Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986
This medicine is dispensed with a doctor's prescription only

Somavert® 10 mg	**Somavert® 15 mg**	**Somavert® 20 mg**	**Somavert® 25 mg**	**Somavert® 30 mg**

Powder and solvent for solution for injection

Composition:

Each vial contains:	Each vial contains:	Each vial contains:	Each vial contains:	Each vial contains:
pegvisomant 10 mg	pegvisomant 15 mg	pegvisomant 20 mg	pegvisomant 25 mg	pegvisomant 30 mg

Inactive ingredients and allergens: See section 2 under 'Important information about some of this medicine's ingredients' and section 6 'Further information'.

Read the entire leaflet carefully before using this medicine. This leaflet contains concise information about this medicine. If you have any further questions about using this medicine, consult your doctor or pharmacist. This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

1. WHAT IS THIS MEDICINE INTENDED FOR?

Treatment of adult patients with acromegaly (gigantism) who are responding inadequately to surgery and/or radiation therapy, and in whom medical treatment with synthetic somatostatin analogues did not normalize IGF-I growth factor levels or was not tolerated.

Acromegaly (gigantism) is a hormonal disorder resulting from the increased secretion of growth hormone (GH) and insulin-like growth factor 1 (IGF-1), which is characterised by overgrowth of bone, soft tissue swelling, heart disease and other related disorders.

Therapeutic group:
growth hormone receptor antagonist.

2. BEFORE USING THIS MEDICINE

Do not use this medicine if:

You are sensitive (allergic) to the active ingredient or to any of the other ingredients in this medicine (see section 6).

Special warnings regarding use of the medicine

Consult your doctor before starting treatment with Somavert®.

- If you experience disturbed vision or headaches, contact your doctor immediately.
- Your doctor or nurse will monitor the levels of insulin-like growth factor 1 (IGF-1) in your blood and adjust the dose of Somavert® if necessary.
- Your doctor should also monitor your benign tumour (adenoma).
- Your doctor or nurse will also monitor the levels of liver enzymes in your blood every 4-6 weeks for the first six months of treatment with Somavert®. Somavert® treatment should be discontinued if signs of liver disease persist.
- If you are diabetic, your doctor may adjust the amount of insulin or other medicines you are using.
- Fertility in women 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 contraception. See also the section 'Pregnancy, breastfeeding, and fertility', below.

Children and adolescents
This medicine is not intended for children and adolescents under 18 years old.

Drug interactions
If you are taking, or have recently taken, other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist. Particularly, if you are taking other medicines for the treatment of acromegaly or medicines for the treatment of diabetes.

As part of your treatment you may be given additional medicines. It is important to keep using all your medicines as well as Somavert® unless you are told otherwise by your doctor.

Pregnancy, breastfeeding, and fertility
The use of Somavert® in pregnant women is not recommended. If you are of childbearing age, you must use contraception during treatment with this medicine. It is not known if this medicine passes into breast milk. Do not breastfeed while taking Somavert®, unless you have consulted your doctor about this.

If you are pregnant or breastfeeding, think you are pregnant or are planning to become pregnant, consult your doctor before taking this medicine.

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

Important information about some of this medicine's ingredients
Somavert® contains sodium
This medicine contains less than 1 mmol (23 mg) of sodium per dose i.e. essentially 'sodium-free'.

3. HOW TO USE THIS MEDICINE?

Always use this medicine according to your doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.

The dosage and treatment regimen will be determined by your doctor only.

The standard dosage is usually:
A starting dose of 80 mg will be given subcutaneously (injected under the skin) by your doctor. Following this, the usual daily dose of Somavert® is 10 mg given by subcutaneous injection.

Every four to six weeks your doctor will make appropriate dose adjustments, made in increments of 5 mg/day, based on your blood insulin-like growth factor-1 (IGF-1) levels to achieve an optimal therapeutic response.

Do not exceed the recommended dose.

Method of administration:
Somavert® is injected subcutaneously (injected under the skin). The injection can be self-administered or given by another person, for example a doctor. The detailed instructions on injection procedure provided at the end of this leaflet must be followed. Adhere to the treatment as recommended by your doctor.

Somavert® comes as a powder and must be dissolved before use. The injection must not be mixed in the same syringe or vial as any other medicine.

Fatty tissue 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 3 of the 'Instructions for preparation and injection of Somavert®' section of this leaflet. This allows your skin and the area under your skin to recover before receiving another injection 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 or nurse.

If you have accidentally injected a higher dosage
If you accidentally inject a higher dose of Somavert® than determined for you by your doctor, it is unlikely to be serious, but you should contact your doctor or nurse immediately.

If you forget to take the medicine
If you forget to give yourself an injection at the scheduled time, you should inject the next dose as soon as you remember and then continue to inject Somavert® at the usual time as prescribed by your doctor. Do not inject a double dose to make up for forgotten doses.

Even if your health improves, do not stop taking this medicine without consulting your doctor or pharmacist.

Do not take medicines in the dark! Check the label and dose <u>each time</u> you take medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Somavert®, may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of 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 effects: swelling of the face, tongue, lips, or throat; wheezing or trouble breathing (spasm of the larynx); generalised skin rash, urticaria or itching; or dizziness. Refer to a doctor immediately if you develop any of these symptoms.

Very common side effects (affect more than 1 in 10 people):
- headache.
- diarrhoea.
- joint pain.

Common side effects (may affect up to 1 in 10 people):
- shortness of breath.
- increased levels of liver enzymes (a measure of liver function) seen in blood tests.
- blood in the urine.
- increased blood pressure.
- constipation, nausea (feeling sick), vomiting (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, inflammation of the joints (arthritis).
- high cholesterol levels in the blood, weight gain, increased or decreased blood sugar levels.
- flu-like illness, fatigue.
- abnormal dreams.
- eye pain.

Uncommon side effects (may affect up to 1 in 100 people):
- allergic reaction after administration (fever, rash, pruritus and, in severe cases, difficulty breathing, rapid swelling of skin, requiring urgent medical attention) may occur immediately, or several days after taking this medicine.
- protein in the urine, increased urine, kidney problems.
- lack of interest, feeling confused, increased sex drive, panic attack, loss of memory, problems sleeping.
- low level of platelets in the blood, high or low level of white blood 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, raised itchy bumps on the skin (urticaria).
- increased level of fat in the blood, increased appetite.
- dry mouth, increased saliva, tooth problems, haemorrhoids.

- abnormal sense of taste, migraine.

Side effects of unknown frequency (the frequency of these effects has not been established yet):

- anger.
- severe breathlessness (laryngospasm).
- rapid swelling of skin and underlying tissue and inner lining 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.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects or by using the link: https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

- Prevent poisoning! This and any other medicine should be kept in a closed place, out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use this medicine after the expiry date which is stated on package. The expiry date refers to the last day of that month.

Storage conditions powder:

- Store the powder vial in a refrigerator (2°C – 8°C). Do not freeze.
- The powder vial may be stored below 25°C for a period of up to 30 days. Do not return to the refrigerator during this period. Write the date on which it was removed from the refrigerator on the carton. Discard at the end of this period.
- Store in the outer package in order to protect from light.

Storage conditions solvent:

- Store the pre-filled syringe with solvent below 25°C or in the refrigerator. Do not freeze.
- Use the solvent supplied in the package to dilute the powder.
- Use immediately after preparing the solution.
- Do not use this medicine if you notice that the solution is cloudy or contains particles.
- Handling waste: Never reuse the syringe and needle. Dispose of needles and syringes as you were instructed by a healthcare professional.

6. FURTHER INFORMATION

In addition to the active ingredient, this medicine also contains:
glycine, mannitol, disodium phosphate anhydrous, sodium dihydrogen phosphate monohydrate, water for injection.

What the medicine looks like and contents of the pack:
Each pack contains a powder vial (either 10 mg, 15 mg, 20 mg, 25 mg or 30 mg pegvisomant) and 1 ml of solvent in a pre-filled syringe.

The powder is white, and the solvent is clear and colourless.

This medicine is available in packs of 30 units (unit=powder vial+syringe with solvent).

Registration holder's name and address: Pfizer Pharmaceuticals Israel Ltd., 9 Shenkar St., Herzliya Pituach 46725.

Registration number of the medicine in the Ministry of Health's National Drug Registry:
Somavert® 10mg: 135-41-31357
Somavert® 15mg: 135-42-31358
Somavert® 20mg: 135-43-31359
Somavert® 25mg: 158-92-34994
Somavert® 30mg: 158-93-34995

Revised in 03/2021 according to MOH guidelines.

INSTRUCTIONS FOR PREPRATION AND INJECTION OF SOMAVERT®:

Somavert® powder in vial for single use with solvent in a pre-filled syringe.

Somavert® comes as a white powder in a vial. You must mix Somavert® with a liquid (solvent) before you can use the medicine.
The solvent comes in a pre-filled syringe.

Do not use any other solvent with Somavert®.

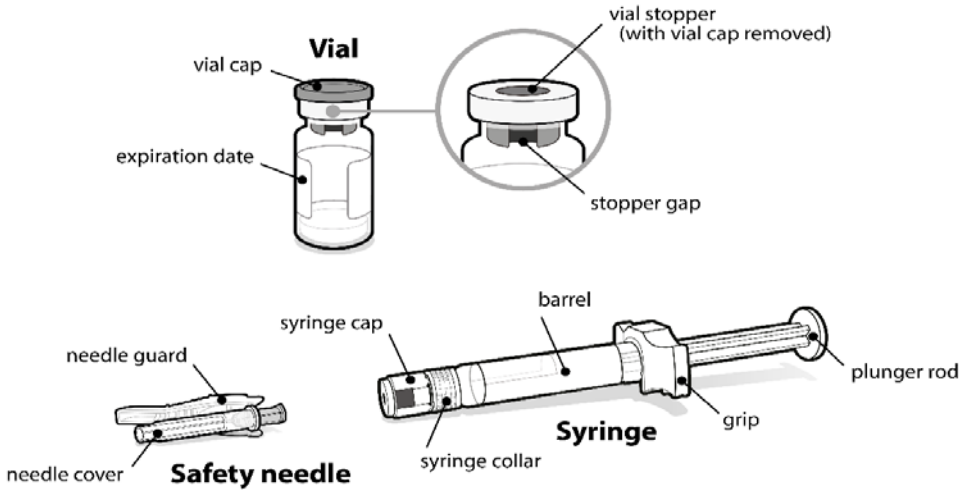
It is important that you do not try to give yourself or someone else an injection before you have been trained to do so by your healthcare provider (doctor/nurse).

Store the powder vial in a refrigerator (2°C – 8°C). Do not freeze.
The powder vial may be stored below 25°C for a period of up to 30 days. Do not return to the refrigerator during this period. Write the date on which it was removed from the refrigerator on the carton. Discard at the end of this period.
Store in the outer package in order to protect from light.

Store the pre-filled solvent syringe below 25°C or in the refrigerator. Do not freeze.

Keep out of the reach and sight of children.

1. **Things you need**
   - 1 vial of powder
   - 1 pre-filled syringe with solvent
   - a safety needle
   - a cotton ball
   - an alcohol swab
   - a sharps container.

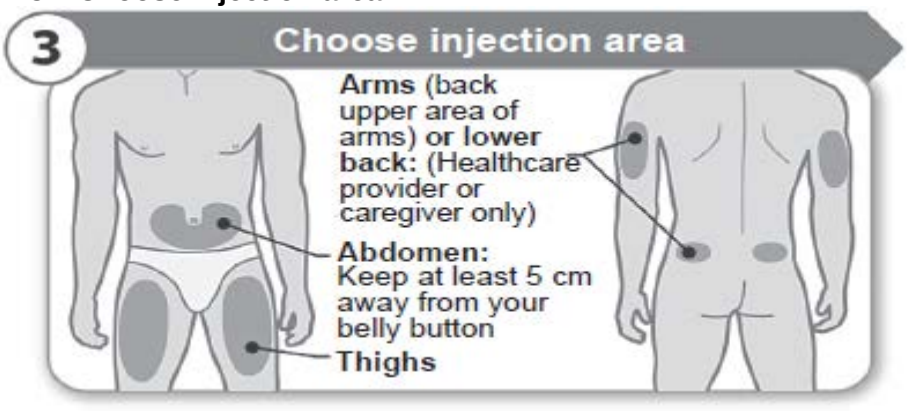


2. Getting ready for injection

Before you start:

- Only mix Somavert® and the solvent when you are ready to inject your dose.
- Remove one Somavert® vial (powder) and one solvent syringe from the refrigerator and allow them 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 contaminated
  - their expiration date has passed
  - they have frozen, even if they have now thawed (syringe only).

3. Choose injection area



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

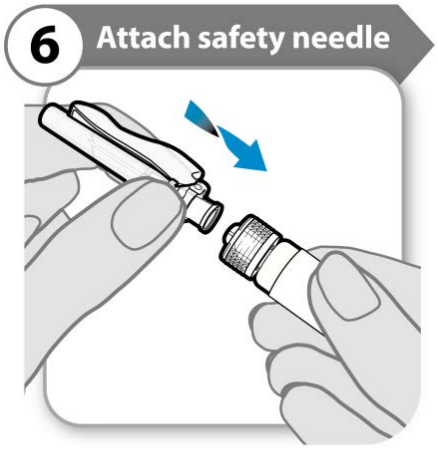
4. Remove vial cap

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

5. Remove syringe cap

- Snap off the syringe cap. It may take more effort to snap off than you might expect.
- Throw the 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 after the syringe cap is off.

6. Attach safety needle

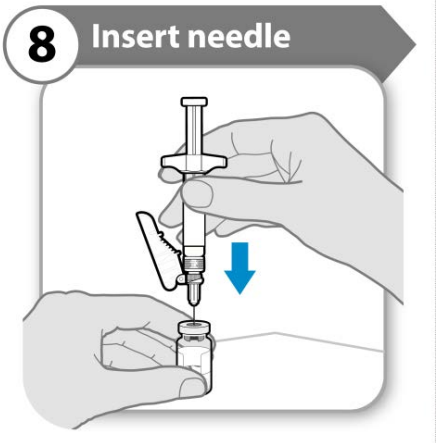


- Twist the safety needle firmly onto the syringe as far as it will go.

7. Remove needle cover

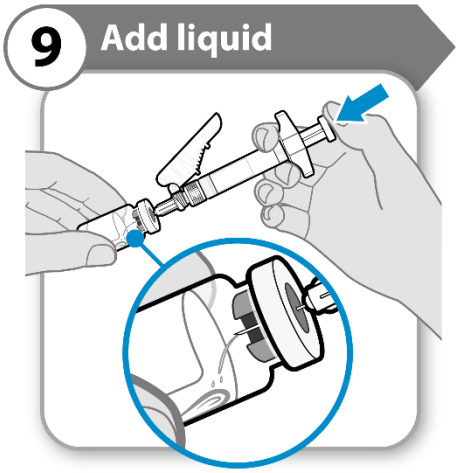
- Fold the needle guard out of the way of the needle cover.
- Carefully pull the needle cover straight off.
- Throw the needle cover away; it is not needed again.
  Caution: Do not let the needle touch anything.

8. Insert needle



- Push the needle through the centre of the vial stopper, as shown in the illustration.
- 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 in the figure.
- 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.**

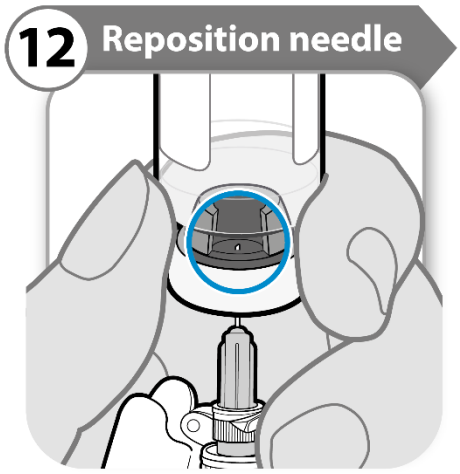
10. Swirl vial contents

- Support both the syringe and vial, as shown in the illustration.
- 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 procedure may take up to 5 minutes.

11. Check solution

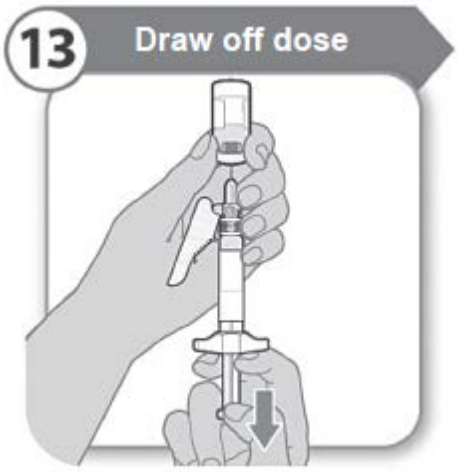
- Keeping the needle in the vial, look carefully at the solution. It must be clear and free of particles.
- Do not use if:
  - the solution is cloudy
  - the solution has any colour at all
  - there are any particles or there is a layer of foam in the vial.

12. Reposition needle



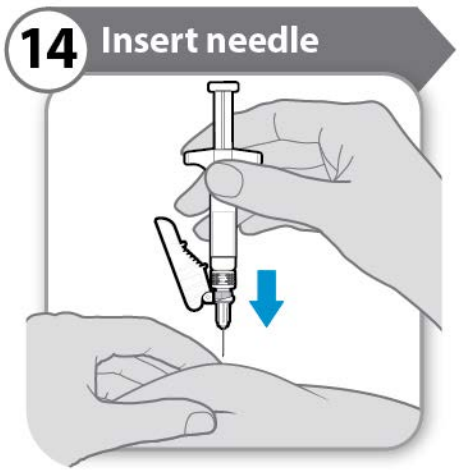
- Turn the vial so that you can see the stopper, as shown in the figure.
- Pull the needle down so that the needle tip is at the lowest point in the liquid. This will help you to draw off as much solution as possible.
- Check that the plunger rod has not moved. If it has moved, push it back all the way 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 solution as possible. **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

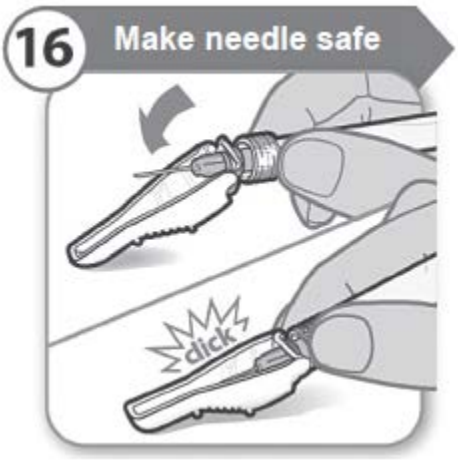


- Gently pinch the skin at the site of injection.
- Insert the needle to its full depth into the pinched skin.

15. Inject solution

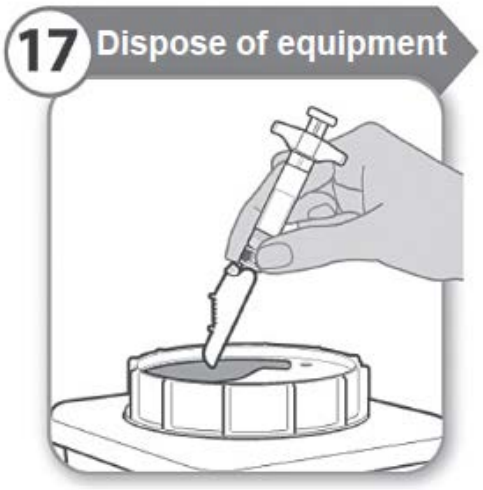
- Push the plunger rod down slowly until the barrel is empty.
  Note: Make sure you keep needle fully in skin.
- Release the pinched skin and pull the needle straight out.

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 of equipment



- 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 regulations.

18. After injection

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