Oral treprostinil (Orenitram®)

Issued by PHA's Scientific Leadership Council
Information is based on the United States Food and Drug Administration drug labeling
Last Updated June 2015

WHAT IS ORAL TREPROSTINIL?

Treprostinil is an oral medication approved for the treatment of pulmonary arterial hypertension (PAH) in World Health Organization (WHO) Group 1 PAH patients to improve exercise capacity.

The study that established its effectiveness included predominately PAH patients with etiologies of idiopathic or heritable PAH (75 percent), or PAH associated with connective tissue disease (19 percent), who were symptomatic in WHO functional class II-III. The most significant effect was achieved when oral treprostinil was used alone, without other PAH therapies, in which case the improvement in exercise was about 10 percent.

Oral treprostinil was approved for PAH by the United States Food and Drug Administration (FDA) in December 2013.

HOW DOES ORAL TREPROSTINIL WORK?

Treprostinil is a synthetic analogue of prostacyclin, a naturally occurring substance in the body that dilates blood vessels. The major actions of oral treprostinil appear to be similar to the actions of another prostacyclin, epoprostenol (Flolan® or Veletri®), and include vasodilatation of the pulmonary and systemic vascular beds (widening of narrowed blood vessels in the lung and other parts of the body).

HOW IS ORAL TREPROSTINIL SUPPLIED?

Oral treprostinil is available in the following four doses: a white 0.125 mg pill, a green 0.25 mg pill, a yellow 1 mg pill and a pink 2.5 mg pill.

HOW DO PATIENTS OBTAIN ORAL TREPROSTINIL?

Oral treprostinil cannot be purchased at a local pharmacy. It must be prescribed by a healthcare provider such as a physician or advanced practice provider who has experience prescribing PH medications.

Insurance approval must be obtained prior to starting therapy. The drug is provided directly from specialty pharmacies (Accredo Health Group, Inc. and CVS Caremark) that provide support through a team of clinical pharmacists and nurses. They assist with all aspects involved in the initiation and long-term usage of oral treprostinil, including

Oral treprostinil (Orenitram®)

Continued

insurance issues, titration of medication, education on drug, and managing possible side effects.

WILL INSURANCE PAY FOR ORAL TREPROSTINIL?

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.

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.

HOW IS ORAL TREPROSTINIL GIVEN?

The recommended starting dose of oral treprostinil is 0.25 mg twice daily (BID), taken approximately 12 hours apart. Another common starting dose is 0.125 mg three times daily (TID), taken approximately 8 hours apart. Your healthcare provider will tell you how to increase the dose to get the best benefit from this medicine. The medication is started at a very low dose and is up-titrated on a regular basis until benefits are achieved in the setting of mild side effects. Your healthcare provider will be monitoring you closely during this up-titration period. Maximum dose is determined by tolerability.

Oral treprostinil should be taken with food at every dose. Oral treprostinil tablets should be swallowed whole; do not crush, split or chew the tablets.

Avoid abrupt discontinuation since it could lead to a worsening of pulmonary hypertension symptoms. If a dose of medication is missed, the patient should take the missed dose as soon as possible, with food.

Oral treprostinil (Orenitram®)

Continued

WHAT ARE THE MAIN SIDE EFFECTS WITH ORAL TREPROSTINIL?

The side effects of oral treprostinil are similar to those seen with all prostacyclin medications and include:

- Headache
- Diarrhea
- Nausea
- Flushing of the skin
- Jaw pain
- Pain in hands or feet
- Low systemic blood pressure.

WHAT ARE CONSIDERATIONS FOR USE OF ORAL TREPROSTINIL IN SPECIAL POPULATIONS?

Oral treprostinil is considered Pregnancy Category C. Animal reproductive studies with treprostinil diolamine have shown an adverse effect on the fetus. There are no adequate and well-controlled studies in humans.

It is not known whether treprostinil is excreted in human milk or absorbed systemically after ingestion. Because many drugs are excreted in human milk, choose oral treprostinil OR breastfeeding.

Safety and efficacy in pediatric patients has not been established.

Exercise caution with use of oral treprostinil in patients with mild liver impairment.

There is an increase in the systemic exposure of the medication due to the liver's inability to clear the medication, as well. Avoid its use in patients with moderate liver impairment. DO NOT use in patients with severe liver impairment. No dose adjustments are required in patients with renal impairment. Oral treprostinil is not removed by dialysis.

COULD A PATIENT BE ALLERGIC TO ORAL TREPROSTINIL?

This is possible, but not likely. If you are concerned that you may be allergic, please contact your healthcare provider immediately.

Oral treprostinil (Orenitram®)

Continued

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

No medications are prohibited with the use of oral treprostinil.

When oral treprostinil is given along with CYP2C8 enzyme inhibitors (medicines like gemfibrozil) that interact with liver enzymes that can change drug levels, systemic levels of treprostinil will be increased. Significant reduction in oral treprostinil dose is suggested under the direction of your healthcare provider.

Oral treprostinil may be taken with anticoagulants, such as Coumadin. Note that oral treprostinil inhibits platelet aggregation, so there is an increased risk of bleeding, particularly among patients receiving anticoagulants.

Do not take oral treprostinil with alcohol, as release of treprostinil from the tablet may occur at a faster rate than intended, causing more side effects.

Always discuss all medications at each visit with your healthcare provider.

ARE THERE OTHER WAYS OF ADMINISTERING TREPROSTINIL?

Inhaled treprostinil (Tyvaso®) is approved and available for use in patients with PAH. It is discussed in depth on a separate Treatment Fact Sheet.

Intravenous and subcutaneous treprostinil (Remodulin®) are approved and available for use in patients with PAH. They are discussed in depth on a separate Treatment Fact Sheet.

MISCELLANEOUS CONSIDERATIONS WHEN TAKING ORAL TREPROSTINIL

The cover of the pill that contains the medicine is not dissolved in your stomach. You may see the small shell of this empty pill eliminated in the feces.

Ask your doctor about taking this medication if you know you have diverticulosis.