PACKAGE LEAFLET: INFORMATION FOR THE USER

Bosentan Zentiva 62.5 mg film-coated tablets
Bosentan Zentiva 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 ZENTIVA IS AND WHAT IT IS USED FOR

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

Bosentan Zentiva 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 Zentiva 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 Zentiva 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 Zentiva 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 Zentiva reduces the number of new finger and toe ulcers that appear.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE BOSENTAN ZENTIVA

Do not take Bosentan Zentiva
- **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 Zentiva".
- **if you are taking ciclosporin A** (a medicine used after a transplant or to treat psoriasis).

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

Warnings and precautions
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 childbearing potential.

Some patients taking Bosentan Zentiva have been found to have abnormal liver function tests and anaemia (low haemoglobin).

Tests your doctor will do during treatment
During treatment with Bosentan Zentiva, 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 Zentiva tablets). It is important that you have these regular blood tests as long as you are taking Bosentan Zentiva. 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 Zentiva. 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 Zentiva may get anaemia.
If these results are abnormal, your doctor may decide to reduce your dose or stop treatment with Bosentan Zentiva and to perform further tests to investigate the cause.

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

Other medicines and Bosentan Zentiva
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), which must not be used together with Bosentan Zentiva.
- Sirolimus or tacrolimus, which are medicines used after transplants, as these are not recommended to be used together with Bosentan Zentiva.
- Glibenclamide (a diabetes medicine), rifampicin (a tuberculosis medicine), fluconazole (a medicine against fungal infections), ketoconazole (a medicine used to treat Cushing's syndrome), or nevirapine (an HIV medicine) as these medicines are not recommended to be used together with Bosentan Zentiva.
- Other medicines for the treatment of HIV infection, which may require special monitoring if used together with Bosentan Zentiva.
- Hormonal contraceptives, which are not effective as the sole method of contraception when you take Bosentan Zentiva. Inside your pack of Bosentan Zentiva 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).

Driving and using machines
Bosentan Zentiva has no or negligible influence on the ability to drive and use machines. However, Bosentan Zentiva 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 Zentiva, do not drive or operate any tools or machines.

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 Bosentan Zentiva.

Women of childbearing age
Do NOT take Bosentan Zentiva if you are pregnant or planning to become pregnant.

Pregnancy tests
Bosentan Zentiva 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 Zentiva, and regularly while you are taking Bosentan Zentiva.

Contraceptives

If it is possible that you could become pregnant, use a reliable form of birth control (contraception) while you are taking Bosentan Zentiva. Your doctor or gynaecologist will advise you about reliable contraceptive methods while taking Bosentan Zentiva. Because Bosentan Zentiva 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 Zentiva 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 Zentiva and are of childbearing age.

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

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

Fertility
If you are a man taking Bosentan Zentiva, 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.

Bosentan Zentiva 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 ZENTIVA

Treatment with Bosentan Zentiva 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 Zentiva.

Children and adolescents
The dose recommendation in children is only for PAH. For children aged 1 year and older, treatment with Bosentan Zentiva is usually started with 2 mg per kg bodyweight twice daily (morning and evening). Your doctor will advise you on your dosing.
Bosentan Zentiva should not be administered to children with a body weight below 31 kg, and an alternative product containing bosentan should be used.

If you have the impression that the effect of Bosentan Zentiva 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 Zentiva
Tablets should be taken (morning and evening), swallowed with water. The tablets can be taken with or without food.

If you take more Bosentan Zentiva 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 Zentiva
If you forget to take Bosentan Zentiva, 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 Zentiva
Suddenly stopping your treatment with Bosentan Zentiva may lead to your symptoms getting worse. Do not stop taking Bosentan Zentiva 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 Zentiva 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 Zentiva (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).
- Gastroesophageal reflux disease (acid reflux).
- Diarrhoea.
- Syncope (fainting).
- Palpitations (fast or irregular heartbeats).
- 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 1,000 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), autoimmune hepatitis (inflammation of the liver caused by the body's own defence system attacking liver cells) which may occur even several months to years after initiation of treatment.

Blurred vision has also been reported at an unknown frequency (frequency cannot be estimated from the available data).

Side effects in children and adolescents
The side effects that have been reported in children treated with Bosentan Zentiva 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:
HPRA Pharmacovigilance
Website: www.hpra.ie

By reporting side effects, you can help provide more information on the safety of this medicine.

5. HOW TO STORE BOSENTAN ZENTIVA

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 carton and 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.
This medicine does not require any special storage conditions.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Bosentan Zentiva contains
The active substance is bosentan.
Each film-coated tablet contains bosentan as monohydrate equivalent to 62.5 mg of bosentan.
Each film-coated tablet contains bosentan as monohydrate equivalent to 125 mg of bosentan.
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The other ingredients are maize starch, povidone, sodium starch glycolate, pregelatinized maize starch, glycerol dibehenate, magnesium stearate, polyvinyl alcohol (E 1203), titanium dioxide (E 171), macrogol (E 1521), talc (E 553b), iron oxide yellow (E 172) and iron oxide red (E 172)).

What Bosentan Zentiva looks like and contents of the pack
Bosentan Zentiva 62.5 mg are round, biconvex-shaped, light orange coloured film-coated tablets with the diameter approx. 6 mm.
Bosentan Zentiva 125 mg are oval, biconvex-shaped, light orange coloured film-coated tablets with length approx. 11 mm and width approx. 5 mm.

Size of packing:
Bosentan Zentiva 62.5 mg: 14, 56 and 112 film-coated tablets.
Bosentan Zentiva 125 mg: 14, 56, 112 and 120 film-coated tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Zentiva k.s, U kabelovny 130, Dolní Měcholupy 102 37 Prague 10, Czech Republic

Manufacturer

ITC Production s.r.l.
Via Pontina KM 29
00071 Pomezia (Rome) – Italy

This medicine is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:

Bosentan Zentiva in United Kingdom (Northern Ireland), Ireland, Germany, Austria, Croatia, Denmark, Netherlands, Latvia, Lithuania, Sweden, Bulgaria.

This leaflet was last updated in September 2025