

Bosentan (Tracleer®)

Issued by PHA's Scientific Leadership Council

Information is based on the United States Food and Drug Administration drug labeling

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WHAT IS BOSENTAN?

Bosentan is an oral medication classified as an endothelin receptor antagonist (ERA) which is approved for the treatment of pulmonary arterial hypertension (PAH) in World Health Organization (WHO) Group 1 patients. The goal of this therapy is to improve exercise ability and slow progression of the disease. Research studies showing the effectiveness of the medication included mostly patients with symptoms that were rated as WHO Functional Class II-III. Bosentan was approved for PAH by the United States Food and Drug Administration (FDA) in 2001.

HOW DOES BOSENTAN WORK?

Bosentan works by blocking endothelin, a substance made by the body. Endothelin causes blood vessels to narrow (constrict). It also causes abnormal growth of the muscle in the walls of the blood vessels in the lungs. This narrowing increases the pressure required to push the blood through the lungs to get oxygen. By blocking the action of endothelin, causing vessels to relax, bosentan decreases the pulmonary blood pressure to the heart and improves its function. This generally results in the ability to be more active. Research studies have verified this improvement.

HOW IS BOSENTAN GIVEN?

Bosentan is taken orally, with or without food. There are two FDA approved doses; 62.5 mg (orange-white and round) or 125 mg (orange-white and oval). Patients' physicians will decide which strength is right for them.

HOW DO PATIENTS OBTAIN BOSENTAN?

Bosentan is a limited distribution medication, which means it cannot be purchased at a local pharmacy. It must be prescribed by a physician through the Tracleer® Access Program (TAP) and insurance approval must be obtained prior to starting therapy. TAP will forward the request to a specialty pharmacy. Bosentan is then sent to patients monthly by any of the following specialty pharmacies: Accredo Health Group Inc., Aetna Specialty Pharmacy, CVS Caremark, Cigna Tel-Drug, CuraScript, Kaiser Permanente Specialty Pharmacy and Walgreens Specialty Pharmacy (Medmark).

WILL INSURANCE PAY FOR BOSENTAN?

It is expected that most insurance plans will pay for bosentan prescriptions; however, plans with a set co-payment may result in large cost to the patient.

Medicaid and most state-run insurance plans will pay for bosentan. Medicare will also cover bosentan in most cases under Part D.

Actelion PAH Pathways® (866-288-3546) may assist with either partial or full drug coverage for any patient with qualifying financial circumstances. Caring Voice Coalition (888-267-1440), an organization that provides grants to assist with drug cost for patients with chronic illnesses, may

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also provide coverage if the patient qualifies for such assistance.

WHAT ARE THE FREQUENT SIDE EFFECTS OF BOSENTAN?

Bosentan is generally well tolerated. The most frequent side effects are:

- Swelling of legs or abdomen (fluid retention)
- Respiratory tract infections

Fluid retention is a known side effect of ERAs. This was first seen in the clinical trial studies of bosentan. The swelling was generally mild and occurred more frequently in older adult patients. It is important to notify your physician if you experience swelling or any other side effects. Treatment may be required including reducing salt and fluid in your diet, as well as a water pill (diuretic) to promote increased fluid removal through the kidneys.

The red blood cell count may decrease in some patients but rarely requires blood transfusion.

The development of elevated liver function tests (LFTs) are performed, measured in blood samples to more than three times the upper limit of normal may be observed in up to 10% of patients receiving this medication.

Decreases in sperm count have been observed in men taking bosentan.

HOW ARE SIDE EFFECTS OF BOSENTAN MONITORED?

Because of the potential of damage to the liver, liver function tests (LFTs) must be obtained before initiating therapy and every month as long as a patient is receiving bosentan. A physician will guide a patient in managing their liver enzymes if they become elevated. This may require a patient stop the medication.

Bosentan should be stopped if the blood tests for liver enzymes (LFTs) are accompanied by signs and symptoms of abnormal liver function or injury, or by an increased total bilirubin (another blood test for liver function) to more than 2 times normal.

Because of the potential harm to the fetus, women must also have a pregnancy test before initiating therapy and on a monthly basis as they are receiving bosentan.

Red blood cell counts should be checked at one and three months after initiation of bosentan therapy. This should then be monitored once every three months as long as a patient is receiving bosentan.

WHAT ARE CONSIDERATIONS FOR USE OF BOSENTAN IN SPECIAL POPULATIONS?

Bosentan should not be used in pregnancy. Bosentan has been shown to be harmful to the fetus in research studies of rats and rabbits. Patients should not become pregnant while taking bosentan. Bosentan has been shown to be harmful to the fetus in research studies of rats and

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rabbits. Therefore, two forms of contraception are recommended when taking bosentan to prevent pregnancy: Surgical treatment to prevent pregnancy, such as a tubal ligation and; a Copper T380A or LNG 20 intrauterine device (IUD). In addition, a pregnancy test prior to the initiation of bosentan and monthly thereafter is advised. If a patient becomes pregnant while taking bosentan, she you should stop the bosentan and immediately notify her doctor. It is not known whether bosentan passes into breast milk; therefore, nursing mothers should not take bosentan.

There has not been research to determine whether bosentan is safe or effective for children.

Bosentan is not recommended in patients with significant liver disease.

For patients with significant kidney disease, the dose of bosentan does not need to be changed.

COULD A PATIENT BE ALLERGIC TO BOSENTAN?

This is possible but not likely.

WHAT ARE IMPORTANT DRUG INTERACTIONS WITH BOSENTAN? (PLEASE SEE PACKAGE INSERT FOR FULL DETAILS)

Bosentan is broken down by the body in a way that may result in important interactions with other drugs the patient may be taking at the same time.

Bosentan may reduce the ability of birth control pills to prevent pregnancy.

Bosentan should not be used with cyclosporine A or glyburide.

Ritonavir or ritonavir-containing combination drugs require a special approach and dose changes if used with bosentan. The dosing should be adjusted by the doctor.

In patients receiving cholesterol-lowering medications, cholesterol levels should be monitored carefully to determine if the cholesterol medication dose requires a change.

For patients taking rifampin and bosentan, drug levels may be altered. LFTs should also be carefully monitored.

Based on animal studies, caution should be exercised if tacrolimus and bosentan are used together. This has not been studied in humans.

Bosentan blood levels may be increased if used with ketoconazole.

While there are changes in drug levels in the blood with combined use of sildenafil and bosentan, the differences do not appear to be clinically important.

Patients should discuss with the medications (including over the counter and herbal preparations) they are currently taking with their physician so that any potential or known drug to drug interactions can be avoided.