UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2021 P 1076-10
Program	Prior Authorization/Notification –PAH Agents
Medication	Adcirca®* (tadalafil), Adempas® (riociguat), Letairis® (ambrisentan), Opsumit® (macitentan), Orenitram™ (treprostinil), Revatio® Solution* (sildenafil citrate), Tracleer® (bosentan), Tyvaso® (treprostinil), Uptravi® (selexipag), Ventavis® (iloprost) **Note:** These criteria only apply to the oral solution 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
Effective Date	9/1/2021; 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 (ERA). Letairis is indicated for the treatment of PAH (WHO Group 1) to improve exercise ability and delay clinical worsening. [2] 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. 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. [3] Opsumit is indicated for the treatment of PAH (WHO Group I) to reduce the risks of disease progression and hospitalization for PAH. [8]

Revatio* (sildenafil) and Adcirca* (tadalafil) are oral PDE-5 inhibitors. Revatio* is indicated for the treatment of PAH (WHO Group I) in adults to improve exercise ability and delay clinical worsening.[4] Adcirca* is indicated for the treatment of PAH (WHO Group 1) to improve exercise ability.[5]

Ventavis (iloprost) and Tyvaso (treprostinil) are prostacyclin analogs administered as inhalation solutions. 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 is indicated for the treatment of PAH (WHO Group 1) to improve exercise ability. It is

also indicated for the treatment of pulmonary hypertension associated with interstitial lung disease (WHO Group 3) to improve exercise ability.[7]

Orenitram (treprostinil) is an orally administered prostacyclin analog indicated for the treatment of pulmonary arterial hypertension (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 I) 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. Pulmonary Arterial Hypertension

1. **Initial Authorization**

a. **Adcirca*, Adempas, Letairis, Opsumit, Orenitram, Revatio*, Tracleer, Tyvaso, 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, Letairis, Opsumit, Orenitram, Revatio*, Tracleer, Tyvaso, 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** 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** will be approved based on the following criterion:

(1) Documentation of positive clinical response to Tyvaso therapy

Authorization will be issued for 12 months.

Additional Information regarding the endothelian 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 (Revatio* and Adcirca*): Administration of the oral PDE-5 inhibitors to patients taking any form of organic nitrate, either regularly or intermittently, is contraindicated.[4,5] In addition, the concomitant administration of oral PDE-5 inhibitors with Adempas is contraindicated.[9]

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.

- Adcirca* and Revatio* 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.; January 2021.
4. Revatio [package insert]. New York, NY: Pfizer Labs; February 2020.
5. Adcirca [package insert]. Indianapolis, IN: Eli Lilly and Company; September 2020.
6. Ventavis [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; January 2021.
7. Tyvaso [package insert]. Research Triangle Park, NC: United Therapeutics Corp.; March 2021.
8. Opsumit [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US Inc.; January 2021.
9. Orenitram [package insert]. Research Triangle Park, NC: United Therapeutics Corp.; October 2019.
10. Adempas [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; January 2018.
11. Uptravi [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc; January 2021.

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.