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.

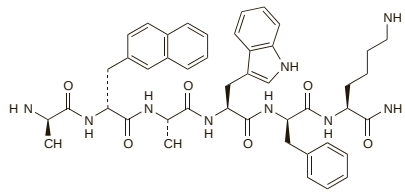
Pralmorelin Dihydrochloride *(USAN, rINNM)* ⊗

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-