UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2024 P 2020-21
Program	Prior Authorization/Medical Necessity – PAH Agents
Medication	Adempas® (riociguat), Letairis®* (ambrisentan), Liqrev® (sildenafil) oral suspension*, Opsumit® (macitentan), Opsynvi® (macitentan/tadalafil)*, Orenitram™ (treprostinil), Revatio® (sildenafil citrate) oral powder for suspension*, Tadliq® oral suspension (tadalafil), Tracleer® (bosentan), Tyvaso® (treprostinil), Tyvaso DPI™ (treprostinil), Uptravi® (selexipag), Ventavis® (iloprost) **Note:** These criteria only apply to the oral suspension formulations of sildenafil citrate. The intravenous (IV) formulation is not self-administered and is therefore not covered under the pharmacy benefit.
P&T Approval Date	4/2014, 12/2014, 5/2015, 1/2016, 2/2016, 12/2016, 9/2017, 11/2017, 11/2018, 11/2019, 11/2020, 6/2021, 6/2022, 10/2022, 12/2022, 3/2023, 2/2024, 8/2024, 11/2024
Effective Date	2/1/2025

1. Background:

Pulmonary arterial hypertension (PAH) is often a progressive disease characterized by elevated pressure in the vessels that carry blood between the heart and the lungs. This results in ventricular dysfunction, reduced exercise capacity, the potential for right sided heart failure, and even death.

Several mechanisms have been identified in the pathogenesis of PAH, leading to the development of five classes of medications to treat the disorder; endothelin receptor antagonists (ERAs), phosphodiesterase-5 (PDE-5) inhibitors, prostacyclin analogs, soluble guanylate cyclase (sGC) stimulators, and an activin signaling ligand.

Letairis* (ambrisentan), Tracleer (bosentan), and Opsumit (macitentan) are oral endothelin receptor antagonists (ERAs). Letairis is indicated for the treatment of PAH (WHO Group 1) to improve exercise ability and delay clinical worsening. It is also indicated in combination with tadalafil to reduce the risk of disease progression and hospitalization for worsening PAH, and to improve exercise ability.[2] Tracleer is indicated for the treatment of PAH (WHO Group 1) to improve exercise ability and to decrease clinical worsening in adult patients, and improve pulmonary vascular resistance, which is expected to result in an improvement in exercise ability in pediatric patients aged 3 years and older.[3] Opsumit is indicated for the treatment of PAH (WHO Group 1) to reduce the risks of disease progression and hospitalization for PAH. [8]

Revatio* (sildenafil), Liqrev* (sildenafil), and Tadliq (tadalafil) are oral PDE-5 inhibitors. Revatio* is indicated in pediatric patients 1 to 17 years old for the treatment of PAH (WHO Group 1) to improve exercise ability and, in pediatric patients too young to perform standardized exercise testing, pulmonary hemodynamics thought to underly improvements in exercise.[4] Revatio* and Liqrev are indicated in adult patients for the treatment of PAH (WHO Group 1) to improve exercise ability and delay clinical worsening.[4,17] Tadliq is indicated for the treatment of PAH (WHO Group 1) to improve exercise ability. [5, 15-16]

Ventavis (iloprost), Tyvaso (treprostinil), and Tyvaso DPI (treprostinil) are prostacyclin analogs. Ventavis is administered as an inhalation solution, Tyvaso is administered as an inhalation solution, and Tyvaso DPI is administered as a dry powder inhaler. Ventavis is indicated for the treatment of PAH (WHO Group 1) to improve a composite endpoint consisting of exercise tolerance, symptoms (NYHA Class), and lack of deterioration. [6] Tyvaso and Tyvaso DPI are indicated for the treatment of PAH (WHO Group 1) to improve exercise ability. Tyvaso and Tyvaso DPI are also indicated for the treatment of pulmonary hypertension associated with interstitial lung disease (WHO Group 3) to improve exercise ability.[7,13,14]

Orenitram (treprostinil) is an orally administered prostacyclin analog indicated for the treatment of PAH (WHO Group 1) to delay disease progression and to improve exercise capacity. [9]

Adempas (riociguat) is a soluble guanylate cyclase (sGC) stimulator indicated for the treatment of adults with PAH (WHO Group 1) to improve exercise capacity, improve WHO functional class and to delay clinical worsening. Adempas is also indicated for the treatment of adults with persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) (WHO Group 4) after surgical treatment or inoperable CTEPH to improve exercise capacity and WHO functional class.[10]

Uptravi (selexipag) is a prostacyclin receptor agonist indicated for the treatment of PAH (WHO Group 1) to delay disease progression and reduce the risk of hospitalization for PAH.[12]

Opsynvi* (macitentan/tadalafil) is a combination of macitentan, an endothelin receptor antagonist (ERA), and tadalafil, a phosphodiesterase 5 (PDE5) inhibitor, indicated for chronic treatment of pulmonary arterial hypertension (PAH, WHO Group I) in adult patients of WHO functional class (FC) II-III.[18]

Members currently on therapy for the above indications will be approved for initial authorization.

2. Coverage Criteria[a]:

A. <u>Pulmonary Arterial Hypertension</u>

1. **<u>Initial Authorization</u>**

a. **Adempas, Letairis*, Opsumit, Opsynvi*, Tracleer, Tyvaso, Tyvaso DPI, or Ventavis** will be approved based on **<u>one</u>** of the following criteria:

(1) **<u>All</u>** of the following:

(a) Pulmonary arterial hypertension is symptomatic
(b) Diagnosis of pulmonary arterial hypertension that is confirmed by right heart catheterization
(c) The medication is prescribed by or in consultation with a cardiologist, pulmonologist, or rheumatologist.

-OR-

(2) **<u>Both</u>** of the following:

(a) Patient is currently on any therapy for the diagnosis of pulmonary arterial hypertension
(b) The medication is prescribed by or in consultation with a cardiologist, pulmonologist, or rheumatologist.

Authorization will be issued for 12 months.

b. **Revatio* oral powder for suspension, Liqrev oral suspension*, or Tadliq oral suspension** will be approved based on **all** of the following criteria:

(1) **One** of the following:

(a) **All** of the following:

ii. Pulmonary arterial hypertension is symptomatic
iii. Diagnosis of pulmonary arterial hypertension that is confirmed by right heart catheterization

-OR-

(b) Patient is currently on any therapy for the diagnosis of pulmonary arterial hypertension

-AND-

(2) Patient is unable to ingest a solid dosage form (e.g., an oral tablet or capsule) due to **one** of the following:

(a) age
(b) oral-motor difficulties
(c) dysphagia

-AND-

(3) Prescribed by or in consultation with a cardiologist, pulmonologist, or rheumatologist

Authorization will be issued for 12 months.

c. **Orenitram or Uptravi** will be approved based on **one** of the following criteria:

(1) **All** of the following:

(a) As continuation of therapy

-AND-

(b) Patient has **not** received a manufacturer supplied sample at no cost in the prescriber's office, or any form of assistance from the manufacturer sponsored support program (e.g., sample card which can be redeemed at a

pharmacy for a free supply of medication) as a means to establish as a current user of Orenitram or Uptravi

-AND-

(c) Patient is not taking Orenitram or Uptravi in combination with a prostanoid/prostacyclin analogue (e.g., epoprostenol, iloprost, treprostinil)

-AND-

(d) Prescribed by or in consultation with a cardiologist, pulmonologist, or rheumatologist

–OR-

(2) **All** of the following:

(a) **One** of the following:

(i) **Both** of the following:

(a) Pulmonary arterial hypertension is symptomatic
(b) Diagnosis of pulmonary arterial hypertension that is confirmed by right heart catheterization

-OR-

(ii) Patient is currently on any therapy for the diagnosis of pulmonary arterial hypertension

-AND-

(b) History of failure, contraindication, or intolerance to **both** of the following:[a]

(i) **One** of the following:

(a) A PDE-5 inhibitor [e.g., sildenafil citrate (generic Revatio), tadalafil (generic Adcirca)]
(b) Adempas

-AND-

(ii) An ERA [e.g., ambrisentan (generic Letairis*), Opsumit, or bosentan (generic Tracleer)]

-AND-

(c) Patient is not taking Orenitram or Uptravi in combination with a prostanoid/prostacyclin analogue (e.g., epoprostenol, iloprost, treprostinil)

-AND-

(d) Prescribed by or in consultation with a cardiologist, pulmonologist or rheumatologist

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Adempas, Opsumit, Opsynvi*, Letairis*, Tracleer, Tyvaso, Tyvaso DPI, or Ventavis** will be approved based on the following criterion:

(1) Documentation the patient is receiving clinical benefit to Adempas, Opsumit, Opsynvi*, Letairis*, Tracleer, Tyvaso, Tyvaso DPI, or Ventavis therapy.

b. **Revatio* oral powder for suspension, Liqrev oral suspension*, or Tadliq oral suspension** will be approved based on **both** of the following criteria:

(1) Documentation the patient is receiving clinical benefit to Revatio* oral powder for suspension, Liqrev oral suspension*, or Tadliq oral suspension therapy.

-AND-

(2) Patient remains unable to ingest a solid dosage form (e.g., an oral tablet) due to **one** of the following:

(a) age
(b) oral-motor difficulties
(c) dysphagia

Authorization will be issued for 12 months.

c. **Orenitram or Uptravi** will be approved based on **both** of the following criteria:

(1) Documentation the patient is receiving clinical benefit to Orenitram or Uptravi therapy.

-AND-

(2) Patient is not taking Orenitram or Uptravi in combination with a prostanoid/prostacyclin analogue (e.g., epoprostenol, iloprost, treprostinil)

Authorization will be issued for 12 months.

B. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

1. **Initial Authorization**

a. **Adempas** will be approved based on **one** of the following criteria:

(1) **All** of the following:

(a) Diagnosis of inoperable or persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH)

-AND-

(b) CTEPH is symptomatic

-AND-

(c) Prescribed by or in consultation with a cardiologist, pulmonologist, or rheumatologist

-OR-

(2) **Both** of the following:

(a) Patient is currently on any therapy for the diagnosis of CTEPH

-AND-

(b) Prescribed by or in consultation with a cardiologist, pulmonologist, or rheumatologist

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Adempas** will be approved based on the following criterion:

(1) Documentation the patient is receiving clinical benefit to Adempas therapy.

Authorization will be issued for 12months.

C. Pulmonary Hypertension Associated with Interstitial Lung Disease

1. **Initial Authorization**

a. **Tyvaso or Tyvaso DPI** will be approved based on **all** of the following criteria:

(1) **All** of the following[13]:

(a) Diagnosis of pulmonary hypertension associated with interstitial lung disease (WHO group 3) confirmed by right heart catheterization

(b) Interstitial lung disease is diagnosed based on evidence of diffuse parenchymal lung disease on computed tomography of the chest
(c) Pulmonary hypertension is symptomatic

-AND-

(2) Prescribed by or in consultation with a cardiologist, pulmonologist, or rheumatologist.

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Tyvaso or Tyvaso DPI** will be approved based on the following criterion:

(1) Documentation of positive clinical response to Tyvaso or Tyvaso DPI therapy (e.g., improved exercise ability)

Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

*Brand Letairis, Liqrev oral suspension, Opsynvi, and Revatio oral powder for suspension are typically excluded from coverage. Tried/Failed criteria may be in place. Please refer to plan specifics to determine exclusion status.

Additional Information regarding the endothelin receptor antagonists (Letairis*, Opsumit, Opsynvi*, and Tracleer): These agents should be used with caution in patients with liver disease. Use is not recommended in moderate to severe hepatic impairment. Tracleer product labeling includes a black box warning regarding the risk of liver injury. Prescribers are cautioned to consider whether benefits of use offset the risk of liver injury in WHO Class II patients. Early liver injury may preclude future use as disease progresses. [3]

Additional Information regarding the oral PDE-5 inhibitors (Liqrev*, Opsynvi*, Revatio powder for oral suspension*, and Tadliq): Administration of the oral PDE-5 inhibitors to patients taking any form of organic nitrate, either regularly or intermittently, is contraindicated.[4,5, 13,14] In addition, the concomitant administration of oral PDE-5 inhibitors with Adempas is contraindicated.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limitations may be in place.

4. References:

1. Pugh ME, Hemnes AR, Robbins IM. Combination therapy in pulmonary arterial hypertension. Clin Chest Med. 2013 Dec ;34(4) :841-55.
2. Letairis [package insert]. Foster City, CA : Gilead Sciences, Inc; August 2019.
3. Tracleer [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; July 2022.
4. Revatio [package insert]. New York, NY: Pfizer Labs; January 2023.
5. Ventavis [package insert]. Titusville, NJ: Actelion Pharmaceuticals US, Inc.; March 2022.
6. Tyvaso [package insert]. Research Triangle Park, NC: United Therapeutics Corp.; May 2022.
7. Opsumit [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US Inc.; June 2023.
8. Orenitram [package insert]. Research Triangle Park, NC: United Therapeutics Corp.; August 2023.
9. Adempas [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; September 2021.
10. Taichman D, Ornelas J, Chung L, et al. Pharmacologic Therapy for Pulmonary Arterial Hypertension in Adults. CHEST 2014;146(2):449-475.
11. Uptravi [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc; July 2022.
12. Waxman, A., Restrepo-Jaramillo, R., et al. Inhaled Treprostinil in Pulmonary Hypertension Due to Interstitial Lung Disease. N Engl J Med. 2021 Jan 28;384(4):325-334.
13. Tyvaso DPI [package insert]. Research Triangle Park, NC: United Therapeutics Corp.; June 2023.
14. Tadliq [package insert]. Farmville, NC: CMP Pharma, Inc.; October 2023.
15. Liqrev [package insert]. Farmville, NC: CMP Pharma, Inc.; April 2023.
16. Opsynvi [package insert]. Titusville, NJ: Actelion Pharmaceuticals US Inc.; March 2024.
17. Humbert, M, Kovacs G, et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. European Respiratory Journal Jan 2022, 2200879

Program	Prior Authorization/Medical Necessity – PAH Agents
Change Control	
4/2014	New program.
12/2014	Added new step requirement for Adcirca, Adempas and Orenitram. Added in criteria for Revatio solution
5/2015	Removed the diagnosis of PAH since we have changed it to Submission of medical records documenting diagnosis of pulmonary arterial hypertension that is confirmed by right heart catheterization. Removed step for Adcirca and Adempas. Removed Tyvaso from Orenitram step. Added Adempas as an alternative to the PDE5 I for the Orenitram step. Decreased Orenitram initial authorization period to 6 months. Decreased Orenitram reauthorization period to 12 months. For reauthorization criteria changed to "Documentation the patient is receiving clinical benefit to therapy."
1/2016	Added Uptravi to the criteria requiring patients to try PDE5/Adempas and an ERA prior to obtaining Uptravi. Changed authorization periods to 12 months due to new regulation and to be consistent with all of the agents.
2/2016	Updated prescriber requirement

7/2016	Added Indiana and West Virginia coverage information.
11/2016	Added California coverage information.
12/2016	Updated background and references.
9/2017	Annual review. Removed medical records requirements and updated sample pack language. Updated references. State mandate reference language updated.
11/2017	Removal of authorization criteria for sildenafil tablets as tablet formulation will no longer require prior authorization.
11/2018	Annual review. Added Adcirca brand tablets to exclusion. Updated background and references.
11/2019	Annual review. Updated references.
11/2020	Annual review. Updated background information with no change to clinical criteria. References updated.
6/2021	Added coverage criteria for additional Tyvaso indication. Updated background and references.
6/2022	Changed Revatio solution to suspension. Added Revatio suspension and Letairis brand tablets to exclusion. Added additional Letairis indication to background. Added generic names to Orenitram/Uptravi step. Updated references.
10/2022	Added coverage criteria for Tyvaso DPI formulation and Alyq per prescribing information. Updated background and references.
12/2022	Added Tadliq oral suspension for PAH. Updated background and references.
3/2023	Updated background with Revatio's expanded indication in pediatric patients with no change in coverage criteria. Updated references.
2/2024	Annual review. Added Liqrev oral suspension for PAH and updated exclusion footnote. Updated background and references.
8/2024	Added coverage criteria for Opsynvi tablets for PAH. Added Opsynvi to additional information section. Updated background and references.
11/2024	Removed Adcirca and Alyq from policy. Added Opsynvi to the list of products that are typically excluded from coverage. Updated references.