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

SANDOSTATIN® 0.05 mg/ml, solution for injection/infusion
Name and quantity of active ingredient:
Each 1 ml ampoule contains 0.05 mg octreotide

SANDOSTATIN® 0.1 mg/ml, solution for injection/infusion
Name and quantity of active ingredient:
Each 1 ml ampoule contains 0.1 mg octreotide

SANDOSTATIN® 0.5 mg/ml, solution for injection/infusion
Name and quantity of active ingredient:
Each 1 ml ampoule contains 0.5 mg octreotide

Inactive ingredients and allergens: see section 6 'Additional information'. See also 'Important information about some of this medicine's ingredients'.

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 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?

This medicine is intended for:

- Preventing complications following pancreatic surgery.

- Controlling symptoms and reducing plasma levels of growth hormone (GH) and insulin-like growth factor 1 (IGF-1) in patients with acromegaly whose illness is inadequately controlled by surgery or radiotherapy. Treatment with SANDOSTATIN is also intended for patients with acromegaly who are unfit or unwilling to undergo surgery or are in the interim period until radiotherapy becomes fully effective.

- Relief of symptoms associated with functional endocrine gastro-entero-pancreatic (GEP) tumors:
  • Carcinoid tumors with features of the carcinoid syndrome
  • VIPomas
  • Glucagonomas
  • Zollinger-Ellison syndrome, usually in combination with proton-pump inhibitors or H_2-antagonists therapy
  • Insulinomas, for pre-operative control of hypoglycemia and maintenance treatment
  • GRFomas

  SANDOSTATIN is not an antitumor therapy and does not cure these patients.

- Emergency management of bleeding gastro-esophageal varices that are secondary to liver cirrhosis, in combination with a certain treatment such as endoscopic sclerotherapy.

Therapeutic group:
somatostatin analogs

SANDOSTATIN is a synthetic compound derived from somatostatin. Somatostatin is normally found in the human body where it inhibits the effect of certain hormones such as growth hormone. SANDOSTATIN 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 markedly reduces the symptoms of acromegaly, which include headache, excessive perspiration, numbness of the hands and feet, tiredness, and joint pain.

Relief of symptoms associated with certain digestive system tumors: In these conditions there is overproduction of specific hormones and other substances in 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 helps to control these symptoms.

Preventing complications following pancreatic surgery: SANDOSTATIN treatment helps lower the risk of complications (such as abscess in the abdomen, inflammation of the pancreas) after the surgery.

Emergency management of bleeding from gastro-esophageal varices: Treatment with SANDOSTATIN helps to control bleeding and reduce the need for blood transfusion due to gastro-esophageal varices in patients suffering from cirrhosis (chronic liver disease).

2. Before using this medicine

Do not use this medicine if:

You are sensitive (allergic) to octreotide or to any of the other ingredients in this medicine (see section 6 'Additional information').

Special warnings about using this medicine

Before using SANDOSTATIN, tell your doctor if:
- you know that you have gallstones now or have had them in the past or you experience any complications like fever, chills, abdominal pain, or yellowing of your skin or eyes, as prolonged use of SANDOSTATIN may cause gallstone formation. Your doctor may wish to check your gallbladder periodically.
- you know that you have problems with blood sugar levels that are either too high (diabetes) or too low (hypoglycemia). When SANDOSTATIN is used to treat bleeding from gastro-esophageal varices, monitoring of blood sugar level is mandatory.
- 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 in children.

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

Your doctor will check your liver function.

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

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

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.

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 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. It is not known whether SANDOSTATIN passes into breast milk.

Driving and using machines
SANDOSTATIN 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, such as dizziness, headache, and tiredness may reduce your ability to drive and use machines safely.
Warn children against riding a bicycle, playing near a road, and similar activities.

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

3. How to use this medicine?

Always use this medicine according to your doctor's instructions.
Check with your doctor or pharmacist if you are not sure about your dosage or about how to take this medicine.
Only your doctor will determine your dose and how you should take this medicine.
Do not exceed the recommended dose.

Depending on the condition being treated, SANDOSTATIN is given by:
• subcutaneous injection (under the skin) or
• intravenous infusion (into a vein).

If you have liver cirrhosis (chronic liver disease), your doctor may need to adjust your maintenance dosage.

Your doctor or nurse will explain how to inject SANDOSTATIN under the skin, but infusion into a vein must always be performed by a healthcare professional.

• Subcutaneous injection

The upper arms, thighs, and abdomen are good areas for subcutaneous injection.

Choose a new site for each subcutaneous injection so that you do not irritate a particular area. Patients who will be injecting themselves must receive precise instructions from their doctor or nurse.

If you store the medicine in the refrigerator, it is recommended that you allow it to reach room temperature before using it. This will reduce the risk of pain at the site of injection. You can warm it up in your hand but do not heat it in any other way.

Some people experience pain at the site of the subcutaneous injection. This pain usually lasts only a short time. If this happens to you, you can relieve it by gently rubbing the site of injection for a few seconds afterwards.
Before using a SANDOSTATIN ampoule, check the solution for particles or a change of color. Do not use it if you see anything unusual.

If you accidentally take a higher dose
No life-threatening reactions have been reported after overdose of SANDOSTATIN.
The symptoms of overdose are: irregular heart beat, low blood pressure, cardiac arrest, reduced supply of oxygen to the brain, severe upper stomach pain, yellow skin and eyes, nausea, loss of appetite, diarrhea, weakness, tiredness, lack of energy, weight loss, abdominal swelling, discomfort, and high level of lactic acid in the blood.
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
Inject one dose as soon as you remember, and then continue as usual.
It will not do any harm if you miss a dose, but you could get some temporary reappearance of symptoms until you get back on schedule.
Do not inject a double dose of SANDOSTATIN to make up for forgotten individual doses.

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

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

Do not take medicines in the dark! Check the label and dose <u>every time</u> you take medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your doctor, nurse, or pharmacist.

4. <u>Side effects</u>

Like with all medicines, using SANDOSTATIN 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 (affect more than one in ten 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 (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;
- swollen, raised areas on the skin that are very itchy (hives).

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 one in ten 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;
- change in color of faeces;
- dizziness;
- loss of appetite;
- change in liver function tests;
- hair loss;

- rash, itchy skin;
- 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.

Some people experience pain at the site of the subcutaneous injection. This pain usually lasts only a short time. If this happens to you, you can relieve the pain by gently rubbing the site of injection for a few seconds afterwards.

If you are taking SANDOSTATIN by subcutaneous injection, it may help to reduce the risk of gastrointestinal side effects if you avoid eating meals around the time of injection. It is therefore recommended that you inject SANDOSTATIN between meals or when you go to bed.

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. You can also use this link: https://sideeffects.health.gov.il/

5. How to store the medicine?

Prevent poisoning! To prevent poisoning, keep this and all other medicines in a closed place, out of the reach and sight of children and/or infants. 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.
Protect from light.
For day-to-day use, may be stored for up to two weeks not above 30°C and protected from light.
Use the ampoule immediately after opening.
Diluted solution should be used immediately after preparation (for intravenous infusion).

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:
mannitol, lactic acid, sodium hydrogen carbonate, water for injections.

What the medicine looks like and contents of the pack:

A 1 ml colorless glass ampoule with two colored rings; the ampoule contains a clear colorless solution:
SANDOSTATIN 0.05 mg/ml: one blue ring and one yellow ring.
SANDOSTATIN 0.1 mg/ml: one blue ring and one green ring.
SANDOSTATIN 0.5 mg/ml: one blue ring and one pink ring.

Each pack contains 5 ampoules.

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

Revised in January 2021 according to MOH guidelines.

Registration number of the medicine in the Ministry of Health National Drug Registry:

SANDOSTATIN 0.05 mg/ml: 047 03 25697

SANDOSTATIN 0.1 mg/ml: 047 01 25698

SANDOSTATIN 0.5 mg/ml: 107 13 27200

The following information is intended for healthcare professionals only:

- **Intravenous infusion (for health-care professionals)**

Inspect the medicinal product visually for discoloration and particulate matter prior to administration. Do not use it if you see anything unusual. For intravenous infusion dilute the product prior to administration. Sandostatin (octreotide acetate) is physically and chemically stable for 24 hours in sterile physiological saline solutions or sterile solutions of dextrose (glucose) 5% in water. However, because Sandostatin can affect glucose homeostasis, it is recommended that physiological saline solutions be used rather than dextrose. The diluted solutions are physically and chemically stable for at least 24 hours below 25°C. From a microbiological point of view, the diluted solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

The contents of one 500 microgram ampoule should normally be dissolved in 60 mL physiological saline, and the resulting solution should be infused by means of an infusion pump. This should be repeated as often as necessary until the prescribed duration of treatment is reached.

How much Sandostatin to use

The dose of Sandostatin depends on the condition being treated.

- **Acromegaly**

Treatment is usually started at 0.05 to 0.1 mg every 8 or 12 hours by subcutaneous injection. It is then changed according to its effect and relief of symptoms (such as tiredness, sweating and headache). In most patients the optimal daily dose will be 0.1 mg 3 times/day. A maximum dose of 1.5 mg/day should not be exceeded.

- **Tumours of the gastrointestinal tract**

Treatment is usually started at 0.05 mg once or twice a day by subcutaneous injection. Depending on response and tolerability, the dosage can be gradually increased to 0.1 mg to 0.2 mg 3 times/day. In carcinoid tumours, therapy should be discontinued if there is no improvement after 1 week of treatment at the maximum tolerated dose.

- **Complications following pancreatic surgery**

The usual dosage is 0.1 mg 3 times/day by subcutaneous injection for 1 week, starting at least 1 hour before surgery.

- **Bleeding gastro-oesophageal varices**

The recommended dosage is 25 micrograms/hour for 5 days by continuous intravenous infusion. Monitoring of blood sugar level is necessary during treatment.