HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use FLOLAN safely and effectively. See full prescribing information for FLOLAN.

FLOLAN (epoprostenol sodium) for injection, for intravenous use
Initial U.S. Approval: 1995

----------RECENT MAJOR CHANGES----------

Dosage and Administration (2.1 - 2.3) 04/2015

----------INDICATIONS AND USAGE----------

FLOLAN is a prostacyclin vasodilator indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group I) to improve exercise capacity. Studies establishing effectiveness included predominantly (97%) patients with NYHA Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH (49%) or PAH associated with connective tissue diseases (51%). (1)

---------- DOSAGE AND ADMINISTRATION ----------

- Initiate intravenous infusion through a central venous catheter at 2 ng/kg/min. (2.2, 2.3)
- Change dose in 1-to 2-ng/kg/min increments at intervals of at least 15 minutes based on clinical response. (2.2)
- Avoid sudden large dose reductions. (2.2, 5.2)

---------- DOSAGE FORMS AND STRENGTHS ----------

For injection: 0.5 mg or 1.5 mg epoprostenol freeze-dried powder in a single use vial for reconstitution with the supplied diluent. (3)

----------CONTRAINDICATIONS----------

- Heart failure with reduced ejection fraction. (4)
- Hypersensitivity to FLOLAN or any of its ingredients. (4)

---------- WARNINGS AND PRECAUTIONS ----------

- Pulmonary edema: Discontinue therapy if pulmonary edema occurs. (5.1)
- Rebound pulmonary hypertension: Do not abruptly discontinue or decrease the dose. (5.2)
- Vasodilation reactions: Monitor blood pressure and symptoms regularly during initiation and after dose change. (5.3)
- Increased risk for bleeding: Increased risk for hemorrhagic complications, particularly for patients with other risk factors for bleeding. (5.4)

---------- ADVERSE REACTIONS ----------

The most common adverse reactions are dizziness, jaw pain, headache, musculoskeletal pain, and nausea/vomiting, and are generally associated with vasodilation. (6)

To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 04/2015

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

FLOLAN® is indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group I) to improve exercise capacity. Trials establishing effectiveness included predominantly (97%) patients with New York Heart Association (NYHA) Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH (49%) or PAH associated with connective tissue diseases (51%).

2 DOSAGE AND ADMINISTRATION

2.1 Reconstitution

Each vial is for single use only; discard any unused diluent or unused reconstituted solution.

Select a concentration for the solution of FLOLAN that is compatible with the infusion pump being used with respect to minimum and maximum flow rates, reservoir capacity, and the infusion pump criteria listed below *[see Dosage and Administration (2.4)]*.

Using aseptic technique, reconstitute FLOLAN only with STERILE DILUENT for FLOLAN or pH 12 STERILE DILUENT for FLOLAN. Table 1 gives directions for preparing several different concentrations of FLOLAN. See Table 2 for storage and administration time limits for the reconstituted FLOLAN.

Table 1. Reconstitution and Dilution Instructions for FLOLAN Using STERILE DILUENT for FLOLAN or pH 12 STERILE DILUENT for FLOLAN.

To make 100 mL of solution with final concentration of:	Directions:
3,000 ng/mL	Dissolve contents of **one 0.5-mg vial** with 5 mL of sterile diluent. Withdraw 3 mL and add to sufficient sterile diluent to make a total of 100 mL.
5,000 ng/mL	Dissolve contents of **one 0.5-mg vial** with 5 mL of sterile diluent. Withdraw entire vial contents and add sufficient sterile diluent to make a total of 100 mL.
10,000 ng/mL	Dissolve contents of **two 0.5-mg vials** each with 5 mL of sterile diluent. Withdraw entire vial contents and add sufficient sterile diluent to make a total of 100 mL.
15,000 ng/mL[a]	Dissolve contents of **one 1.5-mg vial** with 5 mL of sterile diluent. Withdraw entire vial contents and add sufficient sterile diluent to make a total of 100 mL.

[a] Higher concentrations may be prepared for patients who receive FLOLAN long-term.

Table 2. Storage and Administration Limits for Reconstituted FLOLAN

	When Using STERILE DILUENT for FLOLAN	When Using pH 12 STERILE DILUENT for FLOLAN
Stability	When used at room temperature, (15°C to 25°C; 59°F to 77°F) reconstituted solutions: • are stable for up to 8 hours following reconstitution or removal from refrigerated storage • may be stored for up to 40 hours refrigerated at 2°C to 8°C (36°F to 46°F) before use. When used with a cold pack, reconstituted solutions: • are stable for up to 24 hours use • may be stored refrigerated at 2°C to 8°C (36°F to 46°F) before use as long as the total time of refrigerated storage and infusion does not exceed 48 hours • Change cold packs every 12 hours.	Freshly prepared reconstituted solutions or reconstituted solutions that have been stored at 2°C to 8°C (36°F to 46°F) for no longer than 8 days can be administered up to: • 72 hours at up to 25°C (77°F). • 48 hours at up to 30°C (86°F). • 24 hours at up to 35°C (95°F). • 12 hours at up to 40°C (104°F).
• Reconstituted solutions can be used immediately. Refrigerate at 2°C to 8°C (36°F to 46°F) if not used immediately. • Protect from light. • Do not freeze reconstituted solutions.		

2.2 Dosage

Initiate intravenous infusions of FLOLAN at 2 ng/kg/min. Alter the infusion by 1- to 2-ng/kg/min increments at intervals sufficient to allow assessment of clinical response. These intervals should be at least 15 minutes.

During dose initiation, asymptomatic increases in pulmonary artery pressure coincident with increases in cardiac output may occur. In such cases, consider dose reduction, but such an increase does not imply that chronic treatment is contraindicated.

Base changes in the chronic infusion rate on persistence, recurrence, or worsening of the patient's symptoms of pulmonary hypertension and the occurrence of adverse vasodilatory reactions. In general, expect progressive increases in dose.

If dose-related adverse reactions occur, make dose decreases gradually in 2-ng/kg/min decrements every 15 minutes or longer until the dose-limiting effects resolve *[see Adverse Reactions (6.1)]*. Avoid abrupt withdrawal of FLOLAN or sudden large reductions in infusion rates *[see Warnings and Precautions (5.2)]*.

Following establishment of a new chronic infusion rate, measure standing and supine blood pressure for several hours.

Taper doses of FLOLAN after initiation of cardiopulmonary bypass in patients receiving lung transplants.

2.3 Administration

Initiate FLOLAN in a setting with adequate personnel and equipment for physiologic monitoring and emergency care.

Inspect parenteral drug products for particulate matter and discoloration prior to administration whenever solution and container permit. If either particulate matter or discoloration is noted, do not use.

Administer continuous chronic infusion of FLOLAN through a central venous catheter. Temporary peripheral intravenous infusion may be used until central access is established. Do not administer bolus injections of FLOLAN.

The ambulatory infusion pump used to administer FLOLAN should: (1) be small and lightweight, (2) be able to adjust infusion rates in 2-ng/kg/min increments, (3) have occlusion, end-of-infusion, and low-battery alarms, (4) be accurate to ±6% of the programmed rate, and (5) be positive-pressure-driven (continuous or pulsatile) with intervals between pulses not exceeding 3 minutes at infusion rates used to deliver FLOLAN. The reservoir should be made of polyvinyl chloride, polypropylene, or glass. Use a 60-inch microbore non-di-(2-ethylhexyl)phthalate (DEHP) extension set with proximal antisyphon valve, low priming volume (0.9 mL), and in-line 0.22-micron filter.

To avoid interruptions in drug delivery, the patient should have access to a backup infusion pump and intravenous infusion sets.

Do not administer or dilute reconstituted solutions of FLOLAN with other parenteral solutions or medications. Consider a multi-lumen catheter if other intravenous therapies are routinely administered.

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