Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

SANDOSTATIN® LAR® 10 mg powder and solvent for suspension for injection

Name and quantity of active ingredient:

Each vial of powder contains 10 mg octreotide (as octreotide acetate)

SANDOSTATIN® LAR® 20 mg powder and solvent for suspension for injection

Name and quantity of active ingredient:

Each vial of powder contains 20 mg octreotide (as octreotide acetate)

SANDOSTATIN® LAR® 30 mg powder and solvent for suspension for injection

Name and quantity of active ingredient:

Each vial of powder contains 30 mg octreotide (as octreotide acetate)

Inactive ingredients and allergens: see section 6 'Additional information'. See also in section 2 'Important information about some of the ingredients of the medicine'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult the 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?

SANDOSTATIN LAR is used:

- to treat people with acromegaly:
  - whose illness is adequately controlled by standard doses of Sandostatin given by injection under the skin (subcutaneously)
  - when surgery or radiotherapy are inappropriate or ineffective
  - to cover the interim period until the radiotherapy becomes fully effective

- to treat endocrine gastro-entero-pancreatic (GEP) tumors, carcinoid tumors

Therapeutic group:
somatostatin analogues

SANDOSTATIN LAR is a synthetic compound derived from somatostatin. Somatostatin is normally found in the human body, where it inhibits the release of certain hormones such as growth hormone. SANDOSTATIN LAR has advantages over somatostatin; it is stronger and its effects last longer.

Acromegaly is a condition where the body produces too much growth hormone. Normally, growth hormone controls growth of tissues, organs, and bones. Too much growth hormone leads to an increase in the size of bones and tissues, especially in the hands and feet. SANDOSTATIN LAR markedly reduces the symptoms of acromegaly, which include headache, excessive perspiration, numbness of the hands and feet, tiredness, and joint pain.

Overproduction of specific hormones and other related substances can be caused by some rare conditions of the stomach, bowels or pancreas. This upsets the natural hormonal balance of the body and results in a variety of symptoms, such as flushing, diarrhea, low

blood pressure, rash, and weight loss. Treatment with SANDOSTATIN LAR helps to control these symptoms.

2. Before using this medicine

Follow all your doctor's instructions carefully. They may differ from the information contained in this leaflet.

Read the following explanations before you use SANDOSTATIN LAR.

Do not use this medicine if:
you are sensitive (allergic) to octreotide or to any of the other ingredients contained in this medicine (see section 6 'Additional information').

Special warnings about using this medicine

Before using SANDOSTATIN LAR, tell the doctor if:
- you know that you have gallstones now, or have had them in the past or experience any complications like fever, chills, abdominal pain, or yellowing of your skin or eyes, as prolonged use of SANDOSTATIN LAR may cause gallstone formation. Your doctor may wish to check your gallbladder periodically.
- you know that you have diabetes, as SANDOSTATIN LAR can affect blood sugar levels. If you are diabetic, your sugar levels should be checked regularly.
- you have a history of vitamin B12 deficiency; your doctor may wish to check your vitamin B12 level periodically.

Children and adolescents
There is little experience with the use of SANDOSTATIN LAR in children.

Tests and follow-up
If you receive treatment with SANDOSTATIN LAR over a long period of time, your doctor may wish to check your thyroid function periodically.

Your doctor will check your liver function.

Your doctor may want to check your pancreatic enzyme function.

Drug interactions
If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell the doctor or pharmacist.

You can generally continue taking other medicines while you are using SANDOSTATIN LAR. However, certain medicines, such as cimetidine, cyclosporin, bromocriptine, quinidine, and terfenadine have been reported to be affected by SANDOSTATIN LAR.

If you are taking a medicine to control your blood pressure (such as a beta blocker or a calcium channel blocker) or a medicine to control fluid and electrolyte balance, your doctor may need to adjust your dosage.

If you have diabetes, your doctor may need to adjust your insulin dosage.

If you are going to receive lutetium (^{177}Lu) oxodotreotide, a radiopharmaceutical therapy, your doctor may stop and/or adapt SANDOSTATIN LAR treatment for a short period of time.

Pregnancy, breastfeeding, and fertility
If you are pregnant or breastfeeding, think you may be pregnant, or are planning to get pregnant, ask your doctor for advice before taking this medicine.

SANDOSTATIN LAR should only be used during pregnancy if clearly needed.

Women of child-bearing age should use an effective contraceptive method during treatment.
Do not breastfeed while using SANDOSTATIN LAR. It is not known whether SANDOSTATIN LAR passes into breast milk.

Driving and using machines
SANDOSTATIN LAR has no effects or has negligible effects on the ability to drive and use machines. However, some of the side effects you may experience while using SANDOSTATIN LAR, such as headache and tiredness, may reduce your ability to drive and use machines safely.
As for the children, they should be cautioned against riding a bicycle, playing near a road, and similar activities.

Important information about some of this medicine's ingredients
SANDOSTATIN LAR contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'.

3. How to use this medicine?

Always use this medicine according to the doctor's instructions.
Check with the doctor or pharmacist if you are not sure about your dosage or about how to take this medicine.
The dosage and treatment regimen will be determined by the doctor only.
Do not exceed the recommended dose.
SANDOSTATIN LAR must always be administered as an injection into the muscle of the buttocks. With repeated administration, the left and right buttock should be used alternately.
This medicine must be injected by a qualified healthcare professional only.

If you accidentally take a higher dose
No life-threatening reactions have been reported after overdose of SANDOSTATIN LAR.
The symptoms of overdose are: hot flushes, frequent urination, tiredness, depression, anxiety and lack of concentration.
If you think you received an overdose and you experience such symptoms, tell your doctor straight away.
If a child accidentally received an injection with this medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

If you forget to take the medicine
If your scheduled injection is forgotten, it is advisable to get it as soon as you remember, and then continue as usual.
It will not do any harm if a dose is a few days late, but you could get some temporary re-appearance of symptoms until you get back on schedule.

Adhere to the treatment as recommended by the doctor.
Even if your health improves, do not stop taking this medicine without consulting the doctor.

If you stop taking this medicine
If you stop your treatment with SANDOSTATIN LAR your symptoms may come back.
Therefore, do not stop using SANDOSTATIN LAR unless your doctor tells you to.

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 the doctor, pharmacist, or nurse.

4. <u>Side effects</u>

Like with all medicines, using SANDOSTATIN LAR may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Some side effects could be serious. Tell your doctor straight away if you get any of the following side effects:

Very common side effects (may affect more than 1 in 10 users)
- gallstones, may cause sudden back pain;
- too much sugar in the blood.

Common side effects (affect 1-10 in 100 users)
- underactive thyroid gland (hypothyroidism) causing changes in heart rate, appetite or weight, tiredness, feeling cold or swelling at the front of the neck;
- changes in thyroid function tests;
- inflammation of the gallbladder (cholecystitis): symptoms may include pain in the upper right abdomen, fever, nausea, yellowing of the skin and eyes (jaundice);
- too little sugar in the blood;
- impaired glucose tolerance;
- slow heart beat.

Uncommon side effects (affect 1-10 in 1,000 users)
- thirst, low urine output, dark urine, dry flushed skin;
- fast heart beat.

Other serious side effects
- hypersensitivity (allergic) reactions including skin rash;
- a type of an allergic reaction (anaphylaxis) which can cause difficulty in swallowing or breathing, swelling and tingling, possibly with a drop in blood pressure with dizziness or loss of consciousness;
- inflammation of the pancreas gland (pancreatitis): symptoms may include sudden pain in the upper abdomen, nausea, vomiting, diarrhea;
- liver inflammation (hepatitis): symptoms may include yellowing of the skin and eyes (jaundice), nausea, vomiting, loss of appetite, generally feeling unwell, itching, light-colored urine;
- irregular heart beat;
- low platelet count in blood; this could result in increased bleeding or bruising.

Tell your doctor straight away if you notice any of the side effects above.

Other side effects:
Tell your doctor, pharmacist or nurse if you notice any of the side effects listed below. They are usually mild and tend to disappear as treatment progresses.

Very common side effects (affect more than 1 in 10 users):
- diarrhea;
- abdominal pain;
- nausea;
- constipation;
- flatulence;

- headache;
- local pain at the injection site.

Common side effects (affect 1-10 in 100 users)
- abdominal discomfort after meal (dyspepsia);
- vomiting;
- feeling of fullness in the stomach;
- fatty stools;
- loose stools;
- discoloration of feces;
- dizziness;
- loss of appetite;
- change in liver function tests;
- hair loss;
- shortness of breath;
- weakness.

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 the 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
Side effects can also be reported to Novartis using the following e-mail address:
Safetydesk.israel@novartis.com

5. How to store the medicine?

Avoid poisoning! This medicine and any other medicine should be kept in a closed place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by a doctor.

Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.

Storage conditions:
Store in a refrigerator (2-8°C).
Do not freeze.
Store in the original package to protect from light.
SANDOSTATIN LAR may be stored below 25°C on the day of injection.
Use immediately after reconstitution.

Do not use the medicine if you notice any particles or change of color.

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

6. Additional information

In addition to the active ingredient, this medicine also contains:

Powder (in vial):
poly (DL-lactide-co-glycolide) and sterilized mannitol
Solvent (in prefilled syringe):

carmellose sodium, mannitol, poloxamer 188, water for injections

What the medicine looks like and contents of the pack:

The powder in the vial is white to white with yellowish. The solvent is colorless to slightly yellow or brown in a prefilled syringe.

Each pack contains:

- one 6 mL glass vial with rubber stopper, sealed with an aluminum flip-off seal containing powder for suspension for injection.
- one 3 mL colorless prefilled glass syringe with rubber front and plunger stopper containing 2 mL solvent.
- The vial and syringe are packaged together in a rigid plastic tray with one vial adapter and one safety injection needle.

Registration holder and importer:
Novartis Israel Ltd., P.O.B 7126, Tel Aviv.

Revised in August 2024

Registration number of the medicine in the Ministry of Health's National Drug Registry:
SANDOSTATIN LAR 10 mg: 112 50 29488
SANDOSTATIN LAR 20 mg: 112 49 29489
SANDOSTATIN LAR 30 mg: 112 48 29490

The following information is intended for healthcare professionals only:

How much Sandostatin LAR to use

Acromegaly

For patients who are adequately controlled with s.c. Sandostatin, it is recommended to start treatment with the administration of 20 mg Sandostatin LAR at 4-week intervals for 3 months. Treatment with Sandostatin LAR can be started the day after the last dose of s.c. Sandostatin. Subsequent dosage adjustment should be based on serum growth hormone (GH) and insulin-like growth factor-1/somatomedin C (IGF-1) concentrations and clinical symptoms.

For patients in whom, within this 3-month period, clinical symptoms and biochemical parameters (GH; IGF 1) are not fully controlled (GH concentrations still above 2.5 microgram/L), the dose may be increased to 30 mg every 4 weeks.

For patients whose GH concentrations are consistently below 1 microgram/L, whose IGF 1 serum concentrations normalised, and in whom most reversible signs/symptoms of acromegaly have disappeared after 3 months of treatment with 20 mg, 10 mg Sandostatin LAR may be administered every 4 weeks. However, particularly in this group of patients, it is recommended to closely monitor adequate control of serum GH and IGF-1 concentrations, and clinical signs/symptoms at this low dose of Sandostatin LAR.

For patients on a stable dose of Sandostatin LAR, assessment of GH and IGF-1 should be made every 6 months.

For patients in whom surgery or radiotherapy is inappropriate or ineffective, or in the interim period until radiotherapy becomes fully effective, a short test dosing period of s.c. administration of Sandostatin is recommended to assess the response and systemic tolerability of octreotide prior to initiating treatment with Sandostatin LAR as described above.

Gastro-entero-pancreatic endocrine tumours

For patients in whom symptoms are adequately controlled with s.c. Sandostatin, it is recommended to start treatment with the administration of 20 mg Sandostatin LAR at 4-week intervals. The treatment with s.c. Sandostatin should be continued at the previously effective dosage for 2 weeks after the first injection of Sandostatin LAR.

For patients who were not previously treated with s.c. Sandostatin, it is recommended to start with the administration of s.c. Sandostatin at a dosage of 0.1 mg three times daily for a short period (approximately 2 weeks) to assess the response and systemic tolerability of octreotide before initiating the treatment with Sandostatin LAR as described above. For patients in whom symptoms and biological markers are well controlled after 3 months of treatment, the dose may be reduced to 10 mg Sandostatin LAR every 4 weeks.

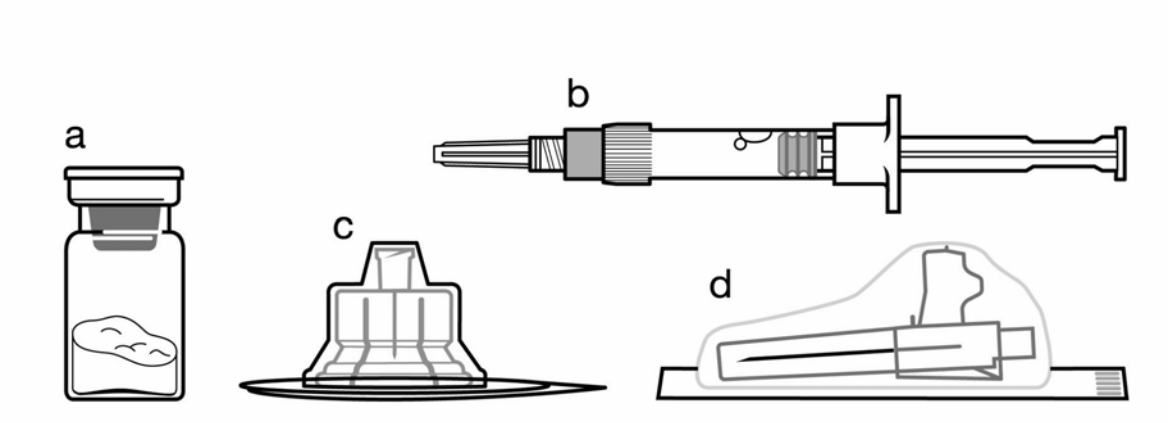
For patients in whom symptoms are only partially controlled after 3 months of treatment, the dose may be increased to 30 mg Sandostatin LAR every 4 weeks.

For days when symptoms associated with gastro-entero-pancreatic tumours may increase during treatment with Sandostatin LAR, additional administration of s.c. Sandostatin is recommended at the dose used prior to the Sandostatin LAR treatment. This may occur mainly in the first 2 months of treatment until therapeutic concentrations of octreotide are reached.

Instructions for preparation and intramuscular injection for Sandostatin LAR

FOR DEEP INTRAMUSCULAR INJECTION ONLY

Included in the injection kit:



a. One vial containing Sandostatin LAR powder
b. One prefilled syringe containing the vehicle solution for reconstitution
c. One vial adapter for drug product reconstitution
d. One safety injection needle

There are 3 critical actions in the reconstitution of Sandostatin LAR. **Not following them could result in failure to deliver the drug appropriately.**

- **The injection kit must reach room temperature**. Remove the injection kit from the fridge and let the kit stand at room temperature for a minimum of 30 minutes before reconstitution, but do not exceed 24 hours.
- After adding the diluent solution, **ensure that the powder is fully saturated** by letting the vial stand for 5 minutes**.**
- After saturation, **shake the vial moderately** in a horizontal direction for a minimum of 30 seconds **until a uniform suspension is formed.** The Sandostatin LAR suspension must only be prepared **immediately** before administration.

Sandostatin LAR should only be administered by a trained healthcare professional.

Step 1

- Remove the Sandostatin LAR injection kit from refrigerated storage.

  ATTENTION: It is essential to start the reconstitution process only after the injection kit reaches room temperature. Let the kit stand at room temperature for a minimum of 30 minutes before reconstitution, but do not exceed 24 hours.

  Note: The injection kit can be re-refrigerated if needed.

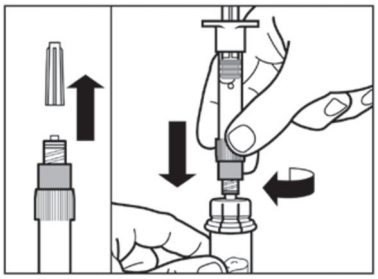
Step 2

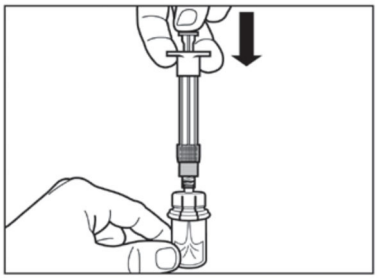
- Remove the plastic cap from the vial and clean the rubber stopper of the vial with an alcohol wipe.
- Remove the lid film of the vial adapter packaging, but do NOT remove the vial adapter from its packaging.
- Holding the vial adapter packaging, position the vial adapter on top of the vial and push it fully down so that it snaps in place, confirmed by an audible “click”.

- Lift the packaging off the vial adapter with a vertical movement.

Step 3

- Remove the cap from the syringe prefilled with diluent solution and screw the syringe onto the vial adapter.
- Slowly push the plunger all the way down to transfer all the diluent solution in the vial.

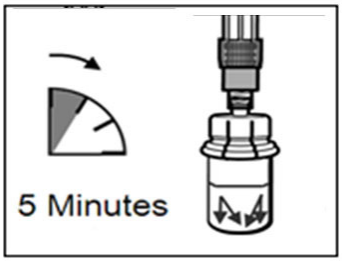




Step 4

ATTENTION: It is essential to let the vial stand for 5 minutes to ensure that the diluent has fully saturated the powder.

Note: It is normal if the plunger rod moves up as there might be a slight overpressure in the vial.

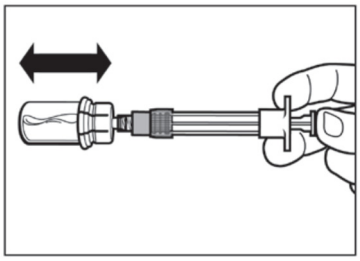


- At this stage prepare the patient for injection.

Step 5

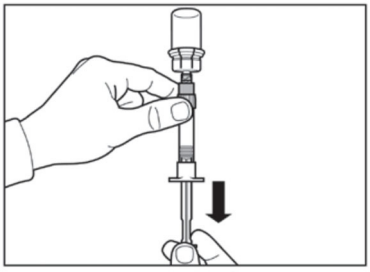
- After the saturation period, make sure that the plunger is pushed all the way down in the syringe.

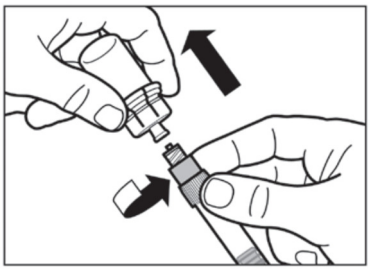
ATTENTION: Keep the plunger pressed and shake the vial **moderately** in a horizontal direction **for a minimum of 30 seconds** so that the powder is completely suspended (milky uniform suspension). **Repeat moderate shaking for another 30 seconds if the powder is not completely suspended.**



Step 6

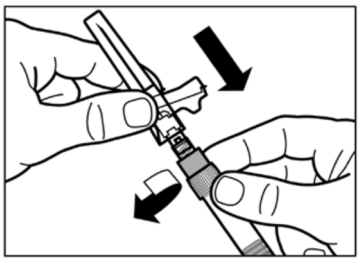
- Prepare injection site with an alcohol wipe.
- Turn syringe and vial upside down, slowly pull the plunger back and draw the entire contents from the vial into the syringe.
- Unscrew the syringe from the vial adapter.

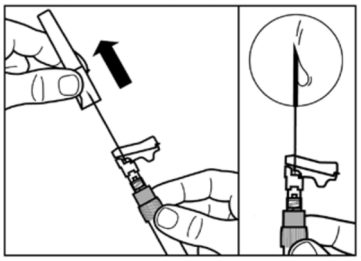




Step 7

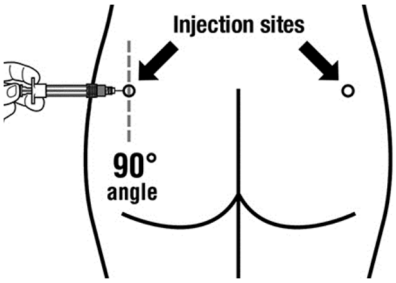
- Screw the safety injection needle onto the syringe.
- Gently re-shake the syringe to ensure a milky uniform suspension.
- Pull the protective cover straight off the needle.
- Gently tap the syringe to remove any visible bubbles and expel them from the syringe. *Verify that injection site has not been contaminated.*
- Proceed **immediately** to Step 8 for administration to the patient. Any delay may result in sedimentation.



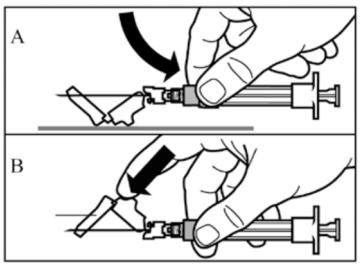


Step 8

- Sandostatin LAR must be given only by deep intramuscular injection, **NEVER** intravenously.
- Insert the needle fully into the left or right gluteus at a 90º angle to the skin.
- Slowly pull back the plunger to check that no blood vessel has been penetrated (reposition if a blood vessel has been penetrated).
- Depress the plunger with steady pressure until the syringe is empty. Withdraw the needle from the injection site and activate the safety guard (as shown in **Step 9**).



Step 9



- Activate the safety guard over the needle in one of the two methods shown:
  - either press the hinged section of the safety guard down onto a hard surface (figure A)
  - or push the hinge forward with your finger (figure B).
- An audible “click” confirms the proper activation.

Dispose of syringe immediately (in a sharps container).