Room Temperature Stable (RTS) Epoprostenol (Veletri®)

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WHAT IS RTS EPOPROSTENOL?

Room temperature stable (RTS) 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 RTS EPOPROSTENOL (VELETRI®) 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 aggregation (clumping). Improved survival and exercise capacity have been shown in a three-month study of intravenous epoprostenol given to patients with idiopathic pulmonary arterial hypertension.

A second trial with intravenous epoprostenol included administration to patients with PAH associated with the scleroderma spectrum of connective tissue disease, and during the trial patients had reduced symptoms and improved exercise capacity.

HOW IS RTS EPOPROSTENOL GIVEN?

RTS 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.

RTS epoprostenol (Veletri®) unlike FLOLAN®, does not need to be refrigerated while it is being used as long as drug concentrations and air temperature are within typical ranges (concentration of diluted drug > 3000 ng/ml and temperature < 86^{o} F). This stability is because RTS epoprostenol contains additional substances in the diluting mixture which stabilize the medicine at room temperature. RTS epoprostenol may be used outside of these conditions typically for limited periods of time.

DOSING OF RTS EPOPROSTENOL (VELETRI®)

Epoprostenol is usually initiated at 2 ng/kg/min, and the dose is gradually increased 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 with a tolerable safety profile; however, like other infusion agents, the dose must be individualized to each patient.

HOW IS RTS EPOPROSTENOL (VELETRI®) SUPPLIED?

RTS epoprostenol is supplied in mL vials containing either 0.5 or 1.5 mg of epoprostenol powder and buffer together. Preparation of medicine requires the addition of sterile water or sterile saline

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to this powder and then transferring 100 mL to an infusion cassette that fits in the small battery-powered pump. This process must be done carefully to prevent bacteria (which could cause infection) from being accidentally added to the medicine.

HOW DO PATIENTS OBTAIN RTS EPOPROSTENOL (VELETRI®)?

RTS 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 RTS EPOPROSTENOL (VELETRI®)?

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 RTS EPOPROSTENOL (VELETRI®) INITIATED?

Patients started on intravenous epoprostenol typically require admission to the hospital for several days. While in the hospital, specialty nurses teach patients central venous catheter (e.g. Hickman) care, CADD pump specifics, and administration of epoprostenol.

WHAT ARE THE MAIN SIDE EFFECTS WITH RTS EPOPROSTENOL (VELETRI®)?

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

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- Swelling
- 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 RTS EPOPROSTENOL IN SPECIAL POPULATIONS?

There are no adequate, well-controlled studies of the potential effect of infused epoprostenol in pregnant humans. Studies in pregnant animals of continuous infusions of epoprostenol sodium, using doses higher than normally used in humans, have revealed no problems with fetal birth defects or miscarriage. Infusion RTS 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. 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.

Epoprostenol clearance appears to be reduced in patients with liver insufficiency. The result is 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 RTS EPOPROSTENOL?

This is possible, but unlikely.

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

No medications are prohibited with the use of RTS epoprostenol.

ARE THERE OTHER WAYS OF ADMINISTERING RTS EPOPROSTENOL (VELETRI®)?

At this time there are no FDA-approved alternate ways of administering RTS epoprostenol.