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 Indications[1]

Uptravi is indicated for the treatment of pulmonary arterial hypertension (PAH, World Health Organization [WHO] Group I):

- In adult patients 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.
- In pediatric patients aged 2 years and older, which reduces N-terminal pro-brain natriuretic peptide (NT-proBNP) and is expected to delay disease progression and reduce the risk of hospitalization for PAH.

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

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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 both 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 millimeters of mercury (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 meters squared (Wood units x m^2) 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 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

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    - 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)

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- 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

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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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