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.

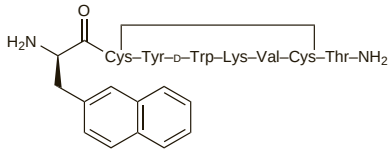
Ланреотид

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

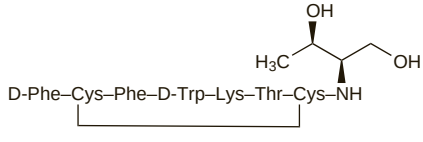
Октреотида Ацетат

$C_{49}H_{66}N_{10}O_{10}S_2.xC_2H_4O_2$ = 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.