New drug approved for pulmonary arterial hypertension

FDA granted marketing approval on June 15 for ambrisentan, or Letairis, an endothelin-receptor antagonist sold by Gilead Sciences Inc. indicated for the once-daily treatment of pulmonary arterial hypertension (PAH), a rare, life-threatening condition characterized by continuous high blood pressure within the arteries of the lungs.

Use of the drug has been shown to improve a patient’s ability to exercise and has delayed clinical worsening of PAH, according to the product’s labeling.

Because of the serious adverse teratogenic and hepatic events associated with the drug, ambrisentan can be prescribed and obtained only through a restricted distribution program known as the Letairis Education and Access Program, or LEAP.

Prescribers and patients must enroll in the program, according to the drug’s labeling. Prescribers are also required to discuss ambrisentan’s medication guide and educational brochures with patients.

Similar to the restricted distribution program for isotretinoin, women of childbearing potential must have a negative pregnancy test before starting ambrisentan and a negative test every month during treatment. Women must also use two “reliable” forms of birth control during treatment with the drug and for one month after stopping therapy.

The drug is supplied only through specialty pharmacies, which mail the product directly to patients enrolled in LEAP.

Ambrisentan is available in 30-count unit-of-use packages of 5- or 10-mg film-coated tablets.

The labeling includes a black-box warning alerting prescribers that ambrisentan can elevate liver aminotransferase values to at least three times the upper limit of normal (ULN).

According to the boxed warning, ambrisentan was associated with aminotransferase elevations of greater than three times the ULN in 0.8% of patients in the 12-week trials and 2.8% of patients in the long-term open-label trials that continued as long as one year.

The black-box warning—FDA’s strongest caution—advises that the patient’s serum aminotransferase levels, and bilirubin if aminotransferase levels are elevated, must be measured before starting the drug and every month during treatment.

The drug is not recommended for use in patients with moderate or severe hepatic impairment.

The boxed warning also strongly caution that women must not be pregnant when they start the drug or become pregnant when taking the medication because of the risk of serious birth defects.

The labeling recommends that treatment should be initiated at 5 mg once daily with or without food. An increase in the dosage to 10 mg once daily could be considered if the 5 mg dosage is well tolerated.

The drug’s approval was based on the results of two short-term, randomized, double-blind, placebo-controlled trials involving 393 patients, according to Gilead. Patients receiving the drug could walk farther after 4 weeks of treatment than those in the placebo group, and a dose–response relationship became apparent after 12 weeks of treatment, the firm said.

The most common adverse effects in patients during the clinical trials were swelling of the legs and ankles, nasal congestion, sinusitis, and skin flushing.

—Donna Young

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