Aerosolized Epoprostenol (Flolan®)

48:48 – Synthetic prostaglandin

GENERAL CONSIDERATIONS:
1. Epoprostenol injection (Flolan® or Veletri ®) is a synthetic prostaglandin that is FDA-approved for the treatment of WHO Group I pulmonary arterial hypertension. Aerosolized epoprostenol (aEPO) can be used as a bridge to alternative interventions or to treat acute pulmonary hypertension due to pulmonary embolism, sarcoidosis, acute right heart dysfunction, or acute respiratory distress syndrome (ARDS). 2. aEPO will be used as a temporary, rescue therapy for mechanically ventilated patients with a diagnosis of ARDS who have failed to respond to conventional management methods for their diseases (i.e. remain ventilator-dependent with high Fi02 and PEEP requirements despite aggressive conventional therapy) or as a bridge to other definitive therapies. a. Selective pulmonary vasodilation has been shown to reverse otherwise refractory declines in patients with ARDS with severe pulmonary hypertension. b. Inhaled epoprostenol demonstrates selective pulmonary vasodilation and has been demonstrated to be safe and cost-effective.

INDICATION & ORDERING:
1. Refractory, moderate or severe ARDS 2. Intra-operative pulmonary hypertension in cardiothoracic surgery patients 3. Right ventricular dysfunction or refractory hypoxemia post-cardiothoracic surgery 4. It can also be used on a temporary basis for pulmonary hypertension related to causes other than WHO classification Type 1 pulmonary arterial hypertension (PAH) as determined by the pulmonologist. 5. Ordering is **restricted** to pulmonologists for patients in the intensive care unit. Treatment must also be approved by the attending physician.

DOSING:
1. **Initiation:** aEPO is initiated at 50 ng/kg/min based on ideal body weight (IBW) rounded to the nearest 10 kg and not to exceed 80 kg continuously via nebulizer **(See Appendix A)** IBW in kg (male) = 50 + 2.3 (Height in inches - 60) IBW in kg (female) = 45 + 2.3 (Height in inches - 60) 2. **Dose Titration:** When the maintenance dose of epoprostenol is ordered, the physician may elect to order an automatic weaning schedule. The order shall specify when the weaning should begin, the time interval between dose reductions, and specific clinical parameters to guide the process (for example: stop weaning process for cardiac index less than 2.2 or Pa02 less than 55). If a weaning schedule is not established, a physician order for weaning will be required as needed based on clinical condition. a. Weaning should be guided by clinical status (including the requirement for other more invasive or morbid interventions) and the continued presence of the indication for aEPO. b. For all weaning schedules: the dose of aEPO will be decreased by 10 ng/kg/min with each successive dose change at the specified time ordered by the physician. i. See Appendix A for dose reductions and weaning interval to be used.

c. If patient does not tolerate weaning always revert to previous minimally effective dose, refer to same procedure as "Intolerance to Dose Reduction during Titration".
d. If the patient is deemed clinically stable for 4 hours by the respiratory therapist, physician, and nurse, begin the dose minimization process. The physician may order this process sooner than 4 hours.

3. **Dose minimization** will occur every 15 minutes in which the dose will be decreased by 10 ng/kg/min to the lowest effective dose.
    a. Monitor patient for rebound pulmonary hypertension and any of the following:
        i. 15% decrease in cardiac output (CO)
        ii. 20% increase in pulmonary vascular resistance
        iii. 10% increase in pulmonary arterial pressure (PAP)
        iv. 10mm Hg decrease in PaO2
        v. 4% decrease in Sa02 (if the reliability of pulse oximetry has been confirmed)

MONITORING:

1. Nursing
    a. During initial dosing:
        i. Hemodynamics (HR, MAP, 02 saturation, and when possible, mPAP, and CO) at baseline, every 15 minutes for the first 30 minutes, then every 30 min for the next 60 minutes, then every 2 hours thereafter.
    b. After any change in dose:
        i. Hemodynamics (HR, MAP, 02 saturation, and when possible, mPAP, and CO) at baseline every 15 minutes for the first 30 minutes, then every 30 min for the next 60 minutes, then every 2 hours thereafter

PHARMACY PREPARATION (aEPO):

1. **At the initiation of the therapy, one epoprostenol syringe or bag** will be compoundedand will be delivered **STAT** to the unit and hand delivered to the RN.
2. **Nusing will med request the next Aerogen epoprostenol syringe two hours before the next syringe is needed**. Pharmacy will compound the next syringe STAT. The Aerogen syringe be delivered **STAT** to the unit and hand delivered to the RN.
3. Epoprostenol Syringe Preparation
    a. Epoprostenol syringe will be changed by a registered nurse (RN) as needed. Epoprostenol in pH 12 Flolan diluent in the Aerogen syringe is considered immediate use and administration must be started within 4 hours of compounding
        i. Using proper aseptic technique, withdraw 5 mL of pH 12 epoprostenol diluent into the 50 mL monoject syringe.
        ii. Inject the 5 mL pH 12 epoprostenol diluent into the 1.5 mg epoprostenol dry powder vial and mix contents gently.
        iii. Withdraw the 5 mL diluted epoprostenol back into the monoject syringe.
        iv. Add the remaining 45 mL of sterile diluent to the syringe and mix gently. *Final concentration of solution: 1.5 mg/50mL = 30,000 ng/mL (nanograms/mL)*
        Transfer the content to the 60 mL Aerogen nebulization syringe using a blunt end needle.
        v. Seal the Aerogen syringe with the nebulization cap
        vi. Adhere patient's label to the syringe
        vii. Adhere auxiliary labels: FOR INHALATION ONLY
        viii. Place syringe in brown bag protected from light
        ix. Document in compounding log

x. Label with **date/time start by as four hours** from compounding time when administration must be started within.

3. Epoprostenol Bag Preparation (ONLY IN RARE CIRCUMSTANCES WHEN AEROGEN SYRINGES ARE NOT AVAILABLE)
    a. Using proper aseptic technique, withdraw 5 mL of pH 12 epoprostenol diluent into the 10 mL syringe.
    b. Inject the 5 mL pH 12 epoprostenol diluent into the 1.5 mg epoprostenol dry powder vial and mix contents gently.
    c. Withdraw the 5 mL diluted epoprostenol back into the monoject syringe and transfer the content to an empty Intravia® bag
    d. Draw up the remaining 45 mL of sterile diluent in a syringe and transfer to Intravia bag. Mix contents gently. *Final concentration of solution: 1.5 mg/50mL = 30,000 ng/mL (nanograms/mL)*
    e. Adhere patient's label to the bag.
    f. Adhere auxiliary labels: REFRIGERATE and FOR INHALATION ONLY
    g. Place bag in brown bag protected from light
    h. Document in compounding log
    i. Label with beyond use date of 8 days referigerate

STABILITY:

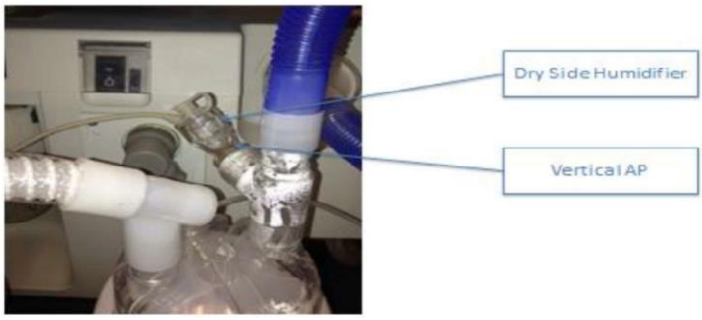
1. Immediate use (start time within 4 hours) in Aerogen Syringe. 8 days refrigerate in bag.
2. Protect from light

RESPIRATORY THERAPIST (RT) – PREPARATION, DELIVERY, & TITRATION:

1. Procedure for Preparation

a. Ventilator circuit/ventilator device needs to contain a heated wire circuit.
b. Place a bacteria filter at the outlet of the expiratory limb to prevent contamination of the expiratory flow monitoring system. The filter should be changed every four hours, or as necessary when the epoprostenol is being administered to prevent increased expiratory flow resistance.
c. The RT will place the Aerogen Solo medication cup with adapter on the dry side (inlet port) of humidifier (see Illustration below).

Aerogen Placement on Dry Side Humidifier



d. Connect the Luer-lock onto the Aerogen solo medication cup.
e. Confirm the Aeroneb is set to continuous mode.
f. Confirm the chamber is not filling past the conical portion of the nebulizer.
g. Confirm there is visible aerosol in the chamber.

h. Calculate patient's ideal body weight (IBW) and round to the nearest 10 kg to determine flow rate for epoprostenol **(See Appendix A):**
    i. All patients will be initiated at a dose of 50 ng/kg/min
    ii. Refer to the infusion rate chart in Appendix A for the dose of Epoprostenol

2. **Procedure for Delivery (RT or RN)**
    a. Double-check calculations, rates, and concentration of epoprostenol.
    b. Begin continuous nebulization via the Aerogen controller.
    c. The epoprostenol syringe or bag should be changed as needed.
    d. Each new syringe or bag should be documented on the eMAR.
    e. Initial dose delivered by pharmacy.
    f. Subsequent syringes will be delivered to the bedside nurse.
    g. Upon initiation or dose change:
        i. If MAP decreases more than 10% within 10 minutes of initiation, discontinue flow to the nebulizer. Notify physician.
            a) When blood pressure recovers restart the medication at 1/2 the dose.
        ii. If there is a clinically significant rebound in targeted response, the physician will be notified immediately and the dose will be increased to the previously effective dose. (See Procedure for Minimal Effective Dose Titration)
    h. Failure to meet goal clinical parameters within 30 minutes of administration indicates no response and the infusion should be discontinued.

3. Respiratory Therapist Monitoring of the Nebulizer Output
    a. The Aerogen nebulizer should be checked often for proper delivery

4. **Procedure for Minimal Effective Dose Titration (Weaning)**
    a. Weaning is by provider order only. Common practice is to:
        i. Decrease the dose every 15 minutes to the lowest effective dose (see Dose titration above and Appendix A below)
        ii. Begin dose titration upon physician order. Usually no sooner than 4 hours after initiation and only if the patient is clinically stable.

5. **Procedure for Intolerance of Dose Reduction during Titration**
    a. If patient does not tolerate dose reduction, restart infusion at last effective dose.

APPENDIX A: CALCULATIONS & INFUSION FLOW RATE CHART

1. Considerations
    a. Aerosolized epoprostenol rate (ml/hr) = [(dose x 60) x IBW] ÷ concentration (30,000 ng/ml)
    b. The aerosolized epoprostenol delivered dose ng/kg/min = (Concentration [30,000 ng/ml] x drip rate [ml/hr]) ÷ IBW (kg) ÷ 60 (min/hr)
    c. Dosing is based on Ideal Body Weight (IBW) rounded to the nearest 10 kg. Maximum dosing rate is 80 kg

****If Actual Body Weight (ABW) is less than Ideal Body Weight, Use ABW****

IBW in kg (male) = 50 + 2.3 (Height in inches - 60)
IBW in kg (female) = 45 + 2.3 (Height in inches - 60)

Aerosolized Epoprostenol (Flolan®)

Height	Male IBW (kg)	Dosing weight (kg)	Female IBW (kg)	Dosing weight (kg)
58 in (4'10")	45.4	50	40.4	40
59 in (4'11")	47.7	50	43.2	40
60 in (5')	50	50	45.5	50
61 in (5'1")	52.3	50	47.8	50
62 in (5'2")	54.6	50	50.1	50
63 in (5'3")	56.9	60	52.4	50
64 in (5'4")	59.2	60	54.7	50
65 in (5'5")	61.5	60	57	60
66 in (5'6")	63.8	60	59.3	60
67 in (5'7")	66.1	70	61.6	60
68 in (5'8")	68.4	70	63.9	60
69 in (5'9")	70.7	70	66.2	70
70 in (5'10")	73	70	68.5 kg	70
71 in (5'11")	75.3	80	70.8 kg	70
72 in (6')	All heights over 71in (5'11") - use 80 kg dosing weight		73.1	70
73 in (6'1")			75.4	80
74 in (6'2")			All heights over 73in (6'1") – use 80 kg dosing weight	

*If patient has ideal body weight > 80 kg, use max dose of 8 ml/hr.

Infusion rate chart (ml per hour)						
Patient's weight	Epoprostenol or NS (ml/hr)	50 ng/kg/min	40 ng/kg/min	30 ng/kg/min	20 ng/kg/min	10 ng/kg/min
40 kg	Epoprostenol	4	3.2	2.4	1.6	0.8
50 kg	Epoprostenol	5	4	3	2	1
60 kg	Epoprostenol	6	4.8	3.6	2.4	1.2
70 kg	Epoprostenol	7	5.6	4.2	2.8	1.4
80 kg	Epoprostenol	8	6.4	4.8	3.2	1.6