

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr **BOSULIF**[®]

bosutinib tablets

Read this carefully before you start taking **BOSULIF** 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 **BOSULIF**.

Serious Warnings and Precautions

Serious side effects with BOSULIF include:

- Drug interactions with inhibitors or inducers of CYP3A4 enzyme. Do NOT use BOSULIF with strong and moderate CYP3A4 inhibitors and inducers (see **Serious Drug and Drug-Food Interactions** below)
- Gastrointestinal problems (vomiting and diarrhea)
- Liver problems
- Heart problems that may lead to death
- Fluid in the lungs and around the heart (fluid retention)
- Bleeding
- Abnormal electrical signal of the heart

What is BOSULIF used for?

BOSULIF is used to treat adults:

- who have a new diagnosis of a white blood cell cancer called Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in a chronic phase or
- who have Ph+ CML in a chronic, accelerated, or blast phase (the blood cancer grows faster in accelerated or blast than in chronic phase) and for whom previous medicines to treat Ph+ CML have either not worked or not been suitable.

A qualified healthcare professional experienced in the use of anticancer therapies and in the treatment of CML should prescribe BOSULIF.

BOSULIF is NOT recommended for use in children less than 18 years of age.

How does BOSULIF work?

BOSULIF works by slowing down the growth and spread of cancer cells in patients with CML.

What are the ingredients in BOSULIF?

Medicinal ingredients: bosutinib

Non-medicinal ingredients: croscarmellose sodium, iron oxide yellow (for 100 mg tablet), iron oxide yellow and iron oxide red (for 400 mg tablet), iron oxide red (for 500 mg tablet), magnesium stearate,

microcrystalline cellulose, poloxamer, polyethylene glycol, polyvinyl alcohol, povidone, talc, and titanium dioxide

BOSULIF comes in the following dosage forms:

Tablets: 100 mg, 400 mg, and 500 mg

Do not use BOSULIF if you:

- are allergic to bosutinib or any of the other ingredients of BOSULIF
- have an abnormal electrical signal of the heart (prolongation of QT interval)
- have uncorrectable low levels of potassium or magnesium
- have liver problems (such as liver failure)

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

- have or have had a liver problem.
- have or have had a heart problem.
- have or have had a pancreas problem.
- have or have had a kidney problem.
- have gastrointestinal problems (vomiting and diarrhea).
- have or have had in the past, a hepatitis B virus infection (a viral infection of the liver). This is because during treatment with BOSULIF, hepatitis B may become active again which can lead to death in some cases. Your doctor will test for signs of this infection before treatment with BOSULIF and while on treatment if required.

Other warnings you should know about:

Female patients:

Pregnancy and birth control

- If you are pregnant or plan to become pregnant, there are specific risks you should discuss with your healthcare professional.
- Do NOT become pregnant while taking BOSULIF. It may cause harm to your unborn child.
- Use highly effective birth control during treatment and for at least one month after your last dose of BOSULIF.
- Tell your healthcare professional right away if you become pregnant.

Breast-feeding

- BOSULIF may pass into your breast milk and harm your baby.
- Do NOT breast-feed during treatment with BOSULIF.
- Talk to your healthcare professional about the best way to feed your baby during treatment with BOSULIF.

Male patients:

- Use highly effective birth control each time you have sex with a woman who is pregnant, may be pregnant or could become pregnant. Continue using birth control for at least 4 weeks after the last dose of BOSULIF.

- Tell your healthcare professional right away if your sexual partner becomes pregnant.

Fertility:

Treatment with BOSULIF may affect your ability to have children in both male and female patients. Talk to your healthcare professional if this is a concern for you.

Driving and using machines:

Before engaging in tasks that require special attention, wait until you know how you respond to BOSULIF. Do NOT drive or use machines if you feel tired, dizzy, or experience any changes in vision while taking BOSULIF.

Monitoring and laboratory tests:

Your healthcare professional will regularly monitor and assess your health before and while you are taking BOSULIF. This may include blood tests, urine tests and ECG recording.

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

Serious Drug and Drug-Food Interactions

Do NOT take any products or juice containing grapefruit, star fruit, pomegranate, Seville oranges or similar fruits while taking BOSULIF. They may change the amount of BOSULIF in your body.

While taking BOSULIF, avoid taking drugs that are used to:

- treat fungal infections such as ketoconazole, itraconazole, voriconazole, posaconazole, and fluconazole
- treat human immunodeficiency virus (HIV) infections such as lopinavir/ritonavir, atazanavir, indinavir, nelfinavir, saquinavir, darunavir/ritonavir, amprenavir, efavirenz, etravirine and fosamprenavir.
- treat high blood pressure such as diltiazem, verapamil, bosentan and mibefradil
- treat depression such as nefazodone and St. John's wort (a herbal preparation obtained without a prescription)
- treat bacterial infections such as erythromycin, clarithromycin, ciprofloxacin and nafcillin
- treat tuberculosis such as rifampicin
- treat epilepsy such as phenytoin and carbamazepine
- prevent and control nausea (feeling sick) and vomiting, such as aprepitant
- treat certain types of sleep disorders, such as modafinil
- treat cancers, such as crizotinib and imatinib
- treat hepatitis C virus, such as telaprevir
- treat low sodium, such as conivaptan

The following may also interact with BOSULIF:

- Vandetanib, sunitinib, nilotinib, lapatinib (other cancer medicines).

- Quinidine, amiodarone and other medicines for heart rhythm problems (anti-arrhythmic medicines).
- Lansoprazole, dexlansoprazole, omeprazole, esomeprazole, pantoprazole, rabeprazole (medicines for reducing stomach acid).
- Amitriptyline and imipramine (medicine for depression).
- Pimozide, ziprasidone, haloperidol (medicine for psychoses).
- Quinine and chloroquine (medicine to treat malaria).
- Domperidone, dolasetron and ondansetron (medicine for nausea and vomiting).
- Formoterol and salmeterol (asthma medicines).
- Water pills, laxatives (medicine that decrease electrolyte levels).

Know the medicines you take. Keep a list of your medicines, both prescription and non-prescription, and show it to your doctor and pharmacist when you get a new medicine. Do NOT take other medicines with BOSULIF until you have discussed with your doctor.

How to take BOSULIF:

- Always take BOSULIF exactly as your healthcare professional has told you. Check with your doctor or pharmacist if you are not sure.
- BOSULIF should be taken with a meal.
- Swallow BOSULIF tablets whole. Do NOT cut, crush or dissolve the tablets.
- Do NOT drink grapefruit juice or eat grapefruit, grapefruit products, star fruit, pomegranate, Seville oranges and other similar fruits. They may change the amount of BOSULIF in your body.

Usual dose:

Adults (18 years of age and older)

- Patients with newly-diagnosed chronic phase Ph+ CML: 400 mg once daily.
- Patients with chronic, accelerated, or blast phase Ph+ CML whose previous medicines to treat Ph+CML have either not worked or not been suitable: 500 mg once daily.

Your healthcare professional will monitor your health during treatment with BOSULIF. They may interrupt, change, or stop your dose. This may occur based on your current health, or if you experience certain side effects.

Overdose:

If you think you have, or a person you are caring for, taken too much BOSULIF, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

If possible, show your healthcare professional the blister pack, or this leaflet. You may require medical attention.

Missed Dose:

If dose is missed by:

- **Less than 12 hours**, take your recommended dose.

- **More than** 12 hours, take your next dose at your regular time on the following day. Do not take a double dose to make up for the forgotten tablets.

What are possible side effects from using BOSULIF?

These are not all the possible side effects you may have when taking BOSULIF. If you experience any side effects not listed here, tell your healthcare professional.

Side effects include:

- Rash
- Nasopharyngitis (common cold virus): sore throat combined with runny nose
- Back pain
- Dysgeusia (altered taste perception): persistent foul, salty, rancid, or metallic taste sensation in the mouth
- Gastrointestinal toxicity: diarrhea, vomiting, stomach pain, nausea, and/or decrease of appetite
- Gastritis (stomach inflammation): stomach irritation
- Arthralgia (Joint pain): mild to severe pain, limited joint motion, locking of the joint, stiffness
- Fatigue
- Headache
- Dizziness
- Fever
- Influenza (viral infection that affects the respiratory system): fever, body aches, fatigue
- Bronchitis (inflammation of the bronchial tubes): cough, chest tightness, wheezing
- Dehydration (excessive loss of body fluid)
- Itching, urticaria (hives), acne (conditions affecting the skin)

Tell your doctor if you have any side effect that bothers you or that does not go away.

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			
Myelosuppression (decrease in bone marrow activity resulting in fewer red blood cells, white blood cells, and platelets): fatigue, shortness of breath, dizziness, weakness, rapid breathing, headache, bleeding, infections,		✓	

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	
and skin pallor			
Dyspnea (difficulty breathing): shortness of breath, chest tightness		✓	
Changes in biochemical markers used to determine if BOSULIF is affecting your liver, kidney, and/or pancreas (shown in test results)		✓	
COMMON			
Hypertension (high blood pressure): headache, nosebleed, fatigue or confusion, vision problems, shortness of breath, chest pain, difficulty breathing, and irregular heartbeat		✓	
Neutropenia (abnormally low number of neutrophils [a type of white blood cell] in the blood): fever, chills or sweating, sore throat, mouth sores, infections, cough, and difficulty breathing		✓	
Pericardial effusion (accumulation of fluid around the heart): chest pain or discomfort, fainting, shortness of breath, nausea, elevated heart rate, elevated breathing rate, swelling of upper and lower extremities, pain in upper right abdomen		✓	
Edema (fluid retention): Swelling of hands, feet or face		✓	
Renal failure, renal impairment (kidney failure, kidney impairment): decreased urine output, fluid retention, swelling of upper and lower extremities, shortness of breath, fatigue, nausea, weakness, and irregular heartbeat		✓	
Hepatotoxicity (liver injury or impairment of liver function): jaundice, abdominal pain in upper right abdomen, fatigue, loss of			✓

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	
appetite, nausea, vomiting, rash, fever, weight loss, itching, and dark-coloured urine			
Pneumonia (inflammation of the lungs caused by infection): cough which may produce green, yellow or bloody mucus, fever, chills, and difficulty breathing, shortness of breath, rapid, shallow breathing, chest pain that worsens with deep breathing or coughing, and fatigue		✓	
Hyperkalemia (abnormally high level of potassium in the blood): abdominal pain, diarrhea, chest pain, abnormal heartbeat, nausea, vomiting, and muscle weakness or numbness		✓	
Hypophosphatemia (abnormally low level of phosphorous in the blood): muscle weakness, fatigue, bone pain and fractures, numbness, confusion, respiratory failure, heart failure, seizures, and coma		✓	
Pleural effusion (fluid around the lungs): cough, shortness of breath, elevated respiration rate, and chest pain, heaviness, or tightness		✓	
UNCOMMON			
Pericarditis (inflammation of the sac-like structure surrounding the heart): chest pain, cough, elevated heart rate, irregular heart rate, fever, shortness of breath, weakness, and fatigue		✓	
Gastrointestinal hemorrhage (bleeding in the stomach or intestine): black, tarry, or bright red stool, blood in vomit, abdominal cramps, dizziness, fatigue, skin pallor, shortness of breath, and weakness		✓	
Long QT syndrome (abnormal		✓	

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	
heartbeat): dizziness, heart palpitations, loss of consciousness, cardiac arrest, and seizures			
Respiratory failure (lack of oxygenated blood leading to respiratory failure): dizziness, difficulty breathing or shortness of breath, rapid breathing, fatigue, elevated heart rate, wheezing, and cyanosis		✓	
Anaphylactic shock (severe potentially life-threatening allergic reaction): dizziness, difficulty breathing and shortness of breath, rapid breathing, cyanosis, nausea or vomiting, elevated heart rate, tongue swelling, difficulty swallowing, facial swelling, and confusion			✓
Pulmonary hypertension (high blood pressure in the blood vessels leading from the heart to the lungs): shortness of breath, dizziness, chest pain/pressure, irregular heartbeat, fatigue, swelling in the upper and lower extremities, and cyanosis		✓	
Erythema multiforme (severe inflammatory skin reaction): exfoliative (scaly, peeling) skin eruptions, fever, headache, mouth sores, fatigue, pruritus, and joint pain		✓	
RARE			
Stevens-Johnson syndrome (severe skin reaction): fever, sore mouth/throat, cough, muscle aches, pruritus, severe red rash that blisters/peels with mouth sores and painful, red, watery eyes			✓
UNKNOWN FREQUENCY			
Hepatitis B (liver infection) virus reactivation: this occurs when a		✓	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
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previous hepatitis B infection becomes active again, which can be fatal in some cases. Symptoms include jaundice, abdominal pain in upper right abdomen, fatigue, loss of appetite, nausea, vomiting, rash, fever, weight loss, itching, and dark-coloured urine			

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:

Store at 20°C to 25°C.

Keep out of the reach and sight of children.

If you want more information about BOSULIF:

- 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 www.pfizer.ca, or by calling 1-800-463-6001.

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