Package leaflet: Information for the user

Bosutinib 100 mg film-coated tablets
Bosutinib 400 mg film-coated tablets
Bosutinib 500 mg film-coated tablets
bosutinib

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Bosutinib is and what it is used for

Bosutinib 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.

If you have any questions about how Bosutinib works or why this medicine has been prescribed for you, ask your doctor.

2. What you need to know before you take Bosutinib

Do not take Bosutinib
- if you are allergic to bosutinib or any of the other ingredients of this medicine (listed in section 6).
- if your doctor has told you that your liver has been damaged and is not working normally

Warnings and precautions
Talk to your doctor, pharmacist or nurse before taking Bosutinib
- **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 Bosutinib and for the first 3 months of treatment with Bosutinib, and as clinically indicated

- **if you 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. In particular, 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 Bosutinib may result in a greater risk of dangerous heart arrhythmias.

- **if you 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.

- **if you 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.

- **if you have fluid retention.** Tell your doctor if you develop any of the following signs and symptoms of fluid retention during Bosutinib 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).

- **if you have heart problems.** Tell your doctor if you have a heart disorder, such as 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 Bosutinib, tell your doctor immediately, as this may be a sign of a serious heart condition.

- **if you 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.

- **if you 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.

- **if you have or have had pancreas problems.** Tell your doctor if you develop abdominal pain or discomfort.

- **if you 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 spreads and blisters and/or other lesions begin to appear in the mucous membrane (e.g., mouth and lips).

- **if you 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 Bosutinib. Your doctor will be aware of this and may ensure you are adequately hydrated and give you other medicines to help prevent it.

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

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

Other medicines and Bosutinib.
Tell your doctor or pharmacist 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 Bosutinib. If you are taking any of them, tell your doctor. Your doctor may change the dose of these medicines, change the dose of Bosutinib, 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 Bosutinib. If you are taking any of them, tell your doctor.

The medicines listed here may not be the only ones that could interact with Bosutinib.

Bosutinib with food and drink
Do not take Bosutinib with grapefruit or grapefruit juice, as it may increase the risk of side effects.

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

Women taking Bosutinib 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 Bosutinib 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 Bosutinib 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.

Bosutinib contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. How to take Bosutinib

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

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

Dose and method of administration
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. In the event that 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 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 the tablet(s) once a day with food. Swallow the tablet(s) whole with water.

If you take more Bosutinib than you should
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.

If you forget to take Bosutinib
If 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 stop taking Bosutinib
Do not stop taking Bosutinib 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 have any further questions on the use of this medicine ask your doctor or pharmacist.

4. Possible side effects

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

You must immediately contact your doctor if you experience any of those serious side effects (see also section 2 “What you need to know before you take Bosutinib”):

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 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 Bosutinib.

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 Bosutinib 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.
- 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 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.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme website www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Bosutinib

Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date which is stated on the blister foil and carton after "EXP". The expiry date refers to the last day of that month.
This medicine does not require any special storage conditions.
Do not use this medicine if you notice that the pack is damaged or shows signs of tampering.
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Bosutinib contains

- The active substance is bosutinib. Bosutinib film-coated tablets come in different strengths.
  Bosutinib 100 mg: each film-coated tablet contains 100 mg bosutinib.
  Bosutinib 400 mg: each film-coated tablet contains 400 mg bosutinib.

Bosutinib 500 mg: each film-coated tablet contains 500 mg bosutinib.

- The other ingredients are: cellulose microcrystalline (E460), croscarmellose sodium (E468), silica, colloidal anhydrous, magnesium stearate. The film-coating contains poly(vinyl alcohol)(E1203), macrogols, talc (E553b), titanium dioxide (E171), iron oxide yellow (E172, for Bosutinib 100 mg and 400 mg), Iron oxide red (E172, for Bosutinib 400 mg and 500 mg).

What Bosutinib looks like and contents of the pack

Bosutinib 100 mg film-coated tablets are yellow, oval biconvex, debossed with "C18" on one side.
Bosutinib 100 mg is available in blisters containing either 28 or 112 film-coated tablets.
Bosutinib 100 mg is available in perforated unit dose blisters containing either 28x1 or 112x1 film-coated tablets.

Bosutinib 400 mg film-coated tablets are orange, oval biconvex, debossed with "C19" on one side.
Bosutinib 400 mg is available in blisters containing 28 film-coated tablets.
Bosutinib 400 mg is available in perforated unit dose blisters containing 28x1 film-coated tablets.

Bosutinib 500 mg film-coated tablets are pink, oval biconvex, debossed with "C20" on one side.
Bosutinib 500 mg is available in blisters containing 28 film-coated tablets.
Bosutinib 500 mg is available in perforated unit dose blisters containing 28x1film-coated tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Dr. Reddy's Laboratories (UK) Ltd.,
410 Cambridge Science Park,
Milton Road,
Cambridge,
CB4 0PE,
United Kingdom

Manufacturer
Coripharma ehf
Reykjavíkurvegur 78
220 Hafnarfjörður
Iceland

This leaflet was last revised in January/2024.