
Continuous Nebulised Epoprostenol in Adult Critical Care [Unlicensed]

Consultant Intensivist Prescription Only

Background

Epoprostenol is a prostaglandin, a potent vasodilator and a powerful inhibitor of platelet aggregation.¹ It is licensed for intravenous administration for treatment of pulmonary arterial hypertension and for inhibition of platelet aggregation in renal dialysis.^{2,3}

When administered by nebulisation into a ventilator circuit, it can act as a pulmonary vasodilator. This may be of benefit in patients with hypoxaemia in conditions such as acute respiratory distress syndrome (ARDS), or in patients with high pulmonary vascular resistance.

Nebulised epoprostenol will only reach alveoli that are being ventilated; it will have minimal effect on areas of non-ventilated lung.

Epoprostenol has a short half-life of 2-3 minutes, and a duration of action of 30-60 minutes, so it should be given as a continuous nebulisation to maintain efficacy.

Indications

Nebulised epoprostenol may be considered for use in patients with:

- ARDS with refractory hypoxaemia
- High pulmonary vascular resistance and right ventricular dysfunction

Cautions^{2,3}

- Active bleeding or high risk of bleeding, particularly pulmonary haemorrhage
- Pregnancy

Contraindications^{2,3}

- Allergy or hypersensitivity to epoprostenol
- Severe left ventricular dysfunction is a contraindication to **intravenous** use.

Adverse events^{2,3}

Epoprostenol has a high pH and may cause coughing and bronchospasm.

Administration via nebuliser rarely causes systemic side effects, although there is potential for these occur.

Intravenous epoprostenol impairs platelet function and **nebulised** epoprostenol therefore carries a theoretical risk of pulmonary haemorrhage. Nebulised epoprostenol must be reviewed if a patient develops new onset pulmonary haemorrhage.

Intravenous epoprostenol can also cause:

- Tachycardia
- Bradycardia
- Facial flushing
- Headache
- Hypotension

Hypotension may necessitate a dose reduction and the prescription should be amended to reflect the patient's maximum tolerated dose.

Abrupt withdrawal of therapy may cause rebound pulmonary hypertension. See '**Infusion Rate**' for weaning recommendations.

There have been reports of epoprostenol infusions eroding connectors when used during renal replacement therapy; the lines and connectors should be checked at each syringe change to ensure patency.

Filters in the expiratory limb are likely become saturated with glycine from the epoprostenol solution causing significant expiratory resistance. See '**Preparation and Administration**' for advice on filter management.

Preparation and administration ⁴

Reconstitute the powder by adding approximately 10mL of the solvent provided to the 500microgram epoprostenol vial. Shake gently until the powder has dissolved.

Draw up the reconstituted solution and inject it into the remaining volume of solvent. Mix well. This contains 500mcg in 50mL (10micrograms/mL = 10,000nanograms/mL)

Draw up into a blue 'Aerogen Continuous Nebulisation' syringe. Attach the blue Aerogen tubing to the syringe and prime the line. Install the syringe into a syringe pump.

Attach the Aerogen Solo device to ventilator circuit in an approved configuration for the circuit type (refer to Aerogen Solo Set-up Guide), and attach the blue tubing to the Aerogen Solo.

Turn the power on to the Aerogen Pro-X controller, ensuring it is connected to the nebuliser then hold the button on the Aerogen controller for over 3 seconds to select continuous mode.

Commence delivery via syringe driver at prescribed rate.

The infusion expires after 24 hours if using the Flolan brand, but 12 hours if using a generic preparation. (The 50mL infusion will last longer than 12 hours if running at less than 4.2mL/hour)

The filter in the expiratory limb of the circuit is likely to become saturated with glycine from the nebulised solution, which can increase expiratory pressures. Filters must therefore be regularly changed whilst on nebulised epoprostenol. **It is recommended that expiratory filters are changed at a minimum of every 8 hours**, although elevated PEEPs may indicate that filters be changed sooner, which is likely to occur at infusion rates over 10mL/hour.⁵

Infusion rate

Start infusion at 20 nanograms/kg/min based on the patient's ideal body weight.⁶

This may be increased to 30 nanograms/kg/minute.⁶

Senior medical staff should provide targets for therapy. Improvements in PaO₂ and O₂ saturations (and pulmonary artery pressure if available) should guide dose adjustments.

If no improvement is seen, discontinuation of therapy should be considered.

Avoid abrupt withdrawal of nebulised epoprostenol as this can cause rebound pulmonary hypertension. Reduce the infusion rate by 50% every hour until it has been running at less than 5mL/hour for 1 hour. The nebulised epoprostenol can then be stopped.

Example Calculation

To administer a dose of 20 nanograms/kg/minute of nebulised epoprostenol to a patient with an ideal body weight of 70kg using a standard solution of 500micrograms in 50mL (10 micrograms/1mL = 10,000 nanograms/1mL):

$$\text{Nebulised epoprostenol infusion rate (mL/hour)} = \frac{20 \text{ nanograms/kg/min} \times 60\text{mins} \times 70\text{kg}}{10,000 \text{ nanograms in 1mL}} = 8.4 \text{ mL/hour}$$

The following specifies the infusion rate (mL per hour) of inhaled epoprostenol 500micrograms in 50mL (10micrograms in 1ml) required for different patient weights:

Ideal body weight (kg)	20 nanograms/kg/minute	30 nanograms/kg/minute
40	4.8 mL/hour	7.2 mL/hour
50	6 mL/hour	9 mL/hour
60	7.2 mL/hour	10.8 mL/hour
70	8.4 mL/hour	12 mL/hour †
80	9.6mL/hour	12 mL/hour †
90	10.8 mL/hour	12 mL/hour †
100	12 mL/hour	12 mL/hour †

† 12mL/hour is the maximum rate of infusion into the Aereoneb Solo nebuliser

References

1. British National Formulary Online accessed on 06/04/2020
2. Summary of product characteristics, Flolan®, GlaxoSmithKline. Last revised 18/11/2019
3. Summary of product characteristics, Epoprostenol 0.5mg, Advanz Pharma (Supplies Mercury Pharmaceuticals Ltd product). Last revised 17/04/2018
4. Injectable Medicines Guide Epoprostenol monograph accessed via <http://www.injguide.nhs.uk> 06/04/2020
5. Nebulised Epoprostenol in Adult Critical Care Guideline. Barts Health NHS Trust. Accessed May 2019.
6. The role of inhaled prostacyclin in treating acute respiratory distress syndrome. Searcy R et al. The Adv Respir Dis. 2015;9(6):302-312

The use of this guideline is subject to professional judgment and accountability. This guideline has been prepared carefully and in good faith for use within the Department of Critical Care at University Hospitals Sussex NHS Foundation Trust (which includes Royal Sussex County Hospital, Princess Royal Hospital, Worthing General Hospital and St Richard’s Hospital).

The decision to implement this guideline is at the discretion of the on-call critical care consultant in conjunction with appropriate critical care medical / nursing staff.