Flolan (epoprostenol)
Veletri (epoprostenol)
epoprostenol (generic)

Line(s) of Business:
HMO; PPO; QUEST Integration
Medicare Advantage

Original Effective Date:
10/01/2015

Current Effective Date:
TBD 10/01/2019

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 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.
Flolan and Veletri are indicated for the treatment of pulmonary arterial hypertension (PAH) WHO Group 1 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.

B. REQUIRED DOCUMENTATION
The following documentation from the medical record is necessary to initiate the prior authorization review (where applicable):
- Report with pretreatment results from right heart catheterization including the following:
  - Mean pulmonary artery pressure (mPAP)
  - Pulmonary capillary wedge pressure (PCWP)
  - Pulmonary vascular resistance (PVR)
  - Doppler US findings for infants if RHC cannot be performed

C. CRITERIA FOR INITIAL APPROVAL

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:
A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
B. PAH was confirmed by either criterion (1) or criterion (2) below:
   1. Pretreatment right heart catheterization with all of the following results:
      i. mPAP ≥ 25 mmHg
1. **Pulmonary arterial hypertension (PAH)**

   Authorization of 12 months may be granted when ALL of the following criteria are met:
   
   a. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (See Appendix A)
   
   b. Member has NYHA functional Class II, III, or IV symptoms prior to initiation of therapy (See Appendix B)
   
   c. PAH was confirmed by one of the following:
      
      i. Pretreatment right heart catheterization with ALL of the following results:
         
         i. Mean pulmonary arterial pressure (mPAP) at rest ≥ 25 mmHg
         
         ii. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
         
         iii. Pulmonary vascular resistance (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:
         
         1. Post cardiac surgery
         
         2. Chronic heart disease
         
         3. Chronic lung disease associated with prematurity
         
         4. Congenital diaphragmatic hernia

D. **CONTINUATION OF THERAPY**

   1. No previous authorization/precertification:
      
      All members (including new members and members currently receiving treatment without prior authorization) must meet criteria for initial approval in section C.

   2. Reauthorization:
      
      Authorization of an additional 12 months may be granted to members requesting authorization for continuation of therapy who are benefiting from epoprostenol therapy and were previously authorized by HMSA/CVS and there is evidence of benefit from therapy.

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**

   **WHO Classification of Pulmonary Hypertension**

   WHO Group 1. Pulmonary Arterial Hypertension (PAH)
   
   1.1 Idiopathic (IPAH)
   
   1.2 Heritable PAH
1. Germline mutations in the bone morphogenetic protein receptor type 2 (BMPR2)
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)
3. Unknown

1. Drug- and toxin-induced

1.1 Connective tissue diseases
1.2 HIV infection
1.3 Portal hypertension
1.4 Congenital heart diseases
1.5 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

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
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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.

G. ADMINISTRATIVE GUIDELINES
Precertification is required. Please refer to the HMSA medical policy web site for the fax form.

H. IMPORTANT REMINDER
The purpose of this Medical Policy is to provide a guide to coverage. This Medical Policy is not intended to dictate to providers how to practice medicine. Nothing in this Medical Policy is intended to discourage or prohibit providing other medical advice or treatment deemed appropriate by the treating physician.

Benefit determinations are subject to applicable member contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

This Medical Policy has been developed through consideration of the medical necessity criteria under Hawaii’s Patients’ Bill of Rights and Responsibilities Act (Hawaii Revised Statutes §432E-1.4), generally accepted standards of medical practice and review of medical literature and government approval status. HMSA has determined that services not covered under this Medical Policy will not be medically necessary under Hawaii law in most cases. If a treating physician disagrees with HMSA/CVS’s determination as to medical necessity in a given case, the physician may request that HMSA reconsider the application of the medical necessity criteria to the case at issue in light of any supporting documentation.

I. REFERENCES


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