SPECIALTY GUIDELINE MANAGEMENT

Uptravi (selexipag)

POLICY

I. 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
Pulmonary Arterial Hypertension
Uptravi is indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH.

Effectiveness was established in a long-term study in PAH patients with WHO Functional Class II-III symptoms. Patients had idiopathic and heritable PAH (58%), PAH associated with connective tissue disease (29%), PAH associated with congenital heart disease with repaired shunts (10%).

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

II. 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:
      - mPAP ≥ 25 mmHg
      - PCWP ≤ 15 mmHg
      - PVR > 3 Wood units
   2. 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

III. CONTINUATION OF THERAPY

Authorization of 12 months may be granted for members with PAH who are currently receiving Uptravi therapy through a paid pharmacy or medical benefit.

IV. APPENDIX

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

V. REFERENCES

1. Uptravi [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; December 2015.
2. Sitbon O, Channick R, Chin K, et al. Selexipag for the treatment of pulmonary arterial hypertension. *N Engl J Med*. 2015;373:2522-33.
3. Simonneau G, Robbins IM, Beghetti M, et al. Updated clinical classification of pulmonary hypertension. *J Am Coll Cardiol.* 2013;62:D34-S41.
4. Rubin LJ; American College of Chest Physicians. Diagnosis and management of pulmonary arterial hypertension: ACCP evidence-based clinical practice guidelines. *Chest*. 2004;126(1 Suppl):7S-10S.
5. McLaughlin V, et al. ACCF/AHA 2009 Expert Consensus Document on Pulmonary Hypertension. *J Am Coll Cardiol*. 2009;53:1573-1619.