sermorelin with the synthetic hexapeptide growth-hormone-releasing peptide-6 has also been reported.[5,6]

1. Thorner MO, *et al.* Human pancreatic growth-hormone-releasing factor selectively stimulates growth-hormone secretion in man. *Lancet* 1983; **i:** 24–8. Correction. *ibid.*; 256.
2. Wood SM, *et al.* Abnormalities of growth hormone release in response to human pancreatic growth hormone releasing factor (GRF (1-44)) in acromegaly and hypopituitarism. *BMJ* 1983; **286:** 1687–91.
3. Grossman A, *et al.* Growth-hormone-releasing factor in growth hormone deficiency: demonstration of a hypothalamic defect in growth hormone release. *Lancet* 1983; **ii:** 137–8.
4. Hindmarsh PC, Swift PGF. An assessment of growth hormone provocation tests. *Arch Dis Child* 1995; **72:** 362–8.
5. Popovic V, *et al.* GH-releasing hormone and GH-releasing peptide-6 for diagnostic testing in GH-deficient adults. *Lancet* 2000; **356:** 1137–42.
6. Leal A, *et al.* A single growth hormone (GH) determination is sufficient for the diagnosis of GH-deficiency in adult patients using the growth hormone releasing hormone plus growth hormone releasing peptide-6 test. *Clin Endocrinol (Oxf)* 2002; **57:** 377–84.

Growth retardation. Sermorelin has been studied in children with growth hormone deficiency (p.1798), usually given in doses of 30 micrograms/kg subcutaneously daily. Although there have been reports of improved growth rates,[1-3] there are limited data directly comparing these with growth hormone. One large study[4] of sermorelin found that, compared with results generally reported for growth hormone therapy, fewer patients responded over a 12-month period and growth responses were poorer.

1. Neyzi O, *et al.* Growth response to growth hormone-releasing hormone(1—29)-NH compared with growth hormone. *Acta Paediatr Suppl* 1993; **388:** 16–21.
2. Lanes R, *et al.* Long term therapy with a single daily subcutaneous dose of growth hormone releasing hormone (1-29) in prepubertal growth hormone deficient children. *J Pediatr Endocrinol* 1994; **7:** 303–8.
3. Ogilvy-Stuart AL, *et al.* Treatment of radiation-induced growth hormone deficiency with growth hormone-releasing hormone. *Clin Endocrinol (Oxf)* 1997; **46:** 571–8.
4. Thorner M, *et al.* Once daily subcutaneous growth hormone-releasing hormone therapy accelerates growth in growth hormone-deficient children during the first year of therapy. *J Clin Endocrinol Metab* 1996; **81:** 1189–96.

Lipodystrophy. In a placebo-controlled study[1] of 31 men with HIV-related lipodystrophy, insulin-like growth factor I (IGF-I) concentrations and body composition measures were improved in those given sermorelin 1 mg twice daily subcutaneously for 12 weeks.

1. Koutkia P, *et al.* Growth hormone-releasing hormone in HIV-infected men with lipodystrophy: a randomized controlled trial. *JAMA* 2004; **292:** 210–18.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Geref; ***Belg.:*** GHRH; ***Denm.:*** Somatrel†; ***Fin.:*** Geref; ***Fr.:*** Stimu-GH; ***Ger.:*** GHRH; ***Gr.:*** Geref; ***Hong Kong:*** Geref†; ***Irl.:*** Geref; ***Ital.:*** Geref; GHRH; ***Neth.:*** GHRH; ***Norw.:*** Geref; ***Port.:*** Geref†; ***Spain:*** Geref; ***Swed.:*** Geref†; ***Switz.:*** Geref†; GHRH; ***UK:*** Geref†; GHRH; ***USA:*** Geref.

Somatostatin *(BAN, rINN)*

GH-RIF; GHRIH; Growth-hormone-release-inhibiting Hormone; Somatostatiini; Somatostatina; Somatostatinas; Somatostatine; Somatostatinum; Somatotrophin-release-inhibiting Factor; Szomatosztatin. Ala-Gly-Cys-Lys-Asn-Phe-Phe-Trp-Lys-Thr-Phe-Thr-Ser-Cys cyclic (3→14) disulphide.

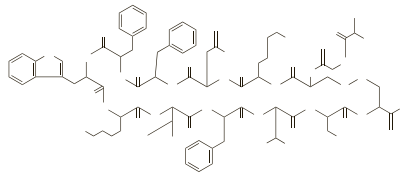
Соматостатин

$C_{76}H_{104}N_{18}O_{19}S_2$ = 1637.9.

CAS — 38916-34-6.

ATC — H01CB01.

ATC Vet — QH01CB01.



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

Ph. Eur. 6.2 (Somatostatin). A cyclic tetradecapeptide having the structure of the hypothalamic hormone that inhibits the release of human growth hormone. It is produced by chemical synthesis and contains not more than 15% w/w of acetic acid. A white amorphous powder. Freely soluble in water and in acetic acid; practically insoluble in dichloromethane. Store in airtight containers at a temperature of 2° to 8°. Protect from light and moisture.

Somatostatin Acetate *(BANM, rINNM)*

Acetato de somatostatina; Somatostatiiniasetaatti; Somatostatin Asetat; Somatostatinacetat; Somatostatine, Acétate de; Somatostatini Acetas.

Соматостатина Ацетат

ATC — H01CB01.

ATC Vet — QH01CB01.

Adverse Effects and Precautions

Abdominal discomfort, flushing, nausea, and bradycardia have been associated with too rapid infusion. Because of the short half-life of somatostatin adverse effects are generally transitory on stopping or reducing the infusion. Giving with parenteral nutrition has been suggested because of the inhibitory effects of somatostatin on intestinal absorption; blood glucose should be monitored since somatostatin may interfere with the secretion of insulin and glucagon.

Effects on the kidneys. Somatostatin has been reported to have an inhibitory effect on renal function[1,2] and severe water retention and hyponatraemia have been reported.[3]

1. Walker BJ, *et al.* Somatostatin and water excretion. *Lancet* 1983; **i:** 1101–2.
2. Vora JP, *et al.* Effect of somatostatin on renal function. *BMJ* 1986; **292:** 1701–2.
3. Halma C, *et al.* Life-threatening water intoxication during somatostatin therapy. *Ann Intern Med* 1987; **107:** 518–20.

Uses and Administration

Somatostatin is a polypeptide obtained from the hypothalamus or by synthesis. The naturally occurring form has a cyclic structure. Although somatostatin derived from the hypothalamus is a 14-amino-acid peptide, a longer, 28-amino-acid form also exists in some tissues. Somatostatin inhibits the release of growth hormone (p.1799) from the anterior pituitary. It also inhibits the release of thyrotrophin (p.2177) and corticotropin (p.1523) from the pituitary, glucagon and insulin from the pancreas, and appears to have a role in the regulation of duodenal and gastric secretions. In the CNS it appears to play a role in the perception of pain.

It has been tried in a variety of disorders such as upper gastrointestinal haemorrhage including variceal haemorrhage (see under Monoethanolamine, p.2346), insulin resistance, and the management of hormone-secreting tumours and other hypersecretory disorders. However, it has a very short duration of action and several analogues of somatostatin have been produced in an attempt to prolong its activity as well as making its inhibitory effects more specific. Octreotide (p.1803) and lanreotide (p.1803) are such analogues.

Somatostatin is usually given as the acetate. In the treatment of gastrointestinal haemorrhage, such as acute bleeding from oesophageal varices, somatostatin acetate equivalent to somatostatin 250 micrograms has been given by intravenous bolus over 3 to 5 minutes, followed by a continuous infusion of 250 micrograms/hour (about 3.5 micrograms/kg per hour) until the bleeding has stopped, which is usually within 12 to 24 hours. The infusion may then be continued for a further 48 to 72 hours to prevent recurrent bleeding. In some cases, the infusion may be continued to a maximum of 120 hours.

Malignant neoplasms. Somatostatin given with melatonin, bromocriptine, and a solution of retinoids (the Di Bella regimen) was ineffective in the treatment of advanced malignancies (see Malignant Neoplasms, under Uses and Administration of Octreotide, p.1806).

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Stilamin†; ***Austria:*** Somatin; Somatolan; ***Belg.:*** Modustatine†; ***Braz.:*** Stilamin; ***Canad.:*** Stilamin; ***Cz.:*** Stilamin†; ***Fr.:*** Modustatine; ***Ger.:*** Aminopan†; ***Gr.:*** Atostan; Eklivan; Sadolin; Somabion; Somargen; Somaritin; Somastin; Stilamin; ***Hong Kong:*** Stilamin; ***Hung.:*** Somatin†; Stilamin†; ***India:*** Somastin; Stilamin†; ***Indon.:*** Stilamin; ***Ital.:*** Etaxene; Ikestatina; Modustatina; Nastoren; Resurmide; Stilamin; Zecnil†; ***Malaysia:*** Stilamin; ***Mex.:*** Stilamin†; ***Neth.:*** Stilamin†; ***Port.:*** Stilamin†; ***S.Afr.:*** Stilamin; ***Singapore:*** Stilamin; ***Spain:*** Somiaton†; Somonal; ***Switz.:*** Stilamin; ***Thai.:*** Etaxene; Stilamin; ***Turk.:*** Somatosan; Stilamin; ***Venez.:*** Ikestatina; Stilamin.

Vapreotide *(BAN, USAN, rINN)*

BMY-41606; RC-160; Vapreotida; Vapréotide; Vapreotidum. D-Phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-L-tryptophanamide cyclic (2→7)-disulfide.

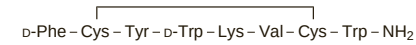
Вапреотид

$C_{57}H_{70}N_{12}O_9S_2$ = 1131.4.

CAS — 103222-11-3.

ATC — H01CB04.

ATC Vet — QH01CB04.



Profile

Vapreotide is a somatostatin analogue similar to octreotide (p.1803). It is under investigation in the management of various disorders, including bleeding oesophageal varices, gastrointestinal and pancreatic fistulas, acromegaly, carcinoid tumours, and for the prevention of postoperative complications following pancreatic surgery.

◊ References.

1. Eriksson B, *et al.* The use of new somatostatin analogues, lanreotide and octastatin, in neuroendocrine gastro-intestinal tumours. *Digestion* 1996; **57** (suppl 1): 77–80.
2. Calès P, *et al.* Early administration of vapreotide for variceal bleeding in patients with cirrhosis. *N Engl J Med* 2001; **344:** 23–8.
3. Anonymous. Vapreotide: BMY 41606, RC 160, Sanvar. *Drugs R D* 2003; **4:** 326–30.