Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Bosentan Taro 62.5 mg

Film-coated tablets

Active ingredient
Each film-coated tablet contains:
bosentan 62.5 mg

Bosentan Taro 125 mg

Film-coated tablets

Active ingredient
Each film-coated tablet contains:
bosentan 125 mg

Inactive ingredients and allergens: see section 2 under 'Important information about some of this medicine's ingredients', and section 6 'Additional information'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about the medicine. If you have any further questions, ask your doctor or pharmacist.
This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

Patient Safety Information Card
In addition to the leaflet, Bosentan Taro also has a patient safety information card about possible harm to the fetus. This card contains important safety information that you should know before and during treatment with Bosentan Taro. Read the patient safety information card and the patient information leaflet before using the medicine. Keep the card and the patient information leaflet for future reference if required.

Do not take Bosentan Taro if you are pregnant, since the medicine may cause harm to the fetus (see section 2 'Before using the medicine' under 'Do not use the medicine if' and 'Pregnancy, breastfeeding, and fertility'). If you are a woman of child-bearing age who could become pregnant, you should take a pregnancy test before you start taking Bosentan Taro and regularly every month while you are taking the medicine as well as a month after end of treatment. A negative result in each pregnancy test must be confirmed. You must use a reliable contraceptive method while taking Bosentan Taro and for one additional month after end of treatment (see section 2, 'Pregnancy, breastfeeding, and fertility').

1. What is this medicine intended for?

- to treat pulmonary arterial hypertension (PAH). PAH is high blood pressure in the blood vessels (the pulmonary arteries) that carry blood from the heart to the lungs. Bosentan Taro widens the pulmonary arteries, making it easier for the heart to pump blood through them. Widening the arteries lowers blood pressure and relieves the symptoms.
- to treat ulcers of the fingers (digital ulcers) in people with a condition called scleroderma. Bosentan Taro reduces the number of new finger ulcers that appear.

Therapeutic group: endothelin receptor antagonist.

2. Before Using the Medicine

Do not use this medicine if:

- you are sensitive (allergic) to the active ingredient (bosentan) or to any of the other ingredients in this medicine (see section 6)
- you have liver problems (consult your doctor)
- you are pregnant or could become pregnant because you are not using reliable contraceptive methods (hormonal contraceptives alone are not effective when taking Bosentan Taro). For additional information, please see the section 'Pregnancy, breastfeeding, and fertility'.
- you are taking cyclosporine A (a medicine used after a transplant or to treat psoriasis).

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

Special warnings about using this medicine
Tests to be performed before, during and after end of treatment - see the sections 'Pregnancy, breastfeeding, and fertility' and 'Tests and follow-up'.

Children and adolescents
Bosentan Taro is not recommended in children who have systemic sclerosis and digital ulcers.

Tests and follow-up
Tests your doctor will do before treatment begins:

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

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

Tests your doctor will do during treatment:
During treatment with Bosentan Taro, your doctor will order regular blood tests to check for changes in your liver function and hemoglobin level.

- Blood tests for liver function:

These tests will be done every month for the duration of treatment with Bosentan Taro. An additional test will be done 2 weeks after an increase in dose.

- Blood tests for anemia:

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

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

Interactions with other medicines:

If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:

- cyclosporine A (a medicine used after transplants and to treat psoriasis) - using together with Bosentan Taro is prohibited

- sirolimus or tacrolimus (medicines used after transplants) - using together with Bosentan Taro is not recommended
- glibenclamide (for diabetes), rifampicin (to treat tuberculosis), fluconazole and ketoconazole (medicines to treat fungal infections) or nevirapine (to treat HIV infection [AIDS]) - using together with Bosentan Taro is not recommended
- hormonal contraceptives (as these are not effective as the sole method of contraception when taking Bosentan Taro). Your doctor and/or gynecologist will determine which method of contraception is appropriate for you. For additional information, please see the section 'Pregnancy, breastfeeding, and fertility' as well as the Patient Safety Information Card.
- other medications for the treatment of pulmonary hypertension: sildenafil and tadalafil
- warfarin (to prevent blood clotting)
- simvastatin (used to treat hypercholesterolemia).

Using this medicine and food
You can take this medicine with or without food.

Pregnancy, breastfeeding, and fertility
Pregnancy:
Bosentan Taro may harm unborn babies that were 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 you start taking Bosentan Taro and regularly every month while you are taking the medicine as well as a month after end of treatment.
A negative result in each pregnancy test must be confirmed.
Do not take the medicine if you are pregnant or planning to become pregnant.
You must use a reliable contraceptive method while taking Bosentan Taro and for one month after end of treatment.
Your doctor or gynecologist will instruct you about reliable contraceptive methods while taking Bosentan Taro.
As Bosentan Taro may make hormonal contraception (e.g., oral, injections, implants, and skin patches) ineffective, this method on its own is not reliable.
Your doctor will recommend one highly effective method of contraception such as an intra-uterine device or tubal sterilization, or a combination of two methods (such as a hormonal method and a barrier method such as a diaphragm, contraceptive sponge, or your partner must also use a condom), or two barrier methods. Consult your doctor about using two methods of contraception.
If the chosen method of contraception is your partner's vasectomy, you must also use hormonal or barrier contraception at the same time.
Tell your doctor immediately if you become pregnant while you are taking Bosentan Taro, think you might be pregnant, or plan to become pregnant in the near future.
Breastfeeding:
If you are breastfeeding or planning to breastfeed, consult your doctor or pharmacist before starting treatment with Bosentan Taro, as it might harm the baby.
You are advised to stop breastfeeding if you are prescribed Bosentan Taro, as it is not known whether this medicine passes into breast milk.
Fertility:
If you are a man and you are taking Bosentan Taro, this medicine may reduce your sperm count. An effect on fertility cannot be ruled out. Talk to your doctor if you have any questions or concerns about this.

Driving and using machines

Bosentan Taro has no or negligible influence on the ability to drive and use machines. However, Bosentan Taro can lower 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 Taro, do not drive or operate any devices or machines.

Important information about some of this medicine's ingredients

This medicine contains less than 1 millimole sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. How to use this medicine?

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.
Treatment with Bosentan Taro may only be initiated and monitored by a doctor who has experience in the treatment of PAH or systemic sclerosis.
Only your doctor will determine your dose and how you should take this medicine. The recommended dosage is usually:
Adults
The treatment in adults is usually started with 62.5 mg twice daily (morning and evening) for the first four weeks. Then your doctor will usually advise you to take a dose of 125 mg twice daily, depending on how you respond to Bosentan Taro.
Swallow the tablet with a glass of water. Do not split, crush or chew the tablets.

Do not exceed the recommended dose.

If you think that the effect of Bosentan Taro is too strong or too weak, tell your doctor in order to find out whether your dose needs to be changed.

If you have accidently taken a higher dosage, contact your doctor immediately.
If you have taken an overdose, or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

If you forget to take this medicine at the scheduled time, take a dose as soon as you remember and continue taking the tablets at the usual time. Do not take a double dose to make up for the forgotten tablets.

If you stop taking this medicine
Suddenly stopping your treatment with Bosentan Taro may lead to your symptoms getting worse. Do not stop taking this medicine unless your doctor tells you to. Your doctor may advise you to reduce the dosage over a few days before stopping the medicine completely. Adhere to the treatment as recommended by your doctor. Even if your health improves, do not stop taking this medicine without consulting your 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 further questions about using this medicine, consult your doctor or pharmacist.

4. Side Effects

Like with all medicines, using Bosentan Taro may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

The most serious side effects with Bosentan Taro treatment:
Abnormal liver function which may affect more than one in 10 users.
Anemia, which may affect 1-10 in 100 users. Anemia may occasionally require blood transfusion.
Your liver function and blood values will be monitored during treatment with Bosentan Taro. It is important that you have these tests as ordered by your doctor.

Consult your doctor immediately if:
You get the following signs that your liver may not be working properly: nausea, vomiting, fever, abdominal pain, jaundice (yellowing of your skin or the whites of your eyes), dark-colored urine, itching of skin, fatigue (unusual tiredness or exhaustion), flu-like syndrome (joint and muscle pain with fever).
Additional side effects:
Very common side effects (appear in more than 1 in 10 users):
- headache
- edema (swelling of the legs and ankles or other signs of fluid retention)

Common side effects (appear in 1-10 in 100 users):
- flushing 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 (appear in 1-10 in 1,000 users):
- thrombocytopenia (low number of platelets)
- neutropenia/leukopenia (low number of white blood cells)
- elevated values in 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 side effects (appear in 1-10 in 10,000 users):
- anaphylaxis (general allergic reaction), angioedema (swelling, most commonly around the eyes, lips, tongue or throat)
- cirrhosis of the liver, liver failure

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

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet or signs of allergic reaction (such as swelling of the face or tongue, rash, itching) while you are taking Bosentan Taro, or if any of the side effects mentioned above worry you, consult your doctor.

Side effects in children and adolescents

The side effects that have been reported in children treated with Bosentan Taro are the same as those reported in adults.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link:
https://sideeffects.health.gov.il

5. How to store the medicine?

- Prevent poisoning! To prevent poisoning, keep this and all other medicines in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.

Storage conditions

- Store below 25°C.
- Medicines should not be disposed of via wastewater or household waste. 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, this medicine also contains:

maize starch, pregelatinised starch, sodium starch glycolate, povidone k-30, glycerol dibehenate, magnesium stearate.

The coating contains:

Opadry 21k520019 (yellow), isopropyl alcohol.

What the medicine looks like and contents of the pack:

Bosentan Taro 62.5 mg tablets are peach to light peach, round, convex, film-coated tablets with one side debossed with "62.5 mg" and the other side blank.

Bosentan Taro 125 mg tablets are peach to light peach, oval, convex, film-coated tablets with one side debossed with "125 mg" and the other side blank.

Approved pack sizes:

packs of 7 tablets and packs of 10 tablets.

Not all pack sizes may be marketed.

Registration holder's name and address:

Taro International Ltd., 14 Hakitor St., Haifa Bay, 2624761.

Manufacturer's name and address:
Sun Pharmaceutical Industries Limited. Industrial Area NO. 03, A.B Road, Dewas – 455001, Madhya Pradesh, (India).

Registration number of the medicine in the Ministry of Health National Drug Registry:
Bosentan Taro 62.5 mg: 35794
Bosentan Taro 125 mg: 35795

This leaflet was revised in December 2021 according to MOH guidelines.