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DRUG POLICY

Pulmonary Arterial Hypertension

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Pulmonary Arterial Hypertension (PAH) drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines and clinical studies. The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Adcirca, Alyq, and Tadalafil (tadalafil)

Adcirca, Alyq, and Tadalafil are oral phosphodiesterase type 5 (PDE5) inhibitors indicated for the 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 and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

Adempas (riociguat)

Adempas is an oral soluble guanylate cyclase stimulator indicated for the treatment of adults with pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to improve exercise capacity, WHO functional class and to delay clinical worsening. Efficacy was shown in patients on Adempas monotherapy or in combination with endothelin receptor antagonists or prostanoids. Studies establishing effectiveness included predominately patients with WHO functional class II–III and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

Adempas is 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.

Flolan/Veletri (epoprostenol)

Epoprostenol/Flolan/Veletri are intravenous prostanoids indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to improve exercise capacity. Studies establishing effectiveness included predominantly patients with New York Heart Association (NYHA) Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

Letairis (ambrisentan)

Letairis is an endothelin receptor antagonist (ERA) indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1):

1. To improve exercise ability and delay clinical worsening
2. 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 trials predominantly in patients with WHO Functional Class II-III symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

Opsumit (macitentan)

Opsumit is an endothelin receptor antagonist (ERA) indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to reduce the risks of disease progression and hospitalization for PAH.

Effectiveness was established in a long-term study in PAH patients with predominantly WHO Functional Class II-III symptoms treated for an average of 2 years. Patients had idiopathic and heritable PAH, PAH caused by connective tissue disorders, and PAH caused by congenital heart disease with repaired shunts.

Opsynvi (macitentan; tadalafil)

Opsynvi is a combination of macitentan, an endothelin receptor antagonist (ERA), and tadalafil, an oral phosphodiesterase type 5 (PDE5) inhibitor, indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to reduce morbidity in adult patients of WHO Functional Class II-III. Individually, macitentan reduces the risk of clinical worsening events and hospitalization, and tadalafil improves exercise ability.

Orenitram (treprostinil)

Orenitram is an oral prostanoid indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to delay disease progression and to improve exercise capacity. The studies 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.

Remodulin (treprostinil)

Remodulin is an intravenous or subcutaneous prostanoid indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to diminish symptoms associated with exercise. Studies establishing effectiveness included patients with New York Heart Association (NYHA)

Functional Class II-IV symptoms and etiologies of idiopathic or heritable PAH, PAH associated with congenital systemic-to-pulmonary shunts, or PAH associated with connective tissue diseases.

In patients with PAH requiring transition from Flolan (epoprostenol sodium), Remodulin/treprostinil is indicated to diminish clinical deterioration. The risks and benefits of each drug should be carefully considered prior to transition.

Revatio and Liqrev (sildenafil)

Revatio (sildenafil) is an oral or intravenous phosphodiesterase type 5 (PDE5) inhibitor indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) in adults to improve exercise ability and delay clinical worsening. Studies establishing effectiveness were short-term (12 to 16 weeks) and included predominately patients with New York Heart Association (NYHA) Functional Class II–III symptoms and idiopathic etiology or associated with connective tissue disease (CTD).

Revatio (sildenafil) is also indicated for the treatment of PAH (WHO Group 1) in pediatric patients 1 to 17 years of age to improve exercise ability and, in pediatric patients too young to perform standardized exercise testing, pulmonary hemodynamics thought to underly improvements in exercise.

Liqrev (sildenafil) an oral phosphodiesterase type 5 (PDE5) inhibitor indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) in adults to improve exercise ability and delay clinical worsening.

Tracleer (bosentan)

Tracleer is an endothelin receptor antagonist indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [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 symptoms and etiologies of idiopathic or heritable PAH, PAH associated with connective tissue diseases, and PAH associated with congenital heart disease with left-to-right shunts.

Tracleer is also indicated 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.

Tyvaso (treprostinil)

Tyvaso is an inhaled prostanoid indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to improve exercise ability. Studies establishing effectiveness predominately included patients with New York Heart Association (NYHA) Functional Class III symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

Tyvaso is also indicated for the treatment of 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) inclusive of idiopathic pulmonary fibrosis (IPF), combined pulmonary fibrosis and emphysema (CPFE), and WHO Group 3 connective tissue disease.

Yutrepia (treprostinil)

Yutrepia (treprostinil) is an inhaled prostanoid indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to improve exercise ability. Studies establishing

effectiveness predominately included patients with New York Heart Association (NYHA) Functional Class III symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

Yutrepia is also indicated for the treatment of 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) inclusive of idiopathic pulmonary fibrosis (IPF), combined pulmonary fibrosis and emphysema (CPFE), and WHO Group 3 connective tissue disease.

Uptravi (selexipag)

Uptravi is an oral prostacyclin receptor indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to delay disease progression and reduce the risk of hospitalization for PAH.

Effectiveness was established in a long-term study in PAH patients with WHO Functional Class II-III symptoms. Patients had idiopathic and heritable PAH, PAH associated with connective tissue disease, PAH associated with congenital heart disease with repaired shunts.

Ventavis (iloprost)

Ventavis is an inhaled prostanoid indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to improve a composite endpoint consisting of exercise tolerance, symptoms (New York Heart Association [NYHA] Class), and lack of deterioration. Studies establishing effectiveness included predominately patients with NYHA Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

Winrevair (sotatercept)

Winrevair is a subcutaneous activin signaling inhibitor indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to increase exercise capacity, improve WHO functional class and reduce the risk of clinical worsening events, including hospitalization for PAH, lung transplantation and death.

Compensial Use

Adcirca, Alyq, and Tadliq (tadalafil)

Secondary Raynaud's phenomenon

Revatio and Liqrev (sildenafil)

Secondary Raynaud's phenomenon

POLICY

Required Documentation (Winrevair only)

Submission of the following is necessary to initiate the prior authorization review for initial requests: chart notes, medical record documentation, or claims history supporting current pulmonary arterial hypertension (PAH) therapy.

Prescriber Specialties (Pulmonary Hypertension indications only)

The requested medication must be prescribed by or in consultation with one of the following:

1. Pulmonologist
2. Cardiologist

Criteria for Initial Approval

I. Adempas (riociguat)

A. Pulmonary Arterial Hypertension (PAH)

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

1. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (Refer to Appendix)
2. PAH was confirmed by right heart catheterization with all of the following pretreatment results:
 - a. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
 - b. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
 - c. Pulmonary vascular resistance (PVR) > 2 Wood units

B. Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

Authorization of 12 months may be granted for treatment of CTEPH when ALL of the following criteria are met:

1. Member has CTEPH defined as WHO Group 4 class of pulmonary hypertension (Refer to Appendix)
2. Member meets either criterion (a) or criterion (b) below:
 - a. Recurrent or persistent CTEPH after pulmonary endarterectomy (PEA)
 - b. Inoperable CTEPH with diagnosis confirmed by BOTH of the following (i. and ii.):
 - i. Computed tomography (CT)/magnetic resonance imaging (MRI) angiography or pulmonary angiography
 - ii. Pretreatment right heart catheterization with all of the following results:
 - Mean pulmonary arterial pressure (mPAP) > 20 mmHg
 - Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
 - Pulmonary vascular resistance (PVR) > 2 Wood units

II. Adcirca, Alyq, and Tadliq (tadalafil)

A. Pulmonary Arterial Hypertension (PAH)

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

1. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
2. PAH was confirmed by either criterion (a) or criterion (b) below:
 - a. Pretreatment right heart catheterization with all of the following results:
 - i. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
 - ii. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
 - iii. Pulmonary vascular resistance (PVR) > 2 Wood units. For pediatric patients, pulmonary vascular resistance index (PVRI) > 3 Wood units x m² is also acceptable.
 - b. For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

B. Secondary Raynaud's Phenomenon

Authorization of 12 months may be granted for treatment of secondary Raynaud's phenomenon when the patient has had an inadequate response to one of the following medications:

1. Calcium channel blockers
2. Angiotensin II receptor blockers
3. Selective serotonin reuptake inhibitors
4. Alpha blockers
5. Topical nitrates

III. Revatio and Liquev (sildenafil)

A. Pulmonary Arterial Hypertension (PAH)

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

1. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
2. PAH was confirmed by either criterion (a) or criterion (b) below:
 - a. Pretreatment right heart catheterization with all of the following results:
 - i. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
 - ii. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
 - iii. Pulmonary vascular resistance (PVR) > 2 Wood units. For pediatric patients, pulmonary vascular resistance index (PVRI) > 3 Wood units x m² is also acceptable.
 - b. For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

B. Secondary Raynaud's Phenomenon

Authorization of 12 months may be granted for treatment of secondary Raynaud's phenomenon when the patient has had an inadequate response to one of the following medications:

1. Calcium channel blockers
2. Angiotensin II receptor blockers
3. Selective serotonin reuptake inhibitors
4. Alpha blockers
5. Topical nitrates

IV. Epoprostenol, Flolan, and Veletri (epoprostenol)

Authorization of 12 months may be granted for treatment of PAH when ALL of the following criteria are met:

- A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
- B. PAH was confirmed by either criterion (1) or criterion (2) below:
 1. Pretreatment right heart catheterization with all of the following results:
 - a. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
 - b. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
 - c. Pulmonary vascular resistance (PVR) > 2 Wood units. For pediatric patients, pulmonary vascular resistance index (PVRI) > 3 Wood units x m² is also acceptable.
 2. For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

V. Ventavis (iloprost)

Authorization of 12 months may be granted for treatment of pulmonary arterial hypertension (PAH) when ALL of the following criteria are met:

- A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
- B. PAH was confirmed by either criterion (1) or criterion (2) below:
 - 1. Pretreatment right heart catheterization with all of the following results:
 - a. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
 - b. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
 - c. Pulmonary vascular resistance (PVR) > 2 Wood units. For pediatric patients, pulmonary vascular resistance index (PVRI) > 3 Wood units x m² is also acceptable.
 - 2. For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

VI. Letairis (ambrisentan)

Authorization of 12 months may be granted for treatment of pulmonary arterial hypertension (PAH) when ALL of the following criteria are met:

- A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
- B. PAH was confirmed by either criterion (1) or criterion (2) below:
 - 1. Pretreatment right heart catheterization with all of the following results:
 - a. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
 - b. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
 - c. Pulmonary vascular resistance (PVR) > 2 Wood units. For pediatric patients, pulmonary vascular resistance index (PVRI) > 3 Wood units x m² is also acceptable.
 - 2. For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

VII. Opsumit (macitentan)

Authorization of 12 months may be granted for treatment of pulmonary arterial hypertension (PAH) when ALL of the following criteria are met:

- A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
- B. PAH was confirmed by either criterion (1) or criterion (2) below:
 - 1. Pretreatment right heart catheterization with all of the following results:
 - a. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
 - b. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
 - c. Pulmonary vascular resistance (PVR) > 2 Wood units. For pediatric patients, pulmonary vascular resistance index (PVRI) > 3 Wood units x m² is also acceptable.
 - 2. For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

VIII. Opsynvi (macitentan; tadalafil)

Authorization of 12 months may be granted for treatment of pulmonary arterial hypertension (PAH) when ALL of the following criteria are met:

- A. Member must experience an inadequate response, adverse event, intolerance, or contraindication to the combined use of the individual ingredients, macitentan and tadalafil.

Treatment failure cannot be caused by a lack of compliance to therapy or the unwillingness to take the two ingredients separately.

- B. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
- C. PAH was confirmed by either criterion (1) or criterion (2) below:
 - 1. Pretreatment right heart catheterization with all of the following results:
 - a. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
 - b. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
 - c. Pulmonary vascular resistance (PVR) > 2 Wood units. For pediatric patients, pulmonary vascular resistance index (PVRI) > 3 Wood units x m² is also acceptable.
 - 2. For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

IX. Orenitram (treprostinil)

Authorization of 12 months may be granted for treatment of pulmonary arterial hypertension (PAH) when ALL of the following criteria are met:

- A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
- B. PAH was confirmed by either criterion (1) or criterion (2) below:
 - 1. Pretreatment right heart catheterization with all of the following results:
 - a. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
 - b. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
 - c. Pulmonary vascular resistance (PVR) > 2 Wood units. For pediatric patients, pulmonary vascular resistance index (PVRI) > 3 Wood units x m² is also acceptable.
 - 2. For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

X. Remodulin (treprostinil)

Authorization of 12 months may be granted for treatment of pulmonary arterial hypertension (PAH) when ALL of the following criteria are met:

- A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
- B. PAH was confirmed by either criterion (1) or criterion (2) below:
 - 1. Pretreatment right heart catheterization with all of the following results:
 - a. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
 - b. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
 - c. Pulmonary vascular resistance (PVR) > 2 Wood units. For pediatric patients, pulmonary vascular resistance index (PVRI) > 3 Wood units x m² is also acceptable.
 - 2. For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

XI. Tracleer (bosentan)

Authorization of 12 months may be granted for treatment of pulmonary arterial hypertension (PAH) when ALL of the following criteria are met:

- A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
- B. PAH was confirmed by either criterion (1) or criterion (2) below:

1. Pretreatment right heart catheterization with all of the following results:
 - a. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
 - b. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
 - c. Pulmonary vascular resistance (PVR) > 2 Wood units. For pediatric patients, pulmonary vascular resistance index (PVRI) > 3 Wood units x m² is also acceptable.
2. For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

XII. Tyvaso, Tyvaso DPI, Yutrepia (treprostinil)

Authorization of 12 months may be granted for treatment of pulmonary hypertension (PH) when both of the following criteria are met:

- A. Member has either of the following:
 1. WHO Group 1 class of pulmonary hypertension (refer to Appendix).
 2. PH associated with interstitial lung disease (WHO Group 3, refer to Appendix)
- B. PH was confirmed by either criterion (1) or criterion (2) below:
 1. Pretreatment right heart catheterization with all of the following results:
 - a. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
 - b. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
 - c. Pulmonary vascular resistance (PVR) > 2 Wood units. For pediatric patients, pulmonary vascular resistance index (PVRI) > 3 Wood units x m² is also acceptable.
 2. For infants less than one year of age, PH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

XIII. Uptravi (selexipag)

Authorization of 12 months may be granted for treatment of pulmonary arterial hypertension (PAH) when ALL of the following criteria are met:

- A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
- B. PAH was confirmed by either criterion (1) or criterion (2) below:
 1. Pretreatment right heart catheterization with all of the following results:
 - a. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
 - b. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
 - c. Pulmonary vascular resistance (PVR) > 2 Wood units. For pediatric patients, pulmonary vascular resistance index (PVRI) > 3 Wood units x m² is also acceptable.
 2. For infants less than one year of age, PAH was confirmed by Doppler echocardiogram if right heart catheterization cannot be performed.

XIV. Winrevair (sotatercept)

Authorization of 6 months may be granted for treatment of pulmonary arterial hypertension (PAH) in members 18 years of age and older when ALL of the following criteria are met:

- A. Member has PAH defined as WHO Group 1 class of pulmonary hypertension (refer to Appendix).
- B. PAH was confirmed by right heart catheterization with all of the following results:
 1. Mean pulmonary arterial pressure (mPAP) > 20 mmHg
 2. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
 3. Pulmonary vascular resistance (PVR) > 2 Wood units
- C. Member has a platelet count greater than or equal to 50,000/mm³
- D. Member is not pregnant nor planning to become pregnant

- E. The requested medication will be used as add-on therapy.
- F. Member is currently receiving PAH therapy with medications from at least two of the following drug classes:
 - 1. Endothelin receptor antagonist (e.g., Letairis, Opsumit, Tracleer)
 - 2. Phosphodiesterase-5 inhibitor (e.g., Adcirca, Revatio)
 - 3. Soluble guanylate cyclase simulator (e.g., Adempas)
 - 4. Prostacyclin analog (e.g., Flolan, Orenitram, Remodulin, Tyvaso, Veletri, Ventavis)
 - 5. Prostacyclin receptor agonist (e.g., Uptravi)

Continuation of Therapy

Pulmonary Arterial Hypertension (PAH)

Authorization of 12 months may be granted for members with PAH who are receiving the requested medication through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

Authorization of 36 months will be granted for members with PAH who are receiving any of the following requested therapies through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement:

- I. Remodulin (treprostinil)
- II. Treprostinil (intravenous or subcutaneous)
- III. Flolan (epoprostenol)
- IV. Veletri (epoprostenol)
- V. Epoprostenol (intravenous)
- VI. Ventavis (iloprost)

Secondary Raynaud's Phenomenon

Authorization of 12 months may be granted for members with secondary Raynaud's phenomenon who are receiving the requested medication (sildenafil or tadalafil) through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

Authorization of 12 months may be granted for members with CTEPH who are receiving Adempas through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

Pulmonary Hypertension associated with Interstitial Lung Disease (WHO Group 3)

Authorization of 12 months may be granted for members with pulmonary hypertension associated with interstitial lung disease (World Health Organization [WHO] Group 3) who are receiving Tyvaso, Tyvaso DPI, or Yutrepia through a paid pharmacy or medical benefit, and who are experiencing benefit from therapy as evidenced by disease stability or disease improvement.

Other

The aforementioned drugs are considered **not medically necessary** for patients who do not meet the criteria set forth above.

Members currently receiving Opsynvi (macitentan; tadalafil) as samples or via the manufacturer's patient assistance program will be required to meet the criteria for initial approval. This ensures that members are treated equally regardless of their provider's ability to access medication samples.

Non-Formulary Exception Criteria

Non-Formulary Exception criteria applies to formularies which do not include the requested product(s) on the formulary drug list. Meeting the criteria above may satisfy some, or all, portions of the Non-Formulary Exception Criteria. A medication that is non-formulary may be covered when the Criteria for Approval AND the following criteria are met:

1. The requested drug must be used for an FDA-approved indication, or an indication supported in the compendia of current literature (examples: AHFS, Micromedex, current accepted guidelines). Diagnostic testing/lab results required when applicable.
2. The prescribed dose/quantity must fall within the FDA-approved labeling or dosing guidelines found in the compendia of current literature.
3. All covered formulary alternative drugs on any tier will be ineffective, have been ineffective, would not be as effective as the non-formulary drug, or would have adverse effects. Documentation is required and must include chart note(s) or other documentation indicating prior treatment failure, severity of the adverse event (if any), and dosage and duration of the prior treatment, or contraindication to formulary alternatives.

Dosing and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limits Apply

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Medication	Standard Limit	FDA-recommended dosing
Adcirca (tadalafil) 20 mg tablets	60 tablets per 30 days	40 mg per day
Alyq (tadalafil) 20 mg tablets	60 tablets per 30 days	
Adempas (riociguat) 0.5 mg tablets	90 tablets per 30 days	The recommended starting dosage is 1 mg taken 3 times a day. For patients who cannot tolerate the hypotensive effect of Adempas, consider a starting dose of 0.5 mg taken three times a day. If systolic blood pressure remains greater than 95 mmHg and the patient has no signs or symptoms of hypotension, up-titrate by 0.5 mg taken three times a day. Dose increases should be no sooner than 2 weeks apart. The dose can be increased to the highest tolerated dosage, up to a maximum of 2.5 mg taken 3 times per day. If at any time, the patient has symptoms of hypotension, decrease the dosage by 0.5 mg taken three times per day.
Adempas (riociguat) 1 mg tablets	90 tablets per 30 days	
Adempas (riociguat) 1.5 mg tablets	90 tablets per 30 days	
Adempas (riociguat) 2 mg tablets	90 tablets per 30 days	
Adempas (riociguat) 2.5 mg tablets	90 tablets per 30 days	
Letairis (ambrisentan) 5 mg tablets	30 tablets per 30 days	Initiate treatment at 5 mg once daily with or without tadalafil 20 mg once daily. At 4-week

Medication	Standard Limit	FDA-recommended dosing
Letairis (ambrisentan) 10 mg tablets	30 tablets per 30 days	intervals, either the dose of Letairis or tadalafil can be increased, as needed and tolerated, to Letairis 10 mg or tadalafil 40 mg.
Liqrev (sildenafil) 10 mg/mL suspension	720 mL per 30 days	Patients ≥ 18 years of age: 20 mg three times a day; may titrate to a maximum dose of 80 mg three times a day
Opsumit (macitentan) 10 mg tablets	30 tablets per 30 days	10 mg per day
Opsynvi (macitentan; tadalafil) 10 mg; 20 mg tablets	30 tablets per 30 days	For treatment naïve patients or patients transitioning from an endothelin receptor antagonist (ERA): 10 mg/20 mg tablet orally once daily and titrate to 10 mg/40 mg tablet orally once daily as the maintenance dose For patients transitioning from a phosphodiesterase 5 (PDE5) inhibitor monotherapy or PDE5 inhibitor and ERA combination: 10 mg/40 mg tablet orally once daily
Opsynvi (macitentan; tadalafil) 10 mg; 40 mg tablets	30 tablets per 30 days	
Orenitram (treprostinil) Month 1 Titration Kit	1 kit per 28 days	Initial dose of 0.125 mg every 8 hours or 0.25 mg every 12 hours, titrate by 0.125 mg every 8 hours or by 0.25 to 0.5 mg every 12 hours no more frequently than every 3 to 4 days. Maximum dose determined by tolerability.
Orenitram (treprostinil) Month 2 Titration Kit	1 kit per 28 days	
Orenitram (treprostinil) Month 3 Titration Kit	1 kit per 28 days	
Orenitram tablets (all strengths)	270 tablets per 30 days	
Revatio (sildenafil) 10 mg/mL suspension*	720 mL per 30 days*	Patients ≥ 18 years of age: 20 mg three times a day; may titrate to a maximum dose of 80 mg three times a day
Revatio (sildenafil) 20 mg tablets	Initial Therapy 90 tablets per 30 days Continuation Therapy** 360 tablets per 30 days	Patients 1 to 17 years of age: • ≤20 kg: 10 mg three times a day • >20 kg to <45 kg: 20 mg three times a day • ≥45 kg: 20 mg three times a day; may be titrated to a maximum dose of 40 mg three times a day
Tadliq (tadalafil) 20 mg/5 mL oral suspension	10 mL per day	40 mg (10 mL) per day

Medication	Standard Limit	FDA-recommended dosing
Tracleer (bosentan) 125 mg tablets	60 tablets per 30 days	Patients >12 years of age and >40 kg: Initiate treatment at 62.5 mg twice daily for 4 weeks and then increase to maintenance dose of 125 mg twice daily. Patients >12 years of age and <40 kg: Initial and maintenance dosing: 62.5 mg twice daily Patients ≤12 years of age: Initial and maintenance dosing: • ≥4-8 kg: 16 mg twice daily • >8-16 kg: 32 mg twice daily • >16-24 kg: 48 mg twice daily • >24-40 kg: 64 mg twice daily
Tracleer (bosentan) 62.5 mg tablets	60 tablets per 30 days	
Tracleer (bosentan) 32 mg tablets	112 tablets per 28 days	
Tyvaso (treprostinil) 0.6 mg/mL inhalation solution	81.2 mL (28 ampules) per 28 days	Up to 72 mcg four times a day
Tyvaso (treprostinil) DPI 16 mcg and 32 mcg Inhalation Powder Titration Kit	196 cartridges per 28 days	Initial dosage: One 16 mcg cartridge per treatment session, four times daily. Dosage should be increased by an additional 16 mcg per treatment session at approximately 1- to 2- week intervals, if tolerated The target maintenance doses of 48 mcg to 64 mcg per treatment sessions, four times daily If the prescribed dose is higher than 80 mcg per treatment session, more than 1 cartridge will be needed per session.
Tyvaso (treprostinil) DPI 16 mcg, 32 mcg, and 48 mcg Inhalation Powder Titration Kit	252 cartridges per 28 days	
Tyvaso (treprostinil) DPI 16 mcg Inhalation Powder Maintenance Kit	112 cartridges per 28 days	
Tyvaso (treprostinil) DPI 32 mcg Inhalation Powder Maintenance Kit	112 cartridges per 28 days	
Tyvaso (treprostinil) DPI 48 mcg Inhalation Powder Maintenance Kit	112 cartridges per 28 days	
Tyvaso (treprostinil) DPI 64 mcg Inhalation Powder Maintenance Kit	112 cartridges per 28 days	
Tyvaso (treprostinil) DPI 80 mcg Inhalation Powder Maintenance Kit	112 cartridges per 28 days	
Tyvaso (treprostinil) DPI 32 mcg and 48 mcg Inhalation Powder Maintenance Kit	224 cartridges per 28 days	

Medication	Standard Limit	FDA-recommended dosing
Uptravi (selexipag) 200 mcg tablets	60 tablets per 30 days	Starting dose: 200 mcg twice daily. Increase the dose by 200 mcg twice daily at weekly intervals to the highest tolerated dose up to 1600 mcg twice daily.
Uptravi (selexipag) 400 mcg tablets	60 tablets per 30 days	
Uptravi (selexipag) 600 mcg tablets	60 tablets per 30 days	
Uptravi (selexipag) 800 mcg tablets	60 tablets per 30 days	
Uptravi (selexipag) 1000 mcg tablets	60 tablets per 30 days	
Uptravi (selexipag) 1200 mcg tablets	60 tablets per 30 days	
Uptravi (selexipag) 1400 mcg tablets	60 tablets per 30 days	
Uptravi (selexipag) 1600 mcg tablets	60 tablets per 30 days	
Uptravi (selexipag) titration pack (200 mcg/800 mcg tablets)	1 pack (140-200mcg tablets, 60- 800 mcg tablets) per 28 days	
Ventavis (iloprost) 10 mcg/mL inhalation solution	9 ampules per day	5 mcg up to nine times per day. The 20 mcg/mL concentration is intended for patients who are maintained at the 5 mcg dose and who have repeatedly experienced extended treatment times which could result in incomplete dosing.
Ventavis (iloprost) 20 mcg/mL inhalation solution	9 ampules per day	
Winrevair (sotatercept) 1 x 45 mg vial kit	1 kit per 21 days	Starting dose: 0.3 mg/kg subcutaneous injection once every 3 weeks Target dose: 0.7 mg/kg subcutaneous injection once every 3 weeks
Winrevair (sotatercept) 1 x 60 mg vial kit		

Medication	Standard Limit	FDA-recommended dosing
Winrevair (sotatercept) 2 x 45 mg vial kit		
Winrevair (sotatercept) 2 x 60 mg vial kit		
Yutrepia (treprostinil) 26.5 mcg inhalation capsule	5 capsules per day	Starting dose: 26.5 mcg 3 to 5 times per day, inhaled in 2 breaths. Dose increases of 26.5 mcg per dose each week may be implemented as tolerated. Target dose: 79.5 mcg to 106 mcg 4 times per day. Doses above 848 mcg per day have not been studied.
Yutrepia (treprostinil) 53 mcg inhalation capsule	5 capsules per day	
Yutrepia (treprostinil) 79.5 mcg inhalation capsule	5 capsules per day	
Yutrepia (treprostinil) 106 mcg inhalation capsule	8 capsules per day	

*For members <18 years of age

**For members who have been titrated without adverse effects and experience clinical benefit with higher doses (tablets ONLY)

APPENDIX

Appendix

WHO Classification of Pulmonary Hypertension

Note: Patients with heritable PAH or PAH associated with drugs and toxins might be long-term responders to calcium channel blockers.

WHO Group 1. Pulmonary Arterial Hypertension (PAH)

- Idiopathic
 - Long-term responders to calcium channel blockers
- Heritable
- Associated with drugs and toxins
- Associated with:
 - Connective tissue diseases
 - HIV infection
 - Portal hypertension
 - Congenital heart diseases
 - Schistosomiasis
- PAH with features of venous/capillary (pulmonary veno-occlusive disease [PVOD]/pulmonary capillary hemangiomatosis [PCH]) involvement
- Persistent PH of the newborn

WHO Group 2. Pulmonary Hypertension (PH) Owing to Left Heart Disease

- Heart Failure
 - With preserved ejection fraction
 - With reduced or mildly reduced ejection fraction
 - Cardiomyopathies with specific etiologies (i.e., hypertrophic, amyloid, Fabry disease, and Chagas disease)
- Valvular Heart Disease
 - Aortic valve disease
 - Mitral valve disease
 - Mixed valvular disease
- Congenital/acquired cardiovascular conditions leading to post-capillary PH

WHO Group 3. Pulmonary Hypertension (PH) associated with Lung Disease and/or Hypoxia

- Chronic obstructive pulmonary disease (COPD) and/or emphysema
- Interstitial lung disease
- Combined pulmonary fibrosis and emphysema
- Other parenchymal lung diseases (i.e., parenchymal lung diseases not included in Group 5)
- Nonparenchymal restrictive diseases:
 - Hypoventilation syndromes
 - Pneumonectomy
- Hypoxia without lung disease (e.g., high altitude)
- Developmental lung diseases

WHO Group 4. Pulmonary Hypertension (PH) Owing to pulmonary artery obstruction

- Chronic thromboembolic PH
- Other pulmonary artery obstructions:
 - Sarcomas (high- or intermediate-grade or angiosarcoma)
 - Other malignant tumors (e.g., renal carcinoma, uterine carcinoma, germ-cell tumors of the testis)
 - Non-malignant tumors (e.g., uterine leiomyoma)
 - Arteritis without connective tissue disease
 - Congenital pulmonary artery stenosis
 - Hydatidosis

WHO Group 5. Pulmonary Hypertension (PH) with Unclear and/or Multifactorial Mechanisms

- Hematological disorders, including inherited and acquired chronic hemolytic anemia and chronic myeloproliferative disorders
- Systemic disorders: Sarcoidosis, Pulmonary Langerhans cell histiocytosis, neurofibromatosis type 1
- Metabolic disorders, including glycogen storage diseases and Gaucher disease
- Chronic renal failure with or without hemodialysis
- Pulmonary tumor thrombotic microangiopathy
- Fibrosing mediastinitis
- Complex congenital heart disease

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD-CM diagnostic codes.

- J1325 Injection, epoprostenol, 0.5 mg
- J3285 Injection, treprostinil, 1 mg
- J3590 Unclassified biologics (when specified as Winrevair [sotatercept-csrk])
- C9399 Unclassified drugs or biologics (when specified as Winrevair [sotatercept-csrk])

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