PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

Sunitinib Taro 12.5 mg
Sunitinib Taro 25 mg
Sunitinib Taro 37.5 mg
Sunitinib Taro 50 mg
Hard capsules

Active ingredient
Sunitinib 12.5 mg, 25 mg, 37.5 mg, 50 mg

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

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them even if it seems to you that their illness is similar to yours.

This medicine is intended for adults above the age of 18.

1. WHAT IS THE MEDICINE INTENDED FOR?

- For treatment of gastrointestinal stromal tumor (GIST) after disease progression on or intolerance to imatinib mesylate.
- For treatment of advanced renal cell carcinoma (aRCC).
- For treatment of differentiated pancreatic neuroendocrine tumors (pNET), that have progressed or cannot be removed with surgery.

Therapeutic group:

Targeted tyrosine kinase receptor 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 in this medicine (see section 6).

Special warnings about using this medicine

Before treatment with Sunitinib Taro, tell the doctor if:

- You are pregnant or planning to become pregnant, breastfeeding or planning to breastfeed.
- You have had a cerebral or cardiac event (e.g., any sort of heart attack, including myocardial infarction, heart failure, bypass surgery, heart muscle disease

(cardiomyopathy), unstable angina pectoris) and/or pulmonary embolism during the 12 months before commencing treatment with the medicine.

- You suffer, or have suffered in the past, from impaired function of: the liver, the kidney/urinary tract, the pancreas, the heart (including arrhythmias), from high blood pressure, blood coagulation problems, electrolyte balance and/or thyroid function, from epilepsy, skin or subcutaneous problems. If you have undergone, or are due to undergo, surgery or invasive dental treatment.
- You have diabetes (monitor blood sugar levels during the treatment with Sunitinib Taro to prevent low blood sugar levels).
- You suffer, or have suffered in the past, from damage in the small blood vessels, a condition called TMA (thrombotic microangiopathy).
- You have or have previously had an aneurysm (enlargement and weakening of a blood vessel wall) or a tear in a blood vessel wall.

Additional warnings

Avoid becoming pregnant during the treatment with the preparation and take appropriate contraceptive measures for this purpose.

During the treatment with this medicine, you should undergo blood tests, monitoring of blood pressure, heart function, ECG, kidney function, electrolytes, liver, pancreas and digestive system enzymes and thyroid gland function.

Have a dental examination before treatment and consider preventive dental treatments.

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:

Medicines which in combination with Sunitinib Taro increase its blood concentration:

ketoconazole, itraconazole (antifungals), erythromycin, clarithromycin (antibiotics), ritonavir (used to treat the AIDS virus), grapefruit juice.

Medicines which in combination with Sunitinib Taro lower its blood concentration:

dexamethasone (a corticosteroid used to treat various conditions such as allergies/breathing disorders or skin diseases), phenytoin, carbamazepine, phenobarbital (used to treat epilepsy and other neurological diseases), rifampin (an antibiotic), the herb Hypericum (St. John's Wort) (used to treat depression).

warfarin (to treat hypercoagulation) – blood coagulation indices values must be under medical surveillance.

medicines from the statins group to lower cholesterol and medicines from the bisphosphonates group (e.g., Fosalan) given intravenously before or during treatment with Sunitinib Taro.

Using this medicine and food

The medicine can be taken with or without food. Swallow the medicine with a small amount of water. Do not drink grapefruit juice or eat grapefruits during treatment with the medicine. Consumption of grapefruits may change the medicine's concentration in your body.

Pregnancy and breastfeeding

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.

If you might get pregnant, you should use effective methods of contraception during treatment with Sunitinib Taro.

If you are breastfeeding, tell your doctor. You should not breastfeed during treatment with Sunitinib Taro.

Driving and using machines

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

Important information about some of this medicine's ingredients

This medicine contains less than 1 mmol (23 mg) sodium per capsule, that is to say essentially 'sodium-free'.

3. HOW TO USE THIS MEDICINE?

Always use this preparation 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.

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

Do not exceed the recommended dose!

There is no information about opening capsules and releasing their content.

Do not use this medicine in children under the age of 18.

If you have taken an overdose or if a child has accidentally swallowed the 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 at the scheduled time, skip the dose and take the next dose the following day at the scheduled time.

Never take a double dose!

Adhere to the treatment as recommended by your doctor.

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

Do not take medicines in the dark! Check the label and dose each time 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 Sunitinib Taro may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Discontinue use and refer to the doctor immediately in case of:

Bleeding in different areas of the body (e.g., from the nose, anus, genitals, gums, digestive system) - the signs of which are: painful and swollen stomach, vomiting blood, bloody stools, blood in the urine, headache or change in mental status, coughing up blood or bloody

sputum from the lungs or airways. Disturbances in heart rhythm and/or function: manifested by shortness of breath, excessive tiredness, swelling of the feet and the ankles.

Arterial embolism (thromboembolism), cerebrovascular disease, transient ischemic attack, cerebral infarction. Hypersensitivity manifested by swelling or edema of the face, lips, throat, legs and hands. Signs of an epileptic seizure e.g., headache, decreased alertness, altered mental functioning and/or loss of sight. Flu or severe infections, necrosis of the jaw bone.

Kidney disorders. Changes in frequency or absence of urination can be symptoms of kidney failure. Tumor destruction leading to a hole in the intestine. Inform the doctor if you have severe abdominal pain, fever, nausea, vomiting, blood in your stool, or changes in irritable bowel patterns.

Refer to the doctor immediately in case of:

Pulmonary embolism, manifested by breathing difficulties, rapid breathing, pain or tightness in the chest, bloody cough, bluish discoloration of the lips and fingertips, collapse. A rise in blood pressure, changes in urinary frequency and amount of urine, pain in the arms, back, neck or jaw, weakness or tingling sensation on one side of the body, difficulty in speaking, symptoms of decreased blood sugar level such as: fatigue, intense palpitations, sweating, hunger, loss of consciousness. Appearance of signs of infection following injury to the skin, such as: fever, pain, redness, swelling or drainage of blood or pus. Such an infection may be life threatening. Symptoms of damage in the small blood vessels, such as: fever, tiredness, exhaustion, bruises on the skin, bleeding, swelling, confusion, loss of vision or seizures.

Additional side effects

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

Diarrhea, constipation, abdominal pain/swelling, nausea, anorexia (loss of appetite), dizziness, fever, inflammation and/or sores and/or dryness of the mouth, digestive disturbances, vomiting, mouth irritation or pain, taste changes, severe allergic rash, skin discoloration/yellowing of the skin, pigmentation of the skin, hair color change, extreme fatigue, weakness, headache, insomnia, back pains, joint pains, limb pains, cough, decreased thyroid activity, decrease in the white, red blood cells and platelet count, swelling caused by fluid under the skin or around the eyes, nose bleed, shortness of breath, high blood pressure, rash on the palms of the hands and soles of the feet, rash, dryness of skin.

Side effects that occur frequently, at a frequency of 1-10 in 100 patients:

Blood clots in the blood vessels, deficiency in blood supply to the heart muscle due to narrowing or obstruction of the coronary arteries, chest pain, reduction in the amount of blood pumped by the heart on each beat, fluid retention including around the lungs, flu-like sick feeling, infections, complication of a severe infection (infection that is present in the blood) that can lead to tissue damage, organ failure and death. Decreased blood sugar level - notify the doctor as soon as possible if you experience signs or symptoms of decreased blood sugar level (fatigue, palpitations, sweating, hunger and loss of consciousness), depression, hemorrhoids, pain in the rectum, gingival bleeding, difficulty or inability to swallow, pains and/or burning sensation on the tongue, inflammation of the esophagus and mucosa, gas in the stomach or intestine, weight loss, muscle and/or bone pains, muscular weakness, muscular fatigue, sudden muscle contraction (spasm), nasal dryness or congestion, excessive tearing, skin effects such as: abnormal sensation in the skin, scaling of the skin, skin peeling, inflammations, blisters on the skin, itching, acne, dehydration, hot flushes, abnormally colored urine, nail discoloration, hair loss, increased uric acid level in the blood, loss of protein in the urine (can lead to swelling), abnormal blood test results, including liver and pancreatic enzyme levels, abnormal sensation in the extremities, increased/decreased sensitivity, particularly to touch, heartburn, chills.

Side effects that occur infrequently, at a frequency of 1-10 in 1,000 patients:

Life-threatening infection of the soft tissue including the ano-genital regions. Refer to a doctor immediately if signs of infection occur 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, fluid around the heart (pericardial effusion), liver failure, abdominal pains due to inflammation of the pancreas. Tumor destruction leading to perforation of the intestine, inflammation of the gallbladder (with or without gallstones), abnormal passage from one body cavity to another body cavity or the skin. Pain in the mouth, teeth and/or jaw, swelling or sores inside the mouth, numbness or a feeling of heaviness in the jaw, or a feeling of loosening of a tooth. These are symptoms of bone damage in the jaw. Contact the doctor and dentist immediately. Overproduction of thyroid hormones, which increase the amount of energy the body uses at rest, problems with wound healing after surgery, increased blood level of enzyme (creatine phosphokinase) from muscle, severe reaction to allergens including allergic rhinitis (hay fever), skin rash, itchy skin, hives, swelling of body parts and trouble breathing. Inflammation of the colon (colitis, ischemic colitis).

Side effects that occur rarely, at a frequency of 1-10 in 10,000 patients:

Severe reactions of the skin and/or mucous membranes (Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme), painful skin ulceration (pyoderma gangrenosum), muscle breakdown (rhabdomyolysis), which can lead to kidney problems.

Tumor lysis syndrome: metabolic complications that can occur during treatment of cancer, due to breakdown of cancerous cells. Effects that are included in this group are: nausea, shortness of breath, irregular heart rate, muscle cramps, convulsions, tiredness and cloudy urine associated with changes in blood test results (increased levels of potassium, uric acid and phosphate and decreased calcium level in the blood) that can lead to changes in kidney function and renal failure, hepatitis - inflammation of the liver, cerebral changes manifested by symptoms such as: headaches, confusion, seizures, loss of sight. Inflammation of the thyroid gland, damage in the small blood vessels, an effect called TMA (thrombotic microangiopathy).

Side effects whose frequency is unknown (cannot be estimated from the available data):

An enlargement and weakening of a blood vessel wall or a tear in a blood vessel wall (aneurysm and artery dissection).

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.

Side effects can be reported to the Ministry of Health by clicking on the link “Report Side Effects of Drug Treatment” found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the 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 unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.

Storage conditions

- Store the medicine below 25°C.

6. FURTHER INFORMATION

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

Sunitinib 12.5 mg:

Cellulose, microcrystalline, mannitol, croscarmellose sodium, povidone, magnesium stearate, hard gelatin capsule shell: red iron oxide, titanium dioxide, gelatin, and printing white ink (containing: shellac, titanium oxide, propylene glycol).

Sunitinib 25 mg:

Cellulose, microcrystalline, mannitol, croscarmellose sodium, povidone, magnesium stearate, hard gelatin capsule shell: black iron oxide, red iron oxide, yellow iron oxide, titanium dioxide, gelatin, and printing white ink (containing: shellac, titanium oxide, propylene glycol).

Sunitinib 37.5 mg:

Cellulose, microcrystalline, mannitol, croscarmellose sodium, povidone, magnesium stearate, hard gelatin capsule shell: yellow iron oxide, titanium dioxide, gelatin, and printing black ink (containing: shellac, black iron oxide, propylene glycol, ammonium hydroxide).

Sunitinib 50 mg:

Cellulose, microcrystalline, mannitol, croscarmellose sodium, povidone, magnesium stearate, hard gelatin capsule shell: black iron oxide, red iron oxide, yellow iron oxide, titanium dioxide, gelatin, and printing white ink (containing: shellac, titanium oxide, propylene glycol).

What the medicine looks like and contents of the pack:

Sunitinib Taro 12.5 mg: an orange capsule with “12.5 mg” imprinted in white ink and that contains yellow-orange granules.

Sunitinib Taro 25 mg: a capsule, the cap of which is caramel-colored and the body of which is orange and imprinted with “25 mg” in white ink and that contains yellow-orange granules.

Sunitinib Taro 37.5 mg: a yellow capsule with "37.5 mg" imprinted in black ink and that contains yellow-orange granules.

Sunitinib Taro 50 mg: a caramel-colored capsule with “50 mg” imprinted in white ink, and that contains yellow-orange granules.

The preparation is marketed in blister packs containing 28 capsules.

Name of importer, registration holder’s name and address: Taro International Ltd., 14 Hakitor St., Haifa Bay 2624761

Revised in December 2021 according to MOH guidelines.

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

Sunitinib Taro 12.5 mg: 167-94-36017-00

Sunitinib Taro 25 mg: 167-95-36030-00

Sunitinib Taro 37.5 mg: 167-96-36031-00

Sunitinib Taro 50 mg: 167-97-36032-00