Flolan (Epoprostenol) Clinical Pearls:

Mechanism of Action: Epoprostenol is also known as prostacyclin and PGI_2. It is a strong vasodilator of all vascular beds. In addition, it is a potent endogenous inhibitor of platelet aggregation. The reduction in platelet aggregation results from epoprostenol's activation of intracellular adenylate cyclase and the resultant increase in cyclic adenosine monophosphate concentrations within the platelets. Additionally, it is capable of decreasing thrombogenesis and platelet clumping in the lungs by inhibiting platelet aggregation.

Dose Titration:

Pulmonary arterial hypertension (PAH): IV: Initial: 2 ng/kg/minute; a lower initial dose may be used if patient is intolerant of starting dose. Increase dose in increments of 1 to 2 ng/kg/minute at intervals of ≥15 minutes until dose-limiting side effects (eg, flushing, jaw pain, headache, hypotension, nausea) are noted or response to epoprostenol plateaus. Usual optimal dose (monotherapy): 25 to 40 ng/kg/minute (McLaughlin 2009); significant patient variability in optimal dose exists. Maximum dose with chronic therapy has not been defined; however, doses as high as 195 ng/kg/minute have been described in children (Rosenzweig 1999).

Dose adjustment during chronic phase of treatment:

If PAH symptoms persist or recur following improvement, increase dose in 1 to 2 ng/kg/minute increments at intervals of ≥15 minutes. May also increase dose at intervals of 24 to 48 hours or longer (eg, every 1 to 2 weeks). **Note:** The need for increased doses should be expected with chronic use; incremental increases occur more frequently during the first few months after the drug is initiated.

In case of dose-limiting pharmacologic events (eg, hypotension, severe nausea, vomiting), decrease dose in 2 ng/kg/minute decrements at intervals of ≥15 minutes until dose-limiting effects resolve. Avoid abrupt withdrawal or sudden large dose reductions. **Note:** Adverse event may resolve without dosage adjustment.

Lung transplant: In patients receiving lung transplants, epoprostenol may be tapered after sequential lung transplantation once the allografts have been reperfused. If cardiopulmonary bypass utilized, epoprostenol may be tapered after pump perfusion has been initiated.

Acute vasodilator testing in patients with PAH (off-label use) (McLaughlin 2009): Note: Acute vasodilator testing should only be done in patients who might be considered candidates for calcium channel blocker therapy.

IV: Initial: 2 ng/kg/minute; increase dose in increments of 2 ng/kg/minute every 10 to 15 minutes; dosing range during testing: 2 to 10 ng/kg/minute

Reconstitution and Dilution Instructions for FLOLAN Using sterile diluent	**Directions:**
3,000 ng/mL *this concentration preferred for diagnostic (cath lab) purposes. Other concentrations useful for patient requiring higher infusion rates when applicable*	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	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.

****NOTE: Use only Flolan diluent provided to dilute****
Only the pH 12 diluent vials are stocked in the Glenwood Talyst**
Room temp stability (see below) when using this diluent.

Diluent located in GW Talyst
(in same bins with both vial sizes – this is not separately inventoried by Talyst)

New starts: due to room temp stability with pH 12 diluent this can be infused at room temperature (empty evacuated bag) and CADD pumps not required for short term, hospital therapy

	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).

Infusion rates may be calculated using the following formula:

Infusion Rate (mL/h) = [Dose (ng/kg/min) x Weight (kg) x 60 min/h]
Final Concentration (ng/mL)

Example calculations for infusion rates are as follows:

Example 1: for a 60-kg person at the recommended initial dose of 2 ng/kg/min using a 3,000-ng/mL concentration, the infusion rate would be as follows:

Infusion Rate (mL/h) **= [2** (ng/kg/min) **x 60** (kg) **x 60 (**min/h)**] = 2.4** (mL/h)
3,000 (ng/mL)

Example 2: for a 70-kg person at a dose of 16 ng/kg/min using a 15,000-ng/mL concentration, the infusion rate would be as follows:

Infusion Rate (mL/h) **= [16** (ng/kg/min) **x 70** (kg) **x 60 (**min/h)**] = 4.48** (mL/h)
15,000 (ng/mL)
(Infusion rate charts are also available)

1 nanogram = 0.000001 milligram

Administration:

*Initiate Flolan in a setting with adequate personnel and equipment for physiologic monitoring and emergency care. (Cath Lab preferred)

*__Access__:

-Chronic infusions should have a central venous catheter.

-Temporary peripheral infusions may be used until central access can be established.

*__Filter__: In-line 0.22 micron filter required.

*****Do not administer or dilute reconstituted solutions of Flolan with other parenteral solutions or medications! Use only sterile diluent provided to dilute drug and further dilute to final concentration.*****

How Supplied:

0.5-mg (500,000 ng) per vial
1.5-mg (1,500,000 ng) per vial

Most patients will have their own supply if they are already on the medication.

Acutely, if you are ask to initiate Flolan. Only use the ph-12 diluent and put in an empty I.V. bag (diluent is located in Talyst along with the Flolan vials – there is not a separate Talyst entry for the diluent vials). Once the dose has been stabilized and you are able to obtain a CADD pump, then you can put in a cassette.

It is important to make up at least one bag/cassette in advance and stress to the nurse to request early so that there is not a delay in therapy.