UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2018 P 1076-7
Program	Prior Authorization/Notification – Standard 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
Effective Date	2/1/2019; 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 delay disease progression.[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.[7]

Orenitram (treprostinil) is an orally administered prostacyclin analog indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to 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.
[Where Revatio brand tablets are excluded from coverage, authorization should be entered for sildenafil citrate only (generic Revatio).]

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 24 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 24 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* 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; October 2015.
3. Tracleer [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; September 2017.
4. Revatio [package insert]. New York, NY: Pfizer Labs; March 2014. February 2018
5. Adcirca [package insert]. Indianapolis, IN: Eli Lilly and Company; August 2017
6. Ventavis [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; October 2017.
7. Tyvaso [package insert]. Research Triangle Park, NC: United Therapeutics Corp.; October 2017
8. Opsumit [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US Inc.; March 2017.
9. Orenitram [package insert]. Research Triangle Park, NC: United Therapeutics Corp.; January 2017.
10. Adempas [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; January 2018.
11. Uptravi [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc; December 2017.

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.