PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Sunitinib Teva 12.5 mg	**Sunitinib Teva 25 mg**	**Sunitinib Teva 37.5 mg**	**Sunitinib Teva 50 mg**
capsules	**capsules**	**capsules**	**capsules**
Composition Each capsule contains: **Sunitinib (as base) 12.5 mg**	**Composition** Each capsule contains: **Sunitinib (as base) 25 mg**	**Composition** Each capsule contains: **Sunitinib (as base) 37.5 mg**	**Composition** Each capsule contains: **Sunitinib (as base) 50 mg**

For information regarding inactive ingredients and allergens, see section 2 under "Important information about some of the ingredients of the medicine" and section 6 – "Additional information".

Read the entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have additional questions, refer to the doctor or the pharmacist.

This medicine has been prescribed for your treatment. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

This medicine is intended for adults over 18 years old.

1. WHAT IS THE MEDICINE INTENDED FOR?

- For treatment of gastrointestinal stromal tumor (GIST) after disease progression or intolerance to imatinib mesylate.
- For treatment of advanced metastatic renal cell carcinoma (aRCC).
- For treatment of metastatic or unresectable well-differentiated pancreatic neuroendocrine tumors (pNET) with disease progression.

Therapeutic class:

A targeted receptor tyrosine kinase inhibitor.

2. Before using the medicine

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient or to any of the other ingredients this medicine contains (see section 6 – "Additional information").

Special warnings regarding the use of the medicine

Before treatment with Sunitinib Teva, tell the doctor if:

- **You have high blood pressure.** Sunitinib Teva can increase blood pressure. The doctor may check your blood pressure during treatment with Sunitinib Teva and you may be given medicines for reducing blood pressure, if needed.
- **You have or have had a blood disease, bleeding problems or bruises.** Treatment with Sunitinib Teva can increase the risk of bleeding or lead to changes in the number of certain cells in the blood which can cause anemia or affect the blood's ability to clot. If you are taking warfarin or acenocoumarol, blood thinning medicines which prevent blood clotting, there may be a greater risk of bleeding. Tell the doctor if you have any bleeding during the treatment with Sunitinib Teva.
- **You have cardiac problems.** Sunitinib Teva can cause cardiac problems. Tell the doctor if you feel increased fatigue, shortness of breath or swelling of the legs and ankles.
- **You have abnormal changes in heart rate.** Sunitinib Teva can cause arrhythmias. The doctor may perform ECG in order to evaluate these problems during the treatment with Sunitinib Teva. Tell the doctor if you feel dizziness, fainting sensation or abnormal heartbeats while taking Sunitinib Teva.
- **You have recently had problems with blood clots in the veins or arteries (types of blood vessels), including stroke, heart attack, embolism or thrombosis.** Refer to the doctor immediately if you have symptoms such as pain or pressure in the chest, pain in the arms, back, neck or jaw, shortness of breath, numbness or weakness in one side of the body, difficulty speaking, headache or dizziness during treatment with Sunitinib Teva.
- **You have or have had damage to the small blood vessels, a phenomenon called thrombotic microangiopathy (TMA).** Tell the doctor if you develop fever, tiredness, bruises, bleeding, swelling, confusion, vision loss and convulsions.
- **You have or have had an aneurysm** (distension and weakening of the blood vessel wall) or a tear in the blood vessel wall.
- **You have thyroid problems.** Sunitinib Teva can cause thyroid problems. Tell the doctor if you get tired more easily, usually feel colder than other people or your voice becomes deeper while taking Sunitinib Teva. Thyroid function should be checked before and during treatment with Sunitinib Teva. If your thyroid gland does not produce enough thyroid hormones, you may receive treatment with thyroid hormone replacement.
- **You have or have had pancreatic or gallbladder disorders.** Tell the doctor if you develop any of the following symptoms or signs: pain in the stomach area (upper abdomen), nausea, vomiting and fever. This can be caused by inflammation of the pancreas or gallbladder.
- **You have or have had liver problems.** Tell the doctor if you develop any of the following symptoms or signs of liver problems during treatment with Sunitinib Teva: itching, yellow eyes or yellow skin, dark urine and pain or discomfort in the right upper part of the stomach area. The doctor will perform blood tests to check your liver function before and during treatment with Sunitinib Teva and as clinically needed.
- **You have or have had kidney problems.** The doctor will monitor your kidney function.
- **You are about to undergo or have recently undergone a surgery.** Sunitinib Teva can affect the way wounds heal. If you undergo a surgery, you will usually stop the treatment with Sunitinib Teva. The doctor will decide when to resume taking Sunitinib Teva.
- **You may be advised to undergo a dental examination before starting treatment with Sunitinib Teva.**
  - Tell the doctor and dentist immediately if you have or have had pain in the mouth, teeth and/or jaw, swelling or sores in the mouth, numbness or a sensation of heaviness in the jaw or sensation of a tooth loosening.
  - If you need to undergo an invasive dental treatment or dental surgery, tell the dentist that you are being treated with Sunitinib Teva, especially if you are also taking or have taken intravenous bisphosphonates. Bisphosphonates are medicines used for preventing bone complications which may have been given for another medical condition.
- **You have or have had skin or subcutaneous disorders.** While taking Sunitinib Teva, pyoderma gangrenosum (painful skin ulcers) or necrotising fasciitis (infection of the skin/soft tissues which spreads rapidly and can be life-threatening) can appear. Refer to the doctor immediately if symptoms of infection appear around injured skin, including fever, pain, redness, swelling or drainage of pus or blood. This event is usually reversible after discontinuation of Sunitinib Teva. Severe skin rashes (Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme) have been reported with the use of Sunitinib Teva, appearing first as red target-like spots or round patches often with central blisters on the body. The rash may progress to extensive blisters or peeling of the skin and can be life-threatening. Refer to the doctor immediately if you develop a rash or these symptoms.
- **You have or have had convulsions.** Tell the doctor as soon as possible if you have high blood pressure, headache or vision loss.
- **You have diabetes.** Blood sugar levels should be checked regularly in diabetic patients in order to assess whether the dosage of diabetes medicines needs to be adjusted to minimize the risk of low blood sugar level. Inform the doctor as soon as possible if you experience signs and symptoms of low blood sugar levels (tiredness, palpitations, sweating, hunger and loss of consciousness).

Children and adolescents

Sunitinib Teva is not intended for children under 18 years of age.

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines and food supplements, tell the doctor or the pharmacist. Especially if you are taking:

- Medicines which, in combination with Sunitinib Teva, increase its concentration in the blood:
  Ketoconazole, itraconazole (antifungals), erythromycin, clarithromycin (antibiotics), ritonavir (for treatment of HIV), grapefruit juice.
- Medicines which, in combination with Sunitinib Teva, decrease its concentration in the blood:
  Dexamethasone (a corticosteroid used for treatment of various conditions, such as allergy/respiratory disorders or skin conditions), phenytoin, carbamazepine, phenobarbital (used for treatment of epilepsy and other neurological diseases), rifampin (an antibiotic), the herb Hypericum (St. John's Wort) (used for treatment of depression).
- Warfarin (used for treatment of hypercoagulation) – your blood coagulation indices levels will need to be monitored.
- Cholesterol-lowering agents of the statin family and intravenous bisphosphonates (such as: Fosalan) before or during treatment with Sunitinib Teva.

Use of the medicine and food

The medicine may be taken with or without food. The medicine should be swallowed with some water.

Do not drink grapefruit juice or eat grapefruit during treatment with the medicine. Grapefruit consumption may alter the concentration of the medicine in your body.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you might be pregnant or are planning to become pregnant, contact your doctor for consultation before taking this medicine.

If you might become pregnant, you must use effective contraception during treatment with Sunitinib Teva.

Inform the doctor if you are breastfeeding. Do not breastfeed during treatment with Sunitinib Teva.

Driving and operating machinery

Use of this medicine may impair alertness and cause dizziness and drowsiness; therefore, caution should be exercised when driving a vehicle, operating dangerous machinery, and in any activity that requires alertness.

Important information about some of the ingredients of the medicine

This medicine contains less than 23 mg of sodium per capsule, and is therefore considered sodium-free.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the medicine according to the doctor's instructions.

Check with the doctor or pharmacist if you are uncertain about the dosage and how to use the medicine.

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

It is recommended to take the medicine at the same time every day.

Do not exceed the recommended dose!

Do not chew! Do not open the capsule and scatter its contents! The effect/efficacy of this manner of administration has not been evaluated.

If you took an overdose or if a child swallowed this medicine by mistake, go to the doctor or to a hospital emergency room immediately and take the package of the medicine with you.

If you forgot to take this medicine at the required time, skip that dose and take the next dose on the following day at the regular time. But under no circumstances should you take a double dose!

Follow the treatment as recommended by the doctor.

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor.

Do not take medicines in the dark! Check the label and the dose every time you take the medicine. Wear glasses if you need them.

If you have any other questions regarding use of the medicine, consult the doctor or the pharmacist.

4. SIDE EFFECTS

As with any medicine, using Sunitinib Teva may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.

Refer to a doctor immediately if you experience any of the following serious side effects (see also section 2 under "Special warnings regarding the use of the medicine"):

Cardiac problems. Tell the doctor if you feel excessive fatigue, shortness of breath or if you have swelling of the legs and ankles. These can be symptoms of cardiac problems which can include heart failure and problems in the heart muscle (cardiomyopathy).

Lung or breathing problems. Tell your doctor if you develop cough, chest pain, sudden appearance of shortness of breath or bloody cough. These can be symptoms of a condition called pulmonary embolism, which occurs when blood clots travel to the lungs.

Renal disorders. Tell the doctor if you experience changes in the frequency of urination or lack of urination which can be symptoms of renal failure.

Bleeding. Tell the doctor if you have any of the following symptoms or severe bleeding during treatment with Sunitinib Teva: painful and swollen abdomen; bloody vomit; black sticky stool; blood in the urine; headache or a change in your mental state; bloody cough or bloody sputum from the lungs or airways.

Tumor destruction that leads to intestinal perforation. Tell the doctor if you have severe abdominal pain, fever, nausea, vomiting, blood in the stool, or changes in irritable bowel habits.

Additional side effects:

Very common side effects (may occur in more than 1 out of 10 people):
Diarrhea, constipation, abdominal pain/swelling, nausea, loss of appetite, dizziness, fever, inflammations and/or sores and/or dryness in the mouth, indigestion, vomiting, irritation or pain in the mouth, changes in taste, severe allergic rash, skin discoloration/yellowing of the skin, skin pigmentation, hair discoloration, extreme fatigue, weakness, headache, insomnia, back pain, joint pain, limb pain, cough, decreased thyroid function, decreased level of platelets, red and/or white blood cells, swelling caused by fluids under the skin or around the eyes, nose bleeding, shortness of breath, high blood pressure, rash on the hands and feet, rash, dry skin.

Common side effects (may occur in up to 1 out of 10 people):
Blood clots in blood vessels, decreased blood supply to the cardiac muscle due to constriction or blockage in the coronary arteries, chest pain, decrease in the amount of blood pumped by the heart with each heartbeat, fluid retention, including around the lungs, flu-like feeling, infections, complication of a severe infection (infection in the blood), which may cause tissue damage, organ failure and death, a decrease in blood sugar level – see section 2 under "Special warnings regarding the use of the medicine", depression, hemorrhoids, rectal pain, bleeding gums, difficulty or inability to swallow, pain and/or burning sensation in the tongue, inflammation of the esophagus and mucosal membranes, gastric or intestinal flatulence, weight loss, muscle and bone pain, muscle weakness, muscle tiredness, sudden muscle cramps (spasm), dry nose, nasal congestion, excessive tearing, abnormal sensation in the skin, inflammation and peeling of the skin, skin blisters, itching, acne, dehydration, hot flashes, abnormal urine color, nail discoloration, hair loss, high levels of uric acid in the blood, loss of protein in the urine (may lead to swelling), abnormal blood test results, including liver and pancreatic enzyme levels, abnormal sensation in the limbs, increased/decreased sensitivity, especially to touch, heartburn, chills.

Uncommon side effects (may occur in up to 1 out of 100 people):
A life-threatening infection of the soft tissues, including anogenital areas – see section 2 under "Special warnings regarding the use of the medicine".
Stroke, heart attack due to decreased or interrupted blood supply to the heart, changes in the electrical activity or heart rhythm disorder, fluids around the heart (pericardial effusion), liver failure, abdominal pain due to inflammation of the pancreas (pancreatitis). Tumor destruction that causes intestinal perforation, inflammation (redness and swelling) of the gallbladder (with or without gallstones), abnormal passage between body cavities or the skin. Pain in the mouth, teeth and/or jaw, swelling or sores in the mouth, numbness or a sensation of heaviness in the jaw, or a sensation of a tooth loosening – these may be symptoms of jawbone damage – see section 2 under "Special warnings regarding the use of the medicine".
Overproduction of thyroid hormones, which increase the amount of energy the body uses at rest, impaired wound healing after surgery, increased level of enzyme from the muscles (creatine phosphokinase) in the blood, a severe reaction to allergens, including allergic rhinitis (hay fever), skin rash, itching of the skin, hives, swelling of body parts and breathing difficulties, inflammation of the colon (colitis, ischemic colitis).

Rare side effects (may occur in up to 1 out of 1000 people):
Serious skin and/or mucous membrane reactions (Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme), painful skin ulceration (pyoderma gangrenosum), rhabdomyolysis, which can lead to kidney problems.
Tumor lysis syndrome: metabolic complications which may occur during cancer treatment due to the breakdown of cancer cells. Effects in this group include: nausea, shortness of breath, irregular heart rhythm, muscle cramps, convulsions, tiredness and cloudy urine accompanied by changes in blood test results (high levels of potassium, uric acid and phosphate and low levels of calcium in the blood) which may lead to changes in kidney function and renal failure, hepatitis – inflammation of the liver, abnormal changes in the brain which can cause a collection of symptoms including headaches, confusion, convulsions and loss of vision. Thyroiditis, damage to the small blood vessels, a phenomenon called thrombotic microangiopathy (TMA).

Side effects with unknown incidence (incidence cannot be estimated from existing data):
Distension and weakening of a blood vessel wall or a tear in a blood vessel wall (aneurysm and arterial dissection); lack of energy, confusion, drowsiness, loss of consciousness/coma – these symptoms can be signs of brain toxicity caused by high levels of ammonia in the blood (hyperammonemic encephalopathy).

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects

Side effects may be reported to the Ministry of Health by clicking on the link "Report side effects due to medicinal treatment" found on the Ministry of Health website homepage (www.health.gov.il), which will direct you to the online form for reporting side effects, or by clicking on the following link: https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

- Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.
- Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.
- **The medicine should be stored below 25°C.**
- **Keep in the original package to protect from humidity.**

6. ADDITIONAL INFORMATION

In addition to the active ingredient the medicine also contains:

Mannitol (Parteck Delta M), Povidone K-25, Croscarmellose sodium, Magnesium stearate, Gelatin, Titanium dioxide (E171), Yellow iron oxide (E172), Red iron oxide (E172), Shellac, Black iron Oxide, Propylene Glycol, Strong Ammonia Solution, Potassium Hydroxide.

What does the medicine look like and what are the contents of the package?

Sunitinib Teva 12.5 mg: an opaque capsule with an orange cap and body; the capsule cap is imprinted with "12.5" in black ink.
Sunitinib Teva 25 mg: an opaque capsule with an orange body and a light orange cap; the capsule cap is imprinted with "25" in black ink.
Sunitinib Teva 37.5 mg: an opaque capsule with a yellow cap and body; the capsule cap is imprinted with "37.5" in black ink.
Sunitinib Teva 50 mg: an opaque capsule with a light orange cap and body; the capsule cap is imprinted with "50" in black ink.

The preparation is marketed in a bottle or a blister pack that contains 30 capsules.

Not all package types may be marketed.

Name and address of the license holder and manufacturer:

Teva Israel Ltd.
124 Dvora HaNevi'a St., Tel Aviv 6944020

This leaflet was revised in May 2024.

Registration number of the medicine in the national drug registry of the Ministry of Health:

Sunitinib Teva 12.5 mg – 163-78-35252
Sunitinib Teva 25 mg – 163-79-35253
Sunitinib Teva 37.5 mg – 163-80-35254
Sunitinib Teva 50 mg – 163-81-35255

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