

BOSNIB 100 & BOSNIB 500

Bosutinib Tablet (100 mg, 500 mg)

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WHAT BOSNIB IS AND WHAT IT IS USED FOR

BOSNIB contains the active substance bosutinib. It is used to treat adult patients who have a type of leukaemia called Philadelphia chromosome-positive (Ph-positive) Chronic Myeloid Leukaemia (CML) and are newly diagnosed or for whom previous medicines to treat CML have either not worked or are not suitable. Ph-positive CML is a cancer of the blood which makes the body produce too many of a specific type of white blood cell called granulocytes.

HOW BOSNIB WORKS

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

BEFORE YOU USE BOSNIB

When you must not use it

- if you are allergic to bosutinib or any of the other ingredients of this medicine
- if your doctor has told you that your liver has been damaged and is not working normally.

Before you start to use it

Talk to your doctor, pharmacist or nurse before taking BOSNIB if you:

- **have, or have had in the past, liver problems.** Tell your doctor if you have a history of liver problems including hepatitis (liver infection or inflammation) of any kind, or a history of any of the following signs and symptoms of liver problems: itching, yellow eyes or skin, dark urine, and pain or discomfort in the

right upper stomach area. Your doctor should do blood tests to check your liver function prior to your starting treatment with BOSNIB and for the first 3 months of treatment with BOSNIB, and as clinically indicated.

- **have diarrhoea and vomiting.** Tell your doctor if you develop any of the following signs and symptoms: an increase in the number of stools (bowel movements) per day over normal, an increase in episodes of vomiting, blood in your vomit, stools (bowel movements) or urine, or have black stools (tarry black bowel movements). You should ask your doctor if use of your treatment for vomiting may result in a greater risk of heart arrhythmias. You should ask your doctor if you want to use a medicine containing domperidone for the treatment of nausea and/or vomiting. Treatment of nausea or vomiting with such medicines together with BOSNIB may result in a greater risk of dangerous heart arrhythmias.
- **suffer from bleeding problems.** Tell your doctor if you develop any of the following signs and symptoms such as abnormal bleeding or bruising without having an injury.
- **have an infection.** Tell your doctor if you develop any of the following signs and symptoms such as fever, problems with urine such as burning on urination, a new cough, or a new sore throat.
- **have fluid retention.** Tell your doctor if you develop any of the following signs and symptoms of fluid retention during BOSNIB treatment such as swelling of the ankles, feet or legs; difficulty breathing chest pain or a cough (these may be signs of fluid retention in the lungs or chest).
- **have heart problems.** Tell your doctor if you have a heart disorder, such as heart failure and decreased blood flow to the heart which can lead to heart attack. Get medical help right away if you get shortness of breath, weight gain, chest pain, or swelling in your hands, ankles or feet.

- **have been told you have an abnormal heart rhythm.** Tell your doctor if you have arrhythmias or an abnormal electrical signal called “prolongation of the QT interval”. This is always important, but especially if you are experiencing frequent or prolonged diarrhoea as described above. If you faint (loss of consciousness) or have an irregular heartbeat while taking BOSNIB, tell your doctor immediately, as this may be a sign of a serious heart condition.
- **have been told that you have problems with your kidneys.** Tell your doctor if you are urinating more frequently and producing larger amounts of urine with a pale colour or if you are urinating less frequently and producing smaller amounts of urine with a dark colour. Also tell your doctor if you are losing weight or have experienced swelling of your feet, ankles, legs, hands or face.
- **have ever had or might now have a hepatitis B infection.** This is because Bosutinib 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.
- **have or have had pancreas problems.** Tell your doctor if you develop abdominal pain or discomfort.
- **have any of these symptoms: serious skin rashes.** Tell your doctor if you develop any of the following signs and symptoms of painful red or purplish rash that spread and blisters and/or other lesions begin to appear in the mucous membrane (e.g., mouth and lips).
- **notice any of these symptoms: pain in your side, blood in your urine or reduced amount of urine.** When your disease is very severe, your body may not be able to clear all the waste products from the dying cancer cells. This is called tumour lysis syndrome and can cause kidney failure and heart problems within 48 hours of the first dose of BOSNIB. Your doctor will be aware of this and may ensure you are adequately hydrated and give

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you other medicines to help prevent it.

Sun/UV protection

You may become more sensitive to the sun or UV rays while taking BOSNIB. It is important to cover sunlight-exposed areas of skin and use sunscreen with high sun protection factors (SPF).

Children and adolescents

BOSNIB is not recommended for people whose age is under 18 years. This medicine has not been studied in children and adolescents.

Taking other medicines

Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription, vitamins, and herbal medicines.

Some medicines can affect the levels of bosutinib in your body. You should inform your doctor if you are taking medicines containing active substances such as those listed below:

The following active substances may increase the risk of side effects with Bosutinib:

- ketoconazole, itraconazole, voriconazole, posaconazole and fluconazole, used to treat fungal infections.
- clarithromycin, telithromycin, erythromycin, and ciprofloxacin, used to treat bacterial infections.
- nefazodone, used to treat depression.
- mibefradil, diltiazem and verapamil, used to lower blood pressure in people with high blood pressure.
- ritonavir, lopinavir/ritonavir, indinavir, nelfinavir, saquinavir, atazanavir, amprenavir, fosamprenavir and darunavir, used to treat human immunodeficiency virus (HIV)/AIDS.
- boceprevir and telaprevir, used to treat hepatitis C.
- aprepitant, used to prevent and control nausea (feeling sick) and vomiting.
- imatinib, used to treat a type of leukaemia.

- crizotinib, used to treat a type of lung cancer called non-small cell lung cancer.

The following active substances may reduce the effectiveness of Bosutinib:

- rifampicin, used to treat tuberculosis.
- phenytoin and carbamazepine, used to treat epilepsy.
- bosentan, used to lower high blood pressure in the lungs (pulmonary artery hypertension).
- nafcillin, an antibiotic used to treat bacterial infections.
- St. John's Wort (a herbal preparation obtained without a prescription), used to treat depression.
- efavirenz and etravirine, used to treat HIV infections/AIDS.
- modafinil, used to treat certain types of sleep disorders.

These medicines should be avoided during your treatment with BOSNIB. If you are taking any of them, tell your doctor. Your doctor may change the dose of these medicines, change the dose of BOSNIB, or switch you to a different medicine.

The following active substances may affect the heart rhythm:

- amiodarone, disopyramide, procainamide, quinidine and sotalol used to treat heart disorder.
- chloroquine, halofantrine used to treat malaria.
- clarithromycin and moxifloxacin antibiotics used to treat bacterial infections.
- haloperidol, used to treat psychotic disease such as schizophrenia.
- domperidone, used to treat nausea and vomiting or to stimulate breast milk production.
- methadone, used to treat pain.

These medicines should be taken with caution during your treatment with BOSNIB. If you are taking any of them, tell your doctor. The medicines listed here may not be the only ones that could interact with BOSNIB.

Bosutinib with food and drink

Do not take BOSNIB with grapefruit or grapefruit juice, as it may increase the risk of side effects.

Pregnancy, breast-feeding and fertility

BOSNIB is not to be used during pregnancy, unless clearly necessary, because BOSNIB could harm an unborn baby. Ask your doctor for advice before taking BOSNIB if you are pregnant or might become pregnant.

Women taking BOSNIB will be advised to use effective contraception during treatment and for at least 1 month after the last dose. Vomiting or diarrhoea may reduce the effectiveness of oral contraceptives.

There is a risk that treatment with BOSNIB will lead to decreased fertility, and you may wish to seek advice about sperm storage before the treatment starts.

If you are breast-feeding, tell your doctor. Do not breast-feed during treatment with BOSNIB as it could harm your baby.

Driving and using machines

If you experience dizziness, have blurred vision or feel unusually tired, do not drive or operate machines until these side effects have gone away.

HOW TO USE BOSNIB

Always take this medicine exactly as your doctor has told you. Check with your doctor, pharmacist or nurse if you are not sure.

BOSNIB will only be prescribed to you by a doctor with experience in medicines to treat leukaemia.

How much to use

The recommended dose is 400 mg once daily for patients with newly-diagnosed CML. The recommended dose is 500 mg once daily for patients whose previous medicines to treat CML have either not worked or are not suitable.

If you have moderate or severe kidney problems, your doctor will reduce your dose by 100 mg once daily for moderate kidney problems and by an

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additional 100 mg once daily for severe kidney problems.

Your doctor may adjust the dose using the 100 mg tablets depending upon your medical conditions, upon your response to treatment and/or on any side effect you may experience. Take tablet(s) once a day with food. Swallow the tablet(s) whole with water.

When & how long to use it

Do not stop taking BOSNIB unless your doctor tells you to do so. If you are not able to take the medicine as your doctor prescribed or you feel you do not need it anymore, contact your doctor right away.

If you forget to use it

If a dose is missed by less than 12 hours, take your recommended dose. If a dose is missed by 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.

If you use too much (overdose)

If you accidentally take too many Bosutinib tablets or a higher dose than you need, contact a doctor for advice right away. If possible, show the doctor the pack, or this leaflet. You may require medical attention.

SIDE EFFECTS

Like all medicines, BOSNIB can cause side effects, although not everybody gets them.

You must immediately contact your doctor if you experience any of those serious side effects:

- **Blood disorders.** Tell your doctor right away if you have any of these symptoms: bleeding, fever or easy bruising (you might have blood or lymphatic system disorder).
- **Liver disorders.** Tell your doctor right away if you have any of these symptoms: itching, yellow eyes or skin, dark urine, and pain or discomfort in the right upper stomach area or fever.
- **Stomach/intestinal disorders.** Tell your doctor if you develop stomach

pain, heartburn, diarrhoea, constipation, nausea and vomiting.

- **Heart problems.** Tell your doctor if you have a heart disorder, such as heart failure, decreased blood flow to the heart, an abnormal electrical signal called “prolongation of the QT interval”, or if you faint (loss of consciousness) or have an irregular heart beat while taking BOSNIB.
- **Hepatitis B reactivation.** Recurrence (reactivation) of hepatitis B infection when you have had hepatitis B in the past (a liver infection).
- **Severe skin reactions.** Tell your doctor right away if you have any of these symptoms: painful red or purplish rash that spreads and blisters and/or other lesions begin to appear in the mucous membrane (e.g. mouth and lips).

Side effects with BOSNIB may include:

Very common side effects (may affect more than 1 in 10 people):

- reduction in the number of platelets, red blood cells and/or neutrophils (type of white blood cells).
- diarrhoea, vomiting, stomach pain, nausea.
- fever, swelling of hands, feet or face, fatigue, weakness.
- respiratory tract infection.
- nasopharyngitis.
- changes in blood test to determine if Bosutinib is affecting your liver and/or pancreas, kidneys.
- decrease of appetite.
- joint pain, back pain.
- headache.
- skin rash, which may be itchy and/or generalised.
- Cough
- shortness of breath.
- feeling of instability (dizziness).
- fluid in the lungs (pleural effusion).
- itching.

Common side effects (may affect up to 1 in 10 people):

- low white blood cells count (leukopenia).
- stomach irritation (gastritis), bleeding from the stomach or intestine.

- chest pain, pain.
- toxic damage to the liver, abnormal hepatic function including liver disorder.
- infection of the lung (pneumonia), influenza, bronchitis.
- when the heart does not pump blood as well as it should (heart failure).
- defect in cardiac rhythm that predisposes to fainting, dizziness and palpitation.
- increase in blood pressure.
- high level of potassium in the blood, low level of phosphorus in the blood, excessive loss of body fluid (dehydration).
- pain in the muscles.
- alteration of the sense of taste (dysgeusia).
- acute kidney failure, kidney failure, kidney impairment.
- fluid around the heart (pericardial effusion).
- ringing in the ears (tinnitus).
- urticaria (hives), acne.
- photosensitivity reaction (sensitivity to UV rays from the sun and other light sources).
- Allergic reaction.
- abnormally high blood pressure in the arteries of the lungs (pulmonary hypertension).
- acute inflammation of the pancreas (acute pancreatitis).
- respiratory failure.

Uncommon side effects (may affect up to 1 in 100 people):

- fever associated with low white blood cell count (febrile neutropenia).
- damage to the liver.
- life-threatening allergic reaction (anaphylactic shock).
- abnormal build-up of fluid in the lungs (acute pulmonary oedema).
- skin eruption.
- inflammation of the sac-like covering of the heart (pericarditis).
- a marked decrease in the number of granulocytes (a type of white blood cells).
- severe skin disorder (erythema multiforme).
- nausea, shortness of breath, irregular heartbeat, muscular cramps, seizure, clouding of urine and tiredness

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associated with abnormal laboratory test results (high potassium, uric acid and phosphorous levels and low calcium levels in the blood) that can lead to changes in kidney function and acute renal failure –(Tumour lysis syndrome (TLS)).

Not known (frequency cannot be estimated from the available data):

- severe skin disorder (Stevens-Johnson syndrome, toxic epidermal necrolysis) due to an allergic reaction, exfoliative (scaly, peeling) rash.
- interstitial lung disease (disorders causing scarring in the lungs): signs include cough, difficulty breathing, painful breathing

You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by visiting the website npra.gov.my [Consumers→ Reporting Side Effects to Medicines (ConSERF) or Vaccines (AEFI)].

STORAGE AND DISPOSAL OF BOSNIB

Storage

- Keep your medicine in the original package until it is time to take.
- Keep your medicine in a cool dry place where the temperature stays below 30°C.
- Keep this medicine out of the sight and reach of children.

Disposal

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

PRODUCT DESCRIPTION

What it looks like

BOSNIB 100: Yellow, oval, biconvex, film coated tablets, debossed with ‘‘100’’ on one side and ‘‘B’’ on other side.

BOSNIB 500: Red, oval, biconvex, film coated tablets, debossed with

‘‘500’’ on one side and ‘‘B’’ on other side.

Ingredients

Active ingredient

Each tablet contains:

Bosutinib 100mg/ Bosutinib 500mg

Inactive ingredients:

Microcrystalline cellulose, crospovidone XL, Poloxamer 188, Povidone K 25, purified water, magnesium stearate, Opadry Yellow 03F520242 (Bosnib 100), Opadry Brown 03B565081 (Bosnib 500mg), isopropyl alcohol, dichloromethane.

MAL number

BOSNIB 100: MALXXXXXXXXA

BOSNIB 500: MALXXXXXXXXA

MANUFACTURER

MSN Laboratories Private Limited,
Formulation Division, Unit-II,
Sy. No, 1277, 1319 To 1324,
Nandigama Village & Mandal,
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509228 Telangana, India

PRODUCT REGISTRATION HOLDER

MEGA LIFESCIENCES SDN BHD
B-28-02, The Ascent, Paradigm.
No.1, Jalan SS7/26A, Kelana Jaya,
47301 Petaling Jaya,
Selangor, Malaysia.

DATE OF REVISION

14/05/2025

SERIAL NUMBER

NPRA (R1) -----