UnitedHealthcare Community Plan

Clinical Pharmacy Program Guidelines for PAH Agents

Program	Prior Authorization – PAH Agents
Medication	Adcirca® (tadalafil), Adempas® (riociguat), Letairis® (ambrisentan), Opsumit® (macitentan), Orenitram™ (treprostinil), Revatio® (sildenafil citrate), sildenafil citrate tablets (generic Revatio), Tracleer® (bosentan), Uptravi® (selexipag), **Note:** These criteria only apply to the oral formulations of sildenafil citrate. The intravenous (IV) formulation is not self-administered and is therefore not covered under the pharmacy benefit. In addition, Revatio brand tablets are typically excluded from coverage effective 1/1/2014.
Issue Date	4/2014
Pharmacy and Therapeutics Approval Date	11/2017
Effective Date	1/2018

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. Studies establishing effectiveness included predominantly patients with NYHA Functional Class II-III symptoms.[2] Tracleer is indicated for the treatment of PAH (WHO Group 1) to improve exercise ability and to decrease clinical worsening. Studies establishing effectiveness included predominately patients with NYHA Functional Class II-IV symptoms.[3] Opsumit is indicated for the treatment of PAH (WHO Group I) to delay disease progression. Studies establishing effectiveness included predominately patients with NYHA Functional Class II-III symptoms.[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. Studies establishing effectiveness included patients with NYHA

Functional Class II-IV symptoms.[4] Adcirca is indicated for the treatment of PAH (WHO Group 1) to improve exercise ability. Studies establishing effectiveness included predominately patients with NYHA Functional Class II-III symptoms.[5]

Orenitram (treprostinil) is an orally administered prostacyclin analog indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise capacity. The study that established effectiveness included predominately patients with WHO functional class II-III symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue disease.[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. Studies establishing effectiveness included predominately patients with NYHA Functional Class II-III symptoms. 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. Pulmonary Arterial Hypertension

1. **Authorization**

a. Adempas, Letairis, Opsumit, sildenafil citrate tablets (generic Revatio), Revatio solution or Tracleer will be approved based on the following criteria:

(1) Diagnosis of pulmonary arterial hypertension

Authorization will be issued for 12 months.

b. Revatio tablets (BRAND NECESSARY REQUESTS) will be approved based on all of the following criteria:

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

(a) Pulmonary arterial hypertension is symptomatic

-AND-

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

-AND-

(2) History of failure, contraindication or intolerance to the following:

(a) Sildenafil citrate tablets (generic Revatio)

Authorization will be issued for 12 months.

c. Adcirca, Orenitram or Uptravi will be approved based on the following criteria:
(1) 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:

(i) **One** of the following
- A PDE-5 inhibitor (e.g. sildenafil citrate (generic Revatio), Adcirca or Revatio)
- Adempas

-AND-

(ii.) An ERA (e.g. Letairis, Opsumit or Tracleer)

-AND-

(c) **One** of the following:
(i.) Patient is not usingOrenitram in combination with a prostanoid/prostacyclin analogue (e.g.epoprostenol, iloprost, treprostinil) as long-term concomitant therapy
NOTE: Concomitant use will be allowable for patients to transition from one of these agents to the other.

-OR-

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

Authorization will be issued for 12 months.

2. Reauthorization

a. Adcirca or Revatio tablets (BRAND NECESSARY REQUESTS) will be approved based on the following criterion:

(1) Documentation the patient is receiving clinical benefit to Adcirca or Revatio tablet (BRAND NECESSARY REQUESTS) therapy

Authorization will be issued for 12 months.

b. 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 will be issued for 12 months.

B. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

1. **Authorization**

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

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

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. 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.; October 2016.
4. Revatio [package insert]. New York, NY: Pfizer Labs; April 2015.
5. Adcirca [package insert]. Indianapolis, IN: Eli Lilly and Company; April 2015.
6. Opsumit [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US Inc.; October 2016.
7. Orenitram [package insert]. Research Triangle Park, NC: United Therapeutics Corp.; January 2016.
8. Adempas [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc.; January 2017.
9. Taichman D, Ornelas J, Chung L, et al. Pharmacologic Therapy for Pulmonary Arterial Hypertension in Adults. CHEST 2014;146(2):449-475.
10. Uptravi [package insert]. South San Francisco, CA: Actelion Pharmaceuticals US, Inc; December 2015.

Program	Prior Authorization – 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.
7/2016	Updated policy template. Updated clinical criteria to align with

	Employer & Individual. Opsumit and Adempas changed to preferred products.
12/2016	Updated background and references.
3/2017	Removed Adcirca from statement regarding use in combination with a prostanoid/prostacyclin analogue (e.g.epoprostenol, iloprost, treprostinil)
9/2017	Removed medical records requirements. Updated references.
9/2017	Removed all clinical criteria besides diagnosis and reauthorization criteria for Opsumit, Tracleer, Letairis, Adempas, sildenafil tablet and Revatio solution. Removed reauthorization criteria and clinical criteria besides diagnosis for Adempas for CTEPH to allow for Dx to Rx implementation. Removed Ventavis and Tyvaso from header due to being covered on medical benefit.
11/2017	Updated Orenitram language to allow for continuation if transitioning between Orenitram and a prostanoid/prostacyclin analogue. Removed Tyvaso and Ventavis from background and updated references.