

Epoprostenol (Flolan®)

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 EPOPROSTENOL?

Epoprostenol is an intravenous medication approved for the treatment of pulmonary arterial hypertension (PAH) in World Health Organization (WHO) Group 1 patients. Epoprostenol is a synthetic analogue of prostacyclin, a naturally occurring substance in the body, which has effects on dilating blood vessels. Epoprostenol was approved for PAH by the United States Food and Drug Administration (FDA) in 1995.

HOW DOES EPOPROSTENOL WORK?

The major actions of epoprostenol are vasodilatation of the pulmonary and systemic vascular beds (widening of narrowed blood vessels in the lung and other parts of the body), and inhibition of platelet clumping (aggregation). Improved survival and exercise capacity has been demonstrated in a 3-month study of intravenous epoprostenol given to patients with idiopathic pulmonary arterial hypertension.

An additional trial with intravenous epoprostenol included administration to patients with PAH associated with the scleroderma spectrum of connective tissue disease. This resulted in reduced symptoms and improved exercise capacity in patients.

HOW IS EPOPROSTENOL GIVEN?

Epoprostenol is given in two ways: long-term and short-term. Long-term epoprostenol is administered through a surgically placed central venous catheter. A small battery-powered pump (CADD Legacy Pump) keeps the medication flowing into the body from outside the body. Short-term, epoprostenol can be administered through a small IV placed in the arm. This may be useful during catheter malfunction.

Epoprostenol is not stable at room temperature. It requires refrigeration for storage and needs to be kept cold with ice while being infused.

DOSING OF EPOPROSTENOL

Epoprostenol is usually initiated at 2 ng/kg/min and the dose is gradually increased at increments of 1-2 ng/kg/min to achieve symptomatic relief. It is not uncommon for some patients to be on a dose of 40-70 ng/kg/min, or higher over time. The goal of dosing is to achieve optimal benefit while staying at a safe level. However, the dose, like other infusion agents, must be individualized to each patient.

HOW IS EPOPROSTENOL SUPPLIED?

Epoprostenol is supplied in mL vials containing either 0.5 or 1.5 mg of epoprostenol powder. A separate vial containing diluent (the chemicals needed to help dissolve epoprostenol) is also supplied. Mixing a final 100 ml of medicine requires first preparing diluent and then dissolving the epoprostenol.

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HOW DO PATIENTS OBTAIN EPOPROSTENOL?

Epoprostenol is a limited distribution medication, which means it cannot be purchased at a local pharmacy. It must be prescribed by a physician, and 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 a team of clinical pharmacists and nurses. They assist with all aspects involved in the long-term usage of epoprostenol, including insurance issues, education on pump function and central line care, providing pumps and supplies and technical troubleshooting with 24-hour hotlines.

WILL INSURANCE PAY FOR EPOPROSTENOL?

It is expected that most insurance plans will pay for epoprostenol prescriptions; however, plans with a set co-payment may result in a large cost to the patient.

Medicaid and most state-run insurance plans will pay for epoprostenol. Medicare will also cover epoprostenol in most cases under Part D.

Accredo Therapeutics (724-778-3980) offers a variety of options to cover either partial or full drug cost for any patient providing evidence of adequate financial need. Caring Voice Coalition (888-267-1440), an organization that provides grants to assist with drug cost for patients with chronic illnesses, may also provide coverage if the patient proves a need for such assistance.

HOW IS EPOPROSTENOL INITIATED?

Patients started on intravenous epoprostenol typically require admission to the hospital for several days. Education on central venous catheter (e.g. Hickman) care, CADD pump specifics, and administration of epoprostenol are taught by specialty nurses before the patient leaves the hospital.

WHAT ARE THE MAIN SIDE EFFECTS WITH EPOPROSTENOL?

The side effects of epoprostenol are similar to those seen with all prostacyclin agents and include:

- Headache
- Diarrhea
- Nausea
- Jaw pain
- Flushing of the skin
- Dizziness
- Swelling

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- Itching
- Muscle or joint pain
- Low systemic blood pressure.

In addition to side effects from the medicine, there may be side effects due to the infusion system. Infection and bleeding can occur at the infusion site.

The half-life of epoprostenol is about 3 minutes. Stopping epoprostenol can be fatal when done abruptly.

WHAT ARE CONSIDERATIONS FOR USE OF EPOPROSTENOL IN SPECIAL POPULATIONS?

There are no adequate, well-controlled studies of the potential effect of infused epoprostenol in pregnant humans. In pregnant animals, studies of continuous infusions of epoprostenol sodium using doses higher than normally used in humans has revealed no problems with fetal birth defects or miscarriage. Infused epoprostenol currently carries an FDA grading of “B” in pregnancy and should be used during pregnancy when the benefit is felt to outweigh any risk.

Safety and efficacy in pediatric patients has not been established. Epoprostenol has been used in children. However, clinical studies of epoprostenol did not include sufficient numbers of patients 16 years of age and under to determine its safety and efficacy in children.

Clinical studies did not include a sufficient number of patients over age 65 to determine either safety or efficacy for this age group.

Epoprostenol clearance appears to be reduced in patients with liver insufficiency. This may result in decreased tolerability. Patients with mild or moderate liver insufficiency may be started at lower initial doses and may be more sensitive to dose increases. Epoprostenol has not been studied in severe liver insufficiency.

Epoprostenol has not been evaluated in patients with impaired kidney function. Since epoprostenol is mainly excreted through the kidney, reduced drug clearance may potentially result in increased exposure to epoprostenol and decreased tolerability. Likewise, the effect of dialysis is unknown.

COULD A PATIENT BE ALLERGIC TO EPOPROSTENOL?

This is possible, but not likely.

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

No medications are prohibited with the use of epoprostenol.

ARE THERE OTHER WAYS OF ADMINISTERING EPOPROSTENOL?

At this time there are no FDA-approved alternate ways of administering epoprostenol as Flolan®.