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

This medicine is dispensed with a doctor's prescription only

Imatinib Taro 100 mg Film-coated tablets	**Imatinib Taro 400 mg** Film-coated tablets

Composition:

Each film-coated tablet contains: imatinib (as mesylate) 100 mg	Each film-coated tablet contains: imatinib (as mesylate) 400 mg

Inactive ingredients and allergens: see section 2 under 'Important information about some of this medicine's ingredients', and section 6 'Additional information'.

Read the entire leaflet carefully before you start using this medicine. Keep this leaflet. 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?

Imatinib Taro is indicated for the treatment of adults and children 3 years of age and above with Philadelphia chromosome-positive chronic myeloid leukemia (CML) in the chronic phase, accelerated phase or blast crisis phase.
Imatinib Taro is indicated for the treatment of adults with Kit-positive (CD117) metastatic malignant and/or unresectable gastrointestinal stromal tumors (GIST).
Imatinib Taro is indicated as an adjuvant therapy in adults after complete tumor resection of Kit-positive (CD117) gastrointestinal stromal tumor (GIST).
Imatinib Taro is indicated for the treatment of adults with newly diagnosed Philadelphia chromosome-positive acute lymphoblastic leukemia (ALL), in combination with chemotherapy.
Imatinib Taro is indicated for the treatment of adults with relapsed or refractory Philadelphia chromosome-positive acute lymphoblastic leukemia (ALL) as monotherapy.
Imatinib Taro is indicated for the treatment of adults with unresectable dermatofibrosarcoma protuberans (DFSP) and adults with recurrent and/or metastatic DFSP who are not eligible for surgery.
Imatinib Taro is indicated for the treatment of adults with myeloproliferative or myelodysplastic diseases (MDS/MPD) associated with genetic changes in the PDGF receptor.
Imatinib Taro is indicated for the treatment of adults with hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL), with or without a mutation in FIP1L1-PDGFRα fusion kinase.
Imatinib Taro is indicated for the treatment of adults with aggressive systemic mastocytosis (ASM) without the D816V c-kit mutation.

Therapeutic group: antineoplastic

Imatinib Taro is a medicine containing the active ingredient of imatinib. This medicine works by inhibiting the production of abnormal cells in the diseases listed below, some of which are certain types of cancer.

Chronic myeloid leukemia (CML) is a cancer of white blood cells. White blood cells usually help the body fight infection. In CML-type leukemia, certain abnormal white blood cells (called myeloid cells) start to grow uncontrollably.
GIST are malignant tumors of the stomach and intestines. They develop due to uncontrolled growth of the cells that support tissues of these organs.
Philadelphia chromosome-positive acute lymphoblastic leukemia (ALL) is a cancer of the white blood cells. The white blood cells usually help the body fight infection. In ALL-type leukemia, certain abnormal white blood cells (called lymphoblasts) start to grow uncontrollably. Imatinib Taro inhibits growth of these cells.
Dermatofibrosarcoma protuberans (DFSP) is a malignant tumor of the tissue beneath the skin in which some cells start growing uncontrollably. Imatinib Taro inhibits growth of these cells.
Myeloproliferative or myelodysplastic diseases (MDS/MPD) are a group of blood diseases in which certain blood cells start to grow uncontrollably. Imatinib Taro inhibits growth of these cells in a certain subtype of these diseases.
Hypereosinophilic syndrome or chronic eosinophilic leukemia (HES/CEL) are a group of blood diseases in which certain blood cells (called eosinophils) start to grow uncontrollably. Imatinib Taro inhibits growth of these cells in a certain subtype of these diseases.
Aggressive systemic mastocytosis (ASM) are malignant tumors which cause the body to produce too many blood cells called mast cells.

2. Before using this medicine

Do not use this medicine if:

You are sensitive (allergic) to imatinib or to any of the other ingredients in this medicine (see section 6). If this applies to you, **tell your doctor without taking Imatinib Taro.**
If you think you may be allergic but are uncertain, consult with your doctor.

Special warnings about using this medicine
Before using Imatinib Taro, tell your doctor if:

- You have or have ever had a liver, kidney or heart problem.
- You are taking the medicine levothyroxine due to removal your thyroid.
- You have ever had, or might now have, a viral hepatitis B infection. Imatinib Taro could cause viral hepatitis B to become active again, which can lead to death in certain cases. Patients will be carefully checked by their doctor to detect signs of this infection before starting treatment.

If any of these apply to you, **tell your doctor before taking Imatinib Taro.**

If you experience signs of bruising, bleeding, fever, tiredness and confusion during the course of treatment with Imatinib Taro, contact your doctor. This may be a sign of damage to blood vessels called thrombotic microangiopathy (TMA).

You may be more sensitive to the sun during treatment with Imatinib Taro. It is important to cover sun-exposed areas of skin and use sunscreen with a high sun protection factor (high SPF). These precautions are also relevant for children.

Imatinib Taro treatment will only be prescribed by a doctor with experience with medicines for treating blood cancer or solid tumors.

Follow your doctor's instructions carefully, even if they differ from the general information appearing in this leaflet.

During treatment with Imatinib Taro, inform your doctor immediately if you gain weight quickly. Imatinib Taro may cause your body to retain water (severe fluid retention).

Children and adolescents (below 18 years of age)
Imatinib Taro is given to children from the age of 3 years and above with CML. For the other indications, Imatinib Taro is not indicated for children and adolescents below 18 years of age. In some children and adolescents taking Imatinib Taro, growth may be slower than normal. The doctor will monitor the growth at regular visits.

Tests and follow up
Your doctor will monitor your condition regularly to check whether the desired effect of Imatinib Taro treatment is being achieved. You will be asked to have blood tests taken regularly to see if you are tolerating Imatinib Taro (e.g., blood cells, liver and kidney functions, thyroid function). You will be also be weighed regularly during the course of treatment with Imatinib Taro.

Drug interactions
If you are taking or have recently taken other medicines, including nonprescription medications (such as paracetamol) and dietary supplements (such as St. John's Wort), tell your doctor or pharmacist. Some medicines can interfere with the effect of Imatinib Taro when taken together. They may increase or decrease the effect of Imatinib Taro, lead to worsening of side effects or make Imatinib Taro less effective. Imatinib Taro may do the same to some other medicines.

In particular, tell your doctor if you are taking:

Medicines which may increase blood Imatinib Taro levels:
Some medicines used to treat AIDS (HIV) such as indinavir, lopinavir/ritonavir, ritonavir, saquinavir or nelfinavir;
Some medicines used to treat viral hepatitis C such as telaprevir or boceprevir;
Some medicines used to treat fungal infections such as ketoconazole, itraconazole, posaconazole, voriconazole;
Some medicines used to treat bacterial infections such as erythromycin, clarithromycin or telithromycin.

Exercise caution if you are taking a medicine which may increase blood Imatinib Taro levels.

Medicines which may lower blood Imatinib Taro levels:
Dexamethasone, an anti-inflammatory steroidal medicine;
Some medicines used to treat epilepsy such as phenytoin, carbamazepine, oxcarbazepine, phenobarbital, fosphenytoin or primidone; rifampicin, a medicine for treatment of tuberculosis;
Hypericum perforatum (also known as St. John's Wort) – an herbal product to treat depression and other conditions.

Use of the above medicines should be avoided during the course of treatment with Imatinib Taro. If you are taking any of the medicines mentioned above, your doctor

may prescribe alternative medicines for you.

Medicines whose blood levels may increase upon use of Imatinib Taro:
Cyclosporine, an immunosuppressant medicine;
Warfarin, a medicine to treat blood coagulation disorders (such as blood clots and thrombosis) or other medicines for treatment blood coagulation disorders;
Tacrolimus, sirolimus – medicines to prevent rejection of a transplanted organ in patients who underwent organ transplantation;
Fentanyl, alfentanil - medicines to treat pain;
Terfenadine – to treat allergy;
Bortezomib, docetaxel – medicines to treat cancer;
Quinidine;
Some medicines from the statin family, which treat high cholesterol level such as simvastatin;
Some medicines to treat mental disorders such as benzodiazepines or pimozide;
Some medicines to treat hypertension or heart disorders such as calcium channel blockers or metoprolol;
Ergotamine, diergotamine to treat migraine;
Paracetamol.

Medicines whose blood levels may decrease following use of Imatinib Taro:
Levothyroxine – a medicine given following removal of the thyroid.

In addition, inform your doctor **if you are taking Imatinib Taro** and have been prescribed a new medicine, including nonprescription medicines, that you have not taken previously during Imatinib Taro treatment.

Using this medicine and food
Take Imatinib Taro with a meal to protect your stomach.

Pregnancy, breast-feeding and fertility
- If you are pregnant or breast-feeding, think you may be pregnant or are planning a pregnancy, consult your doctor before using this medicine. Imatinib Taro is not recommended for use during pregnancy unless clearly necessary, as it may harm your baby. Your doctor will discuss the risks associated with taking Imatinib Taro during pregnancy with you .
- Women of child-bearing age must use effective contraception during the course of treatment with Imatinib Taro and for 15 days after completing the treatment.
- Do not breast-feed during treatment with Imatinib Taro and for 15 days after completing the treatment, as it may harm your baby.
- Patients concerned about their fertility during the course of treatment with Imatinib Taro should consult their doctor.

Driving and using machines
If you feel dizzy or drowsy, or if you have blurred vision while using Imatinib Taro, do not drive a vehicle or operate tools or machines until you feel well.
Regarding children, caution them against riding a bicycle or playing near roads and the like.

Important information about some of this medicine's ingredients
Imatinib Taro contains Sunset Yellow FCF which may cause allergic reactions.

3. How to use this medicine?

The doctor has prescribed Imatinib Taro for you because you suffer from a serious illness. Imatinib Taro may help you fight this disease. Always use this medicine according to your doctor's instructions. It is important that you do so for as long as instructed by your doctor. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine. Only your doctor will determine your dose and how you should take this medicine.

The recommended dosage is usually:

Use in adults
Your doctor will tell you exactly how many tablets of Imatinib Taro to take.

If you are being treated for chronic myeloid leukemia (CML):
Depending on your condition, the recommended dosage is either 400 mg or 600 mg to be taken **once** a day.

If you are being treated for gastrointestinal stromal tumors (GIST):
The recommended dosage is 400 mg to be taken **once** a day.

For treatment of CML and GIST, your doctor may prescribe a higher or lower dosage depending on how you respond to the treatment. If your doctor decides on a daily dosage of 800 mg, take 400 mg in the morning and 400 mg in the evening.

If you are being treated for Ph-positive acute lymphoblastic leukemia (ALL):
The recommended dosage is 600 mg, to be taken **once** a day.

If you are being treated for myeloproliferative or myelodysplastic diseases (MPD/MDS):
The recommended dosage is 400 mg, to be taken **once** a day.

If you are being treated for hypereosinophilic syndrome/chronic eosinophilic leukemia (HES/CEL):
The recommended dosage is 400 mg, to be taken **once** a day.
In certain cases, the doctor may recommend a starting dosage of 100 mg **once** a day, and, if necessary, the doctor will consider increasing the dosage to 400 mg **once** a day, depending on your response to treatment.

If you are being treated for dermatofibrosarcoma protuberans (DFSP):
The recommended dosage is 800 mg per day, to be taken as 400 mg in the morning and 400 mg in the evening.

If you are being treated for aggressive systemic mastocytosis (ASM):
The recommended dosage is 400 mg **once** per day. In certain cases, the doctor may recommend a starting dosage of 100 mg **once** a day, and, if necessary, the doctor will consider increasing the dosage to 400 mg **once** a day, depending on your response to treatment.

A 400 mg dosage can be taken either as one tablet of 400 mg or four tablets of 100 mg.
A 600 mg dosage is to be taken as one tablet of 400 mg plus two tablets of 100 mg.

The dosage determined by the doctor may change, depending on your response to treatment.

Use in children and adolescents
The doctor will instruct you how many tablets of Imatinib Taro to give to your child. The dosage of Imatinib Taro given will depend on your child's condition, body weight and height. For patients with CML, the maximum dosage for children should not exceed 600 mg. The treatment can be given to your child either as a once-daily dose or alternatively, the daily dose can be split into two administrations (half in the morning and half in the evening).

Do not exceed the recommended dose.

Treatment duration
Take Imatinib Taro every day, until your doctor instructs you to stop.

Method of administration
- **Take Imatinib Taro with a meal.** This will help protect you from stomach problems while taking Imatinib Taro.
- **Swallow the tablets whole with a large glass of water.** If necessary, the tablets may be split at the score line.

If you are unable to swallow the tablets, you can dissolve them in a glass of water or apple juice in the following manner:
- Use approximately 50 ml for each 100 mg tablet or 200 ml for each 400 mg tablet.
- Stir with a spoon until the tablet(s) is/are completely dissolved.
- Once the tablet(s) dissolve/s, drink the entire content of the glass immediately. Traces of the dissolved tablet(s) may be left in the glass.

If you have accidentally taken a higher dose
If you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you. You may need medical supervision.

If you forget to take the medicine
- If you forgot to take this medicine at the designated time, take it as soon as you remember. However, if it is almost time to take the next dose, do not take the forgotten dose.
- Then continue taking the medicine according to the normal schedule.
- Do not take a double dose to compensate for the forgotten 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.
If you are unable to take the medicine as prescribed by the doctor or if you feel you no longer need it, consult the doctor immediately.

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 or pharmacist.

4. Side effects

Like with all medicines, using Imatinib 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. Side effects are usually mild to moderate.

Some side effects may be serious.
Refer to a doctor immediately if you experience any of the side effects listed below:

Very common (affect more than 1 in 10 users) or common (affect 1-10 in 100 users) side effects:

- Rapid weight gain. Imatinib Taro may cause your body to retain water (severe fluid retention).
- Signs of infection such as fever, severe chills, sore throat or mouth ulcers. Imatinib Taro may reduce the number of white blood cells, so you might suffer infections more easily.
- Unexpected bleeding or bruising (when you have not been injured).

Uncommon (affect 1-10 in 1,000 users) or rare (affect 1-10 in 10,000 users) side effects:

- Chest pain, irregular heart rhythm (signs of heart disorders).
- Cough, difficulty breathing or pain when breathing (signs of lung disorders).
- Lightheadedness, dizziness or fainting (signs of low blood pressure).
- Nausea with loss of appetite, dark-colored urine, yellowing of the eyes or skin (signs of liver disorders).
- Rash, red skin with blisters on the lips, eyes, skin or mouth, peeling skin, fever, raised red or purple skin patches, itching, burning sensation, pustular rash (signs of a skin disorder).
- Severe abdominal pain, blood in vomit, black or bloody stools (signs of gastrointestinal disorders).
- Blood in the urine.
- Severely decreased urine output, feeling thirsty (signs of kidney disorders).
- Nausea with diarrhea and vomiting, abdominal pain or fever (signs of bowel function disorders).
- Severe headache, weakness or paralysis of limbs or face, difficulty speaking, sudden loss of consciousness (signs of nervous system disorder such as bleeding or swelling in the skull/brain).
- Pale skin, tiredness, breathlessness and dark urine (signs of low levels of red blood cells).
- Eye pain or deterioration in vision, bleeding in the eyes.
- Pain in bones or joints (signs of osteonecrosis).
- Blisters on skin or mucous membranes (signs of pemphigus).
- Numbness or coldness in toes and fingers (signs of Raynaud’s syndrome).
- Sudden swelling and redness of the skin (signs of a skin infection called cellulitis).
- Decreased hearing.
- Muscle weakness and muscle spasms with an abnormal heart rhythm (signs of changes in the level of blood potassium).
- Bruising.
- Stomach pain with nausea.

- Muscle spasms with fever, red-brown urine, muscle pain or weakness (signs of muscle disorders).
- Pelvic pain occasionally accompanied by nausea and vomiting, with unexpected vaginal bleeding, feeling dizzy or fainting due to low blood pressure (signs of an ovary or uterus disorder).
- Nausea, shortness of breath, irregular heartbeat, cloudy urine, tiredness and/or joint discomfort accompanied by abnormal laboratory test values (e.g., high potassium, uric acid and calcium levels and low phosphorous levels in the blood).
- Blood clots in small blood vessels (thrombotic microangiopathy).

Side effects of unknown frequency (the frequency of these effects has not been established yet):

- Combination of a severe and widespread rash, nausea, fever, high levels of certain white blood cells or yellow skin or eyes (signs of jaundice) with breathlessness, chest pain/discomfort, severely decreased urine output and feeling of thirst (signs of a treatment-related allergic reaction).
- Chronic renal failure.
- Recurrence (reactivation) of viral hepatitis B infection if you have had viral hepatitis in the past (a liver infection).

If you experience any of these effects, **refer to your doctor immediately.**

Additional side effects:
Refer to a doctor if any of the side effects listed below affect you severely:

Very common side effects (affect more than 1 in 10 users):
headache or feeling tired; nausea, vomiting, diarrhea or indigestion, abdominal pain; rash; muscle cramps, muscle, bone or joint pain during treatment with Imatinib Taro or after discontinuing treatment with Imatinib Taro; swelling e.g., around the ankles or puffy eyes; weight gain; anemia (reduced red blood cells).

Common side effects (affect 1-10 in 100 users):
anorexia, weight loss or a disturbed sense of taste; feeling dizzy or weak; sleeping difficulties (insomnia); discharge from the eye with itching, redness and swelling (conjunctivitis), watery eyes or blurred vision, swollen eyelids; nosebleeds; pain or swelling in the abdomen, flatulence, heartburn or constipation; itching; unusual hair loss or thinning; numbness of the hands or feet (paresthesia); mouth ulcers; pain with swelling of the joints; dry mouth, dry skin or dry eyes; decreased or increased skin sensitivity; hot flashes, chills or night sweats; erythema; shortness of breath, cough; increased liver enzymes.

Uncommon side effects (affect 1-10 in 1,000 users):
painful red lumps on the skin, skin pain, skin reddening (inflammation of fatty tissue under the skin);
cough, runny or stuffy nose, feeling of heaviness or pain on pressing the area above the eyes or on the sides of the nose, nasal congestion, blocked nose, sneezing, sore throat, with or without headache (signs of upper respiratory tract infection);
severe headache felt as a throbbing pain or pulsing sensation, usually on one side of the head and sometimes accompanied by nausea, vomiting and sensitivity to light or sound (signs of migraine); flu-like symptoms; pain or burning sensation while passing urine, increased body temperature, pain in groin or pelvic area, red- or brown-colored or cloudy urine (signs of urinary tract infection); pain and swelling of the joints (signs

of arthralgia); a constant feeling of sadness and loss of interest, which stops you from carrying out your normal activities (signs of depression); apprehension and worry along with physical symptoms such as pounding heart, sweating, trembling, dry mouth (signs of anxiety); sleepiness, drowsiness, excessive sleep; trembling/shaky movements (tremor); memory disorder; overwhelming urge to move the legs (restless leg syndrome); hearing noises (ringing, humming) in the ears that have no external source (tinnitus); hypertension, hematomas, burping, inflammation of the lips, difficulty swallowing, increased sweating, skin discoloration, brittle nails, red bumps or white-headed pimples around the roots of the hair, possibly with pain, itching or burning sensation (signs of inflammation of the hair follicles called folliculitis); skin rash with flaking or peeling (inflammation of the skin – dermatitis);
breast enlargement in men and women; dull pain or feeling of heaviness in the testicles or lower abdomen, pain during urination, sexual intercourse or ejaculation, blood in urine (signs of edema of the testicles), inability to get or keep an erection (erectile dysfunction); heavy or irregular menstrual period; difficulty achieving/maintaining sexual arousal, decreased sexual desire; nipple pain, generally feeling unwell (malaise), viral infection such as cold sore (herpes);
lower back pain resulting from kidney disorder, increased frequency of passing urine, increased appetite, pain or burning sensation in upper abdomen or chest (heartburn), nausea, vomiting, acid reflux, feeling of fullness and bloating, black-colored stools (signs of stomach ulcer); joint and muscle stiffness; abnormal laboratory test results; eye irritation, eye pain or redness, swelling/itching of the eyelids; excessive heartbeats; peripheral coldness; thickened red patches around the elbows and knees (psoriasis); darkening of the skin; chest pain (angina pectoris); swollen lymph nodes.

Rare side effects (affect 1-10 in 10,000 users):
confusion, nail discoloration, fungal infection, cardiac arrest, seizures, glaucoma, cataract, arthritis.

Side effects of unknown frequency (the frequency of these effects has not been established yet):
reddening and/or swelling of palms of the hands and soles of the feet, which may be accompanied by a tingling sensation and burning pain; skin lesions that are painful and/or covered with blisters; slowed growth in children and adolescents.

Side effects in patients with aggressive systemic mastocytosis:
All patients with aggressive systemic mastocytosis (ASM) experienced at least one side effect at some point. Side effects that were reported at the highest frequency were diarrhea, nausea, ascites, muscle cramps, shortness of breath, tiredness, peripheral edema, anemia, itch, rash and lower respiratory tract inflammation.

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 your 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. 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 below 25˚C. Protect from moisture.

Do not throw away the medicine via wastewater or household waste. Ask the pharmacist how to throw away this medicine (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:

Silicified microcrystalline cellulose, crospovidone, Opadry Yellow (HPMC 2910, titanium dioxide, macrogol 400, iron oxide yellow, sunset yellow FCF aluminum lake, iron oxide red), mannitol, copovidone, magnesium stearate, polyethylene glycol.

What the medicine looks like and contents of the pack:

Imatinib Taro 100 mg – round, yellow, biconvex film-coated tablets. The tablets have '472' printed on one side and a score line on the other side.

Imatinib Taro 400 mg – oval, yellow, biconvex film-coated tablets. The tablets have '475' printed on one side and a score line on the other side.

Imatinib Taro 100 mg is available in packs of 10, 20, 30, 60 tablets packed in a blister tray and in a bottle of 90 tablets.

Imatinib Taro 400 mg is available in packs of 10, 20, 30, 60 tablets packed in a blister tray and a bottle of 30 tablets.

Not all pack sizes may be marketed.

Registration holder’s name and address:

Taro International, 14 Hakitor St., Haifa Bay 2624761.

Manufacturer's name and address:

Sun Pharmaceutical Industries Ltd, Halol Baroda Highway, Halol – 389 350 Gujarat, India.

Revised in November 2022 according to MOH guidelines.

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

Imatinib Taro 100 mg film-coated tablets: 166-54-35760-00

Imatinib Taro 400 mg film-coated tablets: 166-55-35761-00