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

This medicine is dispensed with a doctor's prescription only

Imatinib Taro 100 mg	**Imatinib Taro 400 mg**
Film-coated tablets	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 aged 3 years and older 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 newly diagnosed Philadelphia chromosome-positive acute lymphoblastic leukemia (ALL), combined with chemotherapy.
Imatinib Taro is indicated for the treatment of adults with Kit (CD 117)-positive metastatic malignant and/or unresectable gastrointestinal stromal tumors (GIST).
Imatinib Taro is indicated for adjuvant treatment of adults following complete gross resection of the Kit (CD117)-positive gastrointestinal stromal tumor (GIST).
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 (PDGFR).
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 an active ingredient called imatinib. This medicine works by inhibiting the production of abnormal cells in the diseases listed below, some of which are certain types of cancer.

CML is a blood cancer that causes the body to produce too many abnormal white blood cells called myeloid cells.
GIST are malignant tumors of the stomach and bowels. They develop due to uncontrolled cell growth of the supporting tissues of these organs.
ALL is a blood cancer that causes the body to produce too many abnormal white blood cells called lymphoblastic cells.
DFSP is a cancer of the tissue beneath the skin in which some cells start growing out of control.
MDS/MPD is a group of blood diseases that cause the body to produce too many abnormal blood cells.
HES/CEL is a group of blood diseases that cause the body to produce too many blood cells called eosinophils.
ASM are malignant tumors that 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 listed in section 6 'Additional information' of this leaflet. 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 treatment with 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 of the thyroid.
- You have ever had or might now have a viral hepatitis B infection. Imatinib Taro may cause viral hepatitis B to become active again, which can lead to death in certain cases. Patients will be carefully checked by their doctor for signs of this infection before treatment is started.
- 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).

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

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 treatment of blood cancers or solid tumors.

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

During the 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). During treatment with Imatinib Taro, your doctor will regularly check if the medicine is working. You will also undergo blood tests and be weighed regularly.

Children and adolescents (below the age of 18 years)
Imatinib Taro is administered to children aged 3 years and older to treat CML. For the other indications, Imatinib Taro is not indicated for children and adolescents below the age of 18. Some children and adolescents taking Imatinib Taro may have slower than normal growth. The doctor will monitor the growth at regular visits.

Tests and follow up
Your doctor will regularly monitor your condition to check whether the desired outcome is achieved by Imatinib Taro treatment. You will be asked to have blood tests taken regularly to see how well you are tolerating Imatinib Taro (for example, blood cells, liver and kidney function, thyroid function). You will be also regularly weighed during treatment with Imatinib Taro.

Drug interactions
If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist. Some medicines can interfere with the effect of Imatinib Taro when taken together. They may increase or decrease the action of Imatinib Taro, lead to increased side effects or make Imatinib Taro less effective. Imatinib Taro may do the same to some other medicines.

In particular, tell the doctor if you are taking:

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

You should be careful if you are taking a medicine which may increase the blood levels of Imatinib Taro.

Medicines which may decrease the blood levels of Imatinib Taro:
Dexamethasone, a steroidal anti-inflammatory medicine;
Certain anti-epileptic medicines 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) – a medicinal plant for treatment of depression and other conditions;

Avoid using the above medicines during treatment with Imatinib Taro. If you are taking any of the medicines mentioned above, your doctor may prescribe alternative medicines for you.

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

Medicines the blood levels of which may decrease due to the 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 you have been prescribed a new medicine, including non-prescription medicines you have not taken before, during treatment with Imatinib Taro.

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 breastfeeding, think you may be pregnant or are planning to become pregnant, consult your doctor or pharmacist 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 with you the risks associated with taking Imatinib Taro during pregnancy.
- Women of childbearing age must use effective contraceptives while being treated with Imatinib Taro and for 15 days after completing the treatment. Do not breastfeed while being treated with Imatinib Taro and for 15 days after completing treatment, as it may harm your baby.
- Patients concerned about their fertility during treatment with Imatinib Taro should consult their doctor.

Driving and using machines
If you feel dizziness or drowsiness, or if you have blurred vision while using Imatinib Taro, do not drive a vehicle or operate devices or machines until you feel well.
Regarding children, caution them against riding bicycles or playing near a highway, etc.

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?
Always use this medicine according to your doctor's instructions. It is important that you do so 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 you should 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 dose depending on how you respond to the treatment. If your doctor decides on a daily dose of 800 mg, you should 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 myelodysplastic or myeloproliferative diseases (MDS/MPD):
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 reaction 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 reaction 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 reaction 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 dose prescribed for you.

Duration of treatment
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 as follows:

- Use about 50 ml for each 100 mg tablet or 200 ml for a 400 mg tablet.
- Stir with a tablespoon until the tablet(s) is/are completely dissolved.
- Once the tablet(s) has/have dissolved, drink the entire content of the glass immediately. Traces of the dissolved tablet(s) may remain 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 treatment.

If you forget to take the medicine

- If you forget to take the medicine at the scheduled 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 treatment with the 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. The side effects are usually mild to moderate.

Some side effects may be serious.
Contact your doctor immediately if you experience any of the following side effects:

Very common (occur in more than 1 in 10 users) or common (occur in 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 develop infections more easily.
- Unexpected bleeding or bruising (without injuring yourself).

Uncommon (occur in 1-10 in 1,000 users) or rare (occur in 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 eruption (signs of a skin disorder).
- Severe abdominal pain, vomiting blood, black or bloody stool (signs of gastrointestinal disorders).
- Blood in the urine.
- Severely decreased urine output (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, shortness of breath and dark urine (signs of low levels of red blood cells).
- Eye pain, decreased vision, bleeding in the eyes.
- Pain in the hips or difficulty walking.
- Numb or cold 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 spasms with an abnormal heart rhythm (signs of changes in blood potassium level).
- Bruising.
- Abdominal pain with nausea.
- Muscle spasms with fever, red-brown urine, pain or weakness in the muscles (signs of muscle disorders).
- Pelvic pain sometimes accompanied by nausea and vomiting, with unexpected vaginal bleeding, sensation of dizziness or fainting due to low blood pressure (signs of an ovary or uterus disorder).
- Nausea, shortness of breath, irregular heartbeats, 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 (effects whose frequency has not yet been established):

- 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 shortness of breath, chest pain/discomfort, severely decreased urine output and feeling thirsty (signs of a treatment-related allergic reaction).
- Chronic renal failure.
- Recurrence (reactivation) of viral hepatitis B infection if you have had hepatitis B in the past (a liver infection).

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

Additional side effects:
Contact your doctor if any of the side effects listed below affects you severely:

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

Common side effects (occur in 1-10 in 100 users): anorexia, weight loss or a disturbed sense of taste; sensation of dizziness or weakness; difficulty sleeping (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; joint pain with swelling; dry mouth, dry skin or dry eyes; decreased or increased skin sensitivity; erythema; hot flushes, chills or night sweats; shortness of breath, cough, increased liver enzymes; fever.

Uncommon side effects (occur in 1-10 in 1,000 users): upper respiratory tract infection leading to cough, runny or stuffy nose, nasal congestion, sneezing, sore throat, facial pressure, severe headache sometimes accompanied by nausea, vomiting and photosensitivity (signs of migraine), flu-like symptoms, urinary tract infection, depression, anxiety, drowsiness, tremor, memory impairment, restless leg syndrome, eye irritation, pain or redness in the eye, swelling/itching in the eyelids, sensation of vertigo/dizziness, noise (ringing) in the ears, multiple heart beats, hypertension, bruises, sensation of cold at the periphery of the body, belching, lip inflammation, difficulty swallowing, increased sweating, skin discoloration, breaking of finger and toe nails, folliculitis, thickened and red patches around elbows and knees, skin darkening, breast enlargement in men and women, testicular edema, erectile dysfunction, heavy menstrual bleeding or irregular menstrual periods, reduced libido and sexual function disorder, pain in the nipples, chest pain, feeling generally unwell, viral infection such as a cold

sore, back pain due to renal disorder, increased frequency of urination, increased appetite, gastric ulcer, joint and muscle stiffness, abnormal laboratory test results, swollen lymph nodes.

Rare side effects (occur in 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 hands and feet which may be accompanied by painful sensation of tingling and burning; skin lesions that are painful and/or covered with blisters; slowing of 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 effects, 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/blister tray. The expiry date refers to the last day of that month.
Storage conditions
Store below 25˚C. Protect from moisture.
Do not store different medicines in the same package. Do not use the medicine if the pack is damaged or shows signs of tampering.
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, mannitol, copovidone, crospovidone, magnesium stearate, film coating (contains: opadry yellow (HPMC 2910,

titanium dioxide, macrogol 400, iron oxide yellow, sunset yellow FCF aluminum lake, iron oxide red), 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.

The medicine is available in packs of 10, 20, 30, 60, 90 tablets. Not all pack sizes may be marketed.

Registration holder:
Taro International, 14 Hakitor St., Haifa Bay 2624761.

Manufacturer's name:
Sun Pharmaceutical Industries Ltd, Halol Baroda Highway, Halol – 389 350 Gujarat, India.

Revised in March 2022 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:
Imatinib Taro 100 mg film-coated tablets: 166-54-35760
Imatinib Taro 400 mg film-coated tablets: 166-55-35761