Pharmacy Policy Bulletin: J-0016 Pulmonary Hypertension – Commercial and Healthcare Reform	
Number: J-0016	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Oral = Yes w/ Prior Authorization **Quantity Limits (1., 2., 3., or 4.):** **1.** Rx Mgmt Quantity Limits = Safety/Specialty **2.** Rx Mgmt Quantity Limits = Safety/Specialty + Dose Opt **3.** Rx Mgmt Quantity Limits = Safety/Specialty + Dose Opt + Watchful **4.** Rx Mgmt Performance = MRxC = Yes **Healthcare Reform:** Not applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0016-042	**Original Date:** 03/06/2002
Effective Date: 09/09/2025	**Review Date:** 06/25/2025

Drugs Product(s):	Oral Agents • Adcirca (tadalafil), Alyq, Tadliq • Adempas (riociguat) • Letairis (ambrisentan) • Liqrev (sildenafil) • Opsumit (macitentan) • Opsynvi (macitentan and tadalafil) • Orenitram (treprostinil diolamine) • Revatio (sildenafil) • Tracleer (bosentan) • Uptravi (selexipag) Inhaled Agents • Tyvaso (treprostinil) • Tyvaso DPI (treprostinil) • Ventavis (iloprost) • Yutrepia (treprostinil) Subcutaneous Agents • Winrevair (sotatercept-csrk)

FDA-Approved Indication(s):	• **Adcirca (tadalafil), Alyq, or Tadliq**
	  ○ Treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to improve exercise ability.
	  ▪ Studies establishing effectiveness included predominately patients with New York Heart Association (NYHA) Functional Class II–III symptoms.
	  ○ In combination with Letairis (ambrisentan): Treatment of PAH (WHO Group 1) to reduce the risks of disease progression and hospitalization for worsening PAH, and to improve exercise ability.
	  ▪ Studies establishing effectiveness included predominately patients with WHO Functional Class II–III symptoms.
	• **Adempas (riociguat)**
	  ○ 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.
	  ○ Treatment of adults with PAH (WHO Group 1) to improve exercise capacity, WHO functional class and to delay clinical worsening.
	  ▪ Studies establishing effectiveness included predominately patients with WHO functional class II–III.
	• **Letairis (ambrisentan)**
	  ○ Single agent: Treatment of PAH (WHO Group 1) to improve exercise ability and delay clinical worsening.
	  ▪ Studies establishing effectiveness included predominantly patients with WHO Functional Class II–III symptoms.
	  ○ In combination with tadalafil to reduce the risks of disease progression and hospitalization for worsening PAH, and to improve exercise ability.
	  ▪ Studies establishing effectiveness included predominantly patients with WHO Functional Class II–III symptoms.
	• **Liqrev (sildenafil)**
	  ○ Treatment of PAH (WHO Group I) in adults to improve exercise ability and delay clinical worsening.
	• **Opsumit (macitentan)**
	  ○ Treatment of PAH (WHO Group I) to reduce the risks of disease progression and hospitalization for PAH.
	  ▪ Studies establishing effectiveness included predominately patients with WHO Functional Class II-III symptoms.
	• **Opsynvi (macitentan and tadalafil)**
	  ○ Treatment of PAH (WHO Group I) in adult patients of WHO Functional Class II-III.
	• **Orenitram (treprostinil diolamine)**
	  ○ Treatment of PAH (WHO Group 1) to delay disease progression and to improve exercise capacity.
	  ▪ Studies establishing effectiveness included predominately patients with WHO functional class II-III symptoms.
	• **Revatio (sildenafil)**
	  ○ Treatment of PAH (WHO Group I) in adults to improve exercise ability and delay clinical worsening
	  ○ Treatment of PAH (WHO Group I) in pediatric patients 1 to 17 years old to improve exercise ability and, in pediatric patients too young to perform standardized exercise testing, pulmonary hemodynamics thought to underly improvements in exercise
	• **Tracleer (bosentan)**
	  ○ Treatment of PAH (WHO Group 1) in adults to improve exercise ability and to decrease clinical worsening.

	▪ Studies establishing effectiveness included predominantly patients with WHO Functional Class II-IV. ○ Treatment in pediatric patients aged 3 years and older with idiopathic or congenital PAH to improve pulmonary vascular resistance (PVR), which is expected to result in an improvement in exercise ability. • **Uptravi (selexipag)** ○ Treatment of PAH (WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH. ▪ Studies establishing effectiveness included predominately patients with WHO Functional Class II-III symptoms. • **Tyvaso, Tyvaso DPI, Yutrepia (treprostinil)** ○ Treatment of PAH (WHO Group 1) to improve exercise ability. ▪ Studies establishing effectiveness included predominately patients with NYHA Functional Class III symptoms. ○ Pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) to improve exercise ability. ▪ The study establishing effectiveness predominately included patients with etiologies of idiopathic interstitial pneumonia (IIP) (45%) inclusive of idiopathic pulmonary fibrosis (IPF), combined pulmonary fibrosis and emphysema (CPFE) (25%), and WHO Group 3 connective tissue disease (22%). • **Ventavis (iloprost)** ○ Treatment of PAH (WHO Group 1) to improve a composite endpoint consisting of exercise tolerance, symptoms (NYHA Class), and lack of deterioration. ▪ Studies establishing effectiveness included predominately patients with NYHA Functional Class III-IV symptoms. • **Winrevair (sotatercept-csrk)** ○ Treatment of adults with PAH, WHO Group 1 to increase exercise capacity, improve WHO functional class and reduce the risk of clinical worsening events. ▪ Studies establishing effectiveness included predominately patients with NYHA Functional Class II-III symptoms.

Background:	**Pulmonary Hypertension (PH) - Clinical Classification** • PH is a when the pressure in the blood vessels leading from the heart to the lungs is too high. The arteries in the lungs narrow, blood flow becomes restricted, and results in less oxygen in the blood. • The World Health Organization (WHO) classifies pulmonary hypertension (PH) into 5 categories based on the disease etiology. These diagnostic classifications include: ○ (Group I) pulmonary arterial hypertension ○ (Group II) pulmonary hypertension with left heart disease ○ (Group III) pulmonary hypertension associated with lung disease and/or hypoxemia ○ (Group IV) pulmonary hypertension due to chronic thromboembolic disease ○ (Group V) pulmonary hypertension with unclear multifactorial mechanisms. • Functional assessment of patients with PAH is based on the severity of the disease, which is classified according to the clinical symptoms on a scale of I to IV. Categorization is based on the WHO classification system, which has been modified for PAH from the New York Heart Association (NYHA) functional classifications of patients with cardiac disease. In clinical studies, certain drugs used WHO functional class, while others used NYHA functional

class. In practice, the two classification systems are used interchangeably when characterizing patients with PAH.

- PAH is associated with diverse cardiac, pulmonary, and systemic diseases in neonates, infants, and older children and contributes to significant morbidity and mortality. Clinical literature does provide guidance on management of PAH but therapy in children is based generally on experience, small observational studies, and extrapolation from adult evidence-based recommendations.

Clinical Classification of Pulmonary Hypertension	
Group 1: Pulmonary Arterial Hypertension (PAH)	1.1 Idiopathic PAH 1.2 Heritable PAH 1.3 Drug- and toxin-induced PAH 1.4 PAH associated with: 1.4.1 Connective tissue disease 1.4.2 HIV infection 1.4.3 Portal hypertension 1.4.4 Congenital heart disease 1.4.5 Schistosomiasis 1.5 PAH long-term responders to calcium channel blockers 1.6 PAH with overt features of venous/capillaries (PVOD/PCH) involvement 1.7 Persistent PH of the newborn syndrome
Group 2: Pulmonary Hypertension (PH) due to Left Heart Disease	2.1 PH due to heart failure with preserved LVEF 2.2 PH due to heart failure with reduced LVEF 2.3 Valvular heart disease 2.4 Congenital/acquired cardiovascular conditions leading to post-capillary PH
Group 3: Pulmonary Hypertension (PH) due to lung disease and/or hypoxia	3.1 Obstructive lung disease 3.2 Restrictive lung disease 3.3 Other lung disease with mixed restrictive/obstructive pattern 3.4 Hypoxia without lung disease 3.5 Developmental lung disorders
Group 4: Pulmonary Hypertension (PH) due to pulmonary artery obstructions	4.1 Chronic thromboembolic PH 4.2 Other pulmonary artery obstructions
Group 5: Pulmonary Hypertension (PH) with unclear and/or multifactorial mechanisms	5.1 Hematologic disorders 5.2 Systemic and metabolic disorders 5.3 Others 5.4 Complex congenital heart disease

Class	NYHA Functional Classification
I	No symptoms with ordinary physical activity.
II	Symptoms with ordinary activity. Slight limitation of activity.
III	Symptoms with less than ordinary activity. Marked limitation of activity.
IV	Symptoms with any activity or even at rest.

Class	WHO Functional Classification

I	Patients with pulmonary hypertension but without resulting limitations of physical activity. Ordinary physical activity does not cause undue fatigue or dyspnea, chest pain, or heart syncope.
II	Patients with pulmonary hypertension resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity results in undue fatigue or dyspnea, chest pain, or heart syncope.
III	Patients with pulmonary hypertension resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary physical activity causes undue fatigue or dyspnea, chest pain, or heart syncope.
IV	Patients with pulmonary hypertension resulting in inability to carry on any physical activity without symptoms. These patients manifest signs of right heart failure. Dyspnea and/or fatigue may be present even at rest. Discomfort is increased by physical activity.

Drugs	**Mechanism of Action**	**Drug Interactions**
– bosentan – ambrisentan – macitentan	Endothelin-1 receptor antagonists (ERAs) help prevent blood vessels from narrowing.	– CYP3A4 inducers and inhibitors – Hormonal contraceptives
– sildenafil – tadalafil	Phosphodiesterase Inhibitors (PDE 5 inhibitors) help the lungs to produce more of its own natural vasodilators by increasing the concentration of cyclic guanosine monophosphate (cGMP).	– Alpha blockers – Antihypertensives – CYP3A4 inhibitors and inducers – Nitrates – Protease inhibitors
– riociguat	Soluble guanylate cyclase (sGC) stimulators, a cardiopulmonary enzyme, increase the interaction of sGC with nitric oxide to help the blood vessels in the lungs relax.	– CYP and P-gp/ BCRP inhibitors – Nitrates – PDE-5 inhibitors
– treprostinil diolamine – treprostinil	Prostacyclin analogue that directly vasodilates pulmonary and systemic arterial vascular beds. It also inhibits platelet aggregation and smooth muscle cell proliferation. This allows the blood vessels in the lungs to relax.	– Anticoagulants – Antihypertensives – Gemfibrozil – Rifampin
– iloprost	Synthetic analogue of prostacyclin PGI(2) that dilates systemic and pulmonary arteries. The relevance of its effects on platelet aggregation is unknown.	– Anticoagulants – Antihypertensives
– selexipag	Selective prostacyclin receptor (IP) agonist, structurally distinct from prostacyclin, targets and activates a prostacyclin receptor to help the blood vessels in the lungs relax	– CYP2C8 inhibitors and inducers
– sotatercept-csrk	Recombinant activin receptor type IIA-Fc (ActRIIA-Fc) fusion protein, is an activin signaling inhibitor that binds to activin A and other TGF- β superfamily ligands. As a result, this improves the balance between the	– No major drug-drug interactions

	pro-proliferative and anti-proliferative signaling to modulate vascular proliferation. This induces cellular changes associated with thinner vessel walls, partial reversal of right ventricular remodeling, and improved hemodynamics.	

PH - Abbreviations

- Mean pulmonary arterial pressure (mPAP)
- Pulmonary wedge pressure (PWP)* may also be referred to as pulmonary arterial wedge pressure (PAWP), pulmonary capillary wedge pressure (PCWP), pulmonary venous wedge pressure (PVWP), pulmonary artery occlusion pressure (PAOP), or left ventricular end-diastolic pressure (LVEDP).
- Pulmonary vascular resistance (PVR)

PAH - Pediatrics

- Physicians who treat children with pulmonary hypertensive vascular disease agree that cardiac catheterization is required to confirm the diagnosis and evaluate severity and prognosis. Cardiac catheterization can be applied uniformly across all age groups and neurodevelopmental stages to demonstrate disease progression or regression and response to therapy. Cardiac catheterization is recommended before initiation of PAH-targeted therapy. Cardiac catheterization should include acute vasoreactivity testing (AVT) unless there is a specific contraindication.
    - Exceptions may include critically ill patients requiring immediate initiation of empirical therapy or established Eisenmenger syndrome. Risks and benefits of catheterization should be assessed in each case, and it may be appropriate in some children to treat without catheterization.
- Tracleer (bosentan) and Revatio (sildenafil) are the only agents approved for pediatric use. Individual consideration may be warranted by health care professionals by weighing the benefits compared to potential risks associated with use of these agents in the pediatric population.
- Tadliq is not FDA approved for pediatric use. Sildenafil tablets can be crushed or mixed with food. Tadalafil tablets cannot be crushed or mixed with food. Patients unable to swallow tablets or food may benefit from Tadliq's oral suspension formulation. Individual consideration may be warranted by health care professionals by weighing the benefits compared to the potential risks associated with use of this agent in the pediatric population.

PAH - Combination Therapy

- Combination therapy of PAH agents is an accepted therapeutic approach for those not responding to monotherapy. Therapeutic approach is up to the prescribing physician, but should not include more than one agent from the same therapeutic class (ERA, PDE5-inhibitors, prostacyclines). Where multiple drug options are provided, there is no comparative effectiveness data to suggest greater benefit of one therapy over the other.
- However, substituting tadalafil plus ambrisentan for sildenafil plus bosentan, while are drugs in the same family, does not result in any beneficial effect on exercise capacity. The increased metabolism and additional reduction in plasma concentration of sildenafil by bosentan may explain the contradictory outcomes associated with this combination.

- Winrevair was studied in adults with PAH, WHO Group 1 to increase exercise capacity, improve WHO Functional Class and reduce the risk of clinical worsening events in with PAH (WHO Group 1 Functional Class II or III). Most participants were receiving either three (61%) or two (35%) background drugs for PAH, and 40% were receiving prostacyclin infusion. Thirteen percent of patients were on monotherapy as background therapy.

PAH - Step Therapy

- An exception for generic tadalafil may be made if the prescriber believes it will increase patient adherence or convenience.
- The 2019 American College of Chest Physicians (CHEST) guideline states that in patients with PAH who remain symptomatic on stable and appropriate doses of an ERA or a PDE5I, addition of inhaled treprostinil to improve six-minute walk distance (6MWD) is suggested.

PH-ILD

- ILD is a group of lung diseases characterized by significant fibrosis (scarring) of the bronchioles and alveolar sacs within the lungs. Increased fibrotic tissue prevents oxygenation and free gas exchange causing shortness of breath with activity, labored breathing, and fatigue. PH complicates the course of patients with ILD and may contribute to worse functional status.

CTEPH

- Recurrent blood clots in the lung clog the arteries, and over time scars develop. As the blood vessels become narrower and more clogged, pulmonary pressure grows causing PH.

Prescribing Considerations:

- **PH**
    - PH is a chronic and progressive condition. High-volume specialized centers have shown the best outcomes for patients, with lower complication rates and shorter length of hospital stays. The current guidelines recommend referral of PH diagnosed patients to expert centers.
    - Efforts must be made to ensure appropriate diagnosis of PAH, ruling out other groups of PH. PAH cannot be determined without first ruling out left heart disease, chronic lung disease, venous thromboembolism, or other contributory diseases. Cardiac catheterization is the current gold standard diagnostic tool, and it is recommended to be performed in expert centers to ensure appropriate technique.
    - In symptomatic patients with idiopathic pulmonary arterial hypertension (IPAH), AVT is recommended to determine if the patient may be a candidate for long-term calcium channel blocker therapy (CCB) (for example, amlodipine, diltiazem, nifedipine). In patients with PAH who demonstrate a positive response to acute vasoreactivity testing, in the absence of right-heart failure or contraindications to calcium-channel blocker (CCB) therapy, treatment with high dose CCB's may be warranted when deemed appropriate by treating physician.
        - PAH patients who are not vasoreactive or are vasoreactive but not responding appropriately to CCBs (after at least 3-months of therapy) may be considered for advanced therapies. Contraindications to vasoreactivity testing include low systemic blood pressure, low cardiac output or the

	presence of functional class (FC) IV symptoms. Vasoreactivity testing should be performed by individuals with appropriate training in test performance and interpretation. CCB use is not recommended empirically, in the absence of demonstrated acute vasoreactivity. ○ Select advance therapies addressed in this policy pose a risk to the fetus, and require additional cautionary steps (for example, Special access programs (L.E.A.P., T.A.P., REMS), use of contraception, pregnancy testing for female patients). Examples of these agents include: bosentan (Tracleer), ambrisentan (Letairis), macitentan (Opsumit), riociguat (Adempas). The treating physician should take into consideration and address these safety concerns prior to the patient initiating therapy. ○ The recommended dose of Revatio in adults is 20 mg three times a day; however, the dose may be titrated to a maximum of 80 mg three times a day based on symptoms and tolerability. The recommended dose of Revatio in pediatric patients ≤ 20 kg is 10 mg three times a day and in pediatric patients > 20 kg is 20 mg three times a day. In pediatric patients > 45 kg, the dose may be increased to a maximum of 40 mg three times a day based on symptoms and tolerability. ○ Alyq is a generic version of Adcirca.

Approval Criteria

I. Initial Authorization

A. Adcirca (tadalafil), Alyq, or Tadliq

When a benefit, coverage of Adcirca (tadalafil), Alyq, or Tadliq may be approved when all of the following criteria are met **(1. through 5.)**:

1. The drug is prescribed by or in consultation with a cardiovascular or pulmonary specialist.
2. The member has a diagnosis of WHO Group 1 PAH (ICD-10: I27.0, I27.21).
3. The member has documented NYHA or WHO Functional Class II or III symptoms from baseline.
4. The prescriber has submitted the results of a right heart catheterization substantiating all of the following **(a., b., and c.)**:
  a. A documented mPAP > 20 mmHg at rest.
  b. A documented PWP ≤ 15 mmHg.
  c. A documented PVR ≥ 3 Wood units.
5. The member meets all of the following criteria **(a., b., and c.)**:
  a. If the request is for brand Adcirca, the has member experienced therapeutic failure or intolerance to generic tadalafil or Alyq.
  b. For new starts to generic tadalafil or Alyq therapy, the member has experienced therapeutic failure, contraindication, or intolerance to plan-preferred generic sildenafil.
  c. If the request is for Tadliq, the member meets all of the following **(i. and ii.)**:
    i. The member has experienced therapeutic failure, contraindication, or intolerance to plan-preferred generic sildenafil.
    ii. The member meets one (1) of the following **(A) or B))**:
      A) The member has experienced therapeutic failure or intolerance to plan-preferred generic tadalafil or Alyq.
      B) The member has an inability to swallow tablets.

B. Adcirca (tadalafil), Alyq, or Tadliq plus Letairis (ambrisentan)

When a benefit, coverage of Adcirca (tadalafil), Alyq, or Tadliq plus Letairis (ambrisentan) may be approved when all of the following criteria are met **(1. through 5.)**:

1. The drugs are prescribed by or in consultation with a cardiovascular or pulmonary specialist.
2. The member has a diagnosis of WHO Group 1 PAH (ICD-10: I27.0, I27.21).
3. The member has documented NYHA or WHO Functional Class II or III symptoms from baseline.
4. The prescriber has submitted the results of a right heart catheterization substantiating all of the following **(a., b., and c.)**:
   - **a.** A documented mPAP > 20 mmHg at rest.
   - **b.** A documented PWP ≤ 15 mmHg.
   - **c.** A documented PVR ≥ 3 Wood units.
5. The member meets all of the following criteria **(a. through d.)**:
   - **a.** If the request is for brand Adcirca, the member experienced therapeutic failure or intolerance to generic tadalafil or Alyq.
   - **b.** If the request is for brand Letairis, the member experienced therapeutic failure or intolerance to generic ambrisentan.
   - **c.** If the request is for Tadliq, the member has experienced therapeutic failure, contraindication, or intolerance to all of the following plan-preferred generic products **(i. and ii.):**
     - **i.** sildenafil
     - **ii.** tadalafil or Alyq
   - **d.** For new starts to dual therapy, the member has experienced therapeutic failure, contraindication, or intolerance to plan-preferred generic sildenafil monotherapy.

C. Adempas (riociguat)

1. PAH

When a benefit, coverage of Adempas may be approved when all of the following criteria are met **(a. through d.)**:

- **a.** The drug is prescribed by or in consultation with a cardiovascular or pulmonary specialist.
- **b.** The member has a diagnosis of WHO Group 1 PAH (ICD-10: I27.0, I27.21).
- **c.** The member has documented NYHA or WHO Functional Class II or III symptoms from baseline.
- **d.** The prescriber has submitted the results of a right heart catheterization substantiating all of the following **(i., ii., and iii.)**:
  - **i.** A documented mPAP > 20 mmHg at rest.
  - **ii.** A documented PWP ≤ 15 mmHg.
  - **iii.** A documented PVR ≥ 3 Wood units.

2. CTEPH

When a benefit, coverage of Adempas may be approved when all of the following criteria are met **(a. through d.)**:

- **a.** The drug is prescribed by or in consultation with a cardiovascular or pulmonary specialist.
- **b.** The member has a diagnosis of WHO Group 4 CTEPH (ICD-10: I27.24).
- **c.** The prescriber has submitted the results of a right heart catheterization and V/Q scan substantiating all of the following **(i., ii., and iii.)**:
  - **i.** A documented mPAP > 20 mmHg at rest.
  - **ii.** A documented PWP ≤ 15 mmHg.
  - **iii.** Documented presence of occlusive thrombi within the pulmonary arteries.
- **d.** The member is using Adempas for recurrent or residual pulmonary hypertension after surgery or if disease is inoperable.

D. Letairis (ambrisentan)

When a benefit, coverage of Letairis (ambrisentan) may be approved when all of the following criteria are met **(1. through 5.)**:

1. The drug is prescribed by or in consultation with a cardiovascular or pulmonary specialist.
2. The member has a diagnosis of WHO Group 1 PAH (ICD-10: I27.0, I27.21).

3. The member has documented NYHA or WHO Functional Class II or III symptoms from baseline.
4. The prescriber has submitted the results of a right heart catheterization substantiating all of the following **(a., b., and c.)**:
   a. A documented mPAP > 20 mmHg at rest.
   b. A documented PWP ≤ 15 mmHg.
   c. A documented PVR ≥ 3 Wood units.
5. The member meets all of the following criteria **(a. and b.)**:
   a. If the request is for brand Letairis, the member experienced therapeutic failure or intolerance to generic ambrisentan
   b. For new starts to ambrisentan therapy, the member has experienced therapeutic failure, contraindication, or intolerance to plan-preferred generic sildenafil.

E. Liqrev (sildenafil)

When a benefit, coverage of Liqrev may be approved when all of the following criteria are met **(1. through 4.)**:

1. The drug is prescribed by or in consultation with a cardiovascular or pulmonary specialist.
2. The member has a diagnosis of WHO Group 1 PAH (ICD-10: I27.0, I27.21).
3. The prescriber has submitted the results of a right heart catheterization substantiating all of the following **(a., b., and c.)**:
   a. A documented mPAP > 20 mmHg at rest.
   b. A documented PWP ≤ 15 mmHg.
   c. A documented PVR ≥ 3 Wood units.
4. The member meets one (1) of the following **(a. or b)**:
   a. The member has experienced therapeutic failure or intolerance to plan-preferred, generic sildenafil tablets.
   b. The member has an inability to swallow tablets.

F. Opsumit (macitentan)

When a benefit, coverage of Opsumit may be approved when all of the following criteria are met **(1. through 4.)**:

1. The drug is prescribed by or in consultation with a cardiovascular or pulmonary specialist.
2. The member has a diagnosis of WHO Group 1 PAH (ICD-10: I27.0, I27.21).
3. The member has documented NYHA or WHO Functional Class II or III symptoms from baseline.
4. The prescriber has submitted the results of a right heart catheterization substantiating all of the following **(a., b., and c.)**:
   a. A documented mPAP > 20 mmHg at rest.
   b. A documented PWP ≤ 15 mmHg.
   c. A documented PVR ≥ 3 Wood units.

G. Opsynvi (macitentan and tadalafil)

When a benefit, coverage of Opsynvi may be approved when all of the following criteria are met **(1. through 5.)**:

1. The drug is prescribed by or in consultation with a cardiovascular or pulmonary specialist.
2. The member has a diagnosis of WHO Group 1 PAH (ICD-10: I27.0, I27.21).
3. The member has documented NYHA or WHO Functional Class II or III symptoms from baseline.
4. The prescriber has submitted the results of a right heart catheterization substantiating all of the following **(a., b., and c.)**:
   a. A documented mPAP > 20 mmHg at rest.
   b. A documented PWP ≤ 15 mmHg.
   c. A documented PVR ≥ 3 Wood units.
5. The member has experienced therapeutic failure, contraindication, or intolerance to an agent in at least one (1) of the following drug classes **(a., b., or c.)**:

a. generic ERA
b. generic PDE5 Inhibitors
c. sGC stimulators

H. Orenitram (oral treprostinil)
When a benefit, coverage of Orenitram may be approved when all of the following criteria are met **(1. through 4.)**:
1. The drug is prescribed by or in consultation with a cardiovascular or pulmonary specialist.
2. The member has a diagnosis of WHO Group 1 PAH (ICD-10: I27.0, I27.21).
3. The member has documented NYHA or WHO Functional Class II or III symptoms from baseline.
4. The prescriber has submitted the results of a right heart catheterization substantiating all of the following **(a., b., and c.)**:
a. A documented mPAP > 20 mmHg at rest.
b. A documented PWP ≤ 15 mmHg.
c. A documented PVR ≥ 3 Wood units.

I. Revatio (sildenafil)
When a benefit, coverage of Revatio (sildenafil) may be approved when all of the following criteria are met **(1. through 4.)**:
1. The drug is prescribed by or in consultation with a cardiovascular or pulmonary specialist.
2. The member has a diagnosis of WHO Group 1 PAH (ICD-10: I27.0, I27.21).
3. The member meets one (1) of the following criteria **(a. or b.)**:
a. The prescriber has submitted the results of a right heart catheterization substantiating all of the following **(i., ii., and iii.)**:
i. A documented mPAP > 20 mmHg at rest.
ii. A documented PWP ≤ 15 mmHg.
iii. A documented PVR ≥ 3 Wood units.
b. An exception to right heart catheterization may be allowed when all of the following criteria are met **(i., ii., and iii.)**:
i. The member is 17 years of age or younger.
ii. The risk of right heart catheterization outweighs the benefit.
iii. The prescriber submits alternative studies such as contrast-enhanced computed tomography (CT) scan, magnetic resonance imaging (MRI), or other specified testing ruling out other causes of PH (for example, for congenital metabolic diseases, gastroesophageal reflux disease).
4. If the request is for brand Revatio, the member experienced therapeutic failure or intolerance to generic sildenafil.

J. Tracleer (bosentan)
When a benefit, coverage of Tracleer (bosentan) may be approved when all the following criteria are met **(1. through 6.)**:
1. The drug is prescribed by or in consultation with a cardiovascular or pulmonary specialist.
2. The member has a diagnosis of WHO Group 1 PAH (ICD-10: I27.0, I27.21).
3. The member has documented NYHA or WHO Functional Class II, III or IV symptoms from baseline.
4. The member meets one (1) of the following criteria **(a. or b.)**:
a. The prescriber has submitted the results of a right heart catheterization substantiating all of the following **(i., ii., and iii.)**:
i. A documented mPAP > 20 mmHg at rest.
ii. A documented PWP ≤ 15 mmHg.
iii. A documented PVR ≥ 3 Wood units.
b. An exception to right heart catheterization may be allowed when all of the following criteria are met **(i., ii., and iii.)**:
i. The member is 17 years of age or younger.
ii. The risk of right heart catheterization outweighs the benefit.

iii. The prescriber submits alternative studies such as contrast-enhanced computed tomography (CT) scan, magnetic resonance imaging (MRI), or other specified testing ruling out other causes of PH (for example, for congenital metabolic diseases, gastroesophageal reflux disease).

5. If the request is for brand Tracleer oral tablets, the member has experienced therapeutic failure or intolerance to generic bosentan oral tablets.
6. If the request is for Tracleer tablets for oral suspension, the member meets one (1) of the following **(a. or b.)**:
   a. The member has experienced therapeutic failure or intolerance to generic bosentan oral tablets.
   b. The member has an inability to swallow tablets.

K. Tyvaso inhalation solution, Tyvaso DPI (inhaled treprostinil), or Yutrepia

1. PAH

When a benefit, coverage of Tyvaso, Tyvaso DPI, or Yutrepia may be approved when all of the following criteria are met **(a. through e.)**:

a. The drug is prescribed by or in consultation with a cardiovascular or pulmonary specialist.
b. The member has a diagnosis of WHO Group 1 PAH (ICD-10: I27.0, I27.21).
c. The member has documented NYHA or WHO Functional Class III symptoms from baseline.
d. The prescriber has submitted the results of a right heart catheterization substantiating all of the following **(i., ii., and iii.)**:
   i. A documented mPAP > 20 mmHg at rest.
   ii. A documented PWP ≤ 15 mmHg.
   iii. A documented PVR ≥ 3 Wood units.
e. For new starts to Tyvaso or Yutrepia therapy, the member has experienced therapeutic failure, contraindication, or intolerance to one (1) of the following generic products **(i. or ii.)**:
   i. sildenafil
   ii. ambrisentan

2. PH-ILD

When a benefit, coverage of Tyvaso, Tyvaso DPI, or Yutrepia may be approved when all of the following criteria are met **(a. through d.)**:

a. The drug is prescribed by or in consultation with a cardiovascular or pulmonary specialist.
b. The member has diagnoses of all of the following (ICD-10: I27.23) **(i. and ii.)**:
   i. WHO Group 3 PH
   ii. Interstitial lung disease
c. The prescriber has submitted the results of a right heart catheterization substantiating all of the following **(i., ii., and iii.)**:
   i. A documented mPAP > 20 mmHg at rest.
   ii. A documented PWP ≤ 15 mmHg.
   iii. A documented PVR ≥ 3 Wood units.
d. The member is a non-smoker or is currently engaged in smoking cessation.

L. Uptravi (selexipag)

When a benefit, coverage of Uptravi may be approved when all of the following criteria are met **(1. through 5.)**:

1. The drug is prescribed by or in consultation with a cardiovascular or pulmonary specialist.
2. The member has a diagnosis of WHO Group 1 PAH (ICD-10: I27.0, I27.21).
3. The member has documented NYHA or WHO Functional Class II or III symptoms from baseline.
4. The prescriber has submitted the results of a right heart catheterization substantiating **all** of the following **(a., b., and c.)**:

a. A documented mPAP > 20 mmHg at rest.
b. A documented PWP ≤ 15 mmHg.
c. A documented PVR ≥ 3 Wood units.

5. For new starts to Uptravi therapy, the member has experienced therapeutic failure, contraindication, or intolerance to one (1) of the following plan-preferred generic products **(a. or b.)**:
a. sildenafil
b. ambrisentan

M. Ventavis (inhaled iloprost)

When a benefit, coverage of Ventavis may be approved when all of the following criteria are met **(1. through 5.)**:

1. The drug is prescribed by or in consultation with a cardiovascular or pulmonary specialist.
2. The member has a diagnosis of WHO Group 1 PAH (ICD-10: I27.0, I27.21).
3. The member has documented NYHA or WHO Functional Class III or IV symptoms from baseline.
4. The prescriber has submitted the results of a right heart catheterization substantiating **all** of the following **(a., b., and c.)**:
a. A documented mPAP > 20 mmHg at rest.
b. A documented PWP ≤ 15 mmHg.
c. A documented PVR ≥ 3 Wood units.
5. For new starts to Ventavis therapy with NYHA or WHO Functional Class III, the member has experienced therapeutic failure, contraindication, or intolerance to one (1) of the following plan-preferred generic products **(a. or b.)**:
a. sildenafil
b. ambrisentan

N. Winrevair (sotatercept-csrk)

When a benefit, coverage of Winrevair may be approved when all of the following criteria are met **(1. through 8.)**:

1. The drug is prescribed by or in consultation with a cardiovascular or pulmonary specialist.
2. The member has a diagnosis of WHO Group 1 PAH (ICD-10: I27.0, I27.21).
3. The member has documented NYHA or WHO Functional Class II or III symptoms from baseline.
4. The prescriber has submitted the results of a right heart catheterization substantiating **all** of the following **(a., b., and c.)**:
a. A documented mPAP > 20 mmHg at rest.
b. A documented PWP ≤ 15 mmHg.
c. A documented PVR ≥ 3 Wood units.
5. The member meets one (1) of the following **(a. or b.)**:
a. The member is currently receiving at least two (2) agents from two (2) different classes of the following medications **(i. through iv.):**
i. generic ERA
ii. generic PDE5 inhibitor
iii. sGC
iv. generic prostacyclin agent
b. If the member is only on one PAH-specific agent, the prescriber attests the member is unable to tolerate dual background therapy.
6. The prescriber attests the member is on maximally tolerated PAH-specific background therapy.
7. The member will continue background therapy with PAH-specific therapies while being treated with Winrevair.
8. The member has unresponsive or progressive disease despite established PAH-specific therapies.

II. Reauthorization

When a benefit, reauthorization of pulmonary hypertension agents may be approved when all of the following criteria are met **(A. through E.)**:

A. The prescriber attests that the member has experienced positive clinical response to therapy.

B. If the request is for brand Adcirca, the member has experienced therapeutic failure or intolerance to generic tadalafil or Alyq.

C. If the request is for brand Letairis, the member has experienced therapeutic failure or intolerance to generic ambrisentan.

D. If the request is for brand Revatio, the member has experienced therapeutic failure or intolerance to generic sildenafil.

E. If the request is for brand Tracleer oral tablets, the member has experienced therapeutic failure or intolerance to generic bosentan oral tablets.

III. Quantity Limits

A. Revatio (sildenafil)

When a benefit, additional quantities of Revatio (sildenafil) may be approved when all of the following criteria are met **(1. and 2.)**:

1. If the member is 1 to 17 years of age, the member weighs > 45 kg.

2. For requests exceeding the coded quantity limit, Revatio (sildenafil) may be authorized in quantities as follows:

Drug	Coded Quantity Limit	Patient Age	Approvable Quantity
Revatio (sildenafil) 20 mg oral tablets	3 tablets per day	≥ 18 years	12 tablets per day
		< 18 years	6 tablets per day
Revatio (sildenafil) 10 mg/mL	2 bottles (224 mL) per 25 days; 6 bottles (672 mL) per 75 days	≥ 18 years	7 bottles (784 mL) per 25 days or 21 bottles (2,352 mL) per 75 days
		< 18 years	4 bottles (448 mL) per 25 days or 12 bottles (1,344 mL) per 75 days

IV. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. The prescriber has ruled out other causes of pulmonary hypertension (for example, left heart disease, chronic lung disease, venous thromboembolism, or other contributory diseases).

II. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

III. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None.

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