

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrTASIGNA®

nilotinib capsules (as nilotinib hydrochloride monohydrate)

Read this carefully before you start taking **Tasigna** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Tasigna**.

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 failure or 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 chronic myeloid leukemia (CML).

What is Tasigna 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.

How does Tasigna work?

CML is caused by a change in your DNA (genetic material) that triggers a signal in your body to produce abnormal white blood cells. Tasigna blocks this signal to stop of making these abnormal cells.

What are the ingredients in Tasigna?

Medicinal ingredients: Nilotinib.

Non-medicinal ingredients: Capsules: 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.

Tasigna comes in the following dosage forms:

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.

Do not use Tasigna if:

- You have a condition that causes an abnormal electrical signal in your heart (prolongation of QT interval).
- You have uncorrectable low levels of potassium or magnesium.
- You are allergic (hypersensitive) to nilotinib or any of the other ingredients of Tasigna.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Tasigna. Talk about any health conditions or problems you may have, including if you:

- 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 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.

Other warnings you should know about:

Lactose Intolerance:

Tasigna contains lactose. Tell your doctor if you have lactose intolerance or one of the following rare hereditary diseases:

- Galactose intolerance
- Lapp lactase deficiency
- Glucose-galactose malabsorption.

Heart Conditions:

Tasigna can cause sudden cardiac death or other serious heart conditions such as QTc prolongation. QTc prolongation causes an irregular heart beat, which can be life threatening. These heart rhythm disturbances are more likely if;

- you have a heart condition,
- you have a family history of heart conditions, or
- you are taking medicines that affect your 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”).

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.

Growth and Development:

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

Medical Tests:

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.

Driving and Heavy Machinery:

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

Reproductive Health:

Men who take Tassigna must use highly effective birth control during treatment with Tassigna, and for at least 4 weeks after ending treatment. Tell your doctor right away if your female partner becomes pregnant.

Pregnancy and Breastfeeding:

Tassigna 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 Tassigna and for at least 4 weeks after ending treatment.

You should not breast feed while taking Tassigna and for two weeks after the last dose.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following medicines may interact with Tassigna, used to treat/or:

- **Anti-HIV medicine from the class “antiproteases”:**
Ritonavir;
- **Asthma:**
Formoterol, salmeterol;
- **Blood coagulation disorders (such as blood clots or thromboses):**
Warfarin;
- **Cancers:**
Imatinib, lapatinib, sunitinib, vorinostat;
- **Dementia:**
Dihydroergotamine and ergotamine;
- **Epilepsy:**
Carbamazepine, phenobarbital, phenytoin;
- **Gastrointestinal motility disorder:**
Domperidone;
- **Herbal product (also known as Hypericum Perforatum):**
St. John’s Wort;
- **High blood pressure and some types of irregular heart beat:**
Verapamil;
- **High level of fats in blood (class of drugs):**
Statins (such as simvastatin and lovastatin);
- **Infections:**
Cefazolin, ciprofloxacin, clarithromycin, erythromycin, fluconazole, itraconazole, ketoconazole, levofloxacin, rifampin, tacrolimus, telithromycin, voriconazole;

- **Irregular Heartbeat:**
Antiarrhythmics such as amiodarone, digoxin, disopyramide, flecainide, ibutilide, procainamide, propafenone, quinidine, sotalol;
- **Malaria:**
Chloroquine;
- **Medicines that can disturb electrolyte levels:**
Amphotericin B, enemas, high dose corticosteroids, laxatives, water pills;
- **Medicines that may have an unwanted effect on the function of the heart (QT prolongation):**
Bepidil, chloroquine, clarithromycin, halofantrine, haloperidol, methadone, moxifloxacin, pimozone;
- **Mood disorder:**
Citalopram, fluoxetine, tricyclic/tetracyclic antidepressants (e.g.: amitriptyline, imipramine, maprotiline), venlafaxine;
- **Nausea:**
Dolasetron, metoclopramide, ondansetron, prochlorperazine;
- **Opioids dependence (substitute treatment):**
Buprenorphine-;
- **Pain (moderate to severe):**
Methadone, morphine;
- **Pain and used as a sedative before or during surgery or medical procedure:**
Alfentanil and fentanyl;
- **Pneumocystis carinii pneumonia:**
Pentamidine;
- **Prevent organ transplantations rejections, and to treat autoimmune conditions:**
Cyclosporine A;
- **Prevent the rejection of transplanted organs such as liver, heart and kidney:**
Cyclosporine, sirolimus and tacrolimus - medicines that suppress the “self-defense” ability of the body and fight infections;
- **Relieve anxiety before surgery:**
Midazolam;
- **Stabilize thinking and behaviour:**
Chlorpromazine, droperidol, ziprasidone;
- **Thyroid deficiency:**
Levothyroxine;
- **Tuberculosis:**

Rifampicin;

Taking Tasigna with Antacids:

While taking Tasigna, speak with your healthcare professional 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 or 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 2 hours after you take Tasigna.

Taking Tasigna with Food and Drink:

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.

How to take Tasigna:

- Always take Tasigna exactly as your healthcare professional has told you.
- Your healthcare professional may lower your dose or stop treatment. This may be based on a specific blood test result or if you feel unwell.
- If treatment with Tasigna is stopped, your healthcare professional will continue to carefully monitor your CML. Your doctor may tell you to re-start Tasigna if you require it.
- 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.

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**.

Usual dose

Adults:

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:

- 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
200 mg	Take two 50 mg capsules twice a day
300 mg	Take one 150 mg capsule twice a day
400 mg	Take one 200 mg capsule twice a day
500 mg	Take one 50 mg and one 200 mg capsule twice a day
600 mg	Take two 150 mg capsules twice a day
700 mg	Take one 200 mg and one 150 mg capsule twice a day
800 mg	Take two 200 mg capsules twice a day

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.

What are possible effects from using Tasigna?

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.

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON			
Changes in blood test results: Chills, fever, easy bruising, frequent, infections, fatigue		✓	
High levels of 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		✓	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
fever			
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 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:		✓	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
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 accompanied by nausea, vomiting and sensitivity to light		✓	
UNCOMMON OR UNKNOWN			
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 (hypothyroid): Weight gain, tiredness, hair		✓	
UNKNOWN FREQUENCY			

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
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		✓	
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		✓	
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:		✓	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Nausea, shortness of breath, irregular heartbeat, clouding of urine, tiredness and/or joint discomfort associated 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.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

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.

Storage:

- Keep out of the reach and sight of children.
- Store at room temperature (15-30°C).
- Store in the original package.

If you want more information about Tasigna:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website (<http://www.novartis.ca>), or by calling 1-800-363-8883.

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