Ambrisentan (Letairis)
Updated June 2023

Ambrisentan treats pulmonary arterial hypertension (PAH), also known as Group 1 pulmonary hypertension. This medication aims to improve exercise ability and slow progression of the disease.

The Food and Drug Administration (FDA) approved Letairis in 2007 to treat PAH. Letairis also is available as a generic drug, ambrisentan.

How ambrisentan works
Ambrisentan is an endothelin receptor antagonist. It works by blocking endothelin, a substance made by the body that causes the blood vessels in the arteries of the lungs to constrict. Endothelin causes abnormal growth of the muscular layer in the vessel wall, which narrows the lumen, or space inside the blood vessel.

This narrowing causes the pressure to increase, making it harder for the right side of the heart to push the blood through the lungs to get oxygen. By blocking the action of endothelin, ambrisentan helps relax the blood vessels so the lung blood pressure goes down. Lower lung pressures reduce stress on the right heart so heart function improves. Improved heart function generally results in the ability to be more active. Research studies have verified this improvement.

Dosage
- Ambrisentan is taken orally, with or without food.
- Tablet must be swallowed whole. Do not split, crush, or chew tablets.
- Available in two doses: 5 mg and 10 mg.
- Your healthcare provider will determine which strength is the right dose for you.

Obtaining ambrisentan
Because of the risk of serious birth defects, ambrisentan is available to women only through a restricted distribution program required by the FDA. The program is known as Risk Evaluation and Mitigation Strategy (REMS) for ambrisentan. All women, regardless of reproductive potential, must enroll in the Ambrisentan REMS before starting this therapy. Women of reproductive potential must comply with monthly pregnancy testing and contraception requirements.

Healthcare providers must be enrolled in the Ambrisentan REMS program to prescribe this therapy. Ambrisentan has limited distribution, which means you can’t buy it at a local pharmacy. Insurance approval usually is required before starting therapy. The drug is dispensed by a specialty pharmacy per insurance preference. Ambrisentan is delivered to patients monthly through the following mail-order specialty pharmacies: Accredo, Aetna, Alliance Rx Walgreens Prime, Axium, BriovaRx, Cigna, CVS specialty, Humana and Kaiser Permanente.

Male patients don’t have to enroll in the REMS program.
Insurance coverage
Most health insurance plans will pay part of the cost of this medication. However, some plans leave patients with high out-of-pocket costs. Ask your insurance provider for more accurate information about copays or out-of-pocket costs. Depending on your insurance plan, you might be eligible for assistance from the company that manufactures the drug or copay assistance from a non-profit charitable organization. See the list or call 301-565-3004.

Common side effects
Ambrisentan is generally well tolerated. The most common 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.
- Elevated liver-function tests.

Fluid retention is a known side effect of endothelin receptor antagonists such as ambrisentan. In ambrisentan clinical trial studies, where the fluid retention was first noticed, the swelling was generally mild and occurred more frequently in older adults. It’s important to notify your physician if you experience swelling or any other side effects.

For some people, red blood cell count may decrease, but it rarely requires blood transfusion.

Elevated liver function can occur in patients taking endothelin receptor antagonists. However, it appears to be less common with ambrisentan. Elevated live enzymes can indicate liver damage. Liver function is measured through blood samples and is considered elevated when it’s more than three times higher than normal.

Decreased sperm counts have been observed in human and animal studies with another endothelin receptor antagonist and in animal fertility studies with ambrisentan.

Monitoring side effects
Your doctor should measure your red blood cell count before you start therapy and one month after starting the medicine. Your red blood cell count should be monitored periodically as long as you take ambrisentan.

Although the FDA no longer requires monthly blood tests for liver function, it still may be wise to test liver function before beginning treatment and occasionally while taking ambrisentan. Ambrisentan should be stopped if the liver function test 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 twice the normal level or if 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 take ambrisentan.

**Considerations for special populations**

**Pregnancy and breastfeeding:** Ambrisentan should not be used in pregnancy. Ambrisentan has been shown to be harmful to fetuses in research studies of rats and rabbits. Patients should not become pregnant while taking ambrisentan. Therefore, two forms of contraception are recommended to be sure to prevent pregnancy while patients take ambrisentan.

Surgical treatment to prevent pregnancy, such as tubal ligation, is one option. Another is a copper T380A or LNG 20 intrauterine device. If a patient becomes pregnant while taking ambrisentan, she should immediately notify her doctor. It’s not known whether ambrisentan passes into breast milk; therefore, nursing mothers should not take ambrisentan.

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

**Other considerations**

Ambrisentan is not recommended in patients with significant liver disease.

For patients with significant kidney disease, the ambrisentan dose doesn’t need to be changed.

Allergies are possible, but not likely.

**Drug interactions**

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

Use of ambrisentan with sildenafil or tadalafil doesn’t cause significant interactions.

Patients should ask their physicians about medications they take (including over the counter and herbal preparations) that might cause potential or known drug interactions.