PACKAGE LEAFLET

Package leaflet: Information for the patient

Bosentan 62.5 mg film-coated tablets
Bosentan 125 mg film-coated tablets
bosentan

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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Bosentan is and what it is used for

Bosentan 62.5 mg or 125 mg film-coated tablets contain bosentan , which blocks a naturally occurring hormone called endothelin-1 (ET-1) causing blood vessels to narrow. Bosentan therefore causes blood vessels to expand and belongs to the class of medicines called "endothelin receptor antagonists".

Bosentan is used to treat:
- Pulmonary arterial hypertension (PAH): PAH is a disease of severe narrowing of the blood vessels in the lungs resulting in high blood pressure in the blood vessels (the pulmonary arteries) that carry blood form the heart to the lungs. This pressure reduces the amount of oxygen that can get into the blood in the lungs, making physical activity more difficult. Bosentan widens the pulmonary arteries, making it easier for the heart to pump blood through them. This lowers the blood pressure and relieves the symptoms.

Bosentan is used to treat patients with class III pulmonary arterial hypertension (PAH) to improve the ability to carry out physical activity and its symptoms. The 'class' reflects the seriousness of the disease: 'class III' involves marked limitation of physical activity. Some improvements have also been shown in patients with class II PAH. 'Class II' involves slight limitation of physical activity. The PAH for which Bosentan is indicated can be:
- primary (with no identified cause or a family history of);
- caused by scleroderma (also called systemic sclerosis, a disease where there is abnormal growth of the connective tissue that supports the skin and other organs);
- caused by congenital (inborn) heart defects with shunts (abnormal passageways) causing abnormal flow of blood through the heart and lungs.

Bosentan is also used to treat digital ulcers (sores on the fingers and toes) in adult patients with scleroderma. Bosentan reduces the number of new finger and toe ulcers that appear.

You must talk to a doctor if you do not feel better or if you feel worse after taking Bosentan.

2. What you need to know before you take Bosentan

Do not take Bosentan:

- if you are allergic to bosentan or any of the other ingredients of this medicine (listed in section 6).
- if you have liver problems.
- if you are taking ciclosporin A (a medicine used after a transplant or to treat psoriasis).
- if you are pregnant, or could get pregnant because you are not using reliable contraceptive methods. Please read the information under "Contraceptives" and "Other medicines and Bosentan".

If any of these apply to you, tell your doctor.

Warnings and precautions

Tests your doctor will do before you start treatment
- a blood test to check your liver function.
- a blood test to check for anaemia (low haemoglobin).
- a pregnancy test if you are a woman of child-bearing potential.

Some patients taking bosentan have been found to have abnormal liver function tests and anaemia (low haemoglobin) during treatment.

Tests your doctor will do during treatment
During treatment with Bosentan, your doctor will arrange for regular blood tests to check for changes in your liver function and haemoglobin level.

For all these tests please refer also to the Patient Alert Card (inside your pack of Bosentan tablets). It is important that you have these regular blood tests as long as you are taking Bosentan. We suggest you write the date of your most recent test and also of your next test (ask your doctor for the date) on the Patient Alert Card, to help you remember when your next test is due.

Blood tests for liver function
These will be done every month for the duration of treatment with Bosentan. After an increase in dose an additional test will be done after 2 weeks.

Blood tests for anaemia
These will be done every month for the first 4 months of treatment, then every 3 months after that, as patients taking bosentan may get anaemia.

If these results are abnormal, your doctor may decide to reduce your dose or stop treatment with Bosentan and to perform further tests to investigate the cause.

Children and adolescents
Bosentan is not recommended in paediatric patients with systemic sclerosis and ongoing digital ulcer disease. Please see also section 3, "How to take Bosentan".

Other medicines and Bosentan
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription. It is especially important to tell your doctor if you are taking:
- ciclosporin A (a medicine used after transplants and to treat psoriasis), see section "Do not take Bosentan").
- hormonal contraceptives (as these are not effective as the sole method of contraception when you take Bosentan). Inside your pack of Bosentan tablets you will find a Patient Alert Card which you should read carefully. Your doctor and/or gynaecologist will establish the contraception which is appropriate for you.
- glibenclamide (for diabetes - as this combination may increase the risk of side effects).
- tacrolimus, sirolimus or any other medicines used to prevent rejection of transplanted organs (as these medicines may increase the concentrations of bosentan in your blood).

- fluconazole, ketoconazole, itraconazole and voriconazole (to treat fungal infections - as these medicines may increase the concentrations of bosentan in your blood).
- simvastatin (used to treat hypercholesterolemia - high cholesterol levels – as bosentan may reduce the concentrations of this medicine in your blood).
- warfarin (an anticoagulant agent – as bosentan may reduce the concentrations of this medicine in your blood).
- other medications for the treatment of pulmonary hypertension: sildenafil and tadalafil (also used to treat erectile dysfunction – as bosentan may reduce the concentration of this medicine in your blood).
- rifampicin (to treat tuberculosis - as this medicine may reduce the efficacy of bosentan).
- carbamazepine, phenobarbital, phenytoin (medicines normally used for the treatment of epilepsy) or St. John's wort (used to treat depression) - as these medicines may reduce the efficacy of bosentan.
- ritonavir and lopinavir, nevirapine, or other medicines for the treatment of HIV infection.

Pregnancy, breast-feeding and fertility

Women of child-bearing age
Do NOT take Bosentan if you are pregnant or planning to have a baby.

Pregnancy tests
Bosentan may harm unborn babies conceived before starting or during treatment. If you are a woman who could become pregnant, your doctor will ask you to take a pregnancy test before you start taking Bosentan, and then every month while you are taking Bosentan.

Contraceptives
If it is possible that you could become pregnant, use a reliable form of birth control (contraception) while you are taking Bosentan. Your doctor or gynaecologist will advise you about reliable contraceptive methods while taking Bosentan. Because bosentan may make hormonal contraception (e.g., tablets, injection, implant, or skin patches) ineffective, this method on its own is not reliable. Therefore, if you use hormonal contraceptives you must also use a barrier method (e.g. female condom, diaphragm, contraceptive sponge, or your partner must also use a condom). Inside your pack of Bosentan tablets you will find a Patient Alert Card. You should complete this card and take it to your doctor at your next visit so that your doctor or gynaecologist can assess whether you need additional or alternative reliable contraceptive methods. Monthly pregnancy tests are recommended while you are taking Bosentan and are of child-bearing age.

Tell your doctor immediately if you become pregnant while you are taking Bosentan, or plan to become pregnant in the near future.

Breast-feeding
Tell your doctor immediately if you are breast-feeding. You are advised to stop breast-feeding if Bosentan is prescribed for you, because it is not known whether this medicine passes into breast milk.

Fertility
If you are a man taking bosentan, it is possible that this medicine may lower your sperm count. It cannot be excluded that this may affect your ability to father a child. Talk to your doctor if you have any questions or concerns about this.

Driving and using machines
Bosentan has no or negligible influence on the ability to drive and use machines. However, bosentan can induce hypotension (decrease of your blood pressure) which can make you feel faint or dizzy, affect your vision and affect your ability to drive and use machines. Therefore, if you feel dizzy or that your vision is blurred while taking Bosentan Mylan, do not drive or operate any tools or machines.

Bosentan Mylan 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 Bosentan

Treatment with Bosentan should only be started and monitored by a doctor who has experience in the treatment of PAH or systemic sclerosis. Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

If you have the impression that the effect of Bosentan is too strong or too weak, talk to your doctor in order to find out whether your dose needs to be changed.

Recommended dose

Use in adults
The treatment in adults is usually started for the first 4 weeks with the recommended dose of 62.5 mg twice daily (morning and evening), from then your doctor will usually advise you to take a 125 mg tablet twice daily, depending on how you react to Bosentan.

Use in children and adolescents
The dose recommendation in children is only for the treatment of pulmonary arterial hypertension. For children 1 year and older, the recommended dose for treatment with bosentan is usually started with 2 mg per kg of body weight twice daily (morning and evening). Your doctor will advise you on the exact amount to give to your child.

Other forms of this medicine may be more suitable for children, people with low body weight or who have difficulties swallowing; ask your doctor or pharmacist.

How to take Bosentan
Tablets should be taken (morning and evening), swallowed with water. The tablets can be taken with or without food.

If you take more Bosentan than you should
If you take more tablets than you have been told to take, contact your doctor at once.
You may get symptoms such as headache, feeling or being sick, low blood pressure (which may make you feel faint or dizzy), sweating and blurred vision.

If you forget to take Bosentan
If you forget to take Bosentan, take a dose as soon as you remember, then continue to take your tablets at the usual times. Do not take a double dose to make up for forgotten tablets.

If you stop taking Bosentan
Suddenly stopping your treatment with Bosentan may lead to your symptoms getting worse. Do not stop taking Bosentan unless your doctor tells you to. Your doctor may tell you to reduce the dose over a few days before stopping completely.

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.

The most serious side effects with bosentan are:

Abnormal liver function which may affect more than 1 in 10 people
Anaemia (low blood value) which may affect up to 1 in 10 people. Anaemia may occasionally require blood transfusion.

Your liver and blood values will be monitored during treatment with bosentan (see section 2). It is important that you have these tests as ordered by your doctor.

Signs that your liver may not be working properly include:
- nausea (urge to vomit)
- vomiting
- fever (high temperature)
- pain in your stomach (abdomen)
- jaundice (yellowing of your skin or the whites of your eyes)
- dark-coloured urine
- itching of your skin
- lethargy or fatigue (unusual tiredness or exhaustion)
- flu-like syndrome (joint and muscle pain with fever)

If you notice any of these signs **tell your doctor immediately**

Other side effects:

Very common (may affect **more than one in 10** people):
- Headache
- Oedema (swelling of the legs and ankles or other signs of fluid retention)

Common (may affect **up to one in 10** people):
- Flushed appearance or redness of skin
- Hypersensitivity reactions (including skin inflammation, itching and rash)
- Gastrooesophageal reflux disease (acid reflux)
- Diarrhoea
- Stuffy or blocked nose
- Syncope (fainting)
- Palpitations (fast or irregular heart beats)
- Low blood pressure

Uncommon (may affect **up to one in 100** people):
- Thrombocytopenia (low number of blood platelets)
- Neutropenia/leukopenia (low number of white blood cells)
- Elevated liver function tests with hepatitis (inflammation of the liver including possible worsening of existing hepatitis) and/or jaundice (yellowing of the skin or the whites of the eyes)

- **Rare** (may affect **up to one in 1000** people):
- Anaphylaxis (general allergic reaction), angioedema (swelling, most commonly around the eyes, lips, tongue or throat)
- Cirrhosis (scarring) of the liver, liver failure (serious disturbance of liver function)

Not known (cannot be estimated from the available data)
- Blurred vision

Side effects in children and adolescents
The side effects that have been reported in children treated with bosentan are the same as those in adults.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at:

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 Bosentan

Keep this medicine out of the sight and reach of children.

This medicinal product does not require any special storage conditions.

Do not use this medicine after the expiry date which is stated on the carton/blister after 'EXP'. The expiry date refers to the last day of that month.

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 Bosentan contains

The active substance is bosentan.
Each tablet contains 62.5 mg or 125 mg of bosentan (as monohydrate).

The other ingredients are maize starch, pregelatinised maize starch, sodium starch glycolate, povidone, sodium laurilsulfate, glycerol dibehenate, magenesium stearate. The coating ingredients are hypromellose (E464), titanium dioxide (E 171), triacetin, talc, iron oxide yellow (E172) and iron oxide red (E172).

What Bosentan looks like and contents of the pack

[62.5 mg] Orange white, film-coated, round, biconvex, bevelled edge tablet marked with ''M'' on one side of the tablet and "BNI'' on other side.

[125 mg] Orange white, film-coated, oval, biconvex, bevelled edge tablet marked with 'M'' on one side of the tablet and "BN2'' on other side.

The tablets are available in blisters in packs of 14, 14x1 (unit dose blister), 28 x1 (unit dose blister), 56, 56 x 1 (unit dose blister), 112, 112 x1 (unit dose blister).

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Mylan, Potters Bar, Hertfordshire EN6 1TL, United Kingdom

Manufacturer

Gerard Laboratories, 35/36 Baldoyle Industrial Estate, Grange Road, Dublin 13, Ireland.

Mylan Hungary Kft, H-2900, Komárom Mylan útca 1, Hungary.

This leaflet was last revised in July 2021