

Package leaflet – Information for the user

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 Tablet is and what it is used for
2. What you need to know before you take Bosentan Tablets
3. How to take Bosentan Tablets
4. Possible side effects
5. How to store Bosentan Tablets
6. Contents of the pack and other information.

1. What Bosentan Tablet is and what it is used for

Bosentan Tablet contains bosentan, which blocks a naturally occurring hormone called endothelin-1 (ET-1), which causes blood vessels to narrow. Bosentan Tablets therefore causes blood vessels to expand and belongs to the class of medicines called “endothelin receptor antagonists”.

Bosentan Tablet 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 from 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 Tablets 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 Tablet is used to treat patients with class III PAH to improve exercise capacity (the ability to carry out physical activity) and 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 Tablet is indicated can be:

- primary (with no identified cause or familial);
- 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.
- **Digital ulcers** (sores on the fingers and toes) in adult patients with a condition called scleroderma. Bosentan Tablet reduces the number of new finger and toe ulcers that appear.

2. What you need to know before you take Bosentan Tablets

Do not take Bosentan Tablets:

- **if you are allergic to bosentan** or any of the other ingredients of this medicine (listed in section 6)
- **if you have liver problems** (ask your doctor)
- **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 Tablets”
- **if you are taking cyclosporine A** (a medicine used after a transplant or to treat psoriasis)

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

Warnings and precautions

Talk to your doctor or pharmacist before taking Bosentan Cipla

Tests your doctor will do before 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 Tablets have been found to have abnormal liver function tests and anaemia (low haemoglobin).

Tests your doctor will do during treatment

During treatment with Bosentan Tablets, 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 tablets). It is important that you have these regular blood tests as long as you are taking Bosentan Tablets. 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 Tablets. 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 Tablets may get anaemia.

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

Children and adolescents

Bosentan Tablet is not recommended in paediatric patients with systemic sclerosis and ongoing digital ulcer disease. Bosentan Tablets should also not be used in children with a body weight below 31 kg with pulmonary arterial hypertension. Please see also section 3. How to take Bosentan Tablets.

Other medicines and Bosentan Tablets

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:

- cyclosporine A (a medicine used after transplants and to treat psoriasis), which must not be used together with Bosentan Tablets
- sirolimus or tacrolimus, which are medicines used after transplants, as these are not recommended to be used together with Bosentan Tablets
- glibenclamide (a diabetes medicine), rifampicin (a tuberculosis medicine) or fluconazole (a medicine against fungal infections), ketoconazole (a medicine used to treat Cushing's syndrome), nevirapine (an HIV medicine) as these medicines are not recommended to be used together with Bosentan Tablets
- other medicines for the treatment of HIV infection, which may require special monitoring if used together with Bosentan Tablets
- hormonal contraceptives, which are not effective as the sole method of contraception when you take Bosentan Tablets. 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.
- other medications for the treatment of pulmonary hypertension: sildenafil and tadalafil,
- warfarin (an anticoagulant agent),
- simvastatin (used to treat hypercholesterolaemia).

Bosentan Tablets with food

Bosentan Tablets can be taken with or without food.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Women of child-bearing age

Do NOT take Bosentan Tablets if you are pregnant or planning to become pregnant.

Pregnancy tests

Bosentan Tablets 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 Tablets, and regularly while you are taking Bosentan Tablets.

Contraceptives

If it is possible that you could become pregnant, use a reliable form of birth control (contraception) while you are taking Bosentan Tablets. Your doctor or gynaecologist will advise you about reliable contraceptive methods while taking Bosentan Tablets. Because Bosentan Tablets may make hormonal contraception (e.g., oral, 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 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 Tablets and are of child-bearing age.

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

Breast-feeding

Bosentan passes into your breast milk. You are advised to stop breast-feeding if bosentan is prescribed for you, because it is not known if bosentan in breast milk can harm your baby. Talk to your doctor about this.

Fertility

If you are a man taking Bosentan Tablets, 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 Tablets has no or negligible influence on the ability to drive and use machines. However, Bosentan Tablets can induce hypotension (decrease of your blood pressure) which can make you feel 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 Tablets, do not drive or operate any tools or machines.

Bosentan Cipla 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 Tablets

Treatment with Bosentan Tablets 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 has told you. Check with your doctor or pharmacist if you are not sure.

Recommended dose:

Adults:

The treatment in adults is usually started for the first 4 weeks with 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 Tablets.

Children and adolescents

The dose recommendation in children is only for PAH. For children 1 years and older, treatment with Bosentan Tablets is usually started with 2 mg per kg bodyweight twice daily (morning and evening); however, some doses of bosentan are not possible in children with a body weight below 31 kg. For such patients a bosentan tablet with lower strength is needed. Your doctor will advise you on your dosing.

Please note that bosentan is also available as a dispersible 32 mg tablet formulation, which may make correct dosing easier for children and patients with low body weight or difficulties to swallow film-coated tablets.

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.

How to take Bosentan Tablets

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

If you take more Bosentan Tablets than you should

If you take more tablets than you have been told to take, contact your doctor immediately.

If you forget to take Bosentan Tablets

If you forget to take Bosentan Tablets, 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 Tablets

Suddenly stopping your treatment with Bosentan Tablets may lead to your symptoms getting worse. Do not stop taking Bosentan Tablets 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 Tablets 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 Tablets (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 1 in 10** people):

- Headache
- Oedema (swelling of the legs and ankles or other signs of fluid retention)

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

- Flushed appearance or redness of skin
- Hypersensitivity reactions (including skin inflammation, itching and rash)
- Gastrooesophageal reflux disease (acid reflux)
- Diarrhoea
- Syncope (fainting)

- Palpitations (fast or irregular heart beats)
- Low blood pressure
- Nasal congestion

Uncommon (may affect **up to 1 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 exacerbation of underlying hepatitis and/or jaundice (yellowing of the skin or the whites of the eyes)

Rare (may affect **up to 1 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 (frequency 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 Tablets 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 Yellow Card Scheme at: <https://yellowcard.mhra.gov.uk/> . By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Bosentan Tablets

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 and carton after EXP. The expiry date refers to the last day of the month.

This medicinal product does not require any special storage conditions.

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 Tablets contains

The active substances is bosentan.

Bosentan 62.5 mg film-coated tablets:

Each film-coated tablets contains 62.5mg bosentan (as monohydrate).

Bosentan 125 mg film-coated tablets:

Each film-coated tablets contains 125mg bosentan (as monohydrate).

The other ingredients are:

- *Tablet core:* maize starch, sodium starch glycolate (Type B), povidone (PVP K-30), pregelatinised starch maize, glycerol dibehenate, magnesium stearate.
- *Film coat:* hypromellose, titanium dioxide (E171), triacetin, talc, iron oxide yellow (E172), iron oxide red (E172), ethylcellulose, cetyl alcohol, sodium laurilsulfate.

What Bosentan Tablets looks like and contents of the pack

Bosentan film-coated tablets:

Bosentan 62.5 mg film-coated tablets are cream to pale yellow coloured, circular biconvex film coated table, debossed with '62.5' on one side and plain on the other side. Diameter – 6.10 mm ± 0.20 mm.

Bosentan 125 mg film-coated tablets are cream to pale yellow coloured, oblong, biconvex film coated tablet, debossed with '125' on one side and plain on the other side. Length – 11.10± 0.20 mm and breadth – 5.10 ± 0.20 mm

PVC/PE/PVDC, aluminium blister. Blister pack of 14's, 56's and 112 film-coated tablets

Perforated unit dose blister: PVC/PE/PVDC, aluminium.

Pack size 14 x 1 , 56 x 1, 112 x 1 film coated tablets

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Cipla (EU) Limited,
Dixcart House, Addlestone Road,
Bourne Business Park,
Addlestone Surrey,
KT15 2LE
United Kingdom,

Manufacturer

CIPLA (EU) Limited,
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PATIENT ALERT CARD

((Front cover))

**Important Safety Alerts for Patients taking
Bosentan Tablets (bosentan)**

This card contains important information about Bosentan Tablets. Please read this card carefully before starting your treatment with Bosentan Tablets.

Your name: _____

Prescribing doctor: _____

If you have questions about Bosentan Tablets ask your doctor.

Cipla (EU) Limited

((Back cover))

Contraception

Do you currently use or take contraceptives?

Yes No

If Yes, write the names of these here:

Take this card to your doctor or your gynaecologist at your next visit and he/she will be able to advise you on whether you need to use additional or alternative contraceptive methods.

((Inside 1))

If you are a woman of child bearing age read this page carefully

Pregnancy

Bosentan Tablets may harm the development of the foetus. Therefore, you must not take Bosentan Tablets if you are pregnant and you must also not become pregnant while taking Bosentan Tablets.

Moreover, if you are suffering from pulmonary hypertension disease, the occurrence of a pregnancy can severely deteriorate the symptoms of your disease. If you suspect you may be pregnant, tell your doctor or gynaecologist.

Contraception

Birth control based on hormones – such as oral contraceptives or birth control pills, hormone injections, implants, or birth control skin patches don't reliably prevent pregnancy in women who are taking Bosentan Tablets. You need to use a barrier form of birth control – like a condom, diaphragm or vaginal sponge – in addition to any of these kinds of hormonal birth control. Be sure to discuss any questions you may have with your doctor or your gynaecologist – complete the details on the back of this card and take it to your doctor or gynaecologist at your next visit.

You should have a pregnancy test before initiation of Bosentan Tablets and every month during the treatment even if you think that you are not pregnant.

Date of first monthly test: _____

((Inside 2))

Blood Test for Liver Function

Some patients taking Bosentan Tablets were found to have abnormal liver function tests. During treatment with Bosentan Tablets, your doctor will arrange for regular blood tests to check for changes in your liver function.

Remember to have your liver blood test every month.

After an increase in dose, an additional test will be done after 2 weeks.

Date of first monthly test: _____

Your monthly liver blood test schedule:

Jan _____ May _____ Sep _____

Feb _____ Jun _____ Oct _____

Mar _____ Jul _____ Nov _____

Apr _____ Aug _____ Dec _____