Somavert® (pegvisomant)

Prescribing Information

Please refer to the SmPC before prescribing Somavert.

Presentation: Somavert powder and solvent for solution for injection is supplied in vials containing 10mg, 15mg, 20mg, 25mg or 30mg of pegvisomant. After reconstitution, 1mL of solution contains 10mg, 15mg, 20mg, 25mg or 30mg of pegvisomant.

The active substance in Somavert, pegvisomant is known as a growth hormone receptor antagonist.

Therapeutic indications: Somavert is used in the treatment of adult patients with acromegaly who have had an inadequate response to surgery and/or radiation therapy and in whom an appropriate medical treatment with somatostatin analogues did not normalise IGF-I concentrations or was not tolerated.

Posology and method of administration: Adults including elderly: A loading dose of 80 mg should be administered subcutaneously under medical supervision. Following this, 10mg reconstituted in 1mL of solvent should be administered subcutaneously once daily. The site of injection should be rotated daily to help prevent lipohypertrophy. Dose adjustments should be based on serum IGF-I levels, measured every four to six weeks, and appropriate dose adjustments made in increments of 5mg/day in order to maintain the serum IGF-I concentration within the age-adjusted normal range. Prior to the start of Somavert, patients should have an assessment of baseline levels of liver tests (LTs) [serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum total bilirubin (TBIL), and alkaline phosphatase (ALP)]. For recommendations regarding initiation of Somavert based on baseline LTs and recommendations for monitoring of LTs while on Somavert refer to Table A. The maximum dose should not exceed 30 mg/day. Paediatric population: The safety and efficacy of Somavert in children aged 0 to 17 years have not been established. No data are available.

Contraindications: Hypersensitivity to the active substance or to any of the excipients.

Special warnings and precautions for use: Growth hormone-secreting tumours: As growth hormone-secreting pituitary tumours may sometimes expand, causing serious complications (e.g. visual field defects), it is essential that all patients be carefully monitored. If evidence of tumour expansion appears, alternative procedures may be advisable. Serum IGF-1 monitoring: A growth hormone deficient state may result from Somavert administration, despite the presence of elevated serum growth hormone levels. Serum IGF-I concentrations should be monitored and maintained within the age-adjusted normal range by adjustment of pegvisomant dosing. ALT or AST elevations: Prior to the start of SOMAVERT, patients should have an assessment of baseline levels of liver tests [serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum total bilirubin (TBIL), and alkaline phosphatase (ALP)].

Evidence of obstructive biliary tract disease should be ruled out in patients with elevations of ALT and AST or in patients with a prior history of treatment with any somatostatin analogue. Administration of pegvisomant should be discontinued if signs of liver disease persist.

For recommendations regarding initiation of Somavert, based on baseline liver tests (LTs) and recommendations for monitoring of liver tests while on Somavert refer to Table A.

Table A: Recommendations for initiation of Somavert treatment based on baseline LTs and for periodic monitoring of LTs during Somavert treatment

Baseline LT Levels	Recommendations
Normal	• May treat with Somavert. • Serum concentrations of ALT and AST should be monitored at 4- to 6-week intervals for the first 6 months of treatment with Somavert, or at any time in patients exhibiting symptoms suggestive of hepatitis.
Elevated, but less than or equal to 3 times ULN	• May treat with Somavert; however, monitor LTs monthly for at least 1year after initiation of therapy and then bi-annually for the next year.
Greater than 3 times ULN	• Do not treat with Somavert until a comprehensive workup establishes the cause of the patient's liver dysfunction. • Determine if cholelithiasis or choledocholithiasis is present, particularly in patients with a history of prior therapy with somatostatin analogs. • Based on the workup, consider initiation of therapy with Somavert. • If the decision is to treat, LTs and clinical symptoms should be monitored very closely.

If a patient develops LT elevations, or any other signs or symptoms of liver dysfunction while receiving Somavert, the following patient management is recommended (Table B).

Table B. Clinical recommendations based on abnormal liver test results while on SOMAVERT

LT Levels and Clinical Signs/Symptoms	Recommendations
Elevated, but less than or equal to 3 times ULN	• May continue therapy with Somavert. However, monitor LTs monthly to determine if further increases occur.

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Greater than 3 but less than 5 times ULN (without signs/symptoms of hepatitis or other liver injury, or increase in serum TBIL)	• May continue therapy with Somavert. However, monitor LTs weekly to determine if further increases occur (see below). • Perform a comprehensive hepatic workup to discern if an alternative cause of liver dysfunction is present.
At least 5 times ULN, or transaminase elevations at least 3 times ULN associated with any increase in serum TBIL (with or without signs/symptoms of hepatitis or other liver injury)	• Discontinue Somavert immediately. • Perform a comprehensive hepatic workup, including serial LTs, to determine if and when serum levels return to normal. • If LTs normalize (regardless of whether an alternative cause of the liver dysfunction is discovered), consider cautious reinitiation of therapy with Somavert, with frequent LT monitoring.
Signs or symptoms suggestive of hepatitis or other liver injury (e.g., jaundice, bilirubinuria, fatigue, nausea, vomiting, right upper quadrant pain, ascites, unexplained edema, easy bruisability)	• Immediately perform a comprehensive hepatic workup. If liver injury is confirmed, the drug should be discontinued.

Hypoglycaemia: In patients with diabetes mellitus, doses of insulin or hypoglycaemic medicinal products may need to be decreased. Improved fertility: The therapeutic benefits of a reduction in IGF I concentration which results in improvement of the patient's clinical condition could potentially also improve fertility in female patients. Acromegaly control may improve during pregnancy. If pegvisomant is used during pregnancy, IGF-I levels should be closely monitored and pegvisomant doses may need to be adjusted based on IGF-I values.

Fertility, pregnancy and lactation: Somavert is not recommended during pregnancy, breast-feeding and in women of childbearing potential not using contraception.

Interactions with other medicinal products and other forms of interaction: No interaction studies have been performed. The use of Somavert in combination with other medicinal products for the treatment of acromegaly has not been extensively investigated. Patients receiving insulin or oral hypoglycaemic medicinal products may require dose reduction of these therapeutic agents due to the effect of Somavert on insulin sensitivity. Somavert cross-reacts in commercially available growth hormone assays. Treatment should therefore not be monitored or adjusted based on serum growth hormone concentrations reported from these assays. .

Side effects: In clinical trials, for patients treated with Somavert (n=550), the majority of adverse reactions to Somavert were of mild to moderate intensity, of limited duration and did not require discontinuation of treatment. The most commonly reported adverse reactions occurring in ≥ 10% of patients with acromegaly treated with pegvisomant during the clinical trials were headache 25%, arthralgia 16% and diarrhoea 13%. Other common (≥1/100 to <1/10) adverse events reported were: dizziness, somnolence, tremor, hypoaesthesia, constipation, nausea, vomiting, abdominal distension, dyspepsia, flatulence, hyperhidrosis, contusion, pruritis, rash, myalgia, arthritis, haematuria, oedema peripheral, hypercholesterolaemia, weight increased, hyperglycaemia, hypoglycaemia, hypertension, dyspnoea, influenza-like illness, fatigue, asthenia, pyrexia, injection site bruising or bleeding, injection site reaction (including injection site hypersensitivity), injection site hypertrophy (e.g. lipohypertrophy), abnormal liver function tests (e.g. transaminase elevation**)**, abnormal dreams, eye pain. Most injection site reactions characterised as localised erythemas and soreness, spontaneously resolved with local symptomatic treatment, while therapy continued. The development of isolated low-titre anti-growth hormone antibodies was observed in 16.9% of patients. The clinical significance of these antibodies is unknown. Systemic hypersensitivity reactions including anaphylactic/anaphylactoid reactions, laryngospasm, angioedema, generalized skin reactions (rash, erythema, pruritus, urticaria) have been reported in post marketing use. Some patients required hospitalization. Upon re-administration, symptoms did not re-occur in all patients.
Please consult the Summary of Product Characteristics in relation to other side-effects.

Overdose: There is limited experience of overdose with pegvisomant. In the case of overdose, Somavert should be discontinued and not resumed until IGF-I levels return to within or above the normal range.

Legal category: POM

Date of revision: February 2021

Package quantities and basic NHS price:

Somavert 10mg, (30 vials of powder & pre-filled syringes and safety needles), £1500

Somavert 15mg, (30 vials of powder & pre-filled syringes and safety needles), £2250

Somavert 20mg, (30 vials of powder & pre-filled syringes and safety needles), £3000 & (1 vial of powder & pre-filled syringe and safety needle), £100

Somavert 25mg, (30 vials of powder & pre-filled syringes and safety needles), £3750 & (1 vial of powder & pre-filled syringe and safety needle), £125

Somavert 30mg, (30 vials of powder & pre-filled syringes and safety needles), £4500 & (1 vial of powder & pre-filled syringe and safety needle), £150

European Marketing Authorisation numbers:

Somavert 10mg, EU/1/02/240/001

Somavert 15mg, EU/1/02/240/002

Somavert 20mg, EU/1/02/240/003 & EU/1/02/240/004

Somavert 25mg, EU/1/02/240/010 & EU/1/02/240/009

Somavert 30mg, EU/1/02/240/012 & EU/1/02/240/011

European Marketing Authorisation Holder:

Pfizer Europe MA EEIG, Boulevard de la Plaine 17, 1050 Bruxelles, Belgium.

GB Marketing Authorisation numbers

Somavert 10mg, PLGB 00057/1635

Somavert 15mg, PLGB 00057/1636

Somavert 20mg, PLGB 00057/1637
Somavert 25mg, PLGB 00057/1638
Somavert 30mg, PLGB 00057/1639
GB Marketing Authorisation Holder
Pfizer Limited, Ramsgate Road, Sandwich, Kent, CT13 9NJ,
United Kingdom.

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Further information is available on request from: Medical Information Department at Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey KT20 7NS, UK. Tel: +44 (0) 1304 616161

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Pfizer Medical Information on 01304 616161

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