Prior Authorization
Pulmonary Arterial Hypertension – Uptravi® (selexipag tablets)

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Product Identifier(s)

Effective 1/1/23 to 3/21/23: 109526

Effective 3/22/23: 53266

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

National Formulary Medical Necessity

Cigna covers selexipag tablets (Uptravi®) as medically necessary when the following criteria are met for FDA Indications or Other Uses with Supportive Evidence:

Prior Authorization is recommended for prescription benefit coverage of Uptravi (tablets). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of individuals treated with Uptravi as well as the monitoring required for adverse events and long-term efficacy, approval requires Uptravi to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required for initiation of therapy where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes and catheterization laboratory reports. For an individual case in which the documentation requirement of the right heart catheterization upon Prior Authorization coverage review for a different medication indicated for WHO Group 1 PAH has been previously provided, the documentation requirement in this *Pulmonary Arterial Hypertension – Uptravi Prior Authorization Policy* is considered to be met.

Note: Uptravi injection is not included in this policy
FDA Indication(s)

1. **Pulmonary Arterial Hypertension (PAH) [World Health Organization {WHO} Group 1].** Approve for the duration noted if the individual meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 1 year if the individual meets the following criteria (i, ii, iii, and iv):
     - **i.** Individual has a diagnosis of World Health Organization (WHO) Group 1 pulmonary arterial hypertension (PAH); AND
     - **ii.** Individual meets the following criteria (a and b):
       - **a)** Individual has had a right heart catheterization **[documentation required]** (see documentation section above); AND
       - **b)** Results for the right heart catheterization confirm the diagnosis of WHO Group 1 PAH; AND
     - **iii.** Individual meets ONE the of following conditions (a or b):
       - **a)** Individual has tried or is currently receiving at least one oral medication for PAH from one of the three following different categories (either alone or in combination) each for ≥ 60 days: one phosphodiesterase type 5 (PDE5) inhibitor, one endothelin receptor antagonist (ERA), or Adempas (riociguat tablets); OR
         Note: Examples of phosphodiesterase type 5 inhibitors include sildenafil, and tadalafil. Examples of endothelin receptor antagonists include bosentan, ambrisentan, and Opsumit (macitentan tablets).
       - **b)** Individual is currently receiving, or has a history of receiving, one prostacyclin therapy for PAH; AND
         Note: Examples of prostacyclin therapies for PAH include Orenitram (treprostinil tablets), Tyvaso (treprostinil inhalation solution), Tyvaso DPI (treprostinil inhalation solution), Ventavis (iloprost inhalation solution), treprostinil injection, and epoprostenol injection; AND
     - **iv.** The medication is prescribed by, or in consultation with, a cardiologist or a pulmonologist.
   - **B)** Individuals Currently Receiving Uptravi. Approve for 1 year if the individual meets all of the following criteria (i, ii, and iii):
     - **i.** Individual has a diagnosis of World Health Organization (WHO) Group 1 pulmonary arterial hypertension (PAH); AND
     - **ii.** Individual meets the following criteria (a and b):
       - **a)** Individual has had a right heart catheterization; AND
       - **b)** Results of the right heart catheterization confirm the diagnosis of WHO Group 1 PAH; AND
     - **iii.** The medication is prescribed by or in consultation with a cardiologist or a pulmonologist.

Conditions Not Covered

Selexipag (Uptravi®) is considered experimental, investigational or unproven for ANY other use including the following (this list may not be all inclusive):

1. **Concurrent Use with Orenitram, Inhaled Prostacyclin Products, or Parenteral Prostacyclin Agents Used for Pulmonary Hypertension.** Use in combination is not appropriate.
   Note: Examples of medications include Tyvaso (treprostinil inhalation solution), Tyvaso DPI (treprostinil oral inhalation powder), Ventavis (iloprost inhalation solution), epoprostenol intravenous infusion, and treprostinil subcutaneous or intravenous infusion.

Background

Overview
Uptravi, a prostacyclin receptor agonist, is indicated for the treatment of **pulmonary arterial hypertension (PAH) World Health Organization (WHO) Group 1** to delay disease progression and reduce the risk of hospitalization for PAH.[1]

Disease Overview
PAH is a serious but rare condition impacting fewer than 20,000 patients in the US.[2,3] It is classified within Group 1 pulmonary hypertension among the five different groups that are recognized. In this progressive disorder the small arteries in the lungs become narrowed, restricted, or blocked causing the heart to work harder to pump blood, leading to activity impairment. Although the mean age of diagnosis is between 36 and 50 years, patients of any age may be affected, including pediatric patients. PAH is defined as a mean pulmonary artery pressure ≥ 25 mmHg (≥ 20 mmHg at rest) with a pulmonary capillary wedge pressure ≤ 15 mmHg measured by cardiac catheterization. The prognosis in PAH has been described as poor, with the median survival being approximately 3 years. However, primarily due to advances in pharmacological therapies, the long-term prognosis has improved.

Guidelines
Various guidelines address oral prostacyclin products.[3,4]

- **Pulmonary Arterial Hypertension:** The CHEST guideline and Expert Panel Report regarding therapy for pulmonary arterial hypertension (2019) in adults details many medications.[3] It was cited that many agents with varying mechanisms of action are used for the management of PAH. It was noted that the addition of an oral prostanoid product is recommended in patients with PAH who are in Functional Class III without evidence of rapid disease progression or a poor prognosis among those not willing or able to manage parenteral prostanoids. The European Society of Cardiology and the European Respiratory Society guidelines regarding the treatment of pulmonary hypertension (2022) also recognize Uptravi as having a role in therapy, mainly as an agent to be added onto other PAH therapies.[4]

References

1. Uptravi® tablets [prescribing information]. South San Francisco, CA: Actelion/Janssen; October 2021.
2. Ruopp NF, Cockrill BA. Diagnosis and treatment of pulmonary arterial hypertension. A review. *JAMA*. 2022;327(14):1379-1391.
3. Klinger JR, Elliott CG, Levine DJ, et al. Therapy for pulmonary arterial hypertension in adults. Update of the CHEST guideline and Expert Panel Report. *CHEST*. 2019;155(3):565-586.
4. Humbert M, Kovacs G, Hoeper MM, et al, for the ESC/ERS Scientific Document Group. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J*. 2022 Aug 26. [Online ahead of print].

Revision History

Type of Revision	Summary of Changes	Approval Date
Annual Revision	A Note was added that Uptravi injection is not included in this policy. The following other changes were made: **Pulmonary Arterial Hypertension (World Health Organization Group 1):** Tyvaso DPI was added as an example of a prostacyclin product used for pulmonary arterial hypertension. Tadliq was added as an example of an oral agent indicated for pulmonary arterial hypertension. **Conditions Not Recommended for Approval:** It was added that concurrent use with Orenitram, inhaled prostacyclin products, or parenteral prostacyclin agents used for pulmonary hypertension is not permitted. Examples of medications are provided in a Note.	10/05/2022