PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Bosentan Teva 62.5 mg

Film-coated tablets

Each film-coated tablet contains:
Bosentan (as monohydrate) 62.5 mg

Bosentan Teva 125 mg

Film-coated tablets

Each film-coated tablet contains:
Bosentan (as monohydrate) 125 mg

For information regarding inactive ingredients and allergens, see section 2 "Important information about some of the ingredients of the medicine" and section 6 "Additional information".

Read the entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have additional questions, refer to the doctor or the pharmacist.

This medicine has been prescribed for treatment of your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness/medical condition is similar.

Patient safety information card

In addition to the leaflet, the medicine Bosentan Teva has a patient safety information card, regarding possible harm to the fetus.

This card contains important safety information, that you should know, before starting and during treatment with Bosentan Teva. Please review the patient safety information card and the patient leaflet before using the medicine. Keep the card and the leaflet for further reference, if required.

Do not use Bosentan Teva if you are pregnant, since the medicine may cause harm to the fetus (see section 2 "Before using the medicine", sub-sections "Do not use this medicine if" and "Fertility, pregnancy and breastfeeding").

If you are a woman of childbearing age who can become pregnant, take a pregnancy test before you start taking Bosentan Teva and regularly every month while you are taking the medicine, as well as a month after termination of treatment. A negative result in each pregnancy test must be confirmed. You must use a reliable contraceptive method while taking Bosentan Teva and for one additional month after termination of treatment (see section 2 "Fertility, pregnancy and breastfeeding").

1. What is the medicine intended for?

- For the treatment of pulmonary arterial hypertension (PAH). Pulmonary arterial hypertension is high blood pressure in the blood vessels (the pulmonary arteries) that carry blood from the heart to the lungs. Bosentan Teva widens the pulmonary arteries, making it easier for the heart to pump blood through them. Widening the arteries lowers the blood pressure and relieves the symptoms.
- For the treatment of ulcers of the fingers (digital ulcers) in people who suffer from a disease called scleroderma. Bosentan Teva reduces the number of new finger ulcers that occur.

Therapeutic class: Endothelin receptor antagonist.

2. Before using the medicine

Do not use this medicine if:

- You are hypersensitive (allergic) to the active ingredient (bosentan) or to any of the other ingredients this medicine contains as listed in section 6 – "Additional information".
- You have liver problems (consult your doctor).
- You are pregnant or may become pregnant as you are not using reliable contraception methods (hormonal contraceptives alone are not effective when taking Bosentan Teva). For additional information, please see section "Fertility, pregnancy and breastfeeding".
- You are taking cyclosporine A [a medicine used after transplantation or for the treatment of psoriasis].

If any of these cases apply to you, consult your doctor.

Special warnings regarding the use of the medicine

Tests that must be performed before, during and after termination of the treatment – see sections "Fertility, pregnancy and breastfeeding" and "Tests and follow-up".

Drug interactions:

If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or the pharmacist. Especially if you are taking:

- Cyclosporine A (a medicine used after transplantations and for the treatment of psoriasis). Using together with Bosentan Teva is prohibited.
- Sirolimus or tacrolimus (medicines used after transplantations). Using together with Bosentan Teva is not recommended.
- Glibenclamide (for the treatment of diabetes), rifampicin (for the treatment of tuberculosis), fluconazole and ketoconazole (medicines for treatment of fungal infections) or nevirapine [for the treatment of HIV infection (AIDS)]. Using together with Bosentan Teva is not recommended.
- Other medicines for the treatment of HIV infection (AIDS) – special monitoring is required if used together with Bosentan Teva.
- Hormonal contraceptives (as they are not effective as a sole method of contraception when taking Bosentan Teva). Your doctor and/or gynecologist will determine the contraception method which is appropriate for you. For additional information, see section "Fertility, pregnancy and breastfeeding" and also "Patient safety information card".
- Simvastatin for the treatment of hypercholesterolemia.
- Warfarin (for prevention of blood coagulation).
- Other medicines for treatment of pulmonary arterial hypertension: sildenafil and tadalafil.

Use of the medicine and food:

The medicine can be taken with or without food.

Fertility, pregnancy and breastfeeding:

Fertility:

If you are a man taking Bosentan Teva, this medicine may lower your sperm count. It cannot be excluded that this may affect your fertility. Talk to your doctor if you have any questions or concerns about this.

Pregnancy:

- Bosentan Teva may harm fetuses conceived before or during treatment. If you are a woman of child-bearing age who could become pregnant, your doctor will ask you to take a pregnancy test before starting treatment with Bosentan Teva and regularly every month while you are taking the medicine as well as one month after termination of the treatment. A negative result in each pregnancy test must be confirmed.
- Do not take Bosentan Teva if you are pregnant or planning to become pregnant.
- You must use a reliable contraceptive method while taking Bosentan Teva as well as for one month after termination of treatment.
- Your doctor or gynecologist will instruct you about reliable contraception methods while taking Bosentan Teva. As the medicine may make hormonal contraceptives (e.g. oral contraceptives, injections, implants or skin patches) ineffective, this method on its own is not reliable.
  The doctor will recommend you one highly effective method of contraception, such as intra-uterine device or tubal sterilization, or using a combination of methods (such as a hormonal contraception method with an additional barrier contraception method, such as: diaphragm, contraceptive sponge or your partner must also use a condom), or two barrier contraception methods. Consult your doctor regarding the use of two methods of contraception.
- If the chosen method of contraception is the partner's vasectomy, hormonal or barrier contraception must be used concomitantly.

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

Breastfeeding:

- If you are breastfeeding or planning to breastfeed, consult your doctor or pharmacist before initiating treatment with Bosentan Teva, since the medicine may cause harm to the baby.
- You are advised to stop breastfeeding if Bosentan Teva is prescribed for you as it is not known whether this medicine passes into breastmilk.

Driving and operating machinery

Bosentan Teva has no effect or negligible effect on the ability to drive and operate machinery. However, the medicine can lower blood pressure which can make you feel dizzy and affect your vision, and affect your ability to drive and operate machinery. Therefore, if you feel dizzy or that your vision is blurry while taking the medicine, do not drive a vehicle or operate any devices or machines.

Important information about some of the ingredients of the medicine

This medicine contains less than 23 mg of sodium in a tablet, and is therefore considered sodium-free.

3. How should you use the medicine?

- Only a doctor who has experience in the treatment of pulmonary arterial hypertension or systemic sclerosis should initiate and monitor the treatment with Bosentan Teva.
- Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain.

The dosage and treatment regimen will be determined only by the doctor. The generally accepted dosage is:

Adults

The treatment in adults is usually 62.5 mg twice daily (morning and evening) for the first four weeks. Thereafter, your doctor will usually advise you to take a dosage of 125 mg twice daily, depending on how you react to Bosentan Teva. Take the medicine with a glass of water. Do not halve, crush or chew the tablets.

Children and adolescents

Bosentan Teva is not recommended for use in children who suffer from systemic sclerosis and digital ulcers.

Do not exceed the recommended dose.

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

Tests and follow-up:

Tests your doctor will do before treatment:

- A blood test to check your liver function
- A blood test to check for anemia (low hemoglobin)
- A pregnancy test if you are a woman of child-bearing age

Some patients taking Bosentan Teva have been found to have anemia (low hemoglobin) and abnormal liver function tests.

Tests your doctor will do during treatment:

During treatment with Bosentan Teva, your doctor will arrange for regular blood tests to check for changes in your liver function and hemoglobin level.

A blood test to check your liver function:

These tests will be done every month during treatment with Bosentan Teva. An additional test will be done 2 weeks after an increase in dosage.

A blood test to check for anemia:

These tests will be done every month for the first four months of treatment with the medicine, and every three months after that, as patients taking Bosentan Teva may develop anemia.

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

If you have accidentally taken a higher dose refer to your doctor immediately.

If you took an overdose or a child accidentally swallowed this medicine, go to the doctor or the emergency room of the hospital immediately and take the package of the medicine with you.

If you forget to take the medicine at the specified time, take a dose as soon as you remember, and then continue taking the tablets at the usual time. Do not take two doses together to compensate for the forgotten tablets.

Follow the treatment as recommended by the doctor.

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor.

If you stop taking the medicine

Suddenly stopping your treatment with Bosentan Teva may lead to your symptoms getting worse.

Do not stop taking the medicine, unless your doctor has instructed you to do so. Your doctor may tell you to reduce the dosage over a few days before stopping the medicine completely.

Do not take medicines in the dark! Check the label and the dose every time you take the medicine. Wear glasses if you need them.

If you have any other questions regarding the use of the medicine, consult the doctor or the pharmacist.

4. Side effects

As with any medicine, using Bosentan Teva may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.

The most severe side effects that may occur during treatment with Bosentan Teva are:

- Abnormal liver function which may affect more than one in ten users.
- Anemia which may affect 1-10 users out of 100. Anemia may occasionally require blood transfusion.

Liver function and blood test values will be monitored during treatment with Bosentan Teva. It is important that you do these tests according to the doctor's instructions.

Refer to a doctor immediately if:

- You suffer from the following symptoms that indicate an impairment of liver function: nausea, vomiting, fever, abdominal pain, jaundice (yellowing of the skin or the whites of the eyes), dark urine, itching of the skin, fatigue (unusual tiredness or exhaustion), flu-like syndrome (muscle and joint pain with fever).

Additional side effects:

Very common side effects (occur in more than one out of ten users):

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

Common side effects (occur in 1-10 out of 100 users):

- Flushed appearance or redness of the skin
- Hypersensitivity reactions (including skin inflammation, itching and rash)
- Gastroesophageal reflux disease (acid reflux)
- Diarrhea
- Fainting
- Palpitations (fast or irregular heartbeats)
- Low blood pressure
- Nasal congestion

Uncommon side effects (occur in 1-10 out of 1,000 users):

- Thrombocytopenia (low number of blood platelets)
- Neutropenia/leukopenia (low number of white blood cells)
- Elevated liver function test values with hepatitis, including possible exacerbation of underlying hepatitis and/or jaundice (yellowing of the skin or the whites of the eyes)

Rare side effects (occur in 1-10 out of 10,000 users):

- Anaphylactic shock (a general allergic reaction), angioedema (swelling, most commonly around the eyes, lips, tongue, throat)
- Cirrhosis, liver failure

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 Teva are the same as those reported in adults.

If a side effect appears, if one of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, or signs of allergic reaction appear (such as: swelling of the face or tongue, rash, itch) while you are taking Bosentan Teva, or if any of the side effects mentioned above worries you, **consult with your doctor.**

Reporting side effects

Side effects may be reported to the Ministry of Health by clicking on the link "Report side effects due to medicinal treatment" found on the Ministry of Health website homepage (www.health.gov.il), which will direct you to the online form for reporting side effects, or by clicking on the following link: https://sideeffects.health.gov.il/

5. How to store the medicine?

- Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.
- Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.
- **Store below 25°C.**
- Do not discard medicines via wastewater or the trash. Ask your pharmacist how to dispose of medicines no longer in use. These measures will help to protect the environment.

6. Additional information

In addition to the active ingredient the medicine also contains:

Maize starch, sodium starch glycolate type A, pregelatinized starch, glycerol dibehenate, povidone, hypromellose, magnesium stearate, titanium dioxide, talc, triacetin, yellow iron oxide, red iron oxide, ethycellulose, cetyl alcohol, sodium lauryl sulfate

What does the medicine look like and what are the contents of the package:

Package sizes: 7, 14, 56, 60, 112 film-coated tablets. Not all package sizes may be marketed.

Bosentan Teva 62.5 mg: A round, biconvex pink-orange film-coated tablet. On one side it is embossed with the number "62.5".

Bosentan Teva 125 mg: An oval, biconvex pink-orange film-coated tablet. On one side it is embossed with the number "125".

Name and address of the manufacturer and marketing authorization holder: Teva Israel Ltd., 124 Dvora HaNevi'a St., Tel Aviv 6944020

Registration numbers of the medicine in the national drug registry of the Ministry of Health:

Bosentan Teva 62.5 mg 162-01-34905-00
Bosentan Teva 125 mg 162-02-34906-00

The leaflet was revised in June 2022 in accordance with the Ministry of Health guidelines.

teva