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

Do not use Bosentan Teva if you are pregnant, since the use of 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 using Bosentan Teva and for one additional month after termination of treatment (see section 2 subsection "Fertility, pregnancy and breastfeeding").

In addition to the leaflet, the medicine Bosentan Teva has a patient warning card. This card contains important safety information that you should know and act upon before starting treatment and during treatment with Bosentan Teva. Please review the patient warning card and the patient leaflet before starting to use the medicine. Keep the card and the leaflet for further reference, if required.

1. WHAT IS THE MEDICINE INTENDED FOR?

- For the treatment of pulmonary arterial hypertension (PAH) in patients with functional class II-IV according to the WHO (World Health Organization).
- To decrease the number of new ulcers that appear on the fingers (digital ulcers) in patients who suffer from scleroderma with active finger ulcers.

Therapeutic class: endothelin receptor antagonist.

2. BEFORE USING THE MEDICINE

Do not use the 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 subsection "Fertility, pregnancy and breastfeeding".
- You are taking cyclosporine A (a medicine used after transplantation or for the treatment of psoriasis).

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

Special warnings regarding the use of the medicine

Tests and follow-up:

Tests your doctor will perform 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 childbearing age

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

Tests your doctor will perform 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.

For information regarding these tests, also review the patient warning card (included in the preparation package). It is important to have these routine blood tests as long as you are treated with Bosentan Teva. We suggest that you write in the patient warning card the last test as well as the date of the next test (ask the doctor about the date), in order to help you remember when you should have the next test.

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 during the first four months of treatment with the medicine, and every three months after that, as patients taking Bosentan Teva may develop anemia.

If the results of these tests 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.

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 (a medicine for treatment of diabetes), rifampicin (a medicine for treatment of tuberculosis), fluconazole (a medicine for treatment of fungal infections), ketoconazole (a medicine for treatment of Cushing's syndrome) or nevirapine (a medicine for the treatment of HIV infection [AIDS]) – using these medicines 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, please see subsection "Fertility, pregnancy and breastfeeding" as well as the "Patient warning card" included in the package, which you should read.
- Simvastatin for the treatment of hypercholesterolemia.
- Warfarin (for prevention of blood coagulation).
- Other medicines for treatment of pulmonary hypertension: sildenafil and tadalafil.

Use of the medicine and food:

The medicine can be taken with or without food.

Fertility, pregnancy and breastfeeding:

Do not take Bosentan Teva if you are pregnant or planning to become pregnant.

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 childbearing 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.

Contraceptives:

- 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.

A patient warning card is included in the preparation package. You should fill in this card and present it to your doctor at the next appointment, so that your doctor or gynecologist can evaluate if there is a need for additional or alternative reliable contraceptive methods.

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:

- Bosentan Teva passes into your breastmilk.
- You are advised to stop breastfeeding if Bosentan Teva is prescribed for you as it is not known whether the passage of the medicine in breastmilk can harm the baby. Consult the doctor about it.

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, 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 hypertension or systemic sclerosis (scleroderma) should initiate and monitor the treatment with Bosentan Teva.
- Always use the medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and how to use the medicine.

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.

Children and adolescents

Bosentan Teva is not recommended for use in children and adolescents 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.

How to take the medicine

Swallow the medicine with a glass of water, with or without food. Do not crush, halve or chew the tablets.

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

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

If you forgot to take this 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.

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.

Follow the treatment as recommended by the doctor.

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

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

If you have any other questions regarding 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 serious side effects during treatment with Bosentan Teva are:

- Abnormal liver function which may affect more than one user out of 10.
- 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 (see section 2 "Tests and follow-up"). 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 (may occur in more than one user out of 10):

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

Common side effects (may occur in up to one user out of 10):

- 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 (may occur in up to one user out of 100):

- 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 (may occur in up to one user out of 1,000):

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

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

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, ethylcellulose, 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 license 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 2024.

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