CVS Caremark®

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| Reference number(s) |
| 1645-A |

# Specialty Guideline Management Uptravi

## Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

| Brand Name | Generic Name |
| --- | --- |
| Uptravi | selexipag |

## 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 Indications1

Uptravi is indicated for the treatment of pulmonary arterial hypertension (PAH, World Health Organization [WHO] Group I) to delay disease progression and reduce the risk of hospitalization for PAH. Effectiveness of Uptravi tablets was established in a long-term study in PAH patients with WHO Functional Class II-III symptoms. Patients had idiopathic and heritable PAH, PAH associated with connective tissue disease, and PAH associated with congenital heart disease with repaired shunts.

All other indications are considered experimental/investigational and not medically necessary.

## Prescriber Specialties

This medication must be prescribed by or in consultation with a pulmonologist or cardiologist.

## Coverage Criteria

### Pulmonary Arterial Hypertension (PAH)1-6

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

* Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
* PAH was confirmed by either of the following criteria:
  + Pretreatment right heart catheterization with all of the following results:
    - Mean pulmonary arterial pressure (mPAP) > 20 mmHg
    - Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
    - Pulmonary vascular resistance (PVR) > 2 Wood units. For pediatric members, pulmonary vascular resistance index (PVRI) > 3 Wood units x m2 is also acceptable.
  + For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

## Continuation of Therapy

Authorization of 12 months may be granted for members with an indication listed in the coverage criteria section who are currently receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

## Appendix

### WHO Classification of Pulmonary Hypertension (PH)4

Note: Patients with heritable PAH or PAH associated with drugs and toxins might be long-term responders to calcium channel blockers.

#### Group 1: Pulmonary Arterial Hypertension (PAH)

* Idiopathic
  + Long-term responders to calcium channel blockers
* Heritable
* Associated with drugs and toxins
* Associated with:
  + Connective tissue disease
  + Human immunodeficiency virus (HIV) infection
  + Portal hypertension
  + Congenital heart disease
  + Schistosomiasis
* PAH with features of venous/capillary (pulmonary veno-occlusive disease [PVOD]/pulmonary capillary hemangiomatosis [PCH]) involvement
* Persistent PH of the newborn

#### Group 2: PH associated with Left Heart Disease

* Heart failure:
  + With preserved ejection fraction
  + With reduced or mildly reduced ejection fraction
  + Cardiomyopathies with specific etiologies (i.e., hypertrophic, amyloid, Fabry disease, and Chagas disease)
* Valvular heart disease:
  + Aortic valve disease
  + Mitral valve disease
  + Mixed valvular disease
* Congenital/acquired cardiovascular conditions leading to post-capillary PH

#### Group 3: PH associated with Lung Diseases and/or Hypoxia

* Chronic obstructive pulmonary disease (COPD) and/or emphysema
* Interstitial lung disease
* Combined pulmonary fibrosis and emphysema
* Other parenchymal lung diseases (i.e., parenchymal lung diseases not included in Group 5)
* Nonparenchymal restrictive diseases:
  + Hypoventilation syndromes
  + Pneumonectomy
* Hypoxia without lung disease (e.g., high altitude)
* Developmental lung diseases

#### Group 4: PH associated with Pulmonary Artery Obstructions

* Chronic thromboembolic PH
* Other pulmonary artery obstructions:
  + Sarcomas (high- or intermediate-grade or angiosarcoma)
  + Other malignant tumors (e.g., renal carcinoma, uterine carcinoma, germ-cell tumors of the testis)
  + Non-malignant tumors (e.g., uterine leiomyoma)
  + Arteritis without connective tissue disease
  + Congenital pulmonary artery stenoses
  + Hydatidosis

#### Group 5: PH with Unclear and/or Multifactorial Mechanisms

* Hematological disorders, including inherited and acquired chronic hemolytic anemia and chronic myeloproliferative disorders
* Systemic disorders: Sarcoidosis, pulmonary Langerhans cell histiocytosis, and neurofibromatosis type 1
* Metabolic disorders, including glycogen storage diseases and Gaucher disease
* Chronic renal failure with or without hemodialysis
* Pulmonary tumor thrombotic microangiopathy
* Fibrosing mediastinitis
* Complex congenital heart disease

## References

1. Uptravi [package insert]. Titusville, NJ: Actelion Pharmaceuticals US, Inc.; July 2022.
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3. Simonneau G, Montani D, Celermajer DS, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. Eur Respir J*.* 2019;53(1):1801913. doi: 10.1183/13993003.01913-2018
4. Kovacs G, Bartolome S, Denton CP, et al. Definition, classification and diagnosis of pulmonary hypertension. Eur Respir J. 2024;64(4):2401324. doi: 10.1183/13993003.01324-2024
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6. Ivy D, Rosenzweig EB, Abman SH, et al. Embracing the challenges of neonatal and paediatric pulmonary hypertension. Eur Respir J. 2024;64(4):2401345. doi: 10.1183/13993003.01345-2024