ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

SOMAVERT 10 mg powder and solvent for solution for injection
SOMAVERT 15 mg powder and solvent for solution for injection
SOMAVERT 20 mg powder and solvent for solution for injection
SOMAVERT 25 mg powder and solvent for solution for injection
SOMAVERT 30 mg powder and solvent for solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

SOMAVERT 10 mg powder and solvent for solution for injection
One vial contains 10 mg of pegvisomant.
After reconstitution, 1 ml of solution contains 10 mg of pegvisomant.*

Excipient with known effect

The 10 mg strength of the medicinal product contains 0.4 mg of sodium per vial of powder.

SOMAVERT 15 mg powder and solvent for solution for injection
One vial contains 15 mg of pegvisomant.
After reconstitution, 1 ml of solution contains 15 mg of pegvisomant.*

Excipient with known effect

The 15 mg strength of the medicinal product contains 0.4 mg of sodium per vial of powder.

SOMAVERT 20 mg powder and solvent for solution for injection
One vial contains 20 mg of pegvisomant.
After reconstitution, 1 ml of solution contains 20 mg of pegvisomant.*

Excipient with known effect

The 20 mg strength of the medicinal product contains 0.4 mg of sodium per vial of powder.

SOMAVERT 25 mg powder and solvent for solution for injection
One vial contains 25 mg of pegvisomant.
After reconstitution, 1 ml of solution contains 25 mg of pegvisomant.*

Excipient with known effect

The 25 mg strength of the medicinal product contains 0.5 mg of sodium per vial of powder.

SOMAVERT 30 mg powder and solvent for solution for injection
One vial contains 30 mg of pegvisomant.
After reconstitution, 1 ml of solution contains 30 mg of pegvisomant.*

Excipient with known effect

The 30 mg strength of the medicinal product contains 0.6 mg of sodium per vial of powder.

*produced in *Escherichia coli* cells by recombinant DNA technology.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection (powder for injection).

The powder is white to slightly off-white.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

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.

4.2. Posology and method of administration

Treatment should be initiated under the supervision of a physician experienced in the treatment of acromegaly.

Posology

A loading dose of 80 mg pegvisomant should be administered subcutaneously under medical supervision. Following this, SOMAVERT 10 mg reconstituted in 1 ml of solvent should be administered once daily as a subcutaneous injection.

Dose adjustments should be based on serum IGF-I levels. Serum IGF-I concentrations should be measured every four to six weeks and appropriate dose adjustments made in increments of 5 mg/day in order to maintain the serum IGF-I concentration within the age-adjusted normal range and to maintain an optimal therapeutic response.

Assessment of baseline levels of liver enzymes prior to initiation of SOMAVERT
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 in *Special warnings and precautions for use (4.4)*.

The maximum dose should not exceed 30 mg/day.

For the different dose regimens, the following strengths are available: SOMAVERT 10 mg, SOMAVERT 15 mg, SOMAVERT 20 mg, SOMAVERT 25 mg and SOMAVERT 30 mg.

Paediatric population
The safety and efficacy of SOMAVERT in children aged 0 to 17 years have not been established. No data are available.

Elderly
No dose adjustment is required.

Hepatic or renal impairment
The safety and efficacy of SOMAVERT in patients with renal or hepatic insufficiency has not been established.

Method of administration

Pegvisomant should be administered by subcutaneous injection.

The site of injection should be rotated daily to help prevent lipohypertrophy.

For instructions on reconstitution of the medicinal product before administration, see section 6.6.

4.3. Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4. Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

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

Pegvisomant is a potent antagonist of growth hormone action. A growth hormone deficient state may result from administration of this medicinal product, 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 the pegvisomant dose.

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 1 year 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 analogues. • 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.

Abbreviations: ALT = alanine aminotransferase; AST = aspartate transaminase; LT = liver test; ULN = upper limit of normal.

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.
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 normalise (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 oedema, easy bruisability)	• Immediately perform a comprehensive hepatic workup. • If liver injury is confirmed, the drug should be discontinued.

Hypoglycaemia

The study conducted with pegvisomant in diabetic patients treated either by insulin or by oral

hypoglycaemic medicinal products revealed the risk of hypoglycaemia in this population. Therefore, in acromegalic patients with diabetes mellitus, doses of insulin or hypoglycaemic medicinal products may need to be decreased (see section 4.5).

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 (see section 4.6).

Pregnancy

Acromegaly control may improve during pregnancy. Pegvisomant is not recommended during pregnancy (see section 4.6). If pegvisomant is used during pregnancy, IGF-I levels should be closely monitored and pegvisomant doses may need to be adjusted (see section 4.2) based on IGF-I values.

Sodium content

This medicinal product contains less than 1 mmol sodium (23 mg) per dose. Patients on low sodium diets can be informed that this medicinal product is essentially 'sodium-free'.

4.5. Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed. It should be considered whether to continue treatment with somatostatin analogues. The use of this medicine 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 active substances due to the effect of pegvisomant on insulin sensitivity (see section 4.4).

Pegvisomant has significant structural similarity to growth hormone which causes it to cross-react in commercially available growth hormone assays. Since serum concentrations of therapeutically-effective doses of this medicine are generally 100 to 1 000 times higher than the actual serum growth hormone concentrations seen in acromegalics, measurements of serum growth hormone concentrations will be spuriously reported in commercially available growth hormone assays. Pegvisomant treatment should therefore not be monitored or adjusted based on serum growth hormone concentrations reported from these assays.

4.6. Fertility, pregnancy and lactation

Pregnancy

There are limited amount of data from the use of pegvisomant in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3).

SOMAVERT is not recommended during pregnancy and in women of childbearing potential not using contraception.

If pegvisomant is used during pregnancy, IGF-I levels should be closely monitored, especially during the first trimester. It may be necessary to adjust the dose of pegvisomant during pregnancy (see section 4.4).

Breast-feeding

The excretion of pegvisomant in breast milk has not been studied in animals. Clinical data are too limited (one reported case) to draw any conclusion on the excretion of pegvisomant in human breast milk. Therefore, pegvisomant should not be used in breast-feeding women. However, breast-feeding

may be continued if this medicine is discontinued: this decision should take into account the benefit of pegvisomant therapy to the mother and the benefit of breast-feeding to the child.

Fertility

For pegvisomant no data on fertility are available.

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.

4.7. Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8. Undesirable effects

Summary of the safety profile

The list below contains adverse reactions seen in clinical trials with SOMAVERT.

In clinical studies, for patients treated with pegvisomant (n = 550), the majority of adverse reactions to pegvisomant 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%.

Tabulated list of adverse reactions

The list below contains adverse reactions seen in clinical trials or that were spontaneously reported, classified by system organ class and frequency.

Adverse reactions are listed according to the following categories:
Very common: ≥ 1/10
Common: ≥ 1/100 to < 1/10
Uncommon: ≥ 1/1 000 to < 1/100
Not known (cannot be estimated from the available data)

System Organ Class	Very Common (≥ 1/10)	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1 000 to < 1/100)	Frequency Not Known (Cannot Be Estimated From Available Data)
Blood and lymphatic system disorders			thrombocytopenia, leukopenia, leukocytosis, haemorrhagic diathesis	
Immune system disorders			hypersensitivity reactions[b]	anaphylactic reaction[b], anaphylactoid reaction[b]

System Organ Class	Very Common (≥ 1/10)	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1 000 to < 1/100)	Frequency Not Known (Cannot Be Estimated From Available Data)
Metabolism and nutrition disorders		hypercholesterolaemia, hyperglycaemia, hypoglycaemia, weight increased	hypertriglyceridemia	
Psychiatric disorders		abnormal dreams	panic attack, short term memory loss, apathy, confusion, sleep disorder, libido increased	anger
Nervous system disorders	headache	somnolence, tremor, dizziness, hypoaesthesia	narcolepsy, migraine, dysgeusia	
Eye disorders		eye pain	asthenopia	
Ear and labyrinth disorders			Meniere's disease	
Cardiac disorders		oedema peripheral		
Vascular disorders		hypertension		
Respiratory, thoracic and mediastinal disorders		dyspnoea		laryngospasm[b]
Gastrointestinal disorders	diarrhoea	vomiting, constipation, nausea, abdominal distension, dyspepsia, flatulence	haemorrhoids, salivary hypersecretion, dry mouth, tooth disorder	
Hepatobiliary disorders		abnormal liver function tests (e.g. transaminase elevation) (see section 4.4)		
Skin and subcutaneous tissue disorders		hyperhidrosis, contusion, pruritus[b], rash[b]	face oedema, dry skin, increased tendency to bruise, night sweats, erythema[b], urticaria[b]	angioedema[b]
Musculoskeletal and connective tissue disorders	arthralgia	myalgia, arthritis		
Renal and urinary disorders		haematuria	proteinuria, polyuria, renal impairment	

System Organ Class	Very Common (≥ 1/10)	Common (≥ 1/100 to < 1/10)	Uncommon (≥ 1/1 000 to < 1/100)	Frequency Not Known (Cannot Be Estimated From Available Data)
General disorders and administration site conditions		injection site reaction (including injection site hypersensitivity), injection site bruising or bleeding, injection site hypertrophy (e.g. lipohypertrophy)[a], influenza-like illness, fatigue, asthenia, pyrexia	feeling abnormal, impaired healing, hunger	

[a] see Description of selected adverse reactions below
[b] ADR related to hypersensitivity reaction

Description of selected adverse reactions

Most injection site reactions characterised as localised erythemas and soreness, spontaneously resolved with local symptomatic treatment, while pegvisomant therapy continued. Occurrence of injection site hypertrophy has been observed, including lipohypertrophy.

The development of isolated low-titre anti-growth hormone antibodies was observed in 16.9% of patients treated with pegvisomant. The clinical significance of these antibodies is unknown.

Systemic hypersensitivity reactions including anaphylactic/anaphylactoid reactions, laryngospasm, angioedema, generalised skin reactions (rash, erythema, pruritus, urticaria) have been reported in post marketing use. Some patients required hospitalisation. Upon re-administration, symptoms did not re-occur in all patients.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9. Overdose

There is limited experience of overdose with pegvisomant. In the one reported incident of acute overdose, where 80 mg/day was administered for 7 days, the patient experienced a slight increase in fatigue and dry mouth. In the week following discontinuation of treatment the adverse reactions noted were: insomnia, increased fatigue, oedema peripheral, tremor, and weight gain. Two weeks after stopping treatment, leukocytosis and moderate bleeding from injection and vein puncture sites was observed which were considered possibly related to pegvisomant.

In cases of overdose, administration of this medicine should be discontinued and not resumed until IGF-I levels return to within or above the normal range.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Other anterior pituitary lobe hormones and analogues, ATC code: H01AX01.

Mechanism of action

Pegvisomant is an analogue of human growth hormone that has been genetically modified to be a growth hormone receptor antagonist. Pegvisomant binds to growth hormone receptors on cell surfaces, where it blocks growth hormone binding, and thus interferes with intracellular growth hormone signal transduction. Pegvisomant is highly selective for the GH receptor, and does not cross-react with other cytokine receptors, including prolactin.

Pharmacodynamic effects

Inhibition of growth hormone action with pegvisomant leads to decreased serum concentrations of insulin-like growth factor-I (IGF-I), as well as other growth hormone-responsive serum proteins such as free IGF-I, the acid-labile subunit of IGF-I (ALS), and insulin-like growth factor binding protein-3 (IGFBP-3).

Clinical efficacy and safety

Acromegalic patients (n = 112) have been treated in a 12-week, randomised, double-blind, multicentre study comparing placebo and pegvisomant. Dose-dependent, statistically significant reductions in mean IGF-I ($p<0.0001$), free IGF-I ($p<0.05$), IGFBP-3 ($p<0.05$) and ALS ($p<0.05$) were observed at all post-baseline visits in the pegvisomant treatment groups. The serum IGF-1 was normalised at the end of the study (week 12) in 9.7%, 38.5%, 75% and 82% of subjects treated with placebo, 10 mg/day, 15 mg/day or 20 mg/day pegvisomant respectively.

Statistically significant differences from placebo ($p<0.05$) were observed for improvements in the total signs and symptoms score for all dose groups compared to placebo.

A cohort of 38 acromegalic subjects has been followed in a long-term, open-label, dose-titration study for at least 12 consecutive months of daily dosing with pegvisomant (mean = 55 weeks). The mean IGF-I concentration in this cohort fell from 917 ng/ml to 299 ng/ml on pegvisomant, with 92% achieving a normal (age-adjusted) IGF-I concentration.

In different studies and also in Acrostudy, pegvisomant normalised IGF-1 levels in a high percentage of patients (> 70%) and significantly decreased fasting plasma glucose (FPG) and fasting plasma insulin (FPI) levels.

Pegvisomant also improves insulin sensitivity, this is likely due to a blockade of the GH receptors on tissues, mainly the liver and also adipose tissue, kidneys, and skeletal muscles, thereby removing the detrimental effect of GH on insulin signalling, lipolysis, and gluconeogenesis. However, the mechanism of action of all these effects is not known with certainty. A decrease in doses of insulin or hypoglycaemic medicinal products may be needed in acromegalic patients with diabetes mellitus (see sections 4.4 and 4.5).

5.2. Pharmacokinetic properties

Absorption

Absorption of pegvisomant following subcutaneous administration is slow and prolonged, and peak serum pegvisomant concentrations are not generally attained until 33-77 hours after administration. The mean extent of absorption of a subcutaneous dose was 57% relative to an intravenous dose.

Distribution

The apparent volume of distribution of pegvisomant is relatively small (7-12 L).

Biotransformation

The metabolism of pegvisomant has not been studied.

Elimination

The mean total body systemic clearance of pegvisomant following multiple doses is estimated to be 28 ml/h for subcutaneous doses ranging from 10 to 20 mg/day. Renal clearance of pegvisomant is negligible and accounts for less than 1% of total body clearance. Pegvisomant is slowly eliminated from serum, with mean estimates of half-life generally ranging from 74 to 172 hours following either single or multiple-doses.

Linearity/non-linearity

After single subcutaneous pegvisomant administration no linearity is observed with rising doses of 10, 15 or 20 mg. Approximately linear pharmacokinetics is observed at steady state in the population pharmacokinetic studies. The data from 145 patients in two long-term studies who received daily doses of 10, 15, or 20 mg, demonstrate pegvisomant mean serum concentrations (± SD) of approximately 8 800 ± 6 300, 13 200 ± 8 000 and 15 600 ± 10 300 ng/ml, respectively.

The pharmacokinetics of pegvisomant are similar in normal healthy volunteers and acromegaly patients, although heavier individuals tend to have a higher total body clearance of pegvisomant than lighter individuals, and may thus require greater doses of pegvisomant.

5.3. Preclinical safety data

Non-clinical data revealed no special hazard for humans based on studies of repeated dose toxicity in rat and monkey. However, due to the marked pharmacological response in monkey, systemic exposures higher than those achieved in patients at therapeutic doses have not been studied.

Malignant fibrous histiocytomas associated with fibrosis and histiocytic inflammation were observed at injection sites in males in the rat carcinogenicity study at exposure levels equivalent to three times the human exposure based on mean plasma concentrations in two long-term studies at a daily dose of 30 mg. The relevance of this response for humans is currently unknown. The increased incidence of injection site tumours was most probably caused by irritation and the high sensitivity of the rat to repeated subcutaneous injections.

Early embryonic development and embryo-foetal development studies were conducted in pregnant rabbits with pegvisomant at subcutaneous doses of 1, 3, and 10 mg/kg/day. There was no evidence of teratogenic effects associated with pegvisomant administration during organogenesis. At 10 mg/kg/day (6 times the maximum human therapeutic dose based on body surface area), an increase in post-implantation loss was observed in both studies. No fertility study has been conducted.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Powder
Glycine
Mannitol (E421)
Disodium phosphate anhydrous
Sodium dihydrogen phosphate monohydrate

Solvent
Water for Injections

6.2. Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3. Shelf life

3 years.

After reconstitution, the product should be used immediately.

6.4. Special precautions for storage

Store the powder vial(s) in a refrigerator (2°C – 8°C). Do not freeze. Keep the vial(s) in their carton(s) in order to protect from light.

The carton(s) containing the SOMAVERT powder vial(s) may be stored at room temperature up to a maximum of 25°C for a single period of up to 30 days. The Use by date should be written on the carton (up to 30 days from the date removed from the refrigerator). The vial(s) must be protected from light and should not be placed back into the refrigerator. The SOMAVERT powder vial(s) must be discarded if not used within the 30 days of room temperature storage or the expiry date printed on the carton, whichever is earlier.

Store the pre-filled syringe(s) below 30°C or store in a refrigerator (2ºC - 8°C). Do not freeze.

After reconstitution
For storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5. Nature and contents of container

10 mg or 15 mg or 20 mg or 25 mg or 30 mg of pegvisomant in powder in a vial (type I flint glass) with a stopper (chlorobutyl rubber) and 1 ml solvent (water for injections) in a pre-filled syringe (type I borosilicate glass) with a plunger stopper (bromobutyl rubber) and a tip cap (bromobutyl rubber). The colour of the protective plastic cap is specific to the strength of the product.

SOMAVERT 10 mg and 15 mg
Pack size of 30 vials, pre-filled syringes and safety needles.

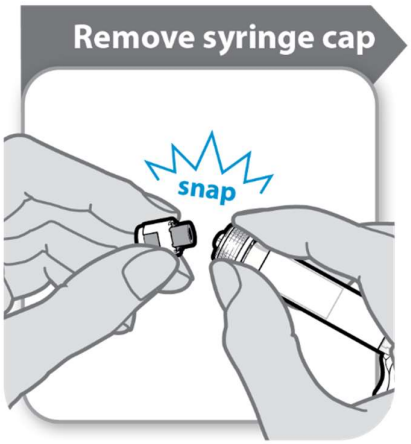
SOMAVERT 20 mg, 25 mg and 30 mg
Pack sizes of 1 and 30 vial(s), pre-filled syringe(s) and safety needle(s).

Not all pack sizes may be marketed.

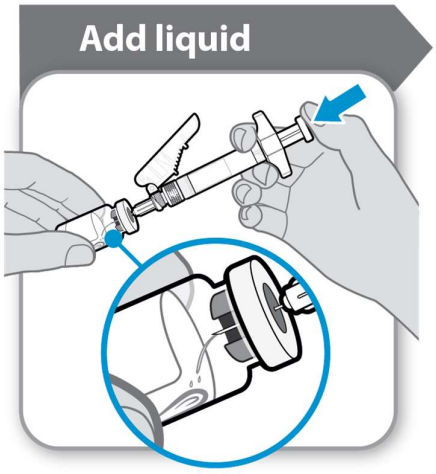
6.6. Special precautions for disposal and other handling

The syringe and safety needle used to administer the injection are provided with the medicinal product.

Before attaching the supplied safety needle the syringe cap will need to be removed from the pre-filled syringe. This is achieved by snapping it off. The syringe should be kept upright to avoid leakage and the end of the syringe should not be allowed to contact anything.



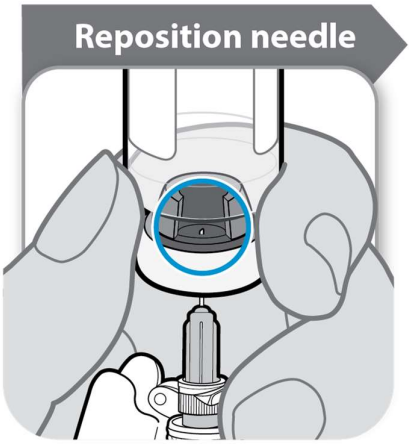
The powder should be reconstituted with 1 ml solvent. When adding the solvent from the syringe the vial and syringe should held at an angle as shown in the diagram below.



Add the solvent to the vial of powder. The solvent should be emptied into the vial slowly to avoid the possibility of a foam forming. This would make the medicine unusable. Gently dissolve the powder with a slow, swirling motion. Do not shake vigorously, as this might cause denaturation of the active substance.

After reconstitution, the reconstituted solution should be inspected visually for extraneous (or for any foreign) particulate matter or any variation in physical appearance prior to administration. In the event of either being observed, discard the medicinal product.

Before withdrawing the dissolved SOMAVERT invert the vial with the syringe still inserted into it and ensure the gap in the stopper can be seen as shown in the diagram below:



Pull the needle down so that the needle tip is at its lowest point in the liquid. Slowly withdraw the plunger in the syringe to withdraw the medicine from the vial. If air is seen in the syringe, tap the barrel to float the bubbles to the top, and then gently push the bubbles out into the vial.

Before disposing of the syringe and needle fold the needle guard over the needle and ensure it clicks into place. The syringe and needle should never be reused.

For single use only. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/02/240/001 10 mg 30 vials
EU/1/02/240/002 15 mg 30 vials
EU/1/02/240/004 20 mg 1 vial
EU/1/02/240/003 20 mg 30 vials
EU/1/02/240/009 25 mg 1 vial
EU/1/02/240/010 25 mg 30 vials
EU/1/02/240/011 30 mg 1 vial
EU/1/02/240/012 30 mg 30 vials

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 13 November 2002
Date of latest renewal: 20 September 2007

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) of the biological active substance(s)

Pfizer Health AB
Mariefredsvagen 37
645 41 Strängnäs
Sweden

Pfizer Ireland Pharmaceuticals Unlimited Company
Grange Castle Business Park
Nangor Road
Dublin 22
D22 V8F8
Ireland

Name and address of the manufacturer(s) responsible for batch release

Pfizer Manufacturing Belgium NV
Rijksweg 12
2870 Puurs-Sint-Amands
Belgium

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

SOMAVERT 10 mg powder and solvent for solution for injection
pegvisomant

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial contains 10 mg pegvisomant
After reconstitution, 1 ml of solution contains 10 mg pegvisomant

3. LIST OF EXCIPIENTS

Glycine
Mannitol (E421)
Disodium phosphate anhydrous
Sodium dihydrogen phosphate monohydrate
Water for Injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

30 vials of powder
30 pre-filled syringes of solvent
30 injection needles

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use. Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use immediately after reconstitution. For single use only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store the powder vial(s) in a refrigerator. Do not freeze.
Keep the powder vial(s) in their carton(s) in order to protect from light.
Refer to the package leaflet for alternative storage details.
Store the pre-filled syringe(s) below 30°C or store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/02/240/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

SOMAVERT 10 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INNER CARTON

1. NAME OF THE MEDICINAL PRODUCT

SOMAVERT 10 mg powder for solution for injection
pegvisomant

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial contains 10 mg pegvisomant
After reconstitution, 1 ml of solution contains 10 mg pegvisomant

3. LIST OF EXCIPIENTS

Glycine
Mannitol (E421)
Disodium phosphate anhydrous
Sodium dihydrogen phosphate monohydrate

4. PHARMACEUTICAL FORM AND CONTENTS

Powder for solution for injection

10 vials of powder

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use. Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use immediately after reconstitution. For single use only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the vial(s) in the carton(s) in order to protect from light.
Powder vial(s) can be stored up to 25°C for a single period of up to 30 days.

If stored at room temperature use by:_____

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/02/240/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

SOMAVERT 10 mg

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

POWDER VIAL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

SOMAVERT 10 mg
powder for injection
pegvisomant
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

10 mg

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

SOMAVERT 15 mg powder and solvent for solution for injection
pegvisomant

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial contains 15 mg pegvisomant
After reconstitution, 1 ml of solution contains 15 mg pegvisomant

3. LIST OF EXCIPIENTS

Glycine
Mannitol (E421)
Disodium phosphate anhydrous
Sodium dihydrogen phosphate monohydrate
Water for Injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

30 vials of powder
30 pre-filled syringes of solvent
30 injection needles

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use. Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use immediately after reconstitution. For single use only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store the powder vial(s) in a refrigerator. Do not freeze.
Keep the powder vial(s) in their carton(s) in order to protect from light.
Refer to package leaflet for alternative storage details.
Store the pre-filled syringe(s) below 30°C or store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/02/240/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

SOMAVERT 15 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INNER CARTON

1. NAME OF THE MEDICINAL PRODUCT

SOMAVERT 15 mg powder for solution for injection
pegvisomant

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial contains 15 mg pegvisomant
After reconstitution, 1 ml of solution contains 15 mg pegvisomant

3. LIST OF EXCIPIENTS

Glycine
Mannitol (E421)
Disodium phosphate anhydrous
Sodium dihydrogen phosphate monohydrate

4. PHARMACEUTICAL FORM AND CONTENTS

Powder for solution for injection

10 vials of powder

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use. Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use immediately after reconstitution. For single use only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the vial(s) in the carton(s) in order to protect from light.
Powder vial(s) can be stored up to 25°C for a single period of up to 30 days.

If stored at room temperature use by:_____

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/02/240/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

SOMAVERT 15 mg

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

POWDER VIAL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

SOMAVERT 15 mg
powder for injection
pegvisomant
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

15 mg

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

SOMAVERT 20 mg powder and solvent for solution for injection
pegvisomant

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial contains 20 mg pegvisomant
After reconstitution, 1 ml of solution contains 20 mg pegvisomant

3. LIST OF EXCIPIENTS

Glycine
Mannitol (E421)
Disodium phosphate anhydrous
Sodium dihydrogen phosphate monohydrate
Water for Injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

30 vials of powder
30 pre-filled syringes of solvent
30 injection needles

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use. Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use immediately after reconstitution. For single use only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store the powder vial(s) in a refrigerator. Do not freeze.
Keep the powder vial(s) in their carton(s) in order to protect from light.
Refer to package leaflet for alternative storage details.
Store the pre-filled syringe(s) below 30°C or store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/02/240/003

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

SOMAVERT 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INNER CARTON

1. NAME OF THE MEDICINAL PRODUCT

SOMAVERT 20 mg powder for solution for injection
pegvisomant

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial contains 20 mg pegvisomant
After reconstitution, 1 ml of solution contains 20 mg pegvisomant

3. LIST OF EXCIPIENTS

Glycine
Mannitol (E421)
Disodium phosphate anhydrous
Sodium dihydrogen phosphate monohydrate

4. PHARMACEUTICAL FORM AND CONTENTS

Powder for solution for injection

10 vials of powder

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use. Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use immediately after reconstitution. For single use only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the vial(s) in the carton(s) in order to protect from light.
Powder vial(s) can be stored up to 25°C for a single period of up to 30 days.

If stored at room temperature use by:_____

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/02/240/003

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

SOMAVERT 20 mg

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

SOMAVERT 20 mg powder and solvent for solution for injection
pegvisomant

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial contains 20 mg pegvisomant
After reconstitution, 1 ml of solution contains 20 mg pegvisomant

3. LIST OF EXCIPIENTS

Glycine
Mannitol (E421)
Disodium phosphate anhydrous
Sodium dihydrogen phosphate monohydrate
Water for Injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

1 vial of powder
1 pre-filled syringe of solvent
1 injection needle

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use. Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use immediately after reconstitution. For single use only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the contents in the carton in order to protect from light.
Carton can be stored up to 25°C for a single period of up to 30 days.

If stored at room temperature use by:_____

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/02/240/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

SOMAVERT 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

POWDER VIAL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

SOMAVERT 20 mg
powder for injection
pegvisomant
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

20 mg

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

SOMAVERT 25 mg powder and solvent for solution for injection
pegvisomant

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial contains 25 mg pegvisomant
After reconstitution, 1 ml of solution contains 25 mg pegvisomant

3. LIST OF EXCIPIENTS

Glycine
Mannitol (E421)
Disodium phosphate anhydrous
Sodium dihydrogen phosphate monohydrate
Water for Injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

30 vials of powder
30 pre-filled syringes of solvent
30 injection needles

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use. Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use immediately after reconstitution. For single use only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store the powder vial(s) in a refrigerator. Do not freeze.
Keep the powder vial(s) in their carton(s) in order to protect from light.
Refer to package leaflet for alternative storage details.
Store the pre-filled syringe(s) below 30°C or store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/02/240/010

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

SOMAVERT 25 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INNER CARTON

1. NAME OF THE MEDICINAL PRODUCT

SOMAVERT 25 mg powder for solution for injection
pegvisomant

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial contains 25 mg pegvisomant
After reconstitution, 1 ml of solution contains 25 mg pegvisomant

3. LIST OF EXCIPIENTS

Glycine
Mannitol (E421)
Disodium phosphate anhydrous
Sodium dihydrogen phosphate monohydrate

4. PHARMACEUTICAL FORM AND CONTENTS

Powder for solution for injection

10 vials of powder

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use. Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use immediately after reconstitution. For single use only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the vial(s) in the carton(s) in order to protect from light.
Powder vial(s) can be stored up to 25°C for a single period of up to 30 days.

If stored at room temperature use by:_____

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/02/240/010

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

SOMAVERT 25 mg

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

SOMAVERT 25 mg powder and solvent for solution for injection
pegvisomant

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial contains 25 mg pegvisomant
After reconstitution, 1 ml of solution contains 25 mg pegvisomant

3. LIST OF EXCIPIENTS

Glycine
Mannitol (E421)
Disodium phosphate anhydrous
Sodium dihydrogen phosphate monohydrate
Water for Injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

1 vial of powder
1 pre-filled syringe of solvent
1 injection needle

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use. Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use immediately after reconstitution. For single use only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the contents in the carton in order to protect from light.
Carton can be stored up to 25°C for a single period of up to 30 days.

If stored at room temperature use by:_____

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/02/240/009

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

SOMAVERT 25 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

POWDER VIAL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

SOMAVERT 25 mg
powder for injection
pegvisomant
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

25 mg

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

SOMAVERT 30 mg powder and solvent for solution for injection
pegvisomant

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial contains 30 mg pegvisomant
After reconstitution, 1 ml of solution contains 30 mg pegvisomant

3. LIST OF EXCIPIENTS

Glycine
Mannitol (E421)
Disodium phosphate anhydrous
Sodium dihydrogen phosphate monohydrate
Water for Injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

30 vials of powder
30 pre-filled syringes of solvent
30 injection needles

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use. Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use immediately after reconstitution. For single use only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store the powder vial(s) in a refrigerator. Do not freeze.
Keep the powder vial(s) in their carton(s) in order to protect from light.
Refer to package leaflet for alternative storage details.
Store the pre-filled syringe(s) below 30°C or store in a refrigerator. Do not freeze.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/02/240/012

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

SOMAVERT 30 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INNER CARTON

1. NAME OF THE MEDICINAL PRODUCT

SOMAVERT 30 mg powder for solution for injection
pegvisomant

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial contains 30 mg pegvisomant
After reconstitution, 1 ml of solution contains 30 mg pegvisomant

3. LIST OF EXCIPIENTS

Glycine
Mannitol (E421)
Disodium phosphate anhydrous
Sodium dihydrogen phosphate monohydrate

4. PHARMACEUTICAL FORM AND CONTENTS

Powder for solution for injection

10 vials of powder

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use. Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use immediately after reconstitution. For single use only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the vial(s) in the carton(s) in order to protect from light.
Powder vial(s) can be stored up to 25°C for a single period of up to 30 days.

If stored at room temperature use by:_____

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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1050 Bruxelles
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12. MARKETING AUTHORISATION NUMBER(S)

EU/1/02/240/012

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

SOMAVERT 30 mg

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

SOMAVERT 30 mg powder and solvent for solution for injection
pegvisomant

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial contains 30 mg pegvisomant
After reconstitution, 1 ml of solution contains 30 mg pegvisomant

3. LIST OF EXCIPIENTS

Glycine
Mannitol (E421)
Disodium phosphate anhydrous
Sodium dihydrogen phosphate monohydrate
Water for Injections

4. PHARMACEUTICAL FORM AND CONTENTS

Powder and solvent for solution for injection

1 vial of powder
1 pre-filled syringe of solvent
1 injection needle

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use. Subcutaneous use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Use immediately after reconstitution. For single use only.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the contents in the carton in order to protect from light.
Carton can be stored up to 25°C for a single period of up to 30 days.

If stored at room temperature use by:_____

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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Boulevard de la Plaine 17
1050 Bruxelles
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/02/240/011

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

SOMAVERT 30 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

POWDER VIAL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

SOMAVERT 30 mg
powder for injection
pegvisomant
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

30 mg

6. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SOLVENT PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Solvent for SOMAVERT
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1 ml water for injections

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

SOMAVERT 10 mg powder and solvent for solution for injection
SOMAVERT 15 mg powder and solvent for solution for injection
SOMAVERT 20 mg powder and solvent for solution for injection
SOMAVERT 25 mg powder and solvent for solution for injection
SOMAVERT 30 mg powder and solvent for solution for injection
pegvisomant

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What SOMAVERT is and what it is used for

SOMAVERT is used for the treatment of acromegaly, a hormonal disorder resulting from the increased secretion of growth hormone (GH) and IGF-I (Insulin-like growth factors), which is characterised by overgrowth of bone, soft tissue swelling, heart disease and related disorders.

The active substance in SOMAVERT, pegvisomant is known as a growth hormone receptor antagonist. These substances decrease the action of GH and levels of IGF-I circulating in the blood.

2. What you need to know before you use SOMAVERT

Do not use SOMAVERT
- If you are allergic to pegvisomant or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before using SOMAVERT.

- If you experience disturbed vision or headaches you must contact your doctor immediately.

- Your doctor or nurse will monitor the levels of IGF-I (Insulin-like growth factors) circulating in the blood and adjust the dose of SOMAVERT if necessary.

- Your doctor should also monitor your adenoma (benign tumour).

- Your doctor will conduct tests of your liver function before starting and during treatment with SOMAVERT. If these test results are not normal, your doctor will discuss treatment options with you. Once treatment begins, your doctor or nurse will monitor the level of liver enzymes in

the blood every 4-6 weeks for the first 6 months of treatment with SOMAVERT. Administration of SOMAVERT should be discontinued if signs of liver disease persist.

- If you are diabetic, your doctor may need to adjust the amount of insulin or other medicines you are using.

- Fertility in women patients may be increased as the disease improves. The use of this medicine in pregnant women is not recommended and women of childbearing age should be advised to use a contraception. See also the section about Pregnancy below.

Other medicines and SOMAVERT
You must tell your doctor if you have previously used other medicines for the treatment of acromegaly or medicines for the treatment of diabetes.

Tell your doctor or pharmacist if you are using or have recently used any other medicines.

As part of your treatment you may be given other medicines. It is important to keep using all your medicines as well as SOMAVERT unless you are told otherwise by your doctor, pharmacist or nurse.

Pregnancy, breast-feeding and fertility
The use of SOMAVERT in pregnant women is not recommended. If you are a women of childbearing age, a contraception should be used during treatment.

It is not known if pegvisomant passes into breast milk. You should not breast-feed while taking SOMAVERT unless your doctor has discussed this with you.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines
No studies on the effects on the ability to drive and use machines have been performed.

SOMAVERT contains sodium
This medicine contains less than 1 mmol of sodium (23 mg) per dose i.e. essentially 'sodium-free'.

3. How to use SOMAVERT

Always inject this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

A starting dose of 80 mg of pegvisomant will be given subcutaneously (just under the skin) by your doctor. Following this, the usual daily dose of pegvisomant is 10 mg, which is given by subcutaneous injection (just under the skin).

Every four to six weeks your doctor will make appropriate dose adjustments, made in increments of 5 mg pegvisomant/day, based on your so-called serum IGF-I levels to maintain an optimal therapeutic response.

Method and route of administration
SOMAVERT is injected under the skin. The injection can be self-administered or given by another person, for example your doctor or his/her assistant. The detailed instructions on injection procedure provided at the end of this leaflet must be followed. You should continue to inject this medicine for as long as instructed by your doctor.

This medicine must be dissolved before use. The injection must not be mixed in the same syringe or vial as any other medicine.

Fatty tissue of the skin can build up at the site of injection. To avoid this, use a slightly different place for your injection each time, as described in Step 2 of the 'instructions for preparing and giving an injection of SOMAVERT' section of this leaflet. This gives your skin and the area under your skin time to recover from one injection before it receives another one in the same place.

If you have the impression that the effect of this medicine is too strong or too weak, talk to your doctor, pharmacist or nurse.

If you inject more SOMAVERT than you should
If you accidentally inject more SOMAVERT than told to by your doctor it is unlikely to be serious, but you should contact your doctor, pharmacist or nurse immediately.

If you forget to use SOMAVERT
If you forget to give yourself an injection you should inject the next dose as soon as you remember and then continue to inject SOMAVERT as prescribed by your doctor. Do not inject a double dose to make up for forgotten individual doses.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Mild to serious allergic (anaphylactic) reactions have been reported in some patients taking SOMAVERT. Symptoms of a serious allergic reaction may include one or more of the following: swelling of the face, tongue, lips, or throat; wheezing or trouble breathing (spasm of the larynx); generalised skin rash, nettle rash (urticaria) or itching; or dizziness. Contact your doctor immediately if you develop any of these symptoms.

Very common: may affect more than 1 in 10 people

- Headache
- Diarrhoea
- Joint pain

Common: may affect up to 1 in 10 people

- Shortness of breath
- Increased levels of substances that measure the function of the liver. These can be seen in the results of blood tests.
- Blood in the urine
- Increased blood pressure
- Constipation, feeling sick, being sick, feeling bloated, indigestion, gas
- Dizziness, sleepiness, uncontrolled trembling, decreased sense of touch
- Bruising or bleeding at injection site, soreness or swelling at injection site, build-up of fat below the surface of the skin at injection site, swelling of the extremities, weakness, fever
- Sweating, itching, rash, tendency to bruise
- Muscle pain, arthritis
- Increased blood cholesterol, weight gain, increased blood glucose, decreased blood glucose
- Flu-like illness, fatigue
- Abnormal dreams
- Eye pain

Uncommon: may affect up to 1 in 100 people

- Allergic reaction after administration (fever, rash, pruritus and, in severe cases, difficulty to breathe, rapid swelling of skin, requiring urgent medical attention). May occur immediately, or several days after administration
- Protein in the urine, increased urine, kidney problems
- Lack of interest, feeling confused, increased sex drive, panic attack, loss of memory, problems sleeping
- Decreased platelets in the blood, increased or decreased white cells in the blood, tendency to bleed
- Feeling abnormal, impaired healing
- Eyestrain, inner ear problems
- Facial swelling, dry skin, night sweats, redness of the skin (erythema), raised itchy bumps on the skin (urticaria)
- Increased fatty substances in the blood, increased appetite
- Dry mouth, increased saliva, tooth problems, haemorrhoids
- Abnormal sense of taste, migraine

Not known: frequency cannot be estimated from the available data

- Anger
- Severe breathlessness (laryngospasm)
- Rapid swelling of skin and underlying tissue and inner lining (mucosa) of organs (angioedema)

About 17% of patients will develop antibodies to growth hormone during treatment. The antibodies do not seem to stop this medicine from working.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store SOMAVERT

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the vial and the carton after EXP. The expiry date refers to the last day of that month.

Store the powder vial(s) in a refrigerator (2°C – 8°C) in their carton(s) in order to protect from light. Do not freeze.
The carton(s) containing the SOMAVERT powder vial(s) may be stored at room temperature up to a maximum of 25°C for a single period of up to 30 days. Write the Use by date on the carton including day/month/year (up to 30 days from the date removed from the refrigerator). The vial(s) must be protected from light. Do not return this medicine to refrigerator.

Discard this medicine if not used by the new Use by date or the expiry date printed on the carton, whichever is earlier.
Store the pre-filled syringe(s) below 30°C or store in a refrigerator (2°C – 8°C). Do not freeze.

After preparing the SOMAVERT solution it must be used immediately.

Do not use this medicine if you notice that the solution is cloudy or contains particulate matter.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What SOMAVERT contains
- The active substance is pegvisomant.
- SOMAVERT 10 mg: One vial of powder contains 10 mg pegvisomant. After reconstitution with 1 ml of solvent, 1 ml of the solution contains 10 mg pegvisomant.
- SOMAVERT 15 mg: One vial of powder contains 15 mg pegvisomant. After reconstitution with 1 ml of solvent, 1 ml of the solution contains 15 mg pegvisomant.
- SOMAVERT 20 mg: One vial of powder contains 20 mg pegvisomant. After reconstitution with 1 ml of solvent, 1 ml of the solution contains 20 mg pegvisomant.
- SOMAVERT 25 mg: One vial of powder contains 25 mg pegvisomant. After reconstitution with 1 ml of solvent, 1 ml of the solution contains 25 mg pegvisomant.
- SOMAVERT 30 mg: One vial of powder contains 30 mg pegvisomant. After reconstitution with 1 ml of solvent, 1 ml of the solution contains 30 mg pegvisomant.
- The other ingredients are glycine, mannitol (E421), disodium phosphate anhydrous and sodium dihydrogen phosphate monohydrate (see section 2 ‘SOMAVERT contains sodium’).
- The solvent is water for injections.

What SOMAVERT looks like and contents of the pack
SOMAVERT is presented as a powder and a solvent for injection (either 10 mg, 15 mg, 20 mg, 25 mg or 30 mg pegvisomant in a vial and 1 ml of solvent in a pre-filled syringe). Pack sizes of 1 and/or 30. Not all pack sizes are marketed. The powder is white and the solvent is clear and colourless.

Marketing Authorisation Holder and Manufacturer:

Marketing Authorisation Holder:

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

Manufacturer:

Pfizer Manufacturing Belgium NV
Rijksweg 12
2870 Puurs-Sint-Amands
Belgium

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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Luxembourg/Luxemburg
Pfizer NV/SA
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Pfizer AS
Tlf: +47 67 52 61 00

Österreich
Pfizer Corporation Austria Ges.m.b.H.
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Polska
Pfizer Polska Sp. z o.o.
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Portugal
Laboratórios Pfizer, Lda.
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România
Pfizer Romania S.R.L.
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Slovenija
Pfizer Luxembourg SARL
Pfizer, podružnica za svetovanje s področja farmacevtske dejavnosti, Ljubljana
Tel: +386 (0)1 52 11 400

Slovenská republika
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Sverige
Pfizer AB
Tel: +46 (0)8 550 520 00

This leaflet was last revised in <{MM/YYYY}>.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu. There are also links to other websites about rare diseases and treatments.

INSTRUCTIONS FOR USE

SOMAVERT powder in vial with solvent in a pre-filled syringe

pegvisomant for injection
For Subcutaneous Injection Only
single dose vial

SOMAVERT comes in a vial as a white block of powder. You must mix SOMAVERT with a liquid (diluent) before you can use it.
The liquid comes in a pre-filled syringe labeled 'Solvent for SOMAVERT'.
Do not use any other liquid to mix with SOMAVERT.
It is important that you do not try to give yourself or someone else an injection unless you have received training from your healthcare provider.

Store the carton(s) of powder vials in the refrigerator at 2°C to 8°C and away from direct sunlight. The carton(s) containing the SOMAVERT powder vial(s) may be stored at room temperature up to a maximum of 25°C for a single period of up to 30 days. Write the Use by date on the carton including day/month/year (up to 30 days from the date removed from the refrigerator). The vial(s) must be protected from light. Do not return this medicine to refrigerator.

Discard this medicine if not used by the new Use by date or the expiry date printed on the carton, whichever is earlier.

The pre-filled solvent syringe may be stored at room temperature. Keep out of reach of children.

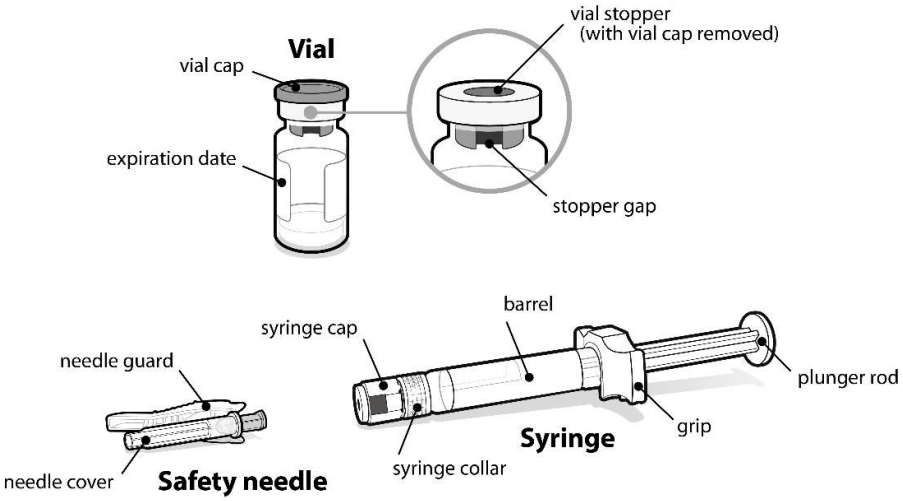
1. Things you need

A single SOMAVERT pack containing:

- A vial of SOMAVERT powder.
- A pre-filled syringe with solvent.
- A safety needle.

You will also need:

- A cotton ball.
- An alcohol swab.
- A suitable sharps container.

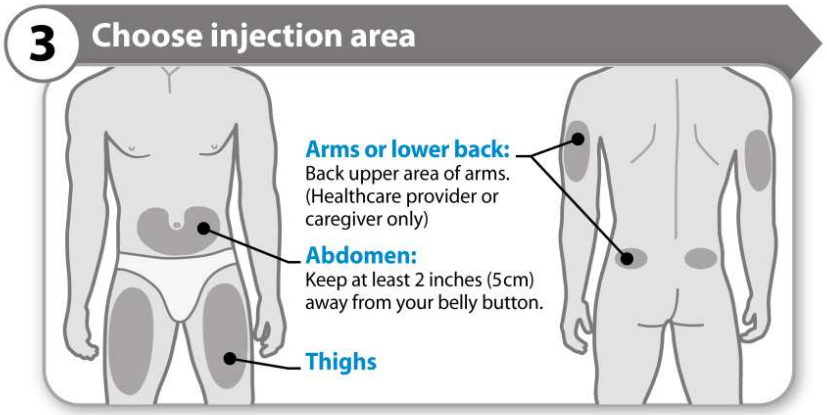


2. Getting ready

Before you start:

- Only mix SOMAVERT and the solvent when you are ready to inject your dose.
- Remove a single SOMAVERT pack from the refrigerator and allow it to come to room temperature naturally in a safe place.
- Wash your hands with soap and water, and dry thoroughly.
- Peel open the packaging of the syringe and safety needle to make it easier to pick up each item as you prepare for your injection.
- Do not use the syringe or vial if:
    - they are damaged or faulty;
    - the expiration date has passed;
    - it has been frozen, even if it has now thawed (syringe only).

3. Choose injection area



- Choose a different location within an area for each injection.
- Avoid bony areas or areas that are bruised, red, sore or hard, or areas that have scars or skin conditions.
- Clean the injection area with the alcohol swab as instructed by your healthcare provider.
- Allow the injection area to dry.

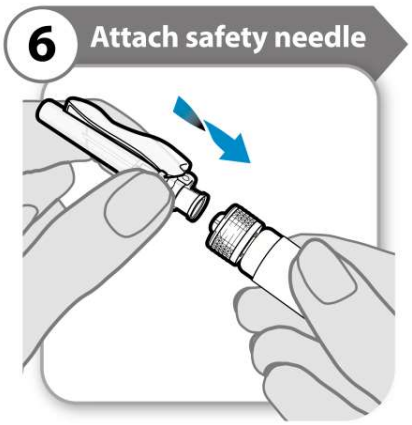
4. Remove vial cap

- Remove the cap from the vial.
- Throw the cap away; it is not needed again.
  Caution: Do not let anything touch the vial stopper.

5. Remove syringe cap

- Snap off the syringe cap. It may take more effort to snap off than you might expect.
- Throw the syringe cap away; it is not needed again.
- Keep the syringe upright to avoid leakage.
  Caution: Do not let the end of the syringe touch anything when the syringe cap is off.

6. Attach safety needle

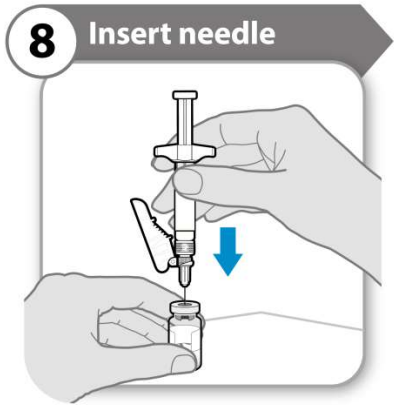


- Twist the safety needle firmly onto the syringe as far as it will go.

7. Remove needle cover

- Fold the needle guard out of the way of the needle cover.
- Carefully pull the needle cover straight off.
- Throw the needle cover away; it is not needed again.
  Caution: Do not let the needle touch anything.

8. Insert needle

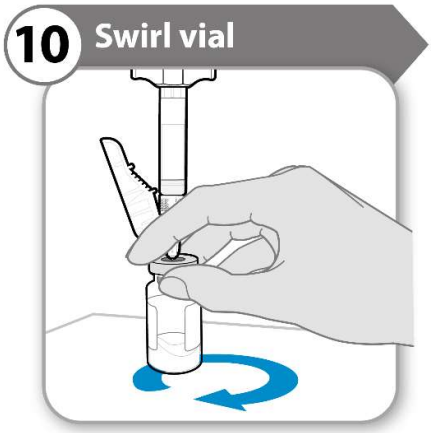


- Push the needle through the centre of vial stopper, as shown.
- Support the syringe while the needle is in the vial stopper to prevent bending the needle.

9. Add liquid

- Tilt both the vial and syringe at an angle, as shown.
- Push the plunger rod down **slowly** until all the liquid has emptied into the vial.
- **Caution:** Do not squirt the liquid directly onto the powder, as this creates foam. Foam makes the medicine unusable.
- **Do not withdraw the needle yet.**

10. Swirl vial

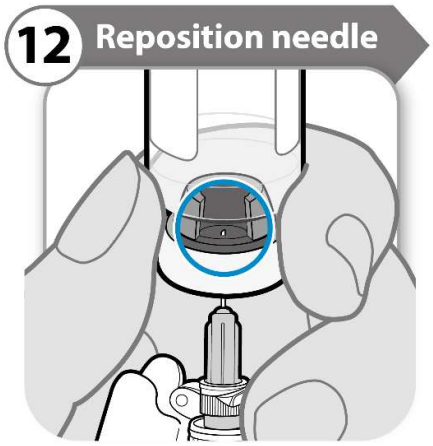


- Support both the syringe and vial in one hand, as shown.
- Gently swirl the liquid, sliding the vial in a circular motion on a flat surface.
- Continue swirling the liquid until all the powder has fully dissolved.
  Note: This may take up to 5 minutes.

11. Check medicine

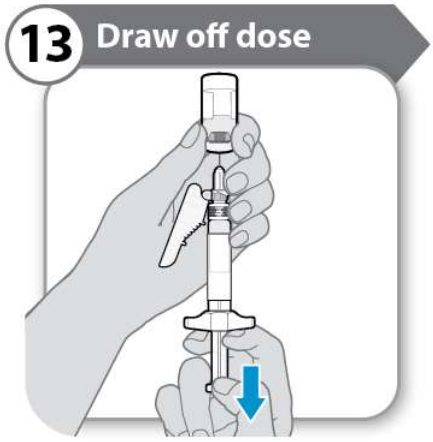
- Keeping the needle in the vial, look carefully at the medicine. It must be clear and free of particles.
- Do not use if:
  - the medicine is cloudy or hazy;
  - the medicine has any colour at all;
  - there are any particles or there is a layer of foam in the vial.

12. Reposition needle



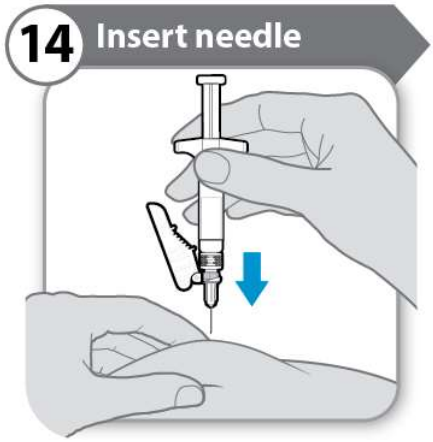
- Turn the vial so that you can see the stopper gap, as shown.
- Pull the needle down so that the needle tip is at the lowest point in the liquid. This will help you to draw off as much liquid as possible.
- Check that the plunger rod has not moved - if it has, then push it back all the way into the syringe. This ensures that all air is removed from the syringe before you draw off the dose.

13. Draw off dose



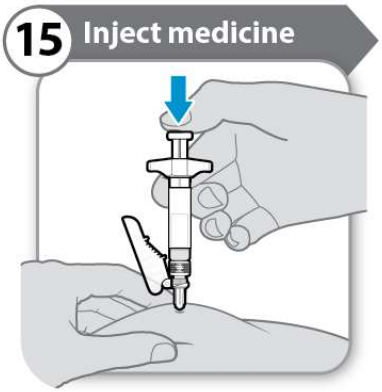
- Slowly pull back the plunger rod to withdraw as much medicine as possible from the vial. **Note:** If you see air in the syringe, tap the barrel to float the bubbles to the top, and then gently push the bubbles out **into the vial**.
- Pull the needle out of the vial.

14. Insert needle



- Gently pinch the skin at the site of injection.
- Insert the needle to its full depth into the pinched skin.

15. Inject medicine



- Push the plunger rod down slowly until the barrel is empty.
  Note: Make sure you keep the needle in at full depth.
- Release the pinched skin and pull the needle straight out.

16. Make needle safe

- Fold the needle guard over the needle.
- **Gently** apply pressure using a hard surface to lock the needle guard in place.
  Note: You will hear a click when the needle guard has been locked.

17. Dispose

- The syringe and needle should **NEVER** be reused. Dispose of the needle and syringe as instructed by your doctor, nurse or pharmacist and in accordance with local health and safety laws.

18. After injection

- If necessary, use a clean cotton ball and press lightly on the injection area.
- **Do not rub the area.**

QUESTIONS & ANSWERS

What should I do if anything has accidentally touched the vial stopper?

- Clean the vial stopper with a fresh alcohol wipe, and leave it to dry completely. If you are unable to clean the stopper, do not use the vial.

What should I do with the syringe if it has been dropped?

- Do not use it - even if it looks undamaged. Dispose of the syringe in the same way as a used syringe. You will need a replacement syringe.

How many times can I safely insert the needle into the vial stopper?

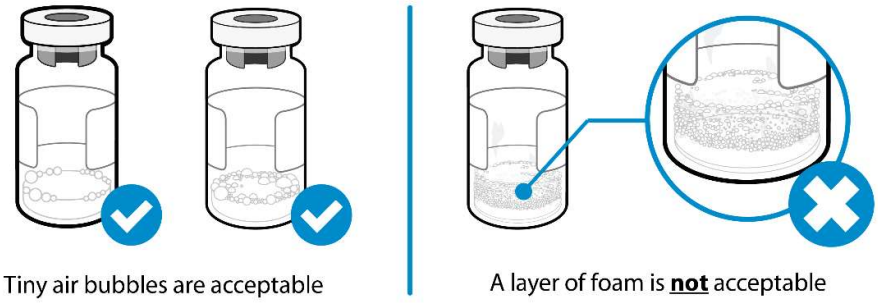
- Once only. Withdrawing and reinserting greatly increases the risk of needle damage, and will blunt the needle. This can cause discomfort and increases risk of skin damage and infection. There is also a risk you may lose some of the medicine.

Is it OK to shake the vial if the powder is not dissolving?

- No - never shake the vial. Shaking can destroy the medicine and create foam. The powder may take a few minutes to dissolve fully, so continue swirling the vial gently until the liquid is completely clear.

How can I tell if there is any foam in the vial?

- Foam looks like a mass of small bubbles that float as a layer to the top of the liquid. Do not inject SOMAVERT if it has foamed.



How can I prevent the medicine from foaming?

- Press the plunger very slowly so that the liquid gently runs down the inside of the vial. Do not spray the liquid directly onto the powder, as this creates foam. This technique will also reduce the swirling time and allow more of the medicine to be drawn off.

I can see some air in the syringe. Is this OK?

- Tiny air bubbles in the liquid are normal and are safe to inject. However, it is possible to accidently draw air into the syringe, which should be removed before injecting. Bubbles or air gaps that float to the top of the liquid should be pushed back out into the vial.

Why can't I get all of the medicine out of the vial?

- The shape of the vial means that a very small amount of the medicine will be left behind in the vial. This is normal. To ensure that only a trace of medicine remains, make sure the needle tip is as low as it can be in the vial when drawing off your dose.

What should I do if I have any doubts about my medicine?

- All questions should be handled by a doctor, nurse or pharmacist familiar with SOMAVERT.