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

The medicine is dispensed with a doctor's prescription only

Dasatinib Taro 20 mg
Dasatinib Taro 50 mg
Dasatinib Taro 70 mg
Dasatinib Taro 80 mg
Dasatinib Taro 100 mg
Dasatinib Taro 140 mg

Film-coated tablets

The active ingredient and its quantity:

Each film-coated tablet contains:

dasatinib 20 mg, dasatinib 50 mg, dasatinib 70 mg, dasatinib 80 mg, dasatinib 100 mg, dasatinib 140 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 ailment. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.

Dasatinib Taro is not intended for use in children and adolescents under 18 years of age. There is limited experience with use of Dasatinib Taro in this age group.

1. WHAT IS THE MEDICINE INTENDED FOR?

Dasatinib Taro is intended for the treatment of adults:

- Newly diagnosed patients suffering from Philadelphia chromosome-positive chronic myeloid leukaemia (CML), at the chronic phase.
- Patients with chronic myeloid leukaemia (CML) at the chronic, accelerated or blast phase with resistance or intolerance to prior treatment, including prior treatment with imatinib mesilate.
- Patients with Philadelphia chromosome-positive acute lymphoblastic leukaemia (ALL) and patients with lymphoid blast-phase chronic myeloid leukaemia (CML) with resistance or intolerance to prior treatment.

Therapeutic group: protein kinase inhibitors

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

You are sensitive (allergic) to the active ingredient (dasatinib) or to any of the other ingredients the medicine contains, which are listed in section 6 'Further information'.

If you could be allergic, ask your doctor for advice.

Special warnings regarding use of the medicine

Before treatment with Dasatinib Taro tell your doctor or pharmacist if:

- You are taking medicines to thin your blood or prevent clots (see the section 'Drug interactions').
- You have or have had liver or heart problems.
- You **start having difficulty breathing, chest pain, or a cough** while being treated with Dasatinib Taro, refer to the doctor. This may be a sign of fluid retention in the lungs or chest (which can be more common in patients aged 65 and older) or due to changes in the blood vessels that supply blood to the lungs.
- You have ever had or currently have a hepatitis B infection. This is because Dasatinib Taro could cause hepatitis B to become active again and be fatal in some cases. Patients will be carefully checked by their doctor for signs of this infection before treatment is started.
- You experience bruising, bleeding, fever, fatigue and confusion during the treatment with Dasatinib Taro, contact your doctor. These may be signs of damage to blood vessels known as thrombotic microangiopathy (TMA).

Children and adolescents

Dasatinib Taro is not intended for use in children and adolescents under 18 years old. There is limited experience with the use of Dasatinib Taro in this age group.

Tests and follow-up

Your doctor will regularly monitor your condition to check whether Dasatinib Taro is having the desired effect. You will also have blood tests regularly while you are taking the medicine.

Drug interactions

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

Dasatinib Taro is primarily cleared by the liver. Certain medicines may interfere with the effect of Dasatinib Taro when taken together.

Do not take the following medicines together with Dasatinib Taro:

- ketoconazole and itraconazole – **antifungal** medicines
- erythromycin, clarithromycin and telithromycin – **antibiotics**
- ritonavir – an **antiviral** medicine
- phenytoin, carbamazepine, phenobarbital – for treatment of **epilepsy**
- rifampicin – a treatment for **tuberculosis**
- famotidine and omeprazole – medicines that **block stomach acid**
- St. John's wort – a herbal-based preparation to treat **depression** (also known as Hypericum perforatum)

Do not take medicines that neutralise stomach acid (**antacids** such as aluminium hydroxide or magnesium hydroxide **to treat heartburn**) **in the 2 hours before or 2 hours after taking Dasatinib Taro.**

Tell your doctor if you are taking **medicines to thin the blood** or prevent clots.

Use of the medicine and food

The medicine can be taken with or without food.

Do not take the medicine with grapefruit or grapefruit juice.

Pregnancy and breast-feeding

If you are pregnant or think you may be pregnant, **tell your doctor immediately**.

Do not take Dasatinib Taro during pregnancy unless clearly necessary. Your doctor will discuss with you the potential risk of taking Dasatinib Taro during pregnancy.

Both men and women taking Dasatinib Taro must consult their doctor regarding the use of effective contraception during treatment.

If you are breast-feeding, tell your doctor. You should stop breast-feeding while you are taking Dasatinib Taro.

Driving and use of machines

Take special care when driving or using machines in case you experience side effects such as dizziness and blurred vision.

Important information about some of this medicine's ingredients

Dasatinib Taro contains lactose. If you have been told by your doctor that you have an intolerance to certain sugars, consult your doctor before taking the medicine.

Dasatinib Taro contains less than 23 mg sodium per tablet and is therefore considered to be essentially sodium free.

3. HOW SHOULD YOU USE THE MEDICINE?

Dasatinib Taro will only be prescribed to you by a doctor with experience in treating leukaemia. Always use Dasatinib Taro according to the doctor's instructions. Check with your doctor or pharmacist if you are not sure about the dosage and the treatment regimen of the medicine. Dasatinib Taro is intended for adults.

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

Take the medicine in accordance with the dosage and duration determined by your doctor. Depending on how you respond to the treatment, the doctor will inform you if a higher or lower dosage of Dasatinib Taro is required or even stopping treatment for a short time. For higher or lower doses, you may need to take combinations of the different tablet strengths.

Do not exceed the recommended dose.

Duration of treatment

Take Dasatinib Taro daily until your doctor tells you to stop. Make sure you take Dasatinib Taro for as long as it is prescribed for you.

Take the medicine at the same time every day.

Swallow the tablets whole. Do not crush, split or chew the tablets (in order to maintain dosing consistency and minimise the risk of skin exposure). Do not disperse the tablets (as the exposure in patients who received a dispersed tablet is lower than in those swallowing a whole tablet). You cannot be sure you will receive the correct dose if you crush, split, chew or disperse the tablets.

The medicine can be taken with or without food. Do not take the medicine with grapefruit or grapefruit juice.

If you are also taking antacids (to treat heartburn), such as medicines that contain aluminium hydroxide or magnesium hydroxide, take the antacids no less than two hours before or two hours after Dasatinib Taro.

Special handling instructions for Dasatinib Taro:

It is unlikely that the Dasatinib Taro tablets will break. But if this happens, persons other than the patient should use gloves when handling Dasatinib Taro.

If you took an overdose or if a child accidentally swallowed the medicine, immediately refer to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forgot to take this medicine at the designated time, do not take a double dose. Take the next dose at the regular time and consult your doctor.

Adhere to the treatment regimen recommended by the doctor.

If you stop taking the medicine

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

Do not take medicines in the dark! Check the label and dose <u>each time</u> you take medicine. Wear glasses if you need them. If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. <u>SIDE EFFECTS</u>

As with any medicine, use of Dasatinib Taro may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Contact your doctor immediately if the following effects, that can be signs of severe side effects, **occur**:

- having chest pain, difficulty breathing, coughing and fainting.
- **unexpected bleeding or bruising** without having sustained an injury.
- having blood in your vomit, stools or urine, or having black stools.
- having **signs of infection** such as fever and severe chills.
- having fever, sore throat or mouth, blistering or peeling of your skin and/or mucous membranes.

Additional side effects:

Very common side effects (effects that occur in more than 1 in 10 users):

- **Infections** (including bacterial, viral, and fungal infections).
- **Heart and lungs:** shortness of breath.
- **Digestive problems:** diarrhoea, nausea, vomiting.
- **Skin, hair, eye, general:** skin rash, fever, swelling around the face, hands and feet, headache, feeling tired or weak, bleeding.
- **Pain:** pain in the muscles (during or after discontinuing treatment), abdominal pain.
- **Tests may show:** low blood platelet count, low white blood cell count (neutropenia), anaemia, fluid around the lungs.

Common side effects (effects that occur in up to 1 in 10 users):

- **Infections:** pneumonia, herpes virus infection (including cytomegalovirus - CMV), upper respiratory tract infection, severe infection of the blood or tissues (including uncommon cases with fatal outcomes).
- **Heart and lungs:** palpitations, irregular heartbeat, congestive heart failure, weak heart muscle, high blood pressure, high blood pressure in the lungs, cough.

- **Digestive problems:** appetite disturbances, taste disturbance, bloated or distended abdomen, inflammation of the colon, constipation, heartburn, mouth ulceration, weight increase, weight decrease, gastritis.
- **Skin, hair, eye, general:** skin tingling, itching, dry skin, acne, inflammation of the skin, persistent noise in ears, hair loss, excessive perspiration, visual disorder (including blurred vision and disturbed vision), dry eye, bruises, depression, insomnia, flushing, dizziness, bruises, anorexia, somnolence, generalized oedema.
- **Pain:** pain in joints, muscular weakness, chest pain, pain around hands and feet, chills, stiffness in muscles and joints, muscle spasm.
- **Tests may show:** fluid around the heart, fluid in the lungs, arrhythmia, febrile neutropenia, gastrointestinal bleeding, high uric acid levels in the blood.

Uncommon side effects (effects that occur in up to 1 in 100 users):

- **Heart and lungs:** heart attack (including fatal outcome), inflammation of the lining (fibrous sack) surrounding the heart, irregular heartbeat, chest pain due to lack of blood supply to the heart (angina), low blood pressure, narrowing of airway that may cause breathing difficulties, asthma, increased blood pressure in the arteries of the lungs, blood clots.
- **Digestive problems:** inflammation of the pancreas, peptic ulcer, inflammation of the food pipe, swollen abdomen, tear in the skin of the anal canal, difficulty in swallowing, inflammation of the gallbladder, blockage of bile ducts, gastro-oesophageal reflux (a condition where acid and other stomach contents come back up into the throat).
- **Skin, hair, eye, general:** allergic reaction including tender, red lumps on the skin (erythema nodosum), anxiety, confusion, mood swings, lower sexual drive, fainting, tremor, inflammation of the eye which causes redness or pain, a skin disease characterized by red, tender, well-defined blotches with the sudden onset of fever and elevated white blood cell count (neutrophilic dermatosis), loss of hearing, sensitivity to light, visual impairment, increased eye tearing, disturbance in skin colour, inflammation of fatty tissue under the skin, skin ulcer, blistering of the skin, change in nails, change in hair, hand-foot disorder, renal failure, urinary frequency, breast enlargement in men, menstrual disorder, general weakness and discomfort, low thyroid function, losing balance while walking, osteonecrosis (a disease of reduced blood flow to the bones, which can cause bone loss and bone death), arthritis, skin swelling anywhere in the body.
- **Pain:** inflammation of a vein which can cause redness, tenderness and swelling, inflammation of the tendon.
- **Brain:** loss of memory.
- **Tests may show:** abnormal blood test results and possibly impaired kidney function caused by removal of tumour waste products (tumour lysis syndrome), low levels of albumin in the blood, low levels of lymphocytes (a type of white blood cell) in the blood, high level of cholesterol in the blood, swollen lymph nodes, bleeding in the brain, irregularity of the electrical activity of the heart, enlarged heart, inflammation of the liver, protein in the urine, elevated creatine phosphokinase (an enzyme mainly found in the heart, brain, and skeletal muscles), elevated troponin (an enzyme mainly found in tissues such as the heart and skeletal muscles), elevated gamma-glutamyl-transferase (an enzyme mainly found in the liver), appearance of milky-appearing fluid around the lungs (chylothorax).

Rare side effects (effects that occur in up to 1 in 1,000 users):

- **Heart and lungs:** enlargement of the right ventricle in the heart, inflammation of the heart muscle, collection of various conditions resulting from blockage of blood supply to the heart muscle (acute coronary syndrome), cardiac arrest (stopping of blood flow from the heart), coronary heart disease, inflammation of the tissue covering the heart and lungs, blood clots (in deep veins), blood clots in the lungs.

- **Digestive problems:** loss of vital nutrients such as protein from your digestive tract, bowel obstruction, anal fistula (an abnormal opening from the anus to the skin around the anus), impairment of kidney function, diabetes.
- **Skin, hair, eye, general:** convulsions, inflammation of the optic nerve that may cause complete or partial loss of vision, blue-purple mottling of the skin, abnormally high thyroid function, inflammation of the thyroid gland, ataxia (coordination disorder), difficulty walking, miscarriage, inflammation of the skin blood vessels, skin fibrosis.
- **Brain:** stroke, temporary episode of neurologic dysfunction caused by impaired blood flow, facial nerve paralysis, dementia.
- **Immune system:** severe allergic reaction.

Additional side effects whose frequency is not known (cannot be estimated from the available data):

- Inflammation of the lungs.
- Bleeding in the stomach or bowels that can cause death.
- Recurrence (reactivation) of hepatitis B virus infection when you have had hepatitis B in the past (a liver infection).
- A reaction with fever, blisters on the skin, and ulceration of the mucous membranes.
- Disease of the kidneys with symptoms including oedema and abnormal laboratory test results such as protein in the urine and low protein level in the blood.
- Damage to blood vessels known as thrombotic microangiopathy (TMA), including decreased red blood cell count, decreased platelets, and formation of blood clots.

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.

Side effects can be reported to the Ministry of Health by clicking on the link: "Reporting of side effects from drug treatment", which can be 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 SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine and any other medicine must be stored 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 below 25°C.
- Do not discard medicines via wastewater or household waste. Ask the pharmacist how to dispose of medicines no longer in use. These measures will help protect the environment.

6. FURTHER INFORMATION

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

Lactose monohydrate, microcrystalline cellulose, hydroxypropyl cellulose, croscarmellose sodium, magnesium stearate, film coating consisting of hypromellose, lactose monohydrate, titanium dioxide (E171), triacetin.

What the medicine looks like and the contents of the package:

Dasatinib Taro 20 mg:

A film-coated tablet that is white to off-white, biconvex, round with a diameter of approximately 6 mm. The tablet is debossed with "D7SB" on one side and “20” on the other side.

Dasatinib Taro 50 mg:

A film-coated tablet that is white to off-white, biconvex, oval, with a length of approximately 11 mm and width of approximately 6 mm. The tablet is debossed with “D7SB” on one side and “50” on the other side.

Dasatinib Taro 70 mg:

A film-coated tablet that is white to off-white, biconvex, round with a diameter of approximately 9 mm. The tablet is debossed with "D7SB" on one side and “70” on the other side.

Dasatinib Taro 80 mg:

A film-coated tablet that is white to off-white, biconvex, triangle, with a length of approximately 10 mm and width of approximately 11 mm. The tablet is debossed with “D7SB” on one side and “80” on the other side.

Dasatinib Taro 100 mg:

A film-coated tablet that is white to off-white, biconvex, oval, with a length of approximately 15 mm and width of approximately 7 mm. The tablet is debossed with “D7SB” on one side and “100” on the other side.

Dasatinib Taro 140 mg:

A film-coated tablet that is white to off-white, biconvex, round, with a diameter of approximately 12 mm. The tablet is debossed with “D7SB” on one side and “140” on the other side.

Dasatinib Taro 20 mg, 50 mg, 70 mg are marketed in packs containing 60 tablets.

Dasatinib Taro 80 mg, 100 mg, 140 mg are marketed in packs containing 30 tablets.

Not all strengths of the medicine may be marketed.

License holder and address: Taro International Ltd., 14 Hakitor St., Haifa Bay 2624761

Manufacturer's name and address: Synthon Hispania, S.L., C/ Castello, 1,08830 Sant Boi de Llobregat, Barcelona, Spain

This leaflet was revised in December 2022 according to MOH guidelines.

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

Dasatinib Taro 20 mg: 168-32-36363-00

Dasatinib Taro 50 mg: 168-33-36364-00

Dasatinib Taro 70 mg: 168-34-36365-00

Dasatinib Taro 80 mg: 168-35-36366-00

Dasatinib Taro 100 mg: 168-36-36367-00

Dasatinib Taro 140 mg: 168-37-36368-00