UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2018 P 2020-11
Program	Prior Authorization/Medical Necessity – 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	4/2014, 12/2014, 5/2015, 1/2016, 2/2016, 12/2016, 9/2017, 11/2017, 11/2018
Effective Date	2/1/2019; Oxford only: 2/1/2019

1. Background:

Pulmonary arterial hypertension (PAH) is 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 endothelian receptor antagonists (ERA). Letairis is indicated for the treatment of PAH (WHO Group 1) to improve exercise ability and delay clinical worsening..[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.[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]

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 I) to delay disease progression and reduce the risk of hospitalization for PAH.[12]

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

2. Coverage Criteria[a]:

A. Pulmonary Arterial Hypertension

1. **Initial Authorization**

a. **Adcirca*, Adempas, Letairis, Opsumit, Tracleer, Tyvaso or Ventavis** will be approved based on **one** of the following criteria:

(1) **All** 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) **Both** 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 solution** 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) **All** 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), Adcirca or Revatio*)

-OR-

(b) Adempas

-AND-

(ii.) An ERA (e.g. Letairis, Opsumit or 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. **Adcirca*, Adempas, , Opsumit, Letairis, Tracleer, Tyvaso, or Ventavis** will be approved based on the following criterion:

(1) Documentation the patient is receiving clinical benefit to Adcirca, Adempas, Opsumit, LetairisTracleer, Tyvaso, or Ventavis therapy.

b. **Revatio solution** will be approved based on the following criteria:

(1) Documentation the patient is receiving clinical benefit to Revatio solution

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 criterion:

(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 for Orenitram and Uptravi 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.

[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 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; 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. Taichman D, Ornelas J, Chung L, et al. Pharmacologic Therapy for Pulmonary Arterial Hypertension in Adults. CHEST 2014;146(2):449-475.
12. Uptravi [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc; December 2017.

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.