Package leaflet: Information for the user

Bosentan Accord 62.5 mg film-coated tablets
Bosentan Accord 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, please 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.

What is in this leaflet

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

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

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

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

Do not take Bosentan Accord

- **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 Accord".
- **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

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 have been found to have abnormal liver function tests and anaemia (low haemoglobin).

Tests your doctor will do during treatment

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

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

Children and adolescents

Bosentan Accord are not recommended in paediatric patients with systemic sclerosis and ongoing digital ulcer disease. Please see also section 3. How to take Bosentan Accord.

Other medicines and Bosentan Accord
Please tell your doctor or pharmacist if you are taking or have recently taken 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 Accord
- sirolimus or tacrolimus, which are medicines used after transplants, as these are not recommended to be used together with Bosentan Accord
- 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 Accord
- other medicines for the treatment of HIV infection, which may require special monitoring if used together with Bosentan Accord
- hormonal contraceptives, which are not effective as the sole method of contraception when you take Bosentan Accord. Inside your pack of Bosentan Accord 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 Accord has no or negligible influence on the ability to drive and use machines. However, Bosentan Accord 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 Accord, do not drive or operate any tools or machines.

Pregnancy, breast-feeding and fertility

Women of child-bearing age
Do NOT take Bosentan Accord if you are pregnant or planning to become pregnant.

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

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

Bosentan Accord 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 Accord

Treatment with Bosentan Accord 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.

Bosentan Accord with food and drink
Bosentan Accord can be taken with or without food.

Recommended dose

Adult
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 Accord.

Use in Children and adolescents
The dose recommendation in children is only for PAH. For children 1 years and older, treatment with is usually started with 2 mg per kg bodyweight twice daily (morning and evening). Your doctor will advise you on your dosing.
Please note that other formulations of bosentan are available, 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 Accord 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 Accord
Tablets should be taken (morning and evening), swallowed with water. The tablets can be taken with or without food.

If you take more Bosentan Accord 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 Accord
If you forget to take Bosentan Accord, 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 a forgotten tablets.

If you stop taking Bosentan Accord
Suddenly stopping your treatment with Bosentan Accord may lead to your symptoms getting worse. Do not stop taking Bosentan Accord 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 Accord 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 Accord (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**

Bosentan Accord <u>Other side effects:</u>

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

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 exacerbation of underlying 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)

Blurred vision have 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 Accord 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 Accord

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 on the blister after "EXP". The expiry date refers to the last day of that month.

Aluminium-aluminium blisters
This medicinal product does not require any special storage condition.

PVC/PE/PVDC-aluminium blisters
Do not store above 30 °C.

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 to protect the environment.

6. Contents of the pack and other information

What Bosentan Accord contains

- **Bosentan Accord 62.5 mg film-coated tablets:** The active substance is bosentan as monohydrate. Each tablet contains 62.5 mg of bosentan (as monohydrate).
- **Bosentan Accord 125 mg film-coated tablets:** The active substance is bosentan as monohydrate. Each tablet contains 125 mg of bosentan (as monohydrate).

- **The other ingredients** in the tablet core are maize starch, pregelatinised starch (maize), sodium starch glycolate (type A), povidone, and magnesium stearate. **The film coat** contains hypromellose, triacetin, talc, titanium dioxide (E171), iron oxide yellow (E172) and iron oxide red (E172).

What Bosentan Accord looks like and contents of the pack

Bosentan Accord 62.5 mg film-coated tablets are Light orange, round, approximately 6.20mm in diameter, biconvex, film-coated tablets debossed with “IB1” on one side and plain on other side

Bosentan Accord 125 mg film-coated tablets are Light orange, oval, approximately 11.00mm in length, 5.00mm in width, biconvex, film-coated tablets debossed with “IB2” on one side and plain on other side

Bosentan Accord 62.5 mg film-coated tablets are packed in Aluminim-aluminium blisters and PVC/PE/PVDC/aluminium-blisters containing 14 film-coated tablets. Cartons contain 14, 56 or 112 film-coated tablets.

Bosentan Accord 125 mg film-coated tablets are packed in Aluminim-aluminium blisters and PVC/PE/PVDC/aluminium-blisters containing 14 film-coated tablets. Cartons contain 56 or 112 film-coated tablets.

Bosentan Accord 125 mg film-coated tablets are packed in Aluminim-aluminium blisters and PVC/PE/PVDC/aluminium-blisters containing 10 film-coated tablets. Cartons contain 120 film-coated tablets.

Not all pack sizes may be marketed.

Marketing authorisation holder and Manufacturer

Marketing Authorisation Holder:

Accord Healthcare Ireland Ltd
Euro House
Euro Business Park
Little Island
Cork T45 K857
Ireland

Manufacturer:

Accord Healthcare Polska Sp.z o.o.,
ul. Lutomierska 50,95-200 Pabianice, Poland

Accord Healthcare B.V.,
Winthontlaan 200,
3526 KV Utrecht,
The Netherlands

This medicinal product is authorised in the Member States of the EEA under the following names:

Member States	Proposed (Invented) Names
UK(NI)	Bosentan Accord 62.5/125 mg Film-coated Tablets
Austria	Bosentan Accord 62,5/125 mg Filmtabletten
Belgium	Bosentan Accord 62.5/125 mg filmomhulde tabletten
Bulgaria	Bosentan Акорд 62.5/125 мг филмирани таблетки
Cyprus	Bosentan Accord 62.5/125 mg Film-coated Tablets
Czech Republic	Bosentan Accord 125 mg potahované tablety
Germany	Bosentan Accord 62.5/125 mg filmtabletten
Denmark	Bosentan Accord 62.5/125 mg filmovertrukne tabletter
Estonia	Bosentan Accord
Finland	Bosentan Accord 62.5/125 mg tabletti, kalvopäällysteinen
France	BOSENTAN ACCORD 62,5/125 mg comprimé pelliculé
Italy	Bosentan Accord
Lithuania	Bosentan Accord 62.5/125 mg plėvele dengtos tabletės
Netherlands	Bosentan Accord 62,5/125 mg filmomhulde tabletten
Norway	Bosentan Accord
Portugal	Bosentan Accord
Sweden	Bosentan Accord 62.5/125 mg filmdragerad tablet
Slovakia	Bosentan Accord 62.5/125 mg filmom obalené tablety
Poland	Bosentan Accord
Romania	Bosentan Accord 125 mg comprimate filmate
Ireland	Bosentan Accord 62.5 mg film-coated tablets Bosentan Accord 125 mg film-coated tablets
Latvia	Bosentan Accord

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