PART III: CONSUMER INFORMATION

PrTASIGNA®
(Nilotinib Capsules)

150 mg and 200 mg nilotinib
(as nilotinib hydrochloride monohydrate)

This leaflet is part III of a three-part "Product Monograph" published when TASIGNA was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about TASIGNA. Contact your doctor or pharmacist if you have any questions about the drug.

Read all of this leaflet carefully before you start taking this medicine.

Keep this leaflet. You may need to read it again.

ABOUT THIS MEDICATION

What the medication is used for:

- TASIGNA is indicated for the treatment of adult patients with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase.
- TASIGNA is also indicated for the treatment of chronic phase and accelerated phase Philadelphia chromosome positive chronic myeloid leukemia (CML) in adult patients resistant to or intolerant of at least one prior therapy, including imatinib.

What it does:

In patients with CML, a change in DNA (genetic material) triggers a signal that tells the body to produce abnormal white blood cells. TASIGNA blocks this signal, and thus stops the production of these abnormal cells.

When it should not be used:
Do not use TASIGNA if you:

- have an abnormal electrical signal of the heart (prolongation of QT interval),
- have uncorrectable low levels of potassium or magnesium,
- are **allergic** (hypersensitive) to nilotinib or any of the other ingredients of TASIGNA.

What the medicinal ingredient is:
Nilotinib.
What the important nonmedicinal ingredients are:
Crospovidone, lactose monohydrate, magnesium stearate, poloxamer, colloidal silicon anhydrous.

- The 150 mg capsule shell is composed of gelatin, titanium dioxide, iron oxide yellow, iron oxide red and the stamping of the imprint includes black iron oxide.
- The 200 mg capsule shell is composed of gelatin, titanium dioxide, iron oxide yellow and the stamping of the imprint includes red iron oxide.

What dosage forms it comes in:

TASIGNA is supplied as a hard capsule.

Each capsule of 150 mg contains 150 mg of nilotinib (as nilotinib hydrochloride monohydrate) and each capsule of 200 mg contains 200 mg of nilotinib (as nilotinib hydrochloride monohydrate).

- The 150 mg capsules are red. A black imprint is stamped on each capsule (“NVR/BCR”).
- The 200 mg capsules are light yellow. A red imprint is stamped on each capsule (“NVR/TKI”).

TASIGNA is available in monthly packs:

- The monthly pack contains 112 capsules divided into 4 individual weekly blister-packs.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions:
TASIGNA should be given under the supervision of a doctor experienced in the use of anti-cancer drugs. Serious side effects with TASIGNA include:
• Sudden cardiac deaths,
• Prolongation of the QT interval (abnormal electrical signal of the heart),
• Ischemic heart disease (heart disorder), ischemic, cerebrovascular events (stroke or other problems due to decreased blood flow to the brain) and peripheral arterial occlusive disease (PAOD) (problems with decreased blood flow to your leg), rare fatal cases have been reported,

• Liver toxicity (increase of liver enzymes), fatal cases have been reported,
• Pancreatitis (inflammation of the pancreas),
•Myelosuppression (decrease of the production of blood cells).
TASIGNA should not be used in patients who have uncorrectable low levels of potassium or magnesium.

TASIGNA should only be stopped under the supervision of a doctor experienced in the treatment of patients with CML.

BEFORE you use TASIGNA talk to your doctor or pharmacist if you:

- have **a heart disorder**, or a heart rhythm disorder (or a family history of heart rhythm disorder) such as an irregular heartbeat or an abnormal electrical signal of the heart called "prolongation of the QT interval",
- have a personal history of fainting spells,
- have a family history of sudden cardiac death at age of less than 50 years,
- are being **treated with medicines** that affect the heart beat (antiarrhythmics) or medicines that may have an unwanted effect on the function of the heart (QT prolongation) (see also other drugs that may interact with TASIGNA under "*INTERACTIONS WITH THIS MEDICATION*"),
- have electrolyte problems (*e.g.*, low blood potassium levels) or conditions that could lead to electrolyte disturbances (*e.g.*, vomiting, diarrhea, dehydration),
- have an eating disorder or are following a strict diet;
- have diabetes, especially with associated nerve disorders;
- had a stroke or other problems due to decreased blood flow to the brain,
- have problems with decreased blood flow to your legs,
- have liver/kidney disease,
- have had pancreatitis (inflammation of the pancreas),
- have intolerance to lactose (milk sugar). TASIGNA contains lactose,
- are pregnant or plan to get pregnant. TASIGNA is not recommended during pregnancy as it may harm the fetus. Women who can get pregnant must use highly effective birth control during treatment with TASIGNA and at least 4 weeks after ending treatment,
- are a male patient and are concerned about your fertility (ability to father a child),
- are a sexually active male. Men who take TASIGNA must use highly effective birth control during treatment with TASIGNA and at least 4 weeks after ending treatment. Tell your doctor right away if your female partner becomes pregnant,
- breast feeding or plan to breast feed. Women should not breast feed while taking TASIGNA and for two weeks after the last dose,
- have had a surgical procedure involving the removal of the entire stomach (total gastrectomy).
- have ever had or might now have a hepatitis B virus infection (a viral infection of the liver). This is because during treatment with TASIGNA, hepatitis B may become active again, which can be fatal in some cases. Your doctor will check for signs of this infection before and during treatment with TASIGNA.

TASIGNA can cause a possible life-threatening heart problem called QTc prolongation. QTc prolongation causes an irregular heart beat, which may uncommonly (0.17%) lead to sudden cardiac death. These heart rhythm disturbances are more likely in patients with risk factors, such as heart disease, or in the presence of certain interacting drugs. If you experience any symptoms of a possible heart rhythm disturbance, such as dizziness, palpitations (sensation of rapid, pounding, or irregular heart beat), fainting, or seizures, you should seek immediate medical attention.

Blood tests will also monitor the level of fatty substances (cholesterol and lipids) and sugar (glucose) in your blood.

Your doctor will check your treatment and may discuss the option of stopping treatment. If you choose to stop taking TASIGNA, your doctor will continue to monitor your CML and may tell you to re-start TASIGNA if your condition requires it.

There is no experience with the use of TASIGNA in children and adolescents.

During the treatment with TASIGNA, you will need to have certain tests, including blood tests, to monitor how TASIGNA works.

TASIGNA may cause dizziness. DO NOT drive or use machines if you feel dizziness or are unable to see well while taking TASIGNA.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor or pharmacist **before taking TASIGNA** if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. This includes in particular:

- antiarrhythmics such as amiodarone, disopyramide, procainamide, quinidine, sotalol, digoxin, ibutilide, flecainide, propafenone - used to treat irregular heart beat;

- verapamil - used to treat high blood pressure and some types of irregular heart beat;
- chloroquine, halofantrine, clarithromycin, haloperidol, moxifloxacin, methadone, bepridil, pimozide - medicines that may have an unwanted effect on the function of the heart (QT prolongation);
- laxatives, enemas, water pills, amphotericin B, high dose corticosteroids - medicines that can disturb electrolyte levels;
- chlorpromazine, droperidol, ziprasidone - used to stabilize thinking and behaviour;
- fluoxetine, citalopram, venlafaxine, tricyclic/tetracyclic antidepressants e.g. amitriptyline, imipramine, maprotiline – used to treat mood disorder;
- pentamidine – used to prevent and treat pneumocystis carinii pneumonia;
- chloroquine – used to treat malaria;
- vorinostat, sunitinib, lapatinib – used to treat cancers;
- salmeterol, formoterol – used to treat asthma;
- ketoconazole, itraconazole, voriconazole, levofloxacin, ciprofloxacin, fluconazole, erythromycin, clarithromycin, telithromycin, tacrolimus, cefazolin - used to treat infections;
- domperidone – used to treat gastrointestinal motility disorder;
- metoclopramide, prochlorperazine, ondansetron and dolasetron- used to treat nausea;
- ritonavir - an anti-HIV medicine from the class "antiproteases";
- carbamazepine, phenobarbital, phenytoin - used to treat epilepsy;
- rifampicin - used to treat tuberculosis;
- St. John's Wort - a herbal product (also known as *Hypericum Perforatum);*
- midazolam - used to relieve anxiety before surgery;
- warfarin - used to treat blood coagulation disorders (such as blood clots or thromboses);
- morphine, methadone - used to treat moderate to severe pain;
- buprenorphine- substitute treatment for opioids dependence;
- cyclosporine A- used to prevent organ transplantations rejections, and to treat autoimmune conditions;
- alfentanil and fentanyl - used to treat pain and used as a sedative before or during surgery or medical procedure;
- cyclosporine, sirolimus and tacrolimus - medicines that suppress the "self-defense" ability of the body and fight infections - commonly used to prevent the rejection of transplanted organs such as liver, heart and kidney;
- dihydroergotamine and ergotamine – used to treat dementia;
- levothyroxine– used to treat thyroid deficiency
- statins (such as simvastatin and lovastatin)- class of drugs used to treat high level of fats in blood.

In addition, if you are taking TASIGNA, discuss with your doctor before taking antacids (medicines against heartburn). These medications need to be taken separately from TASIGNA:

- antacids called H2 blockers which suppress the production of acid in the stomach – should be taken approximately 10 hours before and approximately 2 hours after you take TASIGNA;
- antacids such as those containing aluminum hydroxide, magnesium hydroxide and simethicone which neutralize the high acidity of the stomach – should be taken approximately 2 hours before or approximately 2 hours after you take TASIGNA.

If you need to see other doctors, you should also tell him or her that you are taking TASIGNA.

Do not take TASIGNA with food. Take the capsules at least 2 hours after any food and then wait at least 1 hour before eating again. Taking TASIGNA with food may increase the amount of TASIGNA in the blood, possibly to a harmful level.

Do not take any products or juices containing grapefruit, star fruit, pomegranate, Seville oranges or similar fruits while taking TASIGNA. This may increase the amount of TASIGNA in blood, possibly to a harmful level.

If you are unable to swallow capsules, you may mix the content of each capsule in one teaspoon of applesauce (pureed apple) and swallow the mixture immediately. No other food should be used.

PROPER USE OF THIS MEDICATION

Usual dose:

Always take TASIGNA exactly as your doctor has told you.

Usual starting dose:

- Newly diagnosed Ph+CML in chronic phase: 300 mg (2 capsules of 150 mg) twice a day, approximately every 12 hours.

- Chronic phase and accelerated phase Ph+CML in patients who had a previous treatment: 400 mg (2 capsules of 200 mg) twice a day, approximately every 12 hours.

Capsules to be taken orally on an empty stomach, at least two hours after any food and wait at least 1 hour before eating again.

Swallow the capsules whole with water. Do not open the capsules.

If you are unable to swallow capsules:

- **Open** the capsules
- **Mix** the content of each capsule in one teaspoon of applesauce (pureed apple)

  Use **only one single teaspoon** of applesauce (not more).

  Use **only applesauce** (no other food).

Swallow the mixture **immediately**

Treatment Discontinuation:

Your doctor may discuss with you the option of stopping treatment based on a specific blood test.

If you and your doctor decide you should stop taking TASIGNA, your doctor will continue to carefully monitor your CML. Your doctor may tell you to re-start TASIGNA if your condition requires it.

Overdose:

If you have taken more TASIGNA than you should have, or if someone else accidentally takes your capsules, contact your doctor or the nearest hospital emergency room or a local poison control centre immediately. You may be asked to show them the pack of capsules.

Missed Dose:

If you miss a dose, take your next dose as scheduled. Do not take a double dose to make up for the forgotten capsules.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

As with all medicines, TASIGNA can cause side effects. The side effects of TASIGNA are as follows:

Very common:

- nausea, constipation, vomiting;
- headache;
- muscle pain, pain in joints;
- itching, rash, hives;
- hair loss;
- tiredness (fatigue)
- pain in muscles, joints, bones, the extremities and /or the spine if you stop treatment with TASIGNA.

If any of these affects you severely, tell your doctor.

Common:

- upper respiratory tract infections
- abdominal pain, dyspepsia (digestion problems); diarrhea; eating disorder (anorexia), disturbed sense of taste;
- pain (bone and extremity);
- muscle spasms;
- skin reddening, dry skin;
- insomnia, depression, anxiety;
- weakness;
- dizziness, spinning sensation (vertigo).

If any of these affects you severely, tell your doctor.

TASIGNA may also cause:

- a decrease of the production of blood cells (low levels of white cells, red cells, platelets);

- an increased blood level of lipase or amylase (inflammation of the pancreas);

- an increase in liver enzymes (liver dysfunction or toxicity);
- an increased blood level of creatinine (reduced kidney function), and high or low levels of potassium or low level of magnesium.

- an increase of cholesterol and other fats (lipids) in your blood.

- low blood level of insulin (an enzyme regulating blood sugar level).

- an increase of prothrombin time

- a previous hepatitis B virus infection (a viral infection of the liver) to become active again when you have had a hepatitis B infection in the past (hepatitis B virus reactivation), which can be fatal in some cases

If you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Call your doctor as soon as possible if you faint (loss of consciousness) or have an irregular heartbeat while taking TASIGNA as these may be due to a serious heart condition.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
	Only if severe	In all cases	
Very common or common -Fever, easy bruising, frequent Infections (changes in blood test results).		√	
Common -Sensation of tingling, pain or numbness in fingers and toes (paraesthesia).		√	
- Chest pain, or discomfort, high blood pressure, irregular heart rhythm blue discoloration of the lips, tongue or skin (heart disorders).		√	
-Irregular heartbeat, fainting, loss of consciousness (prolongation of the QT interval).		√	
- Abdominal pain.	√		
- Fever.	√		
-Difficulty breathing or painful, cough, wheezing with or without fever (lung disorders).		√	
- Severe upper (middle or left) abdominal pain (possible signs of inflammation of pancreas)		√	
Common or uncommon -Rapid weight gain, swelling of hands, ankles, feet or face (signs of water retention).		√	
Uncommon - Yellow skin and eyes, nausea, loss of appetite, dark-colored urine (liver damage).		√	
- Chest pain, irregular heart rhythm (fast or slow) (cardiac failure).		√	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
	Only if severe	In all cases	
-Diarrhea.	√		
-Vomiting.	√		
-Nausea.	√		
-Abdominal pain, nausea, vomiting of blood, black stools, constipation, heartburn, swelling or bloating of the abdomen (gastrointestinal disorders).		√	
- pain or discomfort, weakness, or cramping in leg muscles which may be due to decreased blood flow, ulcers that heal slowly or not at all and noticeable changes in color (blueness or paleness) or temperature (coolness) as these symptoms could be signs of artery blockage in the affected limb (leg or arm) and digits (toes and fingers).		√	
-Generally feeling unwell.	√		
-Bone pain.		√	
-Pain in joints.		√	
-Excessive thirst, high urine output, increased appetite with weight loss, tiredness (high level of sugar in the blood).		√	
-Difficulty and pain when passing urine, exaggerated sense of needing to urinate, blood in urine (urinary tract disorders).		√	
-Fast heart beat, bulging eyes, weight loss, swelling at front of the neck (overactive thyroid gland).		√	
-Severe headache often accompanied by nausea, vomiting and sensitivity to light (migraine).		√	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM			
Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
	Only if severe	In all cases	
Uncommon or unknown frequency -Weakness or paralysis of limbs or face, difficulty speaking, severe headache, seeing, feeling or hearing things that are not there, loss of consciousness, confusion, disorientation, trembling (nervous system disorders such as intracranial hemorrhage).		√	
-Thirst, dry skin, irritability, dark urine, decreased urine output (kidney disorders).		√	
- Blurred vision, loss of vision in eye, increased sensitivity of the eyes to light, eye pain or redness, swelling and itching of the eyelids, decreased sharpness of vision, eye irritation (eye disorders).		√	
-Rash, painful red lumps, pain in joints and muscles (skin disorders).		√	
Unknown frequency -Muscle spasms, fever, red-brown urine (rhabdomyolysis).		√	
-Swelling and pain in one part of the body (clotting within a vein).		√	
-Weight gain, tiredness, hair loss, muscle weakness, feeling cold (underactive thyroid gland).		√	
-Dizziness, spinning sensation (hypotension).		√	
-Second malignancies (such as gastric cancer, gastrointestinal stromal tumour, pancreatic carcinoma, pancreatic neuroendocrine tumour, colon cancer).		√	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM			
Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
	Only if severe	In all cases	
Nausea, shortness of breath, irregular heartbeat, clouding of urine, tiredness and/or joint pain associated with tumor lysis syndrome (the sudden, rapid death of cancer cells due to the treatment).		√	
-fever, skin rash, joint pain and inflammation as well as tiredness, loss of appetite, nausea, jaundice (yellowing of the skin or whites of eyes), pain in the upper right abdomen, pale stools and dark urine (possible signs of hepatitis B virus reactivation)		√	
Reported from post-marketing with Unknown frequency: -Difficulty breathing, dizziness (severe allergic reaction).		√	
-Anxiety, restlessness, chest pain (cardiac tamponade).		√	
-Difficulty breathing with wheezing or coughing (bronchospasm).		√	
-Excessive thirst, high urine output, increased appetite with weight loss, tiredness (higher level of sugar in the blood).		√	
-Nausea, shortness of breath, irregular heartbeat, clouding of urine, tiredness and/or joint discomfort associated with abnormal laboratory values (such as high potassium, uric acid, and phosphorous levels and low calcium levels in the blood).		√	
-Spontaneous abortions, stillbirth and fetal malformations		√	

This is not a complete list of side effects. For any unexpected effects while taking TASIGNA, contact your doctor or pharmacist.

HOW TO STORE IT

- Keep out of the reach and sight of children.
- Do not use TASIGNA after the expiry date which is stated on the carton after EXP. The expiry date refers to the last day of that month.
- Store at room temperature (15-30°C).
- Store in the original package.

REPORTING SUSPECTED SIDE EFFECTS

To monitor drug safety, Health Canada through the Canada Vigilance Program collects information on serious and unexpected side effects of drugs. If you suspect you have had a serious or unexpected reaction to this drug you may notify Canada Vigilance:
You can report any suspected adverse reactions associated with the use of health products in the Canada Vigilance Program by one of the following 3 ways:

Report online: www.healthcanada.gc.ca/medeffect
Call toll-free at 1-866-234-2345
Complete a Canada Vigilance Reporting Form and:
. Fax toll-free to 1-866-678-6789, or
. Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701D
Ottawa, ON K1A0K9
Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of the side effect, contact your health care professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

Please consult your doctor or pharmacist with any questions or concerns you may have regarding your individual condition.

This document plus the full product monograph, prepared for health professionals can be found at: http://www.novartis.ca

or by contacting the sponsor
Novartis Pharmaceuticals Canada Inc., at:
1-800-363-8883

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