Bosentan (Tracleer®) for Pediatric Use

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Information is based on the United States Food and Drug Administration drug labeling
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What is bosentan?
Bosentan is a medicine used to treat WHO Group 1 pulmonary hypertension (PH) – pulmonary arterial hypertension (PAH). It is approved for pediatric patients ages 3 years and older with idiopathic (“unknown cause”), genetic (people born with a genetic difference know to increase the risk for PH, or who have family members with PH) and congenital heart disease-associated PAH. The goal of this therapy is to decrease the pulmonary vascular resistance that helps the heart and lungs work better, which is further expected to improve the patient’s ability to breathe more comfortably at rest and with activities, including exercise. Bosentan was approved for pediatric use by the United States Food and Drug Administration (FDA) in 2017.

How does bosentan work?
Bosentan works by blocking endothelin, a substance made by the body that causes blood vessels to narrow. Endothelin also causes abnormal growth of the muscle in the walls of the blood vessels in the lungs, further narrowing the vessels and making it harder for the blood to travel through the lungs to get oxygen. By blocking the action of endothelin, bosentan causes the blood vessels to relax, decreasing the work of the lungs and ultimately, the workload of the heart. This should allow patients to be more active in everyday life.

How is bosentan given?
Bosentan is taken by mouth, with or without food, twice daily. There are film coated tablets (62.5 mg and 125 mg) for use in adults and a pediatric tablet that can be used for oral suspension (32 mg). These pediatric tablets, or half tablets, can be placed and suspended in water and have a fruit flavor. Dosage is typically based on weight. The physician will decide the proper dose for each patient.

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). Insurance approval must be obtained prior to starting therapy. TAP will forward the request to a specialty pharmacy that is contracted with the patient’s prescription insurance plan or based on the provider’s preference. Bosentan is then mailed to the patient monthly by one of the following certified specialty pharmacies:

- Accredo
- Aetna
- AllianceRx Walgreens Prime
- Axium
- BriovaRx
- Cigna
- CVS Specialty
- Humana
- Kaiser Permanente.

Will insurance pay for bosentan?
It is expected that most insurance plans will pay for bosentan prescriptions. Every health plan has specific guidelines. The insurance company may need days or weeks to review the patient’s medical information before making a decision on whether to provide coverage. Medicaid and most state-run insurance plans will pay for bosentan.

Depending on your insurance type, you may be eligible for assistance from the company that manufactures your therapy or from a non-profit charitable assistance organization. For more information visit www.PHAssociation.org/Help or call 301-565-3004.

What are the frequent side effects of bosentan?
Bosentan is generally well tolerated. The most frequent side effects reported in clinical trials in children are sinus/lung congestion or infection, flushing, headache, increased liver enzymes and swelling of the hands and feet (fluid retention).
Elevation of liver enzymes is typically not associated with symptoms but requires regular monitoring of liver function tests (LFTs) and can necessitate stopping of the medication (see below).

Fluid retention is a known side effect of this type of medicine. This was first seen in clinical trial studies of bosentan. The swelling was generally mild and occurred more frequently in older adult patients but can occur in children. It is important to notify your physician if you notice swelling or any other side effects.

The red blood cell count may decrease in some patients (anemia), but patients rarely require blood transfusion. Blood tests should also be monitored regularly for this (see below).

**How are side effects of bosentan monitored?**
Because of the potential damage to the liver, 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 his or her liver enzymes if they become elevated. This may require a patient to stop taking bosentan if the blood tests for liver enzymes are more than three times the upper limit of normal or if accompanied by signs and symptoms of abnormal liver function or injury.

Blood tests to monitor for anemia (hemoglobin and hematocrit) 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.

Because of the potential harm to the fetus, female patients of child bearing age must also have a pregnancy test before initiating therapy and on a monthly basis while they are receiving bosentan.

**What are considerations for use of bosentan in special populations?**
Bosentan should not be used during pregnancy. Bosentan has been shown to be harmful to the fetus in research studies of rats and rabbits. Therefore, two forms of contraception are recommended to prevent pregnancy in females of child bearing age who are taking bosentan. In addition, pregnancy tests should be taken prior to initiation of bosentan and monthly thereafter. If a patient becomes pregnant while taking bosentan, she should stop the medication and immediately notify her doctor. It is not known whether bosentan passes into breast milk; therefore, nursing mothers should not take bosentan. Female caregivers of children with PAH who are pregnant or may become pregnant should discuss safe medication handling practices with their physician or pharmacist.

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 unlikely. Bosentan is contraindicated in patients who have an allergic reaction to the medication.

**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 cause interactions with other drugs, including over the counter medications and herbal supplements. The patient should discuss these possible medication interactions with his/her physician so that any potential or known drug to drug interaction can be avoided. Specifically:

1. Bosentan may reduce the ability of birth control pills to prevent pregnancy.
2. Bosentan should not be used with cyclosporine A or glyburide.
3. Medications for HIV, such as ritonavir or ritonavir-containing combination drugs require a special approach and dose changes if used with bosentan. The dosing should by adjusted by the doctor.
4. In patients receiving cholesterol-lowering medications, cholesterol levels should be monitored carefully to determine if the cholesterol medication dose requires a change.
5. For patients taking rifampin for infection and bosentan, drug levels may be altered. LFTs should be carefully monitored.
6. Based on animal studies, caution should be exercised if tacrolimus and bosentan are used together. This has not been studied in humans.
7. Bosentan blood levels may be increased if used with ketoconazole.