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

The medicine is dispensed with a doctor's prescription only

TASIGNA® 150 MG Capsules

Each capsule contains:
Nilotinib as hydrochloride monohydrate 150 mg

TASIGNA® 200 MG Capsules

Each capsule contains:
Nilotinib as hydrochloride monohydrate 200 mg

Inactive ingredients: See "Important information about some of the medicine's ingredients" section, listed under section 2, and also section 6 "Further information".

Read this package insert carefully in its entirety before using this medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.
Keep this leaflet. You may need to read it again.
This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.
There is no experience with use of Tasigna in children and adolescents (below the age of 18).

1. WHAT IS THE MEDICINE INTENDED FOR?

Tasigna 150 mg and Tasigna 200 mg are used:
For treatment of adult patients with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia - Ph+ CML in the chronic phase.
Tasigna 200 mg **only** is used:
For treatment of patients with Philadelphia chromosome positive chronic myeloid leukemia - Ph+ CML in the chronic or accelerated phase, who are resistant to or who experienced significant toxicity during treatment with imatinib.
Tasigna is used to treat a type of leukemia called Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML).
CML is a cancer of the blood which causes the body to produce too many abnormal white blood cells.
In CML patients, a change in the genetic material (DNA) triggers a signal which causes the body to produce too many abnormal white blood cells. Tasigna blocks this signal and stops the production of these cells.

Therapeutic group: Antineoplastic.

If you have any question about how Tasigna works or why this medicine has been prescribed for you, refer to your doctor.

2. BEFORE USING THE MEDICINE:

Follow all the doctor's instructions carefully. They may differ from the general information contained in this leaflet.

☒ **Do not use the medicine:**
- If you have an allergy (hypersensitivity) to nilotinib or to any of the other ingredients of the medicine listed in section 6 "Further information".

If you think you may be allergic, inform the doctor **before taking** Tasigna.

Special warnings regarding use of the medicine:
Before treatment with Tasigna, inform your doctor if any of the following apply to you:
- If you have had prior cardiovascular events such as a heart attack, chest pain (angina), problems with the blood supply to your brain (stroke), or problems with the blood flow to your leg (claudication) or if you have risk factors for cardiovascular disease such as high blood pressure (hypertension), diabetes, or problems with the level of fats in your blood (lipid disorders).
- If you have a **heart disorder** such as an abnormal electrical signal called "prolongation of the QT interval".
- If you are **being treated with medicines** that affect the heart rate (anti-arrhythmics) or the liver (see below "If you are taking, or have recently taken, other medicines").
- If you suffer from lack of potassium or magnesium.
- If you have a liver or pancreas disorder.
- If you have symptoms such as easy bruising, feeling tired or short of breath or recurrent infections.
- If you underwent surgery for removal of your entire stomach (gastrectomy).
- If you have ever had or might have a hepatitis B infection. Tasigna could cause hepatitis B to become active again, which can be fatal in some cases. Patients will be carefully checked by their doctor for signs of this infection before treatment is started.

During treatment with Tasigna
Refer to your doctor immediately if you faint (lose consciousness), or have irregular heartbeats during treatment with this medicine, as these may occur due to a serious heart condition. Prolongation of the QT interval or irregular heartbeats may lead to sudden death.
Uncommon cases of sudden death have been reported in patients treated with Tasigna.
Refer to your doctor immediately if you have sudden heart palpitations, severe muscle weakness or paralysis, seizures or sudden changes in your thinking or level of alertness, since this may be a sign of the rapid breakdown of cancer cells called "tumor lysis syndrome". Rare cases of tumor lysis syndrome have been reported in patients taking Tasigna.
Refer to your doctor immediately if you develop chest pain or discomfort, numbness or weakness, problems with walking or speech, pain, discoloration or a cold sensation in one of the limbs since this may be a sign of a cardiovascular event. Severe cardiovascular events including problems with blood flow to the leg (peripheral arterial occlusive disease), ischemic heart disease and problems with blood supply to the brain (ischemic cerebrovascular disease) have been reported in patients taking Tasigna. Your doctor should monitor the level of fats (lipids) and sugar in your blood before initiating treatment with Tasigna and during the treatment.
If you develop swelling of the feet or hands, generalized swelling or rapid weight gain, tell your doctor since these may be signs of severe fluid retention. Uncommon cases of severe fluid retention have been reported in patients taking Tasigna.

Tests and follow-up:
During treatment with this medicine, tests should be performed regularly, including blood tests. These tests will monitor:
- the amount of blood cells (white blood cells, red blood cells and platelets) in the body to see how Tasigna is being tolerated.
- pancreas and liver function in the body to see how Tasigna is being tolerated.
- electrolytes in the body (potassium, magnesium). These are important in the functioning of the heart.
- the level of sugar and fats in the blood.

The heart rate will also be checked using a machine that measures the electrical activity of the heart (a test called "ECG").
Your doctor will regularly monitor your treatment and decide whether you should continue taking Tasigna.
If you are told to stop taking this medicine, your doctor will carefully continue to monitor your CML and may instruct you to resume taking Tasigna if necessary, depending on your condition.
Refer to the doctor with any question regarding how Tasigna works or why it was prescribed for you.

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist in order to prevent risks or inefficacy arising from drug interactions. Tasigna may interfere with other medicines. In particular, inform the doctor or pharmacist if you are taking:
- Anti-arrhythmics - used to treat irregular heart rate;
- Chloroquine, halofantrine, clarithromycin, haloperidol, methadone, moxifloxacin - medicines that may have an unwanted effect on the function of the heart;
- Ketoconazole, itraconazole, voriconazole, clarithromycin, Telithromycin – used to treat infections;
- Ritonavir – a medicine for the treatment of AIDS (HIV) from the "antiprotease" group;
- Carbamazepine, phenobarbital, phenytoin - used to treat epilepsy;
- Rifampicin - used to treat tuberculosis;
- St. John's Wort – a herbal product used to treat depression and other conditions (also known as *Hypericum perforatum*);
- Midazolam – used to relieve states of anxiety before surgery;
- Alfentanil and fentanyl - used to treat pain and as a sedative before or during surgery or medical procedures;
- Cyclosporine, sirolimus and tacrolimus - medicines that suppress the "self-defense" capability of the body and ability to fight infections and are usually used to prevent the rejection of transplanted organs such as liver, heart and kidney;
- Dihydroergotamine and ergotamine - used to treat dementia;
- Lovastatin, simvastatin - used to treat high levels of fats in blood;
- Warfarin - used to treat blood coagulation disorders (such as blood clots and thrombosis);
- Astemizole, terfenadine, cisapride, pimozide, quinidine, bepridil.

During treatment with Tasigna avoid taking these medicines. If you are taking one or more of these medicines, the doctor may prescribe alternative medicines for you.
In addition, inform the doctor or pharmacist before taking Tasigna if you are taking antacids (medicines for treatment of heartburn). These medications need to be taken separately from Tasigna:
- Antacids called H2 blockers, which decrease the production of acidity in the stomach - should be taken approximately 10 hours before and, approximately 2 hours, after you take Tasigna.
- Antacids such as those containing aluminium hydroxide, magnesium hydroxide and simethicone, which neutralize high acidity of the stomach - should be taken approximately 2 hours before or 2 hours after taking Tasigna.

You should inform your doctor **if you are already taking Tasigna** and you are prescribed a new medicine, including non-prescription medicines, that you have not taken previously during Tasigna treatment.

Use of Tasigna and food
Do not take the medicine with food. Food may enhance the absorption of Tasigna and therefore increase its amount in the blood, possibly to a harmful level.
Do not drink grapefruit juice or eat grapefruit. It may increase the amount of Tasigna in the blood, possibly to a harmful level.

Elderly people (patients from 65 years and over)
Tasigna can be used by people aged 65 years and over at the same dosages as for other adults.

Pregnancy and breast-feeding
It is not recommended to use Tasigna during pregnancy unless clearly necessary. If you are pregnant or think that you may be pregnant, inform the doctor who will discuss with you whether you can use this medicine during pregnancy.
Women of child-bearing age must use highly effective contraception while using Tasigna and for 2 full weeks after ending treatment.
Do not breast-feed during treatment with Tasigna. Inform your doctor if you are breast-feeding.
If you are pregnant or breast-feeding, think you are pregnant or planning to become pregnant, consult with the doctor or pharmacist before taking this medicine.

Driving and use of machines
If you experience side effects (such as dizziness or visual disorders) that can affect the ability to drive safely or use any tools or machines after taking this medicine, you should refrain from these activities until the effect has passed.

Important information about some of the medicine's ingredients
The preparation contains lactose (milk sugar). If you know that you are lactose intolerant, inform the doctor before taking Tasigna.
Each 150 mg Tasigna capsule contains approximately 117 mg lactose monohydrate.
Each 200 mg Tasigna capsule contains approximately 156 mg lactose monohydrate.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure about the dosage and treatment regimen of the preparation.

The dosage and the treatment regimen will be determined by the doctor only. The usual dosage is generally:
Adult patients with newly diagnosed Ph+ CML: 2 capsules of 150 mg twice daily (300 mg twice daily).
For patients with Ph+ CML in the chronic or accelerated phase who are resistant to or who experienced significant toxicity during treatment with, imatinib: 2 capsules of 200 mg twice daily (400 mg twice daily).
Your doctor may prescribe a lower dosage depending on your response to treatment.
Do not exceed the recommended dose.

When to take Tasigna:
Take the capsules:
- twice a day (approximately every 12 hours)
- at least 2 hours after eating any food
- then wait at least 1 hour before eating again

If you have questions about when to take the medicine, talk to your doctor or pharmacist.
Taking the medicine at the same time each day will help you remember when to take your capsules.

How to take Tasigna:
Swallow the capsules whole with water.
Do not consume any food together with the capsules.
Do not open the capsules unless **you are unable to swallow the capsules whole.**
In this case you may mix the contents of each capsule in **one** teaspoon of applesauce (pureed apple) and take it immediately. Do not use more than one teaspoon of applesauce for each capsule and do not use any food other than applesauce.

Duration of treatment:
Continue taking the medicine every day as long as your doctor instructs you to; this is a long-term treatment. Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.
The doctor will consider stopping the treatment with Tasigna according to specific criteria.
If you have questions regarding how long to take Tasigna, consult your doctor or pharmacist.

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

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

Adhere to 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.
Stopping treatment with the medicine without a doctor's recommendation places you at risk for worsening of your illness which may come with life-threatening consequences. Be sure to discuss with your doctor, nurse and/or pharmacist if you are considering stopping Tasigna.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.

If your doctor recommended discontinuation of Tasigna treatment
Your doctor will regularly monitor your treatment by a certain diagnostic test and will decide if you should continue taking this medicine.
If you have been told to stop taking Tasigna, your doctor will continue to carefully monitor your CML, before, during and after stopping treatment and may instruct you to resume taking Tasigna if necessary, depending on your condition.

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS:

As with any medicine, use of Tasigna 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. Most of the side effects are mild to moderate, and will generally disappear after a few days to a few weeks after starting treatment.

Some side effects can be serious. Contact the doctor immediately in the following cases:
These side effects are common (may affect up to 1 in 10 patients), uncommon (may affect up to 1 in 100 patients) or were reported at unknown frequencies (can not be estimated from the existing data).
- Rapid weight gain, swelling of hands, ankles, feet or face (signs of water retention)
- Chest pain, high blood pressure, irregular heart rate, blue discoloration of the lips, tongue or skin (signs of heart disorders)
- Difficulty breathing, cough, wheezing with or without fever, swelling of legs and feet (signs of lung disorders)
- Fever, easy bruising, frequent infections (signs of blood disorders)
- Weakness or paralysis of limbs or face, difficulty speaking, severe headache, seeing, hearing or feeling things that are not there (signs of nervous system disorders)
- Thirst, dry skin, irritability, dark urine, decreased urine output (signs of kidney disorders)
- Blurred vision, loss of vision, blood in the eyes (signs of eye disorders)
- Swelling and pain in one part of the body (signs of clotting within a vein)
- Abdominal pain, nausea, vomiting of blood, black stools, constipation, swollen abdomen (signs of gastrointestinal disorders)
- Severe upper abdominal pain (a sign of inflammation of pancreas)
- Yellow skin and eyes, nausea, loss of appetite, dark-colored urine (signs of liver disorders)
- Rash, painful red lumps, pain in joints and muscles (signs of skin disorders)
- Excessive thirst, high urine output, increased appetite with weight loss, tiredness (signs of high level of sugar in the blood)
- Fast heartbeats, bulging eyes, weight loss, swelling at front of the neck (signs of overactive thyroid gland)
- Nausea, shortness of breath, irregular heartbeats, clouding of urine, tiredness and/or joint discomfort with abnormal laboratory test results (such as an increase in potassium, uric acid and phosphorous levels and decrease in calcium levels in the blood)
- Pain, discomfort, weakness or cramping in leg muscles, which may be due to decreased blood flow, ulcers on the legs and arms that heal slowly or not at all and noticeable changes in color (blueness or paleness) or temperature (coolness) of the legs and arms, as these symptoms could be signs of artery blockage in the affected limb (leg or arm) and digits (toes and fingers).
- Recurrence (reactivation) of hepatitis B infection when you have had hepatitis B in the past.

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

Additional side effects:
Very common side effects (may affect more than 1 in 10 patients): Diarrhea; headache; tiredness; muscle pain; itching, rash, nausea; vomiting; hair loss; high blood level of bilirubin (liver function); high blood level of lipase (pancreas function); muscle pain, musculoskeletal pains, pain in extremities, pain in joints, bone pain, and back pains with discontinuation of Tasigna treatment.
If one of the effects mentioned above affects you severely, tell your doctor.

Common side effects (may affect up to 1 in 10 patients): Hives (urticaria); abdominal discomfort, stomach discomfort after meals, flatulence, swelling or bloating of the abdomen; bone pain, joint pain, muscle spasms; pain including back pain, neck pain and pain in extremities, pain or discomfort in the side of the body; eye irritation, swelling, discharge, itching or redness, dry eyes (signs of eye disorders); skin redness, dry skin, acne, skin wart, decreased skin sensitivity; weight increase or decrease, loss of appetite, disturbed sense of taste; insomnia, depression, anxiety; night sweats, increased sweating, hot flushes; dizziness, generally feeling unwell, spinning sensation; tingling or numbness; voice disturbance; nose bleed; frequent urine output; palpitations.
If one of the effects mentioned above affects you severely, tell your doctor.

Uncommon side effects (may affect up to 1 in 100 patients): Increased skin sensitivity, skin pain; eyelid swelling; dry mouth, sore throat, mouth sores; heartburn; breast pain; increased appetite; attention disorder; difficulty and pain upon urinating, exaggerated sense of needing to urinate; inability to achieve or maintain an erection; breast enlargement in men; flu-like symptoms, muscle weakness; trembling; decreased sharpness of vision; severe headache occasionally accompanied by nausea, vomiting, sensitivity to light; visual disturbances; vaginal or oral thrush; joint and muscle stiffness; loss of consciousness; weight gain; feeling body temperature change (including feeling hot, feeling cold); thickened patches of red/silver skin (signs of psoriasis); teeth sensitivity.
If one of the effects mentioned above affects you severely, tell your doctor.

The following side effects were reported at unknown frequencies (can not be estimated from the existing data):
Confusion, spatial disorientation, memory loss, disturbed mood, lack of energy; bacterial skin infection; blister, skin cyst, oily skin, thinning of skin, dark patches of skin, skin discoloration; bleeding, tender or enlarged gums; runny or stuffy nose, sneezing; reddening and/or swelling and possibly peeling of the palms of the hands and soles of the feet (named hand-foot syndrome); increased sensitivity of the eyes or skin to light; eye pain or redness, pain, itching of eyelids; difficulty hearing, ear pain, noises (ringing) in the ears; swollen and painful joints (gout); blood in urine, urinary incontinence, abnormal urine color; hemorrhoids; feeling of hardening in the breasts, nipple swelling, heavy periods; symptoms of restless legs syndrome (an urge to move one part of the body, usually the leg, in order to stop uncomfortable sensations).
If the effects mentioned above affect you severely, notify the doctor.

During treatment with Tasigna you may have abnormal blood test results, e.g., low level of blood cells (white blood cells, red blood cells, platelets), high blood level of lipase or amylase (pancreas function), high blood level of bilirubin (liver function), high blood level of creatinine (kidney function), low or high blood level of insulin (a hormone regulating blood sugar level), low or high blood sugar level, high level of fats in the blood.

If one of the effects mentioned above affects you, follow your doctor's advice.
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 with 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://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach of children and/or infants to avoid poisoning.
Do not induce vomiting unless explicitly instructed to do so by the doctor.
Do not use the medicine after the expiry date (exp. date) appearing on the package. Expiry date refers to the last day of that month.
Do not store above 30°C.
Store in the original package in order to protect from moisture.
Do not use a package that is damaged or shows signs of tampering.
Keep out of the reach and sight of children.

6. FURTHER INFORMATION:

In addition to the active ingredient, the medicine also contains:
Lactose monohydrate, Crospovidone, Poloxamer 188, Silica colloidal, anhydrous/Colloidal silicon dioxide, Magnesium stearate.

Tasigna 150 mg capsule shell: Gelatin, Titanium dioxide (E171), Iron oxide yellow (E172), Iron oxide red (E172), and Printing ink: black.
Qualitative composition of printing ink: Shellac, Iron oxide black, n-butyl alcohol, purified water, propylene glycol, dehydrated ethanol, isopropyl alcohol, ammonium hydroxide.

Tasigna 200 mg capsule shell: Gelatin, Titanium dioxide (E171), Iron oxide yellow (E172), Printing ink: red.

Qualitative composition of printing ink a: Shellac, dehydrated alcohol, isopropyl alcohol, butyl alcohol, propylene glycol, strong ammonia solution, Iron oxide red (E172), potassium hydroxide, purified water.
Qualitative composition of printing ink b: Shellac, Iron oxide red (E172), Iron oxide black (E172), n-butyl alcohol, purified water, titanium dioxide (E171), propylene glycol, industrial methylated spirit, isopropyl alcohol.
The printing ink used is 'Printing ink a' or alternatively 'Printing ink b'.
Each 150 mg Tasigna capsule contains approximately 117 mg lactose monohydrate.
Each 200 mg Tasigna capsule contains approximately 156 mg lactose monohydrate.

What does the medicine look like and what are the contents of the package:
A monthly package of Tasigna 150 mg contains 112 capsules. The monthly package contains 4 weekly packs.
A 10-day pack of Tasigna 200 mg contains 40 capsules and a monthly package contains 120 capsules. The monthly package contains 3 10-day packs.
Tasigna 150 mg capsules: White to yellowish powder in red, opaque, size 1 capsules, with black axial imprint "NVR"/"BCR".
Tasigna 200 mg capsules: White to yellowish powder in light yellow, opaque, size 0 capsules, with red axial imprint "NVR"/"TKI".

Registration Holder and address:
Novartis Israel Ltd., 36 Shacham St., Petach-Tikva.

Manufacturer and address:
Novartis Pharma Stein A.G., Stein, Switzerland for Novartis Pharma A.G., Basel, Switzerland.

This leaflet was checked and approved by the Ministry of Health in September 2018.

Drug Registration Number in the National Drug Registry of the Ministry of Health:
Tasigna 150 mg: 145 84 33271
Tasigna 200 mg: 138 17 31681

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