## Prior Authorization Review Panel

**CHC-MCO Policy Submission**

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

| | |
|---|---|
| **Plan: PA Health & Wellness** | **Submission Date: 02/01/2023** |
| **Policy Number: PA.CP.PHAR.192** | **Effective Date: 01/2018**<br>**Revision Date: 01/2023** |
| **Policy Name: Epoprostenol (Flolan, Veletri)** | |

**Type of Submission – Check all that apply:**

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL -** *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

**Please provide any changes or clarifying information for the policy below:**

1Q 2023 annual review: no significant changes; references reviewed and updated.

| | |
|---|---|
| **Name of Authorized Individual (Please type or print):**<br><br>**Venkateswara R. Davuluri, MD** | **Signature of Authorized Individual:** |

# Clinical Policy: Epoprostenol Sodium (Flolan, Veletri)

Reference Number: PA.CP.PHAR.192
Effective Date: 01/2018
Last Review Date: 01/2023

Coding Implications
Revision Log

**Description**
Epoprostenol (Flolan®, Veletri®) is a prostacyclin.

**FDA Approved Indication(s)**
Flolan and Veletri are indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to improve exercise capacity.

Studies establishing effectiveness included predominantly patients with New York Heart Association (NYHA) Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

**Policy/Criteria**
*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of PA Health & Wellness that epoprostenol is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Pulmonary Arterial Hypertension** (must meet all):

1. Diagnosis of PAH;
2. Prescribed by or in consultation with a cardiologist or pulmonologist;
3. Failure of a calcium channel blocker (*see Appendix B*), unless member meets one of the following (a, b, or c):
   a. Inadequate response or contraindication to acute vasodilator testing;
   b. Contraindication or clinically significant adverse effects to a calcium channel blocker are experienced;
   c. Members already taking and stabilized on epoprostenol sodium will not be required to change therapy;
4. If request is for brand Flolan or brand Veletri, member must use generic epoprostenol sodium, unless contraindicated or clinically significant adverse effects are experienced;

**Approval duration: 6 months**

**B. Other diagnoses/indications:** Refer to PA.CP.PMN.53

**II. Continued Approval**

**A. Pulmonary Hypertension** (must meet all)**:**

1. Currently receiving medication via PA Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy.

3. If request is for brand Flolan or brand Veletri, member must use generic epoprostenol sodium, unless contraindicated or clinically significant adverse effects are experienced;

**Approval duration: 12 months**

**B. Other diagnoses/indications** (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
   **Approval duration: Duration of request or 6 months (whichever is less)**; or
2. Refer to PA.CP.PMN.53

## III. Diagnoses/Indications for which coverage is NOT authorized:

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*

FC: functional class
FDA: Food and Drug Administration
NYHA: New York Heart Association
PAH: pulmonary arterial hypertension
PH: pulmonary hypertension
WHO: World Health Organization

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.*

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| nifedipine (Adalat® CC, Afeditab® CR, Procardia®, Procardia XL®) | 60 mg PO QD; may increase to 120 to 240 mg/day | 240 mg/day |
| diltiazem (Dilacor XR®, Dilt-XR®, Cardizem® CD, Cartia XT®, Tiazac®, Taztia XT®, Cardizem® LA, Matzim® LA) | 720 to 960 mg PO QD | 960 mg/day |
| amlodipine (Norvasc®) | 20 to 30 mg PO QD | 30 mg/day |

*Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s):
  - Congestive heart failure due to severe left ventricular systolic dysfunction
  - Pulmonary edema
  - Hypersensitivity to the drug or to structurally related compounds
- Boxed Warning(s): none reported

*Appendix D: Pulmonary Hypertension: WHO Classification*

- Group 1: PAH (pulmonary arterial hypertension)
- Group 2: PH due to left heart disease
- Group 3: PH due to lung disease and/or hypoxemia
- Group 4: CTEPH (chronic thromboembolic pulmonary hypertension)
- Group 5: PH due to unclear multifactorial mechanisms

*Appendix E: Pulmonary Hypertension: WHO/NYHA Functional Classes (FC)*

| Treatment Approach* | FC | Status at Rest | Tolerance of Physical Activity (PA) | PA Limitations | Heart Failure |
|---|---|---|---|---|---|
| Monitoring for progression of PH and treatment of co-existing conditions | I | Comfortable at rest | No limitation | Ordinary PA does not cause undue dyspnea or fatigue, chest pain, or near syncope. | |
| Advanced treatment of PH with PH-targeted therapy - *see Appendix F*** | II | Comfortable at rest | Slight limitation | Ordinary PA causes undue dyspnea or fatigue, chest pain, or near syncope. | |
| | III | Comfortable at rest | Marked limitation | Less than ordinary PA causes undue dyspnea or fatigue, chest pain, or near syncope. | |
| | IV | Dyspnea or fatigue may be present at rest | Inability to carry out any PA without symptoms | Discomfort is increased by any PA. | Signs of right heart failure |

*PH supportive measures may include diuretics, oxygen therapy, anticoagulation, digoxin, exercise, pneumococcal vaccination. **Advanced treatment options also include calcium channel blockers.

*Appendix F: Pulmonary Hypertension: Targeted Therapies*

| Mechanism of Action | Drug Class | Drug Subclass | Drug | Brand/Generic Formulations |
|---|---|---|---|---|
| Reduction of pulmonary arterial pressure through vasodilation | Prostacyclin* pathway agonist<br><br>**Member of the prostanoid class of fatty acid derivatives.* | Prostacyclin | Epoprostenol | Veletri (IV)<br>Flolan (IV)<br>Flolan generic (IV) |
| | | Synthetic prostacyclin analog | Treprostinil | Orenitram (oral tablet)<br>Remodulin (IV)<br>Tyvaso (inhalation) |
| | | | Iloprost | Ventavis (inhalation) |

| Mechanism of Action | Drug Class | Drug Subclass | Drug | Brand/Generic Formulations |
|---|---|---|---|---|
| | | Non-prostanoid prostacyclin receptor (IP receptor) agonist | Selexipag | Uptravi (oral tablet) |
| | Endothelin receptor antagonist (ETRA) | Selective receptor antagonist | Ambrisentan | Letairis (oral tablet) |
| | | Nonselective dual action receptor antagonist | Bosentan | Tracleer (oral tablet) |
| | | | Macitentan | Opsumit (oral tablet) |
| | Nitric oxide-cyclic guanosine monophosphate enhancer | Phosphodiesterase type 5 (PDE5) inhibitor | Sildenafil | Revatio (IV, oral tablet, oral suspension) |
| | | | Tadalafil | Adcirca (oral tablet) |
| | | Guanylate cyclase stimulant (sGC) | Riociguat | Adempas (oral tablet) |

## V. Dosage and Administration

| Drug Name | Dosing Regimen | Maximum Dose |
|---|---|---|
| Epoprostenol (Flolan) | 2 ng/kg/min IV, increased by 1-2 ng/kg/min at intervals of at least 15 minutes | Based on clinical response |
| Epoprostenol (Veletri) | 2 ng/kg/min IV, increased by 2 ng/kg/min every 15 minutes or longer | Based on clinical response |

## VI. Product Availability

| Drug Name | Availability |
|---|---|
| Epoprostenol (Flolan) | Vial with powder for reconstitution: 0.5 mg, 1.5 mg |
| Epoprostenol (Veletri) | Vial: 0.5 mg/10 mL, 1.5 mg/10 mL |

## VII. References

1. Epoprostenol Sodium Prescribing Information. Sellersville, PA: Teva Pharmaceuticals USA; March 2019. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=56733651-d331-4e69-a6a3-303756ccc53c. Accessed November 17, 2022.
2. Flolan Prescribing Information. Research Triangle Park, NC: GlaxoSmithKline; August 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/020444s025lbl.pdf. Accessed November 17, 2022.
3. Veletri Prescribing Information. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; October 2020. Available at: https://www.veletri.com. Accessed November 17, 2022.
4. 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 - developed in collaboration with the American College of Chest Physicians, American Thoracic Society, Inc., and the Pulmonary Hypertension Association. *J Am Coll Cardiol*. 2009; 53(17): 1573-1619.
5. Klinger JR, Elliott CG, Levine DJ, et al. Therapy for pulmonary arterial hypertension in adults: update of the CHEST guideline and expert panel report. *CHEST*. 2019;155(3):565-586.
6. Abman SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: Guidelines from the American Heart Association and American Thoracic Society. *Circulation*. 2015; 132(21): 2037-99.
7. Kim NH, Delcroix M, Jenkins DP, et al. Chronic thromboembolic pulmonary hypertension. *J Am Coll Cardiol*. 2013; 62(25): Suppl D92-99.
8. Galiè N, Humbert M, Vachiery JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Kardiol Pol*. 2015;73(12):1127-206. doi: 10.5603/KP.2015.0242.
9. Simmonneau G, Montani D, Celermajer D, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. *Eur Respir J*. 2019; 53:1801913.
10. Sitbon O, Humber M, Jais X, et al. Long-term response to calcium channel blockers in idiopathic pulmonary arterial hypertension. *Circulation*. 2005;111(23);3105;11.
11. Yaghi S, Novikov A, Trandafirescu T. Clinical update on pulmonary hypertension. *J Investig Med*. 2020; 0:1-7. doi:10.1136/jim-2020-001291.
12. Humbert M, Kovacs G, Hoeper MM, et al. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. European Heart Journal, Volume 43, Issue 38, 7 October 2022, Pages 3618–3731, https://doi.org/10.1093/eurheartj/ehac237.

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

| HCPCS Codes | Description |
|---|---|
| J1325 | Injection, epoprostenol, 0.5 mg |

| Reviews, Revisions, and Approvals | Date | Approval Date |
|---|---|---|
| Removed WHO/NYHA classifications from initial criteria since specialist is involved in care. References reviewed and updated. | 02/2018 | |
| 1Q 2019 annual review: references reviewed and updated. | 01/2019 | |
| Q1 2020: policy retired | 01/2020 | |
| 1Q 2021 annual review: reintroduced policy; no significant changes; references reviewed and updated. | 01/2021 | |
| 1Q 2022 annual review: revised medical justification language to “must use” language for generic redirection and treatment plan; references reviewed and updated. | 01/2022 | |

| Reviews, Revisions, and Approvals | Date | Approval Date |
|---|---|---|
| 1Q 2023 annual review: no significant changes; references reviewed and updated. | 01/2023 | |