

Prior Authorization DRUG Guidelines

**FLOLAN (epoprostenol)**

Effective Date: 10/20/14

Date Developed: 10/14/14

Last Approval Date: 1/26/16, 1/24/17, 1/23/18

**(Archived 1/22/19)**

**Description:** **Epoprostenol** (PGI<sub>2</sub>, PGX, prostacyclin), a metabolite of arachidonic acid, is a naturally occurring prostaglandin with potent vasodilatory activity and inhibitory activity of platelet aggregation.

**Pre-Authorization Criteria:** Treatment of pulmonary arterial hypertension (PAH) in patients with NYHA Class III or IV symptoms to improve exercise capacity.

**Unlabeled use:** Acute vasodilator testing in PAH.

**Note:** Per VCHCP policy, unlabeled uses are not covered unless specific documentation is submitted. See Policy on Coverage of Prescription Medications for Off-Label Use.

**Dosing:** By continuous intravenous infusion via a central venous catheter using an ambulatory infusion pump: initiate at 2 ng/kg/min; increase by same at greater than 15-minute intervals, observing for side effects (thereafter, mean incremental increase is approximately 2-3 ng/kg/min every three weeks); following dosage adjustments, monitor standing and supine blood pressure and heart rate closely for several hours; temporary peripheral intravenous infusion may be used initially until central access is established.

**How Supplied:** 10 mL vials: 0.5mg (500,000 ng), 1.5 mg (1,500,000 ng); 50 mL sterile diluent

**Contraindications/Warnings:** Contraindicated in patients with congestive heart failure due to severe left ventricular systolic dysfunction; must not be reconstituted or mixed with any other parenteral medications or solutions prior to or during administration; only mix with provided diluent; Initiate **epoprostenol** in a setting with adequate personnel and equipment for physiologic monitoring and emergency care; based on clinical trials, the acute hemodynamic response to epoprostenol did not correlate well with improvement in exercise tolerance or survival during chronic use;

**Major Adverse Reactions:** Hypotension, dizziness, tachycardia, pallor; rebound pulmonary hypertension after abrupt withdrawal (**epoprostenol** is metabolized rapidly; even brief interruptions in delivery may result in symptoms associated with rebound pulmonary hypertension)

**Major Drug Interactions:** Additional reductions in blood pressure may occur when **epoprostenol** is administered with diuretics, antihypertensive agents, or other vasodilators; when other antiplatelet agents or anticoagulants are used concomitantly, there is the potential for increased risk of bleeding.

## REFERENCES

1. [www.uptodate.com](http://www.uptodate.com): Epoprostenol: Drug Guidelines.
2. Badesch DB, Abman SH, Simonneau G, et al, "Medical Therapy for Pulmonary Arterial Hypertension: Updated ACCP Evidence-Based Clinical Practice Guidelines," *Chest*, 2007, 131(6):1917-28.
3. Badesch DB, Tapon VF, McGoon MD, et al, "Continuous Intravenous Epoprostenol for Pulmonary Hypertension Due to the Scleroderma Spectrum of Disease. A Randomized, Controlled Trial," *Ann Intern Med*, 2000, 21;132(6):425-34.
4. Barst RJ, Maislin G, and Fishman AP, "Vasodilator Therapy for Primary Pulmonary Hypertension in Children," *Circulation*, 1999, 99(9):1197-208.
5. Barst RJ, Rubin LJ, Long WA, et al, "A Comparison of Continuous Intravenous Epoprostenol (Prostacyclin) With Conventional Therapy for Primary Pulmonary Hypertension. The Primary Pulmonary Hypertension Study Group," *N Engl J Med*, 1996, 334(5):296-302.
6. Cremona G and Higenbottam T, "Role of Prostacyclin in the Treatment of Primary Pulmonary Hypertension," *Am J Cardiol*, 1995, 75(3):67A-71A.
7. De Wet CJ, Affleck DG, Jacobsohn E, et al, "Inhaled Prostacyclin is Safe, Effective, and Affordable in Patients with Pulmonary Hypertension, Right Heart Dysfunction, and Refractory Hypoxemia After Cardiothoracic Surgery," *J Thorac Cardiovasc Surg*, 2004, 127(4):1058-67.
8. Fattouch K, Sbraga F, Sampognaro R, et al, "Treatment of Pulmonary Hypertension in Patients Undergoing Cardiac Surgery With Cardiopulmonary Bypass: A Randomized, Prospective, Double-Blind Study," *J Cardiovasc Med (Hagerstown)*, 2006, 7(2):119-23.
9. Haché, M, Denault A, Bélisle S, et al, "Inhaled Epoprostenol (Prostacyclin) and Pulmonary Hypertension Before Cardiac Surgery," *J Thorac Cardiovasc Surg*, 2003, 125(3):642-9.
10. Higenbottam TW, Spiegelhalter D, Scott JP, et al, "Prostacyclin (Epoprostenol) and Heart-Lung Transplantation as Treatments for Severe Pulmonary Hypertension," *Br Heart J*, 1994, 70:366-70.
11. Jones DK, Higenbottam TW, and Wallwork J, "Treatment of Primary Pulmonary Hypertension Intravenous Epoprostenol (Prostacyclin)," *Br Heart J* 1987, 57(3):270-8.
12. McLaughlin VV, Archer SL, Badesch DB, et al, "ACCF/AHA 2009 Expert Consensus Document on Pulmonary Hypertension. A Report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association," *Circulation*, 2009, 119(16):2250-94.
13. McLaughlin VV, Genthner DE, Panella MM, et al, "Reduction in Pulmonary Vascular Resistance With Long-Term Epoprostenol (Prostacyclin) Therapy in Primary Pulmonary Hypertension," *N Engl J Med*, 1998, 338(5):273-7.
14. McLaughlin VV, Shillington A, and Rich S, "Survival in Primary Pulmonary Hypertension: The Impact of Epoprostenol Therapy," *Circulation*, 2002, 106(12):1477-82.
15. Nakayama T, Shimada H, Takatsuki S, et al, "Efficacy and Limitations of Continuous Intravenous Epoprostenol Therapy for Idiopathic Pulmonary Arterial Hypertension in Japanese Children," *Circ J*, 2007, 71(11):1785-90.

16. Rich S, Kaufmann E, and Levy PS, "The Effect of High Doses of Calcium-channel Blockers on Survival in Primary Pulmonary Hypertension," *N Engl J Med*, 1992, 327(2):76-81.
17. Rosenzweig EB and Barst RJ, "Idiopathic Pulmonary Arterial Hypertension in Children," *Curr Opin Pediatr*, 2005, 17(3):372-80.
18. Rosenzweig EB, Kerstein D, and Barst RJ, "Long-Term Prostacyclin for Pulmonary Hypertension With Associated Congenital Heart Defects," *Circulation*, 1999, 99(14):1858-65.
19. Rosenzweig EB, Widlitz AC, and Barst RJ, "Pulmonary Arterial Hypertension in Children," *Pediatr Pulmonol*, 2004, 38(1):2-22.
20. Rubin LJ, Groves BM, Reeves JT, et al, "Prostacyclin-Induced Acute Pulmonary Vasodilation in Primary Pulmonary Hypertension," *Circulation*, 1982, 66(2):334-8.
21. Sitbon O, Humbert M, Nunes H, et al, "Long-Term Intravenous Epoprostenol Infusion in Primary Pulmonary Hypertension - Prognostic Factors and Survival," *J Am Coll Cardiol*, 2002, 40(40):780-8.
- Sueta CA, Gheorghiadu M, Adams KF, et al, "Safety and Efficacy of Epoprostenol in Patients With Severe Congestive Heart Failure. Epoprostenol Multicenter Research Group," *Am J Cardiol*, 1995, 75(3):34A-43A.
22. van Heerden PV, Barden A, Michalopaoulos N, et al, "Dose-Response to Inhaled Aerosolized Prostacyclin for Hypoxemia Due to ARDS," *Chest*, 2000, 117(3):819-27.
23. Walrath D, Schneider T, Pilch J, et al, "Aerosolised Prostacyclin in Adult Respiratory Distress Syndrome," *Lancet*, 1993, 342(8877):961-2.
24. Widlitz A and Barst RJ, "Pulmonary Arterial Hypertension in Children," *Eur Respir J*, 2003, 21(1):155-76.
25. Zwissler, B, Kemming G, Habler O, et al, "Inhaled Prostacyclin (PGI<sub>2</sub>) Versus Inhaled Nitric Oxide in Adult Respiratory Distress Syndrome," *Am J Respir Crit Care Med*, 1996, 154(6 Pt 1):1671-7. [PubMed 8970353]

## Revision History:

Date Approved by P&T Committee: 10/28/14; QA Committee: 11/25/14

Date Reviewed/No Updates: 1/13/15 by C. Sanders, MD

Date Approved by P&T Committee: 1/27/15

Date Reviewed/Updated: 3/12/15 by C. Sanders, MD; R. Sterling, MD

Date Approved by P&T Committee: 1/26/16

Date Reviewed/No Updates: 1/24/17 by C. Sanders, MD; R. Sterling, MD

Date Approved by P&T Committee: 1/24/17

Date Reviewed/No Updates: 1/23/18 by C. Sanders, MD; R. Sterling, MD

Date Approved by P&T Committee: 1/23/18

Date Reviewed/Archived: 1/22/19 by C. Sanders, MD; R. Sterling, MD

Date Approved by P&T Committee: 1/22/19

| Revision Date | Content Revised (Yes/No) | Contributors | Review/Revision Notes |
|---------------|--------------------------|--------------|-----------------------|
|---------------|--------------------------|--------------|-----------------------|

|         |    |                                            |                      |
|---------|----|--------------------------------------------|----------------------|
| 1/24/17 | No | Catherine Sanders, MD; Robert Sterling, MD | Annual review        |
| 1/23/18 | No | Catherine Sanders, MD; Robert Sterling, MD | Annual review        |
| 1/22/19 | No | Catherine Sanders, MD; Robert Sterling, MD | Archived – check MCG |