

Ambrisentan (Letairis®)

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 AMBRISENTAN?

Ambrisentan 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. Ambrisentan was approved for PAH by the United States Food and Drug Administration (FDA) in 2007.

HOW DOES AMBRISENTAN WORK?

Ambrisentan 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, ambrisentan 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 AMBRISENTAN GIVEN?

Ambrisentan is taken orally, with or without food. There are two FDA approved doses; 5 mg (pale pink and square) or 10 mg (dark pink and oval). Patients' physicians will decide which strength is right for them.

HOW IS AMBRISENTAN SUPPLIED?

Ambrisentan comes in 5 and 10 mg, film-coated, unscored tablets. The 5 mg tablet is pale pink and square. The 10 mg tablet is deep pink and oval.

HOW DO PATIENTS OBTAIN AMBRISENTAN?

Ambrisentan is a limited distribution medication, which means it cannot be purchased at a local pharmacy. It must be prescribed by a physician through the Letairis® Education and Access Program (LEAP) and insurance approval must be obtained prior to starting therapy. LEAP will forward the request to a specialty pharmacy. Ambrisentan 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, Walgreens Specialty Pharmacy (Medmark), and WellCare. Ambrisentan can only be obtained through the Letairis® Education and Access Program (LEAP).

WILL INSURANCE PAY FOR AMBRISENTAN?

It is expected that most health insurance plans will pay part of the cost of this medication. However, some plans still leave patients with a high out-of-pocket responsibility.

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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 AMBRISENTAN?

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

- Swelling of legs or abdomen (fluid retention)
- Nasal stuffiness or congestion
- Inflammation of the sinuses
- Flushing of the skin
- Rapid or skipped heart beats
- Abdominal pain
- Constipation
- Elevated liver function tests

Fluid retention is a known side effect of ERAs. This was first seen in the clinical trial studies of ambrisentan. 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.

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

The development of elevated liver function tests (LFTs), measured in blood samples to over three times the normal levels, may occur in patients taking ERAs but appears to be less common with ambrisentan compared to bosentan.

Decreases in sperm count have been observed in men taking bosentan, another type of ERA. Based on this information and preclinical data from animal studies, it is possible that ambrisentan may also reduce sperm count.

HOW ARE SIDE EFFECTS OF AMBRISENTAN MONITORED?

Red blood cell count should be assessed prior to initiating therapy and after 1 month; this should then be monitored periodically as long as a patient is receiving ambrisentan.

The FDA recently removed the black box warning related to liver injury for ambrisentan because

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it seems unlikely to harm the liver. Although monthly blood tests for liver function are no longer mandated by the FDA, it still may be wise to test liver function (CMP) before beginning treatment and occasionally while the patient is taking ambrisentan.

Ambrisentan should be stopped if the LFT results increase to more than five times normal levels or if two other related problems are present: the total bilirubin level (another blood test of the liver function) increases to more than 2 times the normal level or the patient develops signs and symptoms of liver harm.

Because of the potential harm to the fetus, women must have a pregnancy test before initiating therapy, and every month while they are receiving ambrisentan.

WHAT ARE CONSIDERATIONS FOR USE OF AMBRISENTAN IN SPECIAL POPULATIONS?

Ambrisentan should not be used in pregnancy. Ambrisentan has been shown to be harmful to the fetus in research studies of rats and rabbits. Patients should not become pregnant while taking ambrisentan; therefore, two forms of contraception are recommended when taking ambrisentan in order to be sure to prevent pregnancy. Surgical treatment to prevent pregnancy, such as a tubal ligation, is an option. Another contraception option is for women to use a Copper T380A or LNG 20 intrauterine device (IUD). In addition, a pregnancy test prior to the initiation of ambrisentan and monthly thereafter is advised. If a patient becomes pregnant while taking ambrisentan, she should immediately notify her doctor. It is not known whether ambrisentan passes into breast milk; therefore, nursing mothers should not take ambrisentan.

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

Ambrisentan is not recommended in patients with significant liver disease.

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

COULD A PATIENT BE ALLERGIC TO AMBRISENTAN?

This is possible, but not likely.

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

Ambrisentan can interact with cyclosporine, a medication given to patients who have had transplant surgery. When ambrisentan and cyclosporine are used together, the dose of ambrisentan should be limited to 5 mg daily.

Use of ambrisentan with sildenafil or tadalafil does not result in any important interaction

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.