UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2023 P 1076-14
Program	Prior Authorization/Notification – PAH Agents
Medication	Adcirca®* (tadalafil), Adempas® (riociguat), Alyq™ (tadalafil), Letairis®* (ambrisentan), Opsumit® (macitentan), Orenitram™ (treprostinil), Revatio® oral powder for suspension* (sildenafil citrate), Tadliq® (tadalafil) oral suspension, 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	9/2006, 4/2008, 4/2009, 8/2009, 10/2009, 7/2010, 5/2011, 5/2012, 5/2013, 10/2013, 2/2014, 5/2015, 3/2016, 3/2017, 11/2017, 11/2018, 6/2019, 6/2020, 6/2021, 6/2022, 10/2022, 12/2022, 3/2023
Effective Date	6/1/2023; Oxford only: N/A

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 four classes of medications to treat the disorder. Endothelin receptor antagonists (ERAs), phosphodiesterase-5 (PDE-5) inhibitors, prostacyclin analogs, and soluble guanylate cyclase (sGC) stimulators may be used as monotherapy, sequential combination therapy, or simultaneous combination therapy to treat PAH.[1]

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), Alyq (tadalafil), Adcirca* (tadalafil), 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. Revatio* is also indicated in adult patients for the treatment of PAH (WHO Group 1) to improve exercise ability and and delay clinical worsening.[4] Adcirca*, Alyq, and Tadliq are indicated for the treatment of PAH (WHO Group 1) to improve exercise ability.[5, 13-14]

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, 12]

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

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.[11]

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]

2. Coverage Criteria[a]:

A. Pulmonary Arterial Hypertension

1. **Initial Authorization**

a. **Adcirca*, Adempas, Alyq, Letairis*, Opsumit, Orenitram, Revatio oral powder for suspension*, Tadliq oral suspension, Tracleer, Tyvaso, Tyvaso DPI, Uptravi,** or **Ventavis** will be approved based on the following criterion:

(1) Diagnosis of pulmonary arterial hypertension which is symptomatic

Authorization will be issued for 12 months.

2. **Reauthorization**

a. **Adcirca*, Adempas, Alyq, Letairis*, Opsumit, Orenitram, Revatio oral powder for suspension*, Tadliq oral suspension, Tracleer, Tyvaso, Tyvaso DPI, Uptravi,** or **Ventavis** will be approved based on the following criterion:

(1) Documentation of positive clinical response to therapy

Authorization will be issued for 12 months.

B. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

1. **Initial Authorization**

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

(1) Diagnosis of inoperable or persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) which is symptomatic

Authorization will be issued for 12 months.

2. **Reauthorization**

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

(1) Documentation of positive clinical response to Adempas therapy

Authorization will be issued for 12 months.

C. Pulmonary Hypertension Associated with Interstitial Lung Disease

1. **Initial Authorization**

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

(1) Diagnosis of pulmonary hypertension associated with interstitial lung disease which is symptomatic

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

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.

Additional Information regarding the endothelin receptor antagonists (Letairis*, Opsumit, 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 (Adcirca*, Alyq, Revatio*, 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.
- Revatio* brand suspension and Adcirca*and Letairis* brand tablets are typically excluded from coverage. Tried/Failed criteria may be in place. Please refer to plan specifics to determine exclusion status.

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 2021.
4. Revatio [package insert]. New York, NY: Pfizer Labs; January 2023.
5. Adcirca [package insert]. Indianapolis, IN: Eli Lilly and Company; September 2020.
6. Ventavis [package insert]. Titusville, NJ: Actelion Pharmaceuticals US, Inc.; March 2022.
7. Tyvaso [package insert]. Research Triangle Park, NC: United Therapeutics Corp.; May 2022.
8. Opsumit [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; October 2021.
9. Orenitram [package insert]. Research Triangle Park, NC: United Therapeutics Corp.; May 2021.
10. Adempas [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; September 2021.
11. Uptravi [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc; October 2021.
12. Tyvaso DPI [package insert]. Research Triangle Park, NC: United Therapeutics Corp.; May 2022.
13. Alyq [package insert]. North Wales, PA: Teva Pharmaceuticals USA, Inc..; September 2021.
14. Tadliq [package insert]. Farmville, NC: CMP Pharma, Inc.; October 2022.

Program	Prior Authorization/Notification – PAH Agents
Change Control	
10/2013	Added note that Revatio tablets are typically excluded from coverage effective 1/1/2014.
2/2014	Added Adempas, Orenitram, and Opsumit. Updated Background, Additional Information and References. Extended reauthorization period to 24 months.
5/2015	Annual review. Updated references.
3/2016	Updated to include Uptravi.
3/2017	Annual review. Updated background and references.
11/2017	Removed authorization criteria for generic Revatio tablets as this formulation will no longer require prior authorization. Updated references.
11/2018	Annual review. Added Adcirca brand tablets to exclusion. Updated background and references.
6/2019	Removed "Standard" from title. Removed reference statement regarding Revatio tablet switch to generic.

6/2020	Annual review. Updated background and references. Updated duration of authorization for continuation of therapy.
6/2021	Annual review. Added criteria for PH-ILD for Tyvaso. Updated background and references.
6/2022	Annual review. Changed Revatio solution to suspension. Added Letairis brand tablets to exclusion. Updated references.
10/2022	Added coverage criteria for Tyvaso DPI formulation and Alyq per prescribing information. Added stated mandate footnote. 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.