al.* Octreotide treatment of acromegaly: a randomized, multicenter study. *Ann Intern Med* 1992; **117:** 711–18.
3. van der Lely AJ, *et al.* A risk-benefit assessment of octreotide in the treatment of acromegaly. *Drug Safety* 1997; **17:** 317–24.
4. Freda PU. Somatostatin analogs in acromegaly. *J Clin Endocrinol Metab* 2002; **87:** 3013–18.
5. Colao A, *et al.* Cardiovascular effects of depot long-acting somatostatin analog Sandostatin LAR in acromegaly. *J Clin Endocrinol Metab* 2000; **85:** 3132–40.
6. Colao A, *et al.* Is the acromegalic cardiomyopathy reversible? Effect of 5-year normalization of growth hormone and insulin-like growth factor I levels on cardiac performance. *J Clin Endocrinol Metab* 2001; **86:** 1551–7.
7. McKeage K, *et al.* Octreotide long-acting release (LAR): a review of its use in the management of acromegaly. *Drugs* 2003; **63:** 2473–99.
8. Ayuk J, *et al.* Long-term safety and efficacy of depot long-acting somatostatin analogs for the treatment of acromegaly. *J Clin Endocrinol Metab* 2002; **87:** 4142–6.
9. Bevan JS, *et al.* Primary medical therapy for acromegaly: an open, prospective, multicenter study of the effects of subcutaneous and intramuscular slow-release octreotide on growth hormone, insulin-like growth factor-I, and tumor size. *J Clin Endocrinol Metab* 2002; **87:** 4554–63.
10. Freda PU, *et al.* Long-acting somatostatin analog therapy of acromegaly: a meta-analysis. *J Clin Endocrinol Metab* 2005; **90:** 4465–73.

Carcinoid syndrome and other secretory neoplasms. For a discussion of carcinoid tumours and other secretory neoplasms, including reference to the important role of octreotide, see p.643.

Reviews.

1. Öberg K, *et al.* Consensus report on the use of somatostatin analogs for the management of neuroendocrine tumors of the gastroenteropancreatic system. *Ann Oncol* 2004; **15:** 966–73.
2. Delaunoit T, *et al.* Somatostatin analogues in the treatment of gastroenteropancreatic neuroendocrine tumors. *Mayo Clin Proc* 2005; **80:** 502–6.

Cardiovascular disorders. There have been reports of benefit from octreotide in patients with postprandial hypotension and orthostatic hypotension (p.1530) associated with autonomic neuropathy.[1-5] Octreotide has also produced cardiac improvement in patients with acromegaly (see above). Promising results have been reported in patients with primary hypertrophic cardiomyopathy.[6,7]

1. Hoeldtke RD, *et al.* Treatment of autonomic neuropathy with a somatostatin analogue SMS-201-995. *Lancet* 1986; **ii:** 602–5.
2. Hoeldtke RD, Israel BC. Treatment of orthostatic hypotension with octreotide. *J Clin Endocrinol Metab* 1989; **68:** 1051–9.
3. Woo J, *et al.* Treatment of severe orthostatic hypotension with the somatostatin analogue octreotide. *Aust N Z J Med* 1990; **20:** 822–3.
4. Bordet R, *et al.* Octreotide in the management of orthostatic hypotension in multiple system atrophy: pilot trial of chronic administration. *Clin Neuropharmacol* 1994; **17:** 380–3.
5. Hoeldtke RD, *et al.* Treatment of orthostatic hypotension with midodrine and octreotide. *J Clin Endocrinol Metab* 1998; **83:** 339–43.
6. Günal AI, *et al.* Short term reduction of left ventricular mass in primary hypertrophic cardiomyopathy by octreotide injections. *Heart* 1996; **76:** 418–21.
7. Demirtaş E, *et al.* Effects of octreotide in patients with hypertrophic obstructive cardiomyopathy. *Jpn Heart J* 1998; **39:** 173–81.

Chylous effusion. Chylous effusion results in accumulation of a milky lymphatic fluid containing raised concentrations of

white blood cells, triglycerides, and cholesterol. Chylothorax, when the effusion affects the pleural cavity, is generally a complication of malignancy or chest surgery, or may be idiopathic. Treatment usually involves catheter drainage and dietary modification; surgery is used when these measures fail. Octreotide has been used successfully in a number of cases, given subcutaneously or by continuous infusion, to treat chylothorax;[1-7] there are also reports of octreotide being ineffective.[8] Octreotide has also been used in chyloperitoneum[9-11] and for cervical chylous fistula.[12]

1. Demos NJ, *et al.* Somatostatin in the treatment of chylothorax. *Chest* 2001; **119:** 964–6.
2. Cheung Y, *et al.* Octreotide for treatment of postoperative chylothorax. *J Pediatr* 2001; **139:** 157–9.
3. Ottinger JG. Octreotide for persistent chylothorax in a pediatric patient. *Ann Pharmacother* 2002; **36:** 1106–7.
4. Demos NJ. Octreotide in the treatment of chylothorax. *Chest* 2002; **121:** 2080–1.
5. Al-Zubairy SA, Al-Jazairi AS. Octreotide as a therapeutic option for management of chylothorax. *Ann Pharmacother* 2003; **37:** 679–82.
6. Evans J, *et al.* Chylous effusions complicating lymphoma: a serious event with octreotide as a treatment option. *Hematol Oncol* 2003; **21:** 77–81.
7. Makrilakis K, *et al.* Successful octreotide treatment of chylous pleural effusion and lymphedema in the yellow nail syndrome. *Ann Intern Med* 2004; **141:** 246–7.
8. Mikroulis D, *et al.* Octreotide in the treatment of chylothorax. *Chest* 2002; **121:** 2079–80.
9. Bhatia C, *et al.* Octreotide therapy: a new horizon in treatment of iatrogenic chyloperitoneum. *Arch Dis Child* 2001; **85:** 234–5.
10. Leong RWL, *et al.* Chylous ascites caused by portal vein thrombosis treated with octreotide. *J Gastroenterol Hepatol* 2003; **18:** 1211–13.
11. Hwang J-B, *et al.* Resolution of refractory chylous ascites after Kasai portoenterostomy using octreotide. *J Pediatr Surg* 2004; **39:** 1806–7.
12. Suver DW, *et al.* Somatostatin treatment of massive lymphorrhea following excision of a lymphatic malformation. *Int J Pediatr Otorhinolaryngol* 2004; **68:** 845–50.

Cushing's syndrome. Cushing's syndrome (p.2344) can be caused by excessive secretion from an ectopic ACTH-secreting tumour. Many of these ectopic tumours express somatostatin receptors and it has been suggested that octreotide may be useful in the diagnosis, and possibly the treatment, of selected patients.[1] However, there are 5 types of somatostatin receptor,[2,3] and responses to octreotide have been variable,[4] even in the same patient.[3,5]

1. de Herder WW, Lamberts SWJ. Is there a role for somatostatin and its analogs in Cushing's syndrome? *Metabolism* 1996; **45** (suppl): 83–5.
2. de Herder WW, Lamberts SWJ. Octapeptide somatostatin-analogue therapy of Cushing's syndrome. *Postgrad Med J* 1999; **75:** 65–6.
3. Uwaifo GI, *et al.* Is there a therapeutic role for octreotide in patients with ectopic Cushing's syndrome? *J Endocrinol Invest* 2003; **26:** 710–17.
4. Woodhouse NJY, *et al.* Acute and long-term effects of octreotide in patients with ACTH-dependent Cushing's syndrome. *Am J Med* 1993; **95:** 305–8.
5. Gill GV, *et al.* Carcinoid-associated ectopic ACTH syndrome with variable response to octreotide. *Postgrad Med J* 1999; **75:** 98–101.

Diabetes mellitus. Although octreotide has been reported to impair glucose tolerance, and even precipitate frank diabetes (see Effects on Carbohydrate Metabolism, under Adverse Effects, above), its variable effects on blood glucose and insulin have led to investigations[1,2] of its ability to induce beta cell rest in patients with diabetes mellitus (p.431) who still have residual insulin secretion. There is also some suggestion that it may be of benefit in the treatment or prevention of diabetic nephropathy[3,4] and retinopathy.[5-7] Benefit has been reported from the use of octreotide in patients with diabetic diarrhoea—see under Gastrointestinal Disorders, below.

1. Björk E, *et al.* Induction of β-cell rest in type 1 diabetes. *Diabetes Care* 1998; **21:** 427–30.
2. Vondra K, *et al.* Somatostatin: beneficial effects on remission in young adult patients with newly diagnosed diabetes mellitus type 1. *Physiol Res* 2004; **53:** 115–17.
3. Serri O, *et al.* Somatostatin analogue, octreotide, reduces increased glomerular filtration rate and kidney size in insulin-dependent diabetes. *JAMA* 1991; **265:** 888–92.
4. Clemens A, *et al.* Octreotide (somatostatin analog) treatment reduces endothelial cell dysfunction in patients with diabetes mellitus. *Metabolism* 1999; **48:** 1236–40.
5. Grant MB, *et al.* The efficacy of octreotide in the therapy of severe nonproliferative and early proliferative diabetic retinopathy: a randomized controlled trial. *Diabetes Care* 2000; **23:** 504–9.
6. Boehm BO, *et al.* Octreotide reduces vitreous hemorrhage and loss of visual acuity risk in patients with high-risk proliferative diabetic retinopathy. *Horm Metab Res* 2001; **33:** 300–306.
7. Grant MB, Caballero S. Somatostatin analogues as drug therapies for retinopathies. *Drugs Today* 2002; **38:** 783–91.

Diagnosis and testing. Radiolabelled octreotide or other somatostatin analogues such as pentetreotide and depreotide may be used to visualise various malignant neoplasms which express somatostatin receptors.[1,2] Somatostatin receptor scintigraphy is the most sensitive method for imaging lesions in patients with Zollinger-Ellison syndrome.[3]

Octreotide may also have a role in the diagnosis of Cushing's syndrome, see above.

1. Breeman WAP, *et al.* Somatostatin receptor-mediated imaging and therapy: basic science, current knowledge, limitations and future perspectives. *Eur J Nucl Med* 2001; **28:** 1421–9.
2. van der Lely AJ, *et al.* Octreoscan radioreceptor imaging. *Endocrine* 2003; **20:** 307–11.
3. Gibril F, *et al.* Somatostatin receptor scintigraphy: its sensitivity compared with that of other imaging methods in detecting primary and metastatic gastrinomas: a prospective study. *Ann Intern Med* 1996; **125:** 26–34.

Eye disorders. There are reports of response to octreotide in 2 patients with bilateral cystoid macular oedema, a refractory form of retinal oedema.[1,2] In 1 case the problem recurred when octreotide was twice withdrawn and each time responded to resumption of octreotide injections.[1]

1. Kuijpers RWAM, *et al.* Treatment of cystoid macular edema with octreotide. *N Engl J Med* 1998; **338:** 624–6.
2. Hernaez-Ortega MC, *et al.* Sandostatin LAR for cystoid diabetic macular edema: a 1-year experience. *Diabetes Res Clin Pract* 2004; **64:** 71–2.

Gastrointestinal disorders. Somatostatin inhibits gastric and intestinal secretion and the production of various active substances in the gastrointestinal tract. It also reduces splanchnic arterial blood flow and portal and gastric mucosal blood flow. These properties are made use of, usually in the form of octreotide, in the management of a number of gastrointestinal disorders including bleeding, refractory diarrhoea, fistulae, dumping syndrome, and nausea and vomiting secondary to bowel obstruction (see Other Gastrointestinal Disorders, below).

Octreotide is used particularly in the treatment of carcinoid syndrome arising from endocrine tumours (see Carcinoid Tumours, p.643).

Bleeding. There have been mixed results with octreotide in the treatment of nonvariceal upper gastrointestinal bleeding. Although a large multicentre study[1] showed that octreotide had no benefit compared with placebo in the management of bleeding upper gastrointestinal ulcers, a meta-analysis that included somatostatin and octreotide suggested there might be some benefit.[2] Nevertheless, a later study[3] found that octreotide, given as an adjunct to endoscopic haemostasis using noradrenaline, did not seem to provide any additional benefit, and it is not recommended in the management of nonvariceal bleeding associated with peptic ulcer (p.1702).

Octreotide may be used in the management of variceal haemorrhage (see under Monoethanolamine, p.2346). A systematic review[4] of studies comparing somatostatin or its analogues with either placebo or no drug treatment found that although there was a small benefit in controlling bleeding, it was doubtful whether this benefit was worthwhile, and that deaths were not reduced. There is some evidence that octreotide is as effective as sclerotherapy in the control of acute bleeding.[5] A meta-analysis[6] of studies comparing octreotide with other therapies (including vasopressin, terlipressin, sclerotherapy, or balloon tamponade) for the control of acute variceal bleeding found that octreotide had a similar effect to sclerotherapy in the prevention of rebleeding and was more effective and associated with fewer major complications than vasopressin or terlipressin. However, there was no evidence of mortality benefit associated with octreotide use. Another systematic review[7] also found that sclerotherapy was no better than drug therapy, including octreotide, but associated with more frequent and severe adverse effects. Controlled studies have suggested that combination of octreotide infusion for 5 days with endoscopic ligation[8] or sclerotherapy[9,10] reduces the risk of rebleeding. In another study,[11] sclerotherapy with 48 hours of octreotide infusion was more effective at controlling bleeding than sclerotherapy alone, and octreotide was as effective as sclerotherapy in those with evidence of recent bleeding. However, another study[12] found that octreotide given subcutaneously for up to 29 days after sclerotherapy did not affect the rate of early rebleeding. Octreotide has also produced some benefit (combined with regular sclerotherapy), in the long-term management of patients with cirrhotic portal hypertension.[13]

1. Christiansen J, *et al.* Placebo-controlled trial with the somatostatin analogue SMS 201-995 in peptic ulcer bleeding. *Gastroenterology* 1989; **97:** 568–74.
2. Imperiale TF, Birgisson S. Somatostatin or octreotide compared with H antagonists and placebo in the management of acute nonvariceal upper gastrointestinal hemorrhage: a meta-analysis. *Ann Intern Med* 1997; **127:** 1062–71. Correction. *ibid.* 1998; **128:** 245.
3. Nikolopoulou VN, *et al.* The effect of octreotide as an adjunct treatment in active nonvariceal upper gastrointestinal bleeding. *J Clin Gastroenterol* 2004; **38:** 243–7.
4. Gøtzsche PC, Hróbjartsson A. Somatostatin analogues for acute bleeding oesophageal varices. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2008 (accessed 21/08/08).
5. Jenkins SA, *et al.* A multicentre randomised trial comparing octreotide and injection sclerotherapy in the management and outcome of acute variceal haemorrhage. *Gut* 1997; **41:** 526–33.
6. Corley DA, *et al.* Octreotide for acute esophageal variceal bleeding: a meta-analysis. *Gastroenterology* 2001; **120:** 946–54.
7. D'Amico G, *et al.* Emergency sclerotherapy versus medical interventions for bleeding oesophageal varices in cirrhotic patients. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2002 (accessed 16/09/05).
8. Sung JJY, *et al.* Prospective randomised study of effect of octreotide on rebleeding from oesophageal varices after endoscopic ligation. *Lancet* 1995; **346:** 1666–9.
9. Besson I, *et al.* Sclerotherapy with or without octreotide for acute variceal bleeding. *N Engl J Med* 1995; **333:** 555–60.
10. Zuberi BF, Baloch Q. Comparison of endoscopic variceal sclerotherapy alone and in combination with octreotide in controlling acute variceal hemorrhage and early rebleeding in patients with low-risk cirrhosis. *Am J Gastroenterol* 2000; **95:** 768–71.
11. Freitas DS, *et al.* Octreotide in acute bleeding esophageal varices: a prospective randomized study. *Hepatogastroenterology* 2000; **47:** 1310–14.
12. Primignani M, *et al.* Sclerotherapy plus octreotide versus sclerotherapy alone in the prevention of early rebleeding from esophageal varices: a randomized, double-blind, placebo-controlled, multicenter trial. *Hepatology* 1995; **21:** 1322–7.
13. Jenkins SA, *et al.* Randomised trial of octreotide for long term management of cirrhosis after variceal haemorrhage. *BMJ* 1997; **315:** 1338–41.

Diarrhoea. Octreotide has been tried for its effects on gastrointestinal secretion and intestinal transit time in the management of severe refractory diarrhoea associated with a variety of conditions. A review[1] found that studies were generally small, and that although there appeared to be an overall benefit associated with the use of octreotide, response was influenced by the cause of diarrhoea. There are reports of octreotide controlling diarrhoea associated with amyloidosis,[2-4] diabetes mellitus,[5-11] and bone marrow transplantation.[12,13] Although octreotide was reported to be useful in a case of microvillous atrophy,[14] others have not found it to be effective.[15] There have been reports of benefit in refractory AIDS-associated diarrhoea,[16] and it has been licensed for this use in some countries, but a double-blind, controlled study found octreotide to be no more beneficial than placebo.[17] In patients with the short bowel syndrome and jejunostomies or ileostomies, octreotide may be useful in decreasing faecal mass[18] or jejunal efflux,[19] and increasing small bowel transit time.[20] Octreotide has also been used with some benefit in refractory diarrhoea associated with chemotherapy, particularly with regimens that include fluorouracil[21,22] and irinotecan.[23] In a small series of patients[24] the use of depot octreotide controlled most episodes of diarrhoea, and allowed the continuation of chemotherapy in some cases.

1. Szilagyi A, Shrier I. Systematic review: the use of somatostatin or octreotide in refractory diarrhoea. *Aliment Pharmacol Ther* 2001; **15:** 1889–97.
2. O'Connor CR, O'Dorisio TM. Amyloidosis, diarrhea, and a somatostatin analogue. *Ann Intern Med* 1989; **110:** 665–6.
3. Gilanders IA, *et al.* Octreotide therapy for diarrhoea. *Postgrad Med J* 1997; **73:** 62.
4. Jeong Y-S, *et al.* Successful treatment of protein-losing enteropathy due to AA amyloidosis with somatostatin analogue and high dose steroid in ankylosing spondylitis. *Clin Exp Rheumatol* 2000; **18:** 619–21.
5. Tsai S-T, *et al.* Diabetic diarrhea and somatostatin. *Ann Intern Med* 1986; **104:** 894.
6. Michaels PE, Cameron RB. Octreotide is cost-effective therapy in diabetic diarrhea. *Arch Intern Med* 1991; **151:** 2469.
7. Mourad FH, *et al.* Effective treatment of diabetic diarrhoea with somatostatin analogue, octreotide. *Gut* 1992; **33:** 1578–80.
8. Nakabayashi H, *et al.* Marked improvement of diabetic diarrhea with the somatostatin analogue octreotide. *Arch Intern Med* 1994; **154:** 1863–7.
9. Virally-Monod ML, *et al.* Variable efficacy of octreotide in diabetic diarrhea. *Diabetes Metab* 1996; **22:** 356–8.
10. Murao S, *et al.* Severe diabetic diarrhea successfully treated with octreotide, a somatostatin analogue. *Endocr J* 1999; **46:** 477–8.
11. Meyer C, *et al.* Octreotide treatment of severe diabetic diarrhoea. *Intern Med J* 2003; **33:** 617–8.
12. Crouch MA, *et al.* Octreotide acetate in refractory bone marrow transplant-associated diarrhea. *Ann Pharmacother* 1996; **30:** 331–6.
13. Ippoliti C, *et al.* Use of octreotide in the symptomatic management of diarrhea induced by graft-versus-host disease in patients with hematological malignancies. *J Clin Oncol* 1997; **15:** 3350–4.
14. Couper RTL, *et al.* Clinical response to the long acting somatostatin analogue SMS 201-995 in a child with congenital microvillus atrophy. *Gut* 1989; **30:** 1020–4.
15. Beck NS, *et al.* Microvillus inclusion disease in two Korean infants. *J Korean Med Sci* 1997; **12:** 452–6.
16. Montaner JSG, *et al.* Octreotide therapy in AIDS-related, refractory diarrhea: results of a multicentre Canadian-European study. *AIDS* 1995: **9:** 209–10.
17. Simon DM, *et al.* Multicenter trial of octreotide in patients with refractory acquired immunodeficiency syndrome–associated diarrhea. *Gastroenterology* 1995; **108:** 1753–60. Correction. *ibid.*; **109:** 1024.
18. Ladefoged K, *et al.* Effect of a long acting somatostatin analogue SMS 201-995 on jejunostomy effluents in patients with severe short bowel syndrome. *Gut* 1989; **30:** 943–9.
19. Nightingale JMD, *et al.* Jejunal efflux in short bowel syndrome. *Lancet* 1990; **336:** 765–8.
20. Nehra V, *et al.* An open trial of octreotide long-acting release in the management of short bowel syndrome. *Am J Gastroenterol* 2001; **96:** 1494–8.
21. Goumas P, *et al.* Octreotide acetate in the treatment of fluorouracil-induced diarrhea. *Oncologist* 1998; **3:** 50–3.
22. Zidan J, *et al.* Octreotide in the treatment of severe chemotherapy-induced diarrhea. *Ann Oncol* 2001; **12:** 227–9.
23. Barbounis V, *et al.* Control of irinotecan-induced diarrhea by octreotide after loperamide failure. *Support Care Cancer* 2001; **9:** 258–60.
24. Rosenoff S. Resolution of refractory chemotherapy-induced diarrhea (CID) with octreotide long-acting formulation in cancer patients: 11 case studies. *Support Care Cancer* 2004; **12:** 561–70.

Fistulae. Octreotide has been used in the management of postoperative small-bowel fistulae. There have been mixed reports, but some have found reduced fistula output,[1,2] with the time to spontaneous fistula closure either reduced[1] or unchanged.[2] Octreotide has also been reported to accelerate healing of pancreatic cutaneous fistulae of various causes,[3]

but others[4] have found no benefit from octreotide in preventing pancreatic fistula formation after pancreaticoduodenectomy. A systematic review[5] of controlled trials commented on the variation in trial methods and conflicting results, but concluded that there is probably benefit in giving octreotide preoperatively to prevent complications of pancreatic surgery, and that in established postoperative fistulae it may have a limited role in reducing fistula output and reducing the time to fistula closure. In a series of 5 patients[6] with Crohn's disease who were treated for 8 weeks with high-dose octreotide, enterocutaneous fistulae closed in 4 cases.

1. Nubiola-Calonge P, *et al.* Blind evaluation of the effect of octreotide (SMS 201-995), a somatostatin analogue, on small-bowel fistula output. *Lancet* 1987; **ii:** 672–4.
2. Alivizatos V, *et al.* Evaluation of the effectiveness of octreotide in the conservative treatment of postoperative enterocutaneous fistulas. *Hepatogastroenterology* 2002; **49:** 1010–12.
3. Prinz RA, *et al.* Treatment of pancreatic cutaneous fistulas with a somatostatin analog. *Am J Surg* 1988; **155:** 36–42.
4. Barnett SP, *et al.* Octreotide does not prevent postoperative pancreatic fistula or mortality following pancreaticoduodenectomy. *Am Surg* 2004; **70:** 222–7.
5. Li-Ling J, Irving M. Somatostatin and octreotide in the prevention of postoperative pancreatic complications and the treatment of enterocutaneous pancreatic fistulas: a systematic review of randomized controlled trials. *Br J Surg* 2001; **88:** 190–9.
6. Lavy A, Yasin K. Octreotide for enterocutaneous fistulas of Crohn's disease. *Can J Gastroenterol* 2003; **17:** 555–8.

OTHER GASTROINTESTINAL DISORDERS. Other gastrointestinal disorders in which octreotide might be useful include dumping syndrome[1,2] (p.1695), reactive (or postprandial) hypoglycaemia,[3] and protein-losing enteropathy associated with intestinal lymphangiectasia.[4,5] Nausea and vomiting secondary to bowel obstruction in patients terminally ill with cancer may also be relieved by octreotide.[6,7] The *BNF* states that in palliative care a dose of 300 to 600 micrograms may be given by subcutaneous infusion over 24 hours to reduce intestinal secretions and vomiting.

1. Vecht J, *et al.* Long-term results of octreotide-therapy in severe dumping syndrome. *Clin Endocrinol (Oxf)* 1999; **51:** 619–24.
2. Li-Ling J, Irving M. Therapeutic value of octreotide for patients with severe dumping syndrome—a review of randomised controlled trials. *Postgrad Med J* 2001; **77:** 441–2.
3. Lehnert H, *et al.* Treatment of severe reactive hypoglycemia with a somatostatin analogue (SMS 201-995). *Arch Intern Med* 1990; **150:** 2401–2.
4. Klingenberg RD, *et al.* Type I intestinal lymphangiectasia treated successfully with slow-release octreotide. *Dig Dis Sci* 2003; **48:** 1506–9.
5. Lee HL, *et al.* Successful treatment of protein-losing enteropathy induced by intestinal lymphangiectasia in a liver cirrhosis patient with octreotide: a case report. *J Korean Med Sci* 2004; **19:** 466–9.
6. Ripamonti C, *et al.* The role of somatostatin and octreotide in bowel obstruction: pre-clinical and clinical results. *Tumori* 2001; **87:** 1–9.
7. Mystakidou K, *et al.* Comparison of octreotide administration vs conservative treatment in the management of inoperable bowel obstruction in patients with far advanced cancer: a randomized, double-blind, controlled clinical trial. *Anticancer Res* 2002; **22:** 1187–92.

Hypercalcaemia. There have been individual reports of hypercalcaemia associated with raised plasma concentrations of parathyroid hormone-related protein (hypercalcaemia of malignancy—p.1083) being successfully controlled with octreotide in patients with malignant pancreatic endocrine tumours[1,2] and adrenal phaeochromocytoma.[3] Octreotide also resolved hypercalcaemia occurring in a patient with VIPoma and vasoactive intestinal peptide concentrations declined.[4] In two patients with a parathyroid hormone-related protein secreting carcinoid tumour, octreotide reduced protein concentrations in both patients[5,6] but controlled hypercalcaemia in only one.[6] Octreotide also normalised calcium concentrations in a patient with hypercalcaemia related to B cell lymphoma.[7] In many of these cases, hypercalcaemia had previously been resistant to treatment with bisphosphonates.

1. Wynick D, *et al.* Treatment of a malignant pancreatic endocrine tumour secreting parathyroid hormone related protein. *BMJ* 1990; **300:** 1314–15.
2. Dodwell D, *et al.* Treatment of a pancreatic tumour secreting parathyroid hormone related protein. *BMJ* 1990; **300:** 1653.
3. Harrison M, *et al.* Somatostatin analogue treatment for malignant hypercalcaemia. *BMJ* 1990; **300:** 1313–14. Correction. *ibid.*; **301:** 97 [dosage error].
4. Venkatesh S, *et al.* Somatostatin analogue: use in the treatment of vipoma with hypercalcaemia. *Am J Med* 1989; **87:** 356–7.
5. Mantzoros CS, *et al.* Intractable hypercalcaemia due to parathyroid hormone-related peptide secretion by a carcinoid tumour. *Clin Endocrinol (Oxf)* 1997; **46:** 373–5.
6. Barhoum M, *et al.* Intractable hypercalcemia due to a metastatic carcinoid secreting parathyroid hormone-related peptide and interleukin-6: response to octreotide. *Am J Med Sci* 1999; **318:** 203–5.
7. Pezzilli R, *et al.* Octreotide for the treatment of hypercalcemia related to B cell lymphoma. *Oncology* 1997; **54:** 517–18.

Hyperinsulinism. As well as reactive hypoglycaemia (see under Other Gastrointestinal Disorders, above), octreotide has been used to control inappropriate insulin secretion, both in the short-term and long-term, in children with hypoglycaemia of infancy,[1-4] or nesidioblastosis.[5-7] Although not licensed in the UK for children, the *BNFC* includes a dose of octreotide for persistent hyperinsulinaemic hypoglycaemia unresponsive to diazoxide and glucose. For neonates an initial dose of 2 to 5 micrograms/kg may be given every 6 to 8 hours subcutaneously and adjusted according to response. For children aged from 1 month to 18 years, an initial dose of 1 to 2 micrograms/kg every 4 to 6 hours may be used. Doses up to 7 micrograms/kg every 4 hours may be required in rare cases.

Octreotide has also been used to treat a patient with hyperinsulinaemia induced by quinine.[8,9] For mention of investigations of octreotide for the reverse effect, see Diabetes Mellitus, above.

1. Kirk JMW, *et al.* Somatostatin analogue in short term management of hyperinsulinism. *Arch Dis Child* 1988; **63:** 1493–4.
2. DeClue TJ, *et al.* Linear growth during long-term treatment with somatostatin analog (SMS 201-995) for persistent hyperinsulinemic hypoglycemia of infancy. *J Pediatr* 1990; **116:** 747–50.
3. Thornton PS, *et al.* Short- and long-term use of octreotide in the treatment of congenital hyperinsulinism. *J Pediatr* 1993; **123:** 637–43.
4. Aynsley-Green A, *et al.* Practical management of hyperinsulinism in infancy. *Arch Dis Child Fetal Neonatal Ed* 2000; **82:** F98–F107.
5. Hindmarsh P, Brook CGD. Short-term management of nesidioblastosis using the somatostatin analogue SMS 201-995. *N Engl J Med* 1987; **316:** 221–2.
6. Delemarre-van de Waal HA, *et al.* Long-term treatment of an infant with nesidioblastosis using a somatostatin analogue. *N Engl J Med* 1987; **316:** 222–3.
7. Behrens R, *et al.* Unusual course of neonatal hyperinsulinaemic hypoglycaemia (nesidioblastosis). *Arch Dis Child* 1998; **78:** F156.
8. Phillips RE, *et al.* Effectiveness of SMS 201-995, a synthetic, long-acting somatostatin analogue, in treatment of quinine-induced hyperinsulinaemia. *Lancet* 1986; **i:** 713–16.
9. Phillips RE, *et al.* Hypoglycaemia and counterregulatory hormone responses in severe falciparum malaria: treatment with Sandostatin. *Q J Med* 1993; **86:** 233–40.

Malignant neoplasms. See also Carcinoid Syndrome, above. For mention of the use of octreotide to treat nausea and vomiting associated with malignant gastrointestinal obstruction see under Other Gastrointestinal Disorders, above. Octreotide has also proved of benefit in some patients with cancer pain (see Pain, below). An unconventional regimen using octreotide or somatostatin with melatonin, bromocriptine, and a solution of retinoids (the Di Bella regimen) was investigated in patients with a variety of advanced malignancies and found to be ineffective.[1,2]

1. Italian Study Group for the Di Bella Multitherapy Trials. Evaluation of an unconventional cancer treatment (the Di Bella multitherapy): results of phase II trials in Italy. *BMJ* 1999; **318:** 224–8.
2. Buiatti E, *et al.* Results from a historical survey of the survival of cancer patients given Di Bella multitherapy. *Cancer* 1999; **86:** 2143–9.

HEPATOCELLULAR CARCINOMA. In a study in 58 patients with advanced hepatocellular carcinoma (p.667) treatment with octreotide was associated with prolongation of survival compared with no treatment.[1] In a further case report[2] cancer regression occurred in a patient given octreotide, and a study[3] found better survival in patients treated with octreotide and tamoxifen compared with fluorouracil and mitomycin. However, other studies of octreotide in patients with advanced hepatocellular carcinoma failed to demonstrate any benefit.[4,5]

1. Kouroumalis E, *et al.* Treatment of hepatocellular carcinoma with octreotide: a randomised controlled study. *Gut* 1998; **42:** 442–7.
2. Siveke JT, *et al.* Complete regression of advanced HCC with long acting octreotide. *Gut* 2003; **52:** 1531. Correction. *ibid.*; 1800.
3. Pan D-Y, *et al.* Tamoxifen combined with octreotide or regular chemotherapeutic agents in treatment of primary liver cancer: a randomized controlled trial. *Hepatobiliary Pancreat Dis Int* 2003; **2:** 211–15.
4. Yuen M-F, *et al.* A randomized placebo-controlled study of long-acting octreotide for the treatment of advanced hepatocellular carcinoma. *Hepatology* 2002; **36:** 687–91.
5. Lersch C, *et al.* Treatment of HCC with pravastatin, octreotide, or gemcitabine - a critical evaluation. *Hepatogastroenterology* 2004; **51:** 1099–1103.

MENINGIOMA. Octreotide has been reported to suppress headaches and visual disturbances associated with meningioma in a small number of patients.[1-3] Doses were generally started at 100 micrograms three times daily subcutaneously, but were increased to 500 micrograms three times daily in some cases because of tolerance. Although it was thought that octreotide may have had a beneficial effect on the meningioma size in one case,[1] others found no evidence of tumour shrinkage.[2,3]

1. Rünzi MW, *et al.* Successful treatment of meningioma with octreotide. *Lancet* 1989; **i:** 1074.
2. García-Luna PP, *et al.* Clinical use of octreotide in unresectable meningiomas: a report of three cases. *J Neurosurg Sci* 1993; **37:** 237–41.
3. Jaffrain-Rea M-L, *et al.* Visual improvement during octreotide therapy in a case of episellar meningioma. *Clin Neurol Neurosurg* 1998; **100:** 40–3.

THYMOMA. A patient with thymoma and pure red cell aplasia, in whom corticosteroids alone failed to control anaemia, had complete remission after treatment with octreotide and prednisone, and subsequently remained well on long-term maintenance therapy with octreotide 500 micrograms twice daily subcutaneously and prednisone 200 micrograms/kg daily.[1] In a study[2] that included 32 patients with thymoma and a positive octreotide scan, octreotide therapy alone (500 micrograms subcutaneously three times daily for up to 1 year) or with prednisone (600 micrograms/kg daily) had modest activity; there were 2 complete and 10 partial responses overall.

1. Palmieri G, *et al.* Successful treatment of a patient with a thymoma and pure red-cell aplasia with octreotide and prednisone. *N Engl J Med* 1997; **336:** 263–5. Correction. *ibid.*; 1039.
2. Loehrer PJ, *et al.* Octreotide alone or with prednisone in patients with advanced thymoma and thymic carcinoma: an Eastern Cooperative Oncology Group phase II trial. *J Clin Oncol* 2004; **22:** 293–9. Correction. *ibid.*; 2261.

Nesidioblastosis. For reference to the use of octreotide in nesidioblastosis, see Hyperinsulinism, above.

Obesity. Hypothalamic obesity can be a complication of hypothalamic damage caused by insults such as head trauma, brain tumours, and cranial surgery or irradiation. Octreotide has improved body-weight, body-mass index, and regulation of insulin secretion in small studies of children with hypothalamic obesity.[1,2] Octreotide is also under investigation in the treatment of Prader-Willi syndrome (p.2149).[3]

1. Lustig RH, *et al.* Hypothalamic obesity caused by cranial insult in children: altered glucose and insulin dynamics and reversal by a somatostatin agonist. *J Pediatr* 1999; **135:** 162–8.
2. Lustig RH, *et al.* Octreotide therapy of pediatric hypothalamic obesity: a double-blind, placebo-controlled trial. *J Clin Endocrinol Metab* 2003; **88:** 2586–92.
3. Haqq AM, *et al.* Circulating ghrelin levels are suppressed by meals and octreotide therapy in children with Prader-Willi syndrome. *J Clin Endocrinol Metab* 2003; **88:** 3573–6.

Pain. Octreotide 120 to 480 micrograms daily was given by continuous intrathecal infusion to 6 patients with cancer pain that had been poorly controlled by opioid analgesics.[1] All patients obtained good pain relief, 3 reporting pain to be totally absent. Sustained decrease in incapacitating bone pain has also been reported in a patient with skeletal metastasis of a gastrinoma who was given subcutaneous octreotide 100 micrograms three times daily.[2] The pain of hypertrophic pulmonary osteoarthropathy (a paraneoplastic syndrome of periostitis, arthropathy, and gynaecomastia seen particularly with squamous cell lung cancer) has also been reported to respond to octreotide.[3] However, a controlled study of octreotide in cancer pain found that it was no better than placebo in most patients.[4] (General guidelines for the management of cancer pain are discussed on p.5.) Octreotide has also been reported to ease headache associated with meningioma (above), and pituitary adenoma (see Acromegaly, above, and Pituitary Adenoma, below).

The use of intrathecal octreotide has also been described[5] in 2 patients with severe intractable non-malignant pain. During 5 years of treatment, octreotide provided a beneficial degree of pain relief and allowed a reduction in opioid dosage. However, the dose of octreotide had to be gradually increased, suggesting tolerance to the analgesic effect; one patient was receiving a daily dose of 648 micrograms.

1. Penn RD, *et al.* Octreotide: a potent new non-opiate analgesic for intrathecal infusion. *Pain* 1992; **49:** 13–19.
2. Burgess JR, *et al.* Effective control of bone pain by octreotide in a patient with metastatic gastrinoma. *Med J Aust* 1996; **164:** 725–7.
3. Johnson SA, *et al.* Treatment of resistant pain in hypertrophic pulmonary osteoarthropathy with subcutaneous octreotide. *Thorax* 1997; **52:** 298–9.
4. De Conno F, *et al.* Subcutaneous octreotide in the treatment of pain in advanced cancer patients. *J Pain Symptom Manage* 1994; **9:** 34–8.
5. Paice JA, *et al.* Intrathecal octreotide for relief of intractable nonmalignant pain: 5-year experience with two cases. *Neurosurgery* 1996; **38:** 203–7.

Pancreatic disorders. Octreotide has been tried in the treatment of acute pancreatitis, but was found to be ineffective.[1] For reference to the use of octreotide in the management of pancreatic endocrine tumours, see under Carcinoid Tumours (p.643); for its use in pancreatic fistulae, see under Gastrointestinal Disorders, above.

1. Uhl W, *et al.* A randomised, double blind, multicentre trial of octreotide in moderate to severe acute pancreatitis. *Gut* 1999; **45:** 97–104.

Pituitary adenoma. Octreotide has a role in the management of pituitary adenomas that cause acromegaly (see above). It has also been used in the management of rare tumours such as thyrotropin-secreting pituitary adenomas, usually when surgery or radiotherapy have failed. Octreotide may reduce concentrations of thyrotropin and normalise thyroid hormones in most patients; tumour shrinkage also occurs in at least a third of cases.[1-4] Octreotide has also been tried in the management of other rare adenomas such as clinically nonfunctioning adenomas, but results have been mixed; in a few cases there has been relief of symptoms such as headache without any change in tumour volume.[5]

1. Chanson P, *et al.* Octreotide therapy for thyroid-stimulating hormone-secreting pituitary adenomas: a follow-up of 52 patients. *Ann Intern Med* 1993; **119:** 236–40.
2. Caron P, *et al.* Efficacy of the long-acting octreotide formulation (octreotide-Lar) in patients with thyrotropin-secreting pituitary adenomas. *J Clin Endocrinol Metab* 2001; **86:** 2849–53.
3. Beck-Peccoz P, Persani L. Medical management of thyrotropin-secreting pituitary adenomas. *Pituitary* 2002; **5:** 83–8.
4. Socin HV, *et al.* The changing spectrum of TSH-secreting pituitary adenomas: diagnosis and management in 43 patients. *Eur J Endocrinol* 2003; **148:** 433–42.
5. Colao A, *et al.* Somatostatin analogs in treatment of non-growth hormone–secreting pituitary adenomas. *Endocrine* 2003; **20:** 279–83.

Pretibial myxoedema. Pretibial myxoedema (deposition of glycosaminoglycans in the subcutaneous tissue of the shins) is associated with Graves' disease (see Hyperthyroidism, p.2165). There are reports of apparent benefit from the use of octreotide for this condition. In one case,[1,2] octreotide given for 6 months after surgical removal of the myxoedematous tissue may have prevented its recurrence. In another,[3] octreotide injected intralesionally was reported to improve and control the condition. However, in other cases[4] subcutaneous octreotide has been ineffective.

1. Derrick EK, *et al.* Successful surgical treatment of severe pretibial myxoedema. *Br J Dermatol* 1995; **133:** 317–18.
2. Felton J, *et al.* Successful combined surgical and octreotide treatment of severe pretibial myxoedema reviewed after 9 years. *Br J Dermatol* 2003; **148:** 825–6.
3. Shinohara M, *et al.* Refractory pretibial myxoedema with response to intralesional insulin-like growth factor 1 antagonist (octreotide): downregulation of hyaluronic acid production by the lesional fibroblasts. *Br J Dermatol* 2000; **143:** 1083–6.
4. Rotman-Pikielny P, *et al.* Lack of effect of long-term octreotide therapy in severe thyroid-associated dermopathy. *Thyroid* 2003; **13:** 465–70.

Raised intracranial pressure. For a reference to octreotide being tried in idiopathic intracranial hypertension, see p.1181.

Sulfonylurea overdose. Octreotide has been used in the treatment of severe refractory cases of sulfonylurea-induced hypoglycaemia (see p.461).

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Sandostatin; ***Austral.:*** Sandostatin; ***Austria:*** Sandostatin; ***Belg.:*** Sandostatine; ***Braz.:*** Sandostatin; ***Canad.:*** Sandostatin; ***Chile:*** Sandostatin; ***Cz.:*** Sandostatin; ***Denm.:*** Sandostatin; ***Fin.:*** Sandostatin; ***Fr.:*** Sandostatine; ***Ger.:*** Sandostatin; ***Gr.:*** Sandostatin; ***Hong Kong:*** Sandostatin; ***Hung.:*** Sandostatin; ***India:*** Sandostatin; ***Indon.:*** Sandostatin; ***Irl.:*** Sandostatin; ***Israel:*** Sandostatin; ***Ital.:*** Longastatina; Samilstin; Sandostatina; ***Malaysia:*** Sandostatin; ***Mex.:*** Proclose; Sandostatina; ***Neth.:*** Sandostatine; ***Norw.:*** Sandostatin; ***NZ:*** Sandostatin; ***Philipp.:*** Sandostatin; ***Port.:*** Sandostatina; ***Rus.:*** Sandostatin (Сандостатин); ***S.Afr.:*** Sandostatin; ***Singapore:*** Sandostatin; ***Spain:*** Sandostatin; ***Swed.:*** Sandostatin; ***Switz.:*** Sandostatine; ***Thai.:*** Sandostatin; ***Turk.:*** Sandostatin; ***UK:*** Sandostatin; ***USA:*** Sandostatin; ***Venez.:*** Sandostatin.

Multi-ingredient: ***Pol.:*** Sandostatin.

Pegvisomant *(USAN, rINN)*

B2036-PEG; Pegvisomantti; Pegvisomantum. 18-L-Aspartic acid-21-L-asparagine-120-L-lysine-167-L-asparagine-168-L-alanine-171-L-serine-172-L-arginine-174-L-serine-179-L-threonine growth hormone (human), reaction product with polyethylene glycol.

Пегвизомант

CAS — 218620-50-9.

ATC — H01AX01.

ATC Vet — QH01AX01.

Adverse Effects and Precautions

Adverse effects commonly reported with the use of pegvisomant include gastrointestinal disturbances, elevated liver function tests, flu-like symptoms, fatigue, injection site reactions, arthralgia, myalgia, peripheral oedema, headache, dizziness, somnolence, tremor, sweating, pruritus, rash, sleep disorders, hypercholesterolaemia, weight gain, hyperglycaemia, hunger, and hypertension.

Liver function tests should be measured before starting pegvisomant, then every 4 to 6 weeks for the first 6 months of therapy. In the USA, it is also recommended that further testing take place twice in the next 6 months and then twice in the following year.

Pegvisomant is structurally similar to growth hormone and may cause assays to overestimate growth hormone concentrations.

Effects on the skin. Lipohypertrophy has been described in patients who have consistently injected pegvisomant into the same subcutaneous area.[1,2] The efficacy of pegvisomant was also reduced in one case, but lipohypertrophy resolved and pegvisomant efficacy improved when the patient used the recommended technique of injection site rotation.[2]

1. Maffei P, *et al.* Lipohypertrophy in acromegaly induced by the new growth hormone receptor antagonist pegvisomant. *Ann Intern Med* 2006; **145:** 310–12.
2. Marazuela M, *et al.* Pegvisomant-induced lipohypertrophy: report of a case with histopathology. *Ann Intern Med* 2007; **147:** 741–3.

Interactions

Pegvisomant may increase insulin sensitivity. In patients with diabetes, doses of insulin or oral hypoglycaemics may need to be decreased because of the increased risk of hypoglycaemia. Patients taking opioid analgesics may require higher serum concentrations of pegvisomant to achieve appropriate IGF-I suppression.

Pharmacokinetics

Pegvisomant is absorbed slowly after subcutaneous injection, and peak serum concentrations occur after about 33 to 77 hours. It is slowly eliminated from serum, with a half-life estimated to range from 74 to 172 hours. Renal clearance of pegvisomant is negligible.

Uses and Administration

Pegvisomant is a protein of recombinant DNA origin to which several polyethylene glycol polymers are covalently bound. It is an analogue of human growth hormone that acts as an antagonist at growth hormone receptors, and is used in the treatment of acromegaly (below). A loading dose of 40 or 80 mg is given subcutaneously, followed by 10 mg daily. Further dose adjustments, in increments of 5 mg, are made according to serum concentrations of IGF-I, which should be measured every 4 to 6 weeks. The maintenance dose should not exceed 30 mg daily.

Acromegaly. Pegvisomant may be used in patients with acromegaly (p.1798) who have not responded adequately to surgery, radiotherapy, or somatostatin analogues, or when these therapies are unsuitable or not tolerated. The combination of pegvisomant with a somatostatin analogue is also under investigation in patients whose response to a somatostatin analogue alone is inadequate.

References.

1. Trainer PJ, *et al.* Treatment of acromegaly with the growth hormone-receptor antagonist pegvisomant. *N Engl J Med* 2000; **342:** 1171–7.
2. Herman-Bonert VS, *et al.* Growth hormone receptor antagonist therapy in acromegalic patients resistant to somatostatin analogs. *J Clin Endocrinol Metab* 2000; **85:** 2958–61.
3. van der Lely AJ, *et al.* Long-term treatment of acromegaly with pegvisomant, a growth hormone receptor antagonist. *Lancet* 2001; **358:** 1754–9.
4. Clemmons DR, *et al.* Optimizing control of acromegaly: integrating a growth hormone receptor antagonist into the treatment algorithm. *J Clin Endocrinol Metab* 2003; **88:** 4759–67.
5. Muller AF, *et al.* Growth hormone receptor antagonists. *J Clin Endocrinol Metab* 2004; **89:** 1503–11.
6. Feenstra J, *et al.* Combined therapy with somatostatin analogues and weekly pegvisomant in active acromegaly. *Lancet* 2005; **365:** 1644–6. Correction. *ibid.*; 1620.
7. Jehle S, *et al.* Alternate-day administration of pegvisomant maintains normal serum insulin-like growth factor-I levels in patients with acromegaly. *J Clin Endocrinol Metab* 2005; **90:** 1588–93.
8. Colao A, *et al.* Efficacy of 12-month treatment with the GH receptor antagonist pegvisomant in patients with acromegaly resistant to long-term, high-dose somatostatin analog treatment: effect on IGF-I levels, tumor mass, hypertension and glucose tolerance. *Eur J Endocrinol* 2006; **154:** 467–77.
9. Pivonello R, *et al.* Treatment with growth hormone receptor antagonist in acromegaly: effect on cardiac structure and performance. *J Clin Endocrinol Metab* 2007; **92:** 476–82. Correction. *ibid.*; 1605.
10. Neggers SJCMM, *et al.* Long-term efficacy and safety of combined treatment of somatostatin analogs and pegvisomant in acromegaly. *J Clin Endocrinol Metab* 2007; **92:** 4598–4601.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Somavert; ***Belg.:*** Somavert; ***Braz.:*** Somavert; ***Cz.:*** Somavert; ***Denm.:*** Somavert; ***Fin.:*** Somavert; ***Fr.:*** Somavert; ***Ger.:*** Somavert; ***Gr.:*** Somavert; ***Irl.:*** Somavert; ***Ital.:*** Somavert; ***Neth.:*** Somavert; ***Norw.:*** Somavert; ***Port.:*** Somavert; ***Spain:*** Somavert; ***Swed.:*** Somavert; ***UK:*** Somavert; ***USA:*** Somavert.

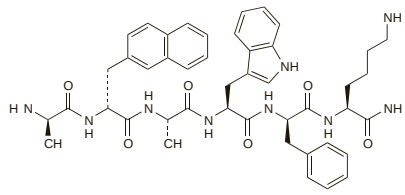
Pralmorelin Dihydrochloride *(USAN, rINNM)* ⊗

Dihidrocloruro de pralmorelina; GHRP-2 (pralmorelin); Growth Hormone-releasing Peptide-2 (pralmorelin); KP-102 (pralmorelin); Pralmoréline, Dichlorhydrate de; Pralmorelini Dihydrochloridum; WAY-GPA-748. D-Alanyl-3-(2-naphthyl)-D-alanyl-L-alanyl-L-tryptophyl-D-phenylalanyl-L-lysinamide dihydrochloride.

Пральморелина Дигидрохлорид

$C_{45}H_{55}N_9O_6$,2HCl = 890.9.

CAS — 158861-67-7 (pralmorelin); 158827-34-0 (pralmorelin dihydrochloride).



(pralmorelin)

Profile

Pralmorelin is a small synthetic peptide that stimulates the release of growth hormone. It is under investigation in the diagnosis of growth hormone deficiency and for the treatment of growth retardation (p.1798).

◊ References.

1. Mericq V, *et al.* Effects of eight months treatment with graded doses of a growth hormone (GH)-releasing peptide in GH-deficient children. *J Clin Endocrinol Metab* 1998; **83:** 2355–60.
2. Mahajan T, Lightman SL. A simple test for growth hormone deficiency in adults. *J Clin Endocrinol Metab* 2000; **85:** 1473–6.
3. Gondo RG, *et al.* Growth hormone-releasing peptide-2 stimulates GH secretion in GH-deficient patients with mutated GH-releasing hormone receptor. *J Clin Endocrinol Metab* 2001; **86:** 3279–83.

Somatomedins ⊗

IGFs; Insulin-like Growth Factors; Somatomedinas; Sulphation Factors.

Description. Somatomedins are a group of polypeptide hormones related to insulin and usually known individually as insulin-like growth factors (IGFs), with molecular weights of about 7000 to 8000. They are synthesised in the liver, kidney, muscle, and other tissues.

Mecasermin *(BAN, USAN, rINN)* ⊗

CEP-151; FK-780; IGF-1; IGF-I; Insulin-like growth factor I (human); Mecasermina; Mécasermine; Mecaserminum; rhIGF-1; Somatomedin C.

Меказермин

$C_{331}H_{512}N_{94}O_{101}S_7$ = 7648.6.

CAS — 68562-41-4; 67763-96-6.

ATC — H01AC03.

ATC Vet — QH01AC03.

Mecasermin Rinfabate *(USAN, rINN)* ⊗

Mecasermina rinfabato; Mécasermine Rinfabate; Mecaserminum Rinfabas; rhIGF-I/rhIGFBP-3. A complex of insulin-like growth factor I (human) with insulin-like growth factor-binding protein IGFBP-3 (human).

Меказермин Ринфабат

CAS — 478166-15-3.

ATC — H01AC05.

ATC Vet — QH01AC05.

Adverse Effects and Precautions

Since the somatomedins are considered to be responsible for many of the actions of growth hormone similar adverse effects (see p.1800) might be expected, and have been seen with mecasermin. Hypoglycaemia is common but symptoms can generally be avoided if mecasermin is given within 20 minutes of food. Tonsillar hypertrophy can develop; patients should be monitored for complications such as snoring, sleep apnoea, and chronic middle ear effusions. Thickening of the soft tissues of the face can also occur. Cardiomegaly and valvulopathy have been reported in a few patients. Although a relationship between cardiac changes and mecasermin therapy has not been confirmed, echocardiogram monitoring has been recommended. Injection site hypertrophy may occur, but can be avoided or resolved by proper rotation of injection sites.

Effects on the eyes. For concerns about an increased risk of retinopathy in diabetic patients receiving mecasermin, see under Diabetes Mellitus, below.

Intravenous administration. Syncope in the absence of hypoglycaemia has been reported in patients given mecasermin by intravenous bolus, accompanied in some cases by convulsions, asystole, bradycardia, hypotension, or dizziness.[1] Reports appear to have ceased since recommendations that mecasermin should not be given intravenously at rates greater than 24 micrograms/kg per hour. Arthralgia, nerve palsies, and hypo-