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Inhaled Epoprostenol

Purpose

The purpose of this guideline is to achieve the following:

- Establish the safe and effective use of inhaled epoprostenol (PGI₂, Flolan) for neonates, pediatrics, and adults.
 - Serve as an educational tool to provide the appropriate indications for administration, management and monitoring of inhaled epoprostenol for physicians, pharmacists, nurses and respiratory care practitioners.
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Description

Epoprostenol is a synthetic prostacyclin that mimics the actions of natural prostacyclins. Prostacyclin is a substance produced by vascular endothelium that stimulates adenylyl cyclase in vascular smooth muscle cells resulting in vasodilatation, antiplatelet aggregation and cytoprotective effects. Epoprostenol is FDA approved for the treatment of primary pulmonary hypertension by intravenous infusion, but its use is limited by adverse effects including systemic hypotension and worsening of intrapulmonary shunt. When administered by IV infusion, epoprostenol is a potent vasodilator of all vascular beds. Epoprostenol administered by inhaled aerosol selectively dilates the pulmonary vascular bed. Hence it reduces pulmonary hypertension and improves oxygenation by matching perfusion and ventilation of lung units.

Epoprostenol must be reconstituted. The reconstituted solution has a very alkaline PH (10.2-10.8) No safety data are available for neonates related to the safety of administering the alkaline diluents utilized with prostacyclin aerosol.

The desired therapeutic effects of aerosolized epoprostenol are:

- In oxygenation by improving ventilation to perfusion matching as a result of redistribution of pulmonary blood flow to ventilated areas of the lung.
- A reduction in pulmonary artery pressure, pulmonary vascular resistance and right ventricular afterload.

Indications

Inhaled prostacyclin therapy is indicated with:

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- Documented PPHTN on echocardiogram without structural disease and/or pre and post ductal oxygen saturation gradient difference of 10%.
- Oxygen index ($Paw \times FIO_2 \times 100/PAO_2$) approaching or >25 on optimal ventilator settings.

- Clinical evidence of hypoxic respiratory failure.
- Patients with respiratory failure per physician's discretions.
- Oxygenation
- Pulmonary Hypertension

Inhaled prostacyclin may be used in conjunction with or in place of Nitric Oxide.

**Contra-
indications** Inhaled prostacyclins should not be used in the treatment of patients known to be dependent on right to left shunting of blood.

Complications Potential complications include but are not limited to the following:

- Rebound hypoxemia and pulmonary hypertension from abrupt withdrawal.
- Systemic hypotension
- Bleeding (decrease in platelet aggregation)
- Tracheitis has been reported in animal studies due to the high alkalinity of the solution.

Any complications should be reported to the ICU faculty.

Accountability

Respiratory Care services with the assistance of nursing are responsible for the setup and administration of aerosolized epoprostenol via the Aeroneb Solo System, and Medfusion 3500 Syringe pump. Infusion pump flow rate is adjusted to deliver prostacyclin solution that will result in a desired aerosolized dose per kilogram per minute.

A double check will be performed and documented at the initiation of therapy and with each change in syringe. The double check will be completed between two of the following Respiratory Care Practitioner, Nurse or Nurse Practitioner.

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Procedure Guidelines for Initiating Therapy

1. Epoprostenol for inhalation use is restricted to neonatology, PICU attending, and adult ICU faculty.
2. This modality may only be administered in a critical care setting. These areas include ISCU, PICU, and adult ICUs.
3. Prior to prostacyclin administration the following clinical/physiological conditions should be assessed.
 - a. Minimize asynchronous or ineffective ventilation.
 - b. Restore blood volume if indicated based on history, hemorrhage, ante partum hemorrhage, HR, etc.
 - c. Initiate inotrope therapy if blood pressure is not at or above the 50th percentile. Consider administration of Milrinone.
 - d. Assess echo for anatomy, contractility and ductal shunting.
4. Blood pressure should be assessed prior to starting the medication. The patient's blood pressure should be taken every 15 minutes for the first hour after starting the medication. Blood pressure should be reassessed after every dose change.
5. Patients that show $\geq 20\%$ increase in PaO₂ or other physiological metrics defined by the responsible physician will be considered responders to treatment. Patient response should be apparent within 10 minutes of initiating treatment.
6. The need to continue therapy should be reassessed every 24 hours and updated in physician's notes.
7. The NNP, PA or Neonatology fellow's order for aerosolized epoprostenol must be approved by Neonatology, PICU attending, or adult ICU faculty.
8. Flolan will be weight adjusted every Monday.

Physician Order Set

Continuous Nebulized Epoprostenol (Flolan®, Prostacyclin)

- A. Pharmacy Orders
 - ///Epoprostenol 50 ml X 3 syringes
 - ///3 mcg/ml
 - ///15 mcg/ml

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///30 mcg/ml

///Adult dose is 10-50 ng/kg/min ordered as 500mcg/50 ml sterile solution

///Dispense in 60 ml blue Aeroneb syringes with blue Aeroneb tubing sets attached and primed

///Dispensed solution 500mcg/50 ml given via medication pump.

///Refrigerate syringes until immediately before use; protect from light

B. Medication Administration

///Epoprostenol to be administered using Medfusion 3500 Syringe Pump

///Initial dose _____ MCG/kg/min via Aeroneb Solo Nebulizer (Initial starting dose: 0.05 MCG/kg/min; range: 0.01 – 0.1 MCG/kg/min) (ISCU)

- Titration increment: 0.01 MCG/kg/min every _____ (30 minutes)
- Change medication syringes and tubing every 72 hours . and tubing every 72 hours or sooner if needed based on rate infusion. Every time a new syringe is hung, new tubing should be used for administration.

C. Medication Administration & Storage Considerations

- Expiration at room temperature is 72 hours; syringes may be stored up to 8 days under refrigeration. Ensure 72 hour expiration upon placing syringe on the pump does not extend beyond original 8 day expiration.
- There should always be at least three syringes dispensed at initiation of therapy. All additional syringes must be stored in the refrigerator
- Nursing should notify pharmacy when only one syringe is remaining in the fridge or patient rate demands new syringe in the next 12 hours.
- Nurse should notify pharmacy and request replacement syringes if any of the additional syringes in the refrigerator expire within 72 hours. It is essential that the patient does not run out of the medication and there are no interruptions in therapy.
- Use AeroNeb syringes and tubing sets ONLY to avoid inadvertent IV administration
- Confirm all tubing set connections between syringe and nebulizer with every syringe and tubing set change
- DOUBLE-CHECK Medfusion Pump settings with a second Provider at the start of therapy and with each syringe and tubing change.

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Pharmacy Order Verification

Before an order can be verified in EPIC the verifying Pharmacist will confirm that the patient is located in an ICU setting. If the patient is not located in an approved setting the pharmacist will contact the physician and inform them that the patient cannot receive inhaled epoprostenol in the non-permitted patient care area.

All orders for inhaled epoprostenol will require **DUAL VERIFICATION** in EPIC when approving the orders (Dual verification requires two Pharmacists to verify the order before it is released)

Medication Preparation and Dispensing

Pharmacy will reconstitute epoprostenol with sterile diluents to approved pediatric or adult concentrations based on patient's weight.

At the time of dispensing the AERONEB syringes of epoprostenol must be labeled with the patient specific EPIC label, a High Alert label, the Inhalation Only Label, The Return Unused Syringe to Pharmacy Label and an expiration date.

Concentration dispensed will be determined by the following table: (ISCU)

Wt. range (kg)	Standard Concentration (mcg/ml)	Starting dose mcg/kg/min
1 -3	3	0.05
3.1 - 6	15	0.05
≥6	30	0.05

- Pharmacy will dispense one syringe per 72 hours.
- All syringes will be refrigerated in the medication fridge.
- Refrigerated stability will be 8 days.
- Refrigerate syringes until immediately before use; protect from light.
- Adult dose will be determined by weight.

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Medication Administration

Administer according to procedure guideline and drip sheet.

Changing/Weaning the dose Pediatrics

- A physician's order is required to change the dose.
- Do **NOT** change the dose by more than 0.01 mcg/kg/min every 30 minutes (pediatrics only).
- To wean decrease the dose by 0.01mcg/kg/min at a time.
- Monitor the patient for rebound hypoxemia and pulmonary hypertension.

Charting

The epoprostenol dose should be charted in EMR, MAR and on the drip sheet. Charting will occur every hour and upon any dose change or change out of syringe. Any adverse reactions should also be charted

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References

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