POLICY
A. INDICATIONS
The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no contraindications or exclusions to the prescribed therapy.

FDA-Approved Indication
Epoprostenol/Flolan/Veletri is indicated for the treatment of pulmonary arterial hypertension (WHO Group I) to improve exercise capacity. Studies establishing effectiveness included predominantly patients with NYHA Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

All other indications are considered experimental/investigational and are not a covered benefit.

B. REQUIRED DOCUMENTATION
The following information is necessary to initiate the prior authorization review (where applicable):
- Report with pretreatment results from right heart catheterization

C. CRITERIA FOR APPROVAL
1. Pulmonary Arterial Hypertension (PAH)
Indefinite authorization may be granted when the following criteria are met (a., b., and c. below):
   a. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to F.1. Appendix A)
   b. PAH was confirmed by i. or ii. below:
      i. Pretreatment right heart catheterization with all of the following results:
         • mPAP ≥ 25 mmHg
         • PCWP ≤ 15 mmHg
         • PVR > 3 Wood units
      ii. For infants less than one year of age with any of the following conditions, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed:
         • Post cardiac surgery
         • Chronic heart disease
         • Chronic lung disease associated with prematurity
         • Congenital diaphragmatic hernia
   c. Member has NYHA functional Class III or IV symptoms (refer to F.2. Appendix B) prior to initiation of epoprostenol therapy

D. CONTINUATION OF THERAPY
All members (including new members) requesting authorization for continuation of therapy must meet ALL initial authorization criteria.

E. DOSAGE AND ADMINISTRATION
Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

F. APPENDICES
1. Appendix A. WHO Classification of Pulmonary Hypertension
   WHO Group 1. Pulmonary Arterial Hypertension (PAH)
      1.1 Idiopathic (IPAH)
      1.2 Heritable PAH
1.2.1 Germline mutations in the bone morphogenetic protein receptor type 2 (BMPR2)
1.2.2 Activin receptor-like kinase type 1 (ALK1), endoglin (with or without hereditary hemorrhagic telangiectasia), Smad 9, caveolin-1 (CAV1), potassium channel super family K member-3 (KCNK3)
1.2.3 Unknown

1.3 Drug- and toxin-induced
1.4. Associated with:
   1.4.1 Connective tissue diseases
   1.4.2 HIV infection
   1.4.3 Portal hypertension
   1.4.4 Congenital heart diseases
   1.4.5 Schistosomiasis

1. Pulmonary veno-occlusive disease (PVOD) and/or pulmonary capillary hemangiomatosis (PCH)
1. Persistent pulmonary hypertension of the newborn (PPHN)

WHO Group 2. Pulmonary Hypertension Owing to Left Heart Disease
2.1 Systolic dysfunction
2.2 Diastolic dysfunction
2.3 Valvular disease
2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies

WHO Group 3. Pulmonary Hypertension Owing to Lung Disease and/or Hypoxia
3.1 Chronic obstructive pulmonary disease
3.2 Interstitial lung disease
3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
3.4 Sleep-disordered breathing
3.5 Alveolar hypoventilation disorders
3.6 Chronic exposure to high altitude
3.7 Developmental abnormalities

WHO Group 4. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

WHO Group 5. Pulmonary Hypertension with Unclear Multifactorial Mechanisms
5.1 Hematologic disorders: Chronic hemolytic anemia, myeloproliferative disorders, splenectomy
5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis: lymphangioleiomyomatosis, neurofibromatosis, vasculitis
5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
5.4 Others: tumoral obstruction, fibrosing mediastinitis, chronic renal failure on dialysis, segmental PH

2. Appendix B. New York Heart Association Functional Classification
   - **Class I**: Patients with pulmonary hypertension but without resulting limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain, or near syncope.
   - **Class II**: Patients with pulmonary hypertension resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity causes undue dyspnea or fatigue, chest pain, or near syncope.
   - **Class III**: Patients with pulmonary hypertension resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes undue dyspnea or fatigue, chest pain, or near syncope.
   - **Class IV**: Patients with pulmonary hypertension with inability to carry out any physical activity without symptoms. These patients manifest signs of right heart failure. Dyspnea and/or fatigue may be present even at rest. Discomfort is increased by any physical activity.

REFERENCES


