

PART III: CONSUMER INFORMATION

PrTASIGNA[®] (Nilotinib Capsules)

50 mg, 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 used to treat adults with:

- newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase.
- chronic phase and accelerated phase Ph+ CML who are no longer benefiting from other therapies for CML including imatinib.

TASIGNA is used to treat children and adolescents 2 years of age and older with:

- newly diagnosed Ph+ CML in chronic phase.
- chronic phase Ph+ CML who are no longer benefiting from other therapies for CML 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 to stop the production of these abnormal cells.

When it should not be used:

Do not use TASIGNA if you or your child:

- 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:

Colloidal silicon anhydrous, crospovidone, gelatin, iron oxide yellow, iron oxide red, lactose monohydrate, magnesium stearate, poloxamer, and titanium dioxide.

The 50 mg and 150 mg capsules also contain black iron oxide.

What dosage forms it comes in:

TASIGNA is supplied as a hard capsule, containing 50 mg, 150 mg or 200 mg nilotinib (as nilotinib hydrochloride monohydrate).

- The 50 mg capsules are red/yellow. A black imprint is stamped on each capsule ("NVR/ABL").
- 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 for 50 mg capsules contains 120 capsules divided into 3 blister-cartons of 40 capsules/carton.
- The monthly pack for 150 mg and 200 mg capsules 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 is not to 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 using TASIGNA talk to your doctor or pharmacist if you or your child:

- 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) or one of the following rare hereditary diseases:
 - Galactose intolerance
 - Lapp lactase deficiency
 - Glucose-galactose malabsorption.

This is because 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 for 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 for at least 4 weeks after ending treatment. Tell your doctor right away if your female partner becomes pregnant,
- are 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. This is called hepatitis B reactivation. 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.

TASIGNA is a treatment for adults, children and adolescents with CML. There is no experience with the use of TASIGNA in children below 2 years of age. The effects of treating children with TASIGNA for long periods of time are not known.

Children and adolescents may grow more slowly when taking TASIGNA. Your child’s doctor will measure their growth at regular visits.

Before and during the treatment with TASIGNA, certain blood tests will be done. These will monitor how TASIGNA is affecting your body. Electrocardiograms

(ECG) may also be done regularly. An ECG is a test that measures how well your heart is working.

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 or your child 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, while taking TASIGNA, speak with the 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 the patient sees other doctors while taking TASIGNA, tell them about TASIGNA use.

Do not take TASIGNA with food. 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.

PROPER USE OF THIS MEDICATION

Adults:

Always take TASIGNA exactly as your doctor has told you.

Newly diagnosed Ph+ CML in chronic phase:

- **Usual daily dose 600 mg:** take two 150 mg capsules two times a day, approximately every 12 hours.
- **Reduced daily dose 400 mg:** take two 200 mg capsules once a day.

Chronic phase and accelerated phase Ph+ CML in patients who are no longer benefitting from previous treatment for CML:

- **Usual daily dose 800 mg:** take two 200 mg capsules two times a day, approximately every 12 hours.
- **Reduced daily dose 400 mg:** take two 200 mg capsules once a day.

Children and adolescents

- Always give TASIGNA to your child exactly as the doctor has told you.
- Your child's dose will depend on their body weight and height. The doctor will calculate the correct dose to use and tell you how many capsules of TASIGNA to give to your child.
- Your child's dose of TASIGNA may change as your child grows.

Pediatric dosing of TASIGNA

Total Daily Dose	How to take this dose	
100 mg	Take one 50 mg capsule twice a day	Morning: 1 x 50 mg Evening: 1 x 50 mg
200 mg	Take two 50 mg capsules twice a day	Morning: 2 x 50 mg Evening: 2 x 50 mg
300 mg	Take one 150 mg capsule twice a day	Morning: 1 x 150 mg Evening: 1 x 150 mg
400 mg	Take one 200 mg capsule twice a day	Morning: 1 x 200 mg Evening: 1 x 200 mg
500 mg	Take one 50 mg and one 200 mg	Morning: 1 x 200 mg and 1 x 50 mg

	capsule twice a day	Evening: 1 x 200 mg and 1 x 50 mg
600 mg	Take two 150 mg capsules twice a day	Morning: 2 x 150 mg Evening: 2 x 150 mg
700 mg	Take one 200 mg and one 150 mg capsule twice a day	Morning: 1 x 200 mg and 1 x 150 mg Evening: 1 x 200 mg and 1 x 150 mg
800 mg	Take two 200 mg capsules twice a day	Morning: 2 x 200 mg Evening: 2 x 200 mg

Swallow capsules whole with water on an empty stomach. Do not consume any food for at least 2 hours before the dose is taken and for at least 1 hour after the dose is taken. Do not open the capsules.

If capsules cannot be swallowed:

- **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:

The doctor may lower the dose, stop the treatment for a short time or discuss the option of stopping treatment completely. This may be based on a specific blood test result or if you or your child feels unwell.

If treatment with TASIGNA is stopped, the doctor will continue to carefully monitor your CML or that of your child. The doctor may tell you or your child to re-start TASIGNA if the condition requires it.

Overdose:

If you or your child have taken more TASIGNA than directed, or if someone else accidentally takes the 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 a dose is missed, take the 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. These are not all the possible side effects that may be experienced when taking TASIGNA. If any side effects not listed here are experienced, or these affect you or your child severely, tell your doctor or pharmacist.

- fatigue;
- weakness;
- muscle pain;
- itching;
- hair loss;
- upper respiratory tract infections;
- dyspepsia (digestion problems), eating disorder (anorexia), disturbed sense of taste;
- skin reddening;
- insomnia, depression, anxiety.

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.

If you are the caregiver of a child who is being treated with TASIGNA, tell the doctor if any of the above conditions apply to your child.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Frequency / Symptom / effect		Talk with your healthcare professional		Stop taking drug and get immediate medical help
		Only if severe	In all cases	
Very Common or Common	Changes in blood test results: Chills, fever, easy bruising, frequent, infections, fatigue		✓	
	High levels of		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Frequency / Symptom / effect		Talk with your healthcare professional		Stop taking drug and get immediate medical help
		Only if severe	In all cases	
	bilirubin in the blood: Yellow skin and eyes, pale stool, dark urine, loss of appetite, fatigue			
	Nausea	✓		
Common	Parasthesia: Sensation of tingling, pain or numbness in fingers and toes		✓	
	Heart Disorders: Chest pain, or discomfort, high blood pressure, irregular heart rhythm blue discoloration of the lips, tongue or skin		✓	
	Heart failure: Chest pain, irregular heart rhythm (fast or slow)		✓	
	Prolongation of QT interval: Irregular heartbeat, fainting, loss of consciousness		✓	
	Abdominal pain	✓		
	Fever	✓		
	Lung Disorders: Difficulty breathing or painful, cough, wheezing with or without fever		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM			
Frequency / Symptom / effect	Talk with your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
	Inflammation of the pancreas (pancreatitis): Severe upper (middle or left) abdominal pain		✓
	Growth Retardation: (when a child is not growing at a normal rate for their age)		✓
Common or uncommon	Water retention: Rapid weight gain, swelling of hands, ankles, feet or face		✓
	High blood sugar: Excessive thirst, high urine output, increased appetite with weight loss, tiredness		✓
Uncommon	Liver Damage: Yellow skin and eyes, nausea, loss of appetite, dark-colored urine		✓
	Diarrhea	✓	
	Vomiting	✓	
	Gastrointestinal disorders: Abdominal pain, nausea, vomiting of blood, black stools, constipation, heartburn, swelling or bloating of the abdomen		✓
	Blocked artery in leg, arm, finger or toe: pain or discomfort, weakness, or cramping in leg		✓

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM			
Frequency / Symptom / effect	Talk with your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
	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)		
	Generally feeling unwell	✓	
	Bone pain		✓
	Pain in joints		✓
	Urinary tract disorders: Difficulty and pain when passing urine, exaggerated sense of needing to urinate, blood in urine		✓
	Overactive thyroid gland (hyperthyroid): Fast heart beat, bulging eyes, weight loss, swelling at front of the neck		✓
	Low levels of growth hormone (growth hormone deficiency): growing more slowly, short stature, weight gain especially around the body, changes in muscle mass, changes in mood, delay in start of puberty	✓	
	Migraine: Severe headache often		✓

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Frequency / Symptom / effect	Talk with your healthcare professional		Stop taking drug and get immediate medical help	
	Only if severe	In all cases		
	accompanied by nausea, vomiting and sensitivity to light			
Uncommon or Unknown Frequency	Nervous system disorders (such as bleeding in the skull): 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		✓	
	Kidney disorders (including kidney failure): Thirst, dry skin, irritability, dark urine, decreased urine output		✓	
	Eye 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		✓	
	Skin disorders: Rash, painful red lumps, pain in joints and muscles		✓	
	Underactive thyroid gland		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Frequency / Symptom / effect	Talk with your healthcare professional		Stop taking drug and get immediate medical help	
	Only if severe	In all cases		
	(hypothyroid): Weight gain, tiredness, hair loss, muscle weakness, feeling cold			
Unknown Frequency	Rhabdomyolysis (breakdown of damaged muscle): Muscle spasms, fever, red-brown urine		✓	
	Blood clot in a vein: Swelling and pain in one part of the body		✓	
	Low blood pressure: Dizziness, spinning, sensation		✓	
	Second malignancies (such as gastric cancer, gastrointestinal stromal tumour, pancreatic carcinoma, pancreatic neuroendocrine tumour, colon cancer)		✓	
	Tumour lysis syndrome (the sudden, rapid death of cancer cells due to the treatment): Nausea, shortness of breath, irregular heartbeat, clouding of urine, tiredness and/or joint pain		✓	

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

Frequency / Symptom / effect	Talk with your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Hepatitis B reactivation (a previous viral infection of the liver becomes active again): 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. Hepatitis B reactivation can be fatal in some cases		✓	
Reported from post-marketing with Unknown Frequency Severe allergic reaction: Rash, hives, swelling of the face, lips tongue or throat, difficulty swallowing or breathing, dizziness		✓	
Cardiac tamponade: Anxiety, restlessness, chest pain		✓	
Bronchospasm: Difficulty breathing with wheezing or coughing		✓	
Abnormal laboratory values: Nausea, shortness of breath, irregular heartbeat, clouding of urine, tiredness and/or joint discomfort associated		✓	

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

Frequency / Symptom / effect	Talk with your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
with blood test results (such as high potassium, uric acid, and phosphorous levels and low calcium levels in the blood)			
Spontaneous abortions, stillbirth and fetal malformations.		✓	
Facial paralysis (weakness and paralysis of face muscles): loss of movement on one side of the face; drooping eye, drooping corner of the mouth, difficulty closing your eye, asymmetry of face		✓	

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 Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

Please consult the 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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