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

Before treatment with Sunitinib Teva, tell the doctor:

- If you are pregnant or planning to become pregnant, breastfeeding or planning to breastfeed.
- If you have had a cerebrovascular accident or cardiac event (such as: a heart attack of any kind, including myocardial infarction, heart failure, bypass surgery, cardiac muscle disease [cardiomyopathy], unstable angina) and/or pulmonary embolism within 12 months prior to starting to use the medicine.
- If you have or have had in the past impaired function of: the liver, the kidney/urinary tract, the pancreas, the heart (including arrhythmias), high blood pressure, problems with blood clotting, electrolyte balance and/or thyroid function, epilepsy, skin or subcutaneous tissue disorders, if you have had or are about to undergo surgery or invasive dental treatment.
- If you are diabetic (blood sugar levels should be monitored during use of Sunitinib Teva to prevent low blood sugar levels).
- If you have or have had in the past damage to small blood vessels, a phenomenon called thrombotic microangiopathy (TMA).
- If you have or have had an aneurysm (distension and weakening of a blood vessel wall) or a tear in a blood vessel wall.

Special warnings regarding the use of the medicine

- If you are sensitive to any type of food or medicine, inform your doctor before starting treatment with this medicine.
- You should avoid becoming pregnant during treatment with the preparation, and use appropriate contraception for that purpose.
- During treatment with this medicine, you should undergo blood tests and tests to check your blood pressure, cardiac function, ECG, renal function, electrolytes, liver enzymes, pancreas and gastrointestinal and thyroid function.
- You should undergo a dental check-up before starting the treatment and consider preventive dental treatments.

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 tablet 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.

This medicine should not be used in children under 18 years of age.

If you took an overdose or if a child swallowed this medicine by mistake, go to the doctor or the emergency room of the hospital 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 <u>every time</u> 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.

Stop using this medicine and refer to a doctor immediately in case of:

- Bleeding in various areas of the body (e.g. nose, anus, genitals, gums, gastrointestinal system) – signs for this include: pain and swelling in the stomach, vomiting blood, bloody stool, blood in the urine, headache or altered mental state, bloody cough or bloody sputum from the lungs or airways.
- Arrhythmias and/or cardiac function disorders: manifest as shortness of breath, fatigue, swelling of the feet and ankles.
- Arterial thromboembolism, cerebrovascular disease, transient ischemic attack, cerebral infarction (stroke).
- Hypersensitivity that manifests as swelling or edema of the face, lips, throat, legs and hands.
- Signs of an epileptic seizure, such as: headache, decreased alertness, altered mental function and/or vision loss.
- Influenza or serious infections, osteonecrosis of the jaw.
- Kidney problems. Changes in the frequency of urination or lack of urination can be symptoms of renal failure.
- Tumor destruction that leads to intestinal perforation. Inform the doctor if you have severe abdominal pain, fever, nausea, vomiting, bloody stool, or changes in irritable bowel habits.

Refer to a doctor immediately in case of:

Pulmonary embolism which manifests as breathing difficulties, rapid breathing, pain or tightness in the chest, coughing blood, cyanosis of the lips and fingertips, collapsing. Rise in blood pressure, changes in the frequency and amount of urine, pain in the arms, back, neck or jaw, weakness or a sensation of numbness in one side of the body, difficulty speaking, symptoms of a decrease in blood sugar level, such as: tiredness, strong heartbeats, sweating, hunger, loss of consciousness.

Appearance of signs of infection due to skin injury, such as: fever, pain, redness, swelling or drainage of blood or pus. This type of infection may be life-threatening.

Symptoms of damage to small blood vessels, such as: fever, tiredness, fatigue, skin bruises, bleeding, swelling, confusion, vision loss or convulsions.

Additional side effects:

Side effects that occur very frequently, with a frequency of more than 1 out of 10 patients:

Diarrhea, constipation, abdominal pain/swelling, nausea, anorexia (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 levels of white and red blood cells and platelets, 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.

Side effects that occur frequently, with a frequency of 1-10 out of 100 patients:

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, decreased blood sugar level – inform the doctor as soon as possible if you experience signs or symptoms of decreased blood sugar level (tiredness, palpitations, sweating, hunger and loss of consciousness), 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/or bone pain, muscle weakness, muscle tiredness, sudden muscle cramps (spasm), nasal dryness or nasal congestion, excessive tearing, skin effects, such as: abnormal sensation in the skin, scaly skin, skin peeling, inflammations, skin blisters, itching, acne, dehydration, hot flashes, abnormal urine color, nail discoloration, hair loss, increase in the level of uric acid in the blood, loss of protein in the urine (may lead to swelling), abnormal blood tests results, including liver and pancreatic enzymes levels, abnormal sensation in the limbs, increased/decreased sensitivity, especially to touch, heartburn, chills.

Side effects that occur infrequently, with a frequency of 1-10 out of 1,000 patients:

A life-threatening infection of the soft tissues, including anogenital areas. Refer to the doctor immediately if signs of infection appear around a skin injury, such as: fever, pain, redness, swelling or drainage of blood or pus.

Stroke, heart attack due to decreased or interrupted blood supply to the heart, changes/disturbances in heart rhythm, fluids around the heart (pericardial effusion), liver failure, abdominal pain due to inflammation of the pancreas (pancreatitis).

Tumor destruction that causes intestinal perforation, gallbladder inflammation (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 loosening of a tooth – these are symptoms of jawbone damage. Refer immediately to a doctor and to a dentist.

Overproduction of thyroid hormones, which increase the amount of energy the body uses at rest, impaired wound healing after surgery, increased blood level of enzymes from muscles (creatine phosphokinase), 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).

Side effects that occur rarely, with a frequency of 1-10 out of 10,000 patients:

Serious skin and/or mucous membranes 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. This includes: nausea, shortness of breath, irregular heart rhythm, muscle cramps, convulsions, tiredness and cloudy urine, accompanied by changes in blood tests results (elevated potassium, uric acid and phosphate levels and decreased calcium levels in the blood), which may lead to changes in kidney function and renal failure, hepatitis – inflammation of the liver, changes in the brain which manifest as symptoms such as: headaches, confusion, convulsions, loss of vision. Thyroiditis, damage to 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).

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 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 marketing authorization holder and manufacturer:

TEVA ISRAEL LTD

124 Dvora HaNevi'a St., Tel Aviv 6944020

This leaflet was revised in April 2021 in accordance with the Ministry of Health guidelines.

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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