Pharmacy Management Drug Policy

SUBJECT: Pulmonary Arterial Hypertension (PAH)
POLICY NUMBER: PHARMACY-42
EFFECTIVE DATE: 6/2005
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If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. Medical or drug policies apply to commercial and Health Care Reform products only when a contract benefit for the specific service exists.

Description:

Pulmonary arterial hypertension (PAH) is a type of pulmonary hypertension characterized by sustained elevation of pulmonary artery pressure. The condition is uncommon but is associated with a high mortality rate. Some causes of and risk factors for pulmonary arterial hypertension include congenital heart defects, connective tissue disease (scleroderma), HIV infection, blood clots, liver disease (portal hypertension) and medication (ex. Fen-phen). The disease can also have an unknown cause: idiopathic pulmonary arterial hypertension (PAH). The most common symptoms caused by PAH are unusual fatigue, shortness of breath, chest pain, fainting, and peripheral edema.

Chronic thromboembolic pulmonary hypertension (CTEPH) is a complication of pulmonary embolism and a major cause of pulmonary hypertension which can lead to right heart failure and death. Common symptoms include dyspnea on exertion, rapid exhaustion and fatigue. Lung ventilation/perfusion (V/Q scan) is the preferred and recommended screening test. Surgery is the only definitive therapy for CTEPH, with pulmonary thromboendarterectomy (PTE) being the surgical procedure of choice.

Careful invasive assessment of pulmonary hemodynamics is critical in the evaluation of any patient with suspected pulmonary hypertension (PH). All patients that are suspected of having PH after non-invasive evaluation (chest X-ray and echocardiogram) must undergo right heart catheterization (RHC) to confirm the diagnosis, assess severity of disease and guide medication therapy. RHC values distinguish PAH [World Health Organization (WHO) Group 1] or CTEPH (WHO Group 4) from other types of Pulmonary Hypertension (WHO Groups 2, 3, 5) as the pharmacological treatment of these groups is vastly different. RHC can be performed safely even in patients with severe PH and right heart failure.

Interpretation of Right Heart Catheterization hemodynamic values:

Pulmonary Artery Pressure: mPAP:

- Normal mean pulmonary artery pressure is typically 11-17mmHg with an upper limit of normal of approximately 20mmHg. When the mPAP is > 20 mmHg this confirms pulmonary hypertension (further testing is necessary to further classify the specific type of pulmonary hypertension and WHO Group AND to determine the appropriate medication treatments)

Pulmonary Capillary Wedge Pressure (PCWP)

- Also referred to as pulmonary artery occlusion pressure (PAOP) or pulmonary artery wedge pressure (PAWP) and estimates the left atrial pressure.
- Normal pulmonary capillary wedge pressure (PCWP) varies from 6 to 15 mmHg with a mean of 9 mmHg and measures the left atrial pressure.
- In the diagnosis of WHO Group 1 PAH the PCWP remains within normal range ≤ 15 mmHg.
- An elevated PCWP > 15 mm Hg is not consistent with a diagnosis of WHO Group 1 PAH.
- Conditions that raise left ventricular end-diastolic pressure result in an elevated wedge pressure (> 15 mm Hg) including left ventricular systolic heart failure, left ventricular diastolic heart failure, mitral and aortic valve disease, hypertrophic cardiomyopathy; hypervolemia, right-to-left shunts, cardiac tamponade, and constrictive and restrictive cardiomyopathies.

Pulmonary Vascular Resistance (PVR)

- A measure of the pulmonary blood vessel resistance to blood flow
- Calculated from RHC hemodynamic values including mPAP, pulmonary capillary wedge pressure and cardiac output.
- PVR (wood units) = $\frac{\text{mPAP – PCWP (mmHg)}}{\text{CO (L/min)}}$
- Sometimes the resistance is reported in dynes/sec/cm^5. To convert this measurement to wood units, divide by 80.
- For reference a calculator is found at www.easycalculation.com/medical/pulmonary.php. Divide result by 80 for wood units.

At the time of RHC, acute Vasoreactivity (VR) testing may be performed to identify those patients who may be effectively managed with calcium channel blockers (CCBs) prior to initiation of advanced therapy. Short-acting vasodilators such as inhaled nitric oxide (iNO), IV prostacyclin (epoprostenol), IV adenosine or inhaled iloprost are typically administered with subsequent measurement of hemodynamic response during the RHC. Patients with a negative vasoreactivity (VR) test are not candidates for calcium channel blocker therapy; however, a small percentage of patients will have a positive response to vasoreactivity test and may benefit from high dose calcium channel blocker therapy. Only advised for patients with idiopathic PAH (IPAH), familial or heritable PAH and drug-induced PAH.

Treatment goals include improvement in both short-term functional symptoms as well as long-term outcomes such as: dyspnea and exercise endurance, lowering pulmonary artery pressure, prevent progression of disease and improve survival. Medical management for PAH includes oral calcium-channel blockers, anticoagulants, oxygen therapy, and advanced therapy including: endothelial-receptor antagonists (bosentan, ambrisentan, macitentan), phosphodiesterase-5 inhibitors (sildenafil, tadalafil) and prostacyclins (iloprost, treprostinil, epoprostenol) and the newer classes of sGC inhibitors (riociguat) and prostacyclin IP receptor agonists (selexipag). Lung and heart-lung transplants have been performed in those patients that are refractory to medical management.

(See appendix for Pulmonary Hypertension WHO and Clinical Classification, NYHA Functional Classification and WHO Pulmonary Hypertension Functional Classification).

This policy is applicable to the following drugs that are FDA approved for the treatment of PAH or CTEPH (Adempas only).

- Adcirca / tadalafil
- Letairis / ambrisentan
- Remodulin / treprostinil
- Tyvaso (treprostinil)
- Ventavis (iloprost)
- Adempas (riociguat)
- Opsumit (macitentan)
- Revatio / sildenafil 20mg
- Uptravi (selexipag)
- Flolan / epoprostenol
- Orenitram (treprostinil)
- Tracleer / bosentan
- Veletri (epoprostenol)

Clinical Policy Criteria:

Based upon our assessment and review of the peer-reviewed literature, Adcirca / tadalafil, Adempas, Flolan / epoprostenol, Letairis / ambrisentan, Opsumit, Orenitram, Remodulin / treprostinil, Revatio / sildenafil, Tracleer / bosentan, Tyvaso, Uptravi, Veletri and Ventavis have been medically proven to be effective and therefore, medically necessary for treatment of PAH when the following Clinical (1,2,3 and 4) AND drug specific criteria have been met:

1. The medication must be prescribed by a cardiologist or pulmonologist experienced in the treatment of Pulmonary Arterial Hypertension; AND
2. The patient must have a diagnosis of World Health Organization (WHO) Group 1 Pulmonary Arterial Hypertension (PAH); AND
3. The diagnosis of PAH must be confirmed by Right Heart Catheterization (RHC) documenting:

- Mean pulmonary artery pressure (mPAP) of > to 20 mmHg at rest **AND**
- Pulmonary capillary wedge pressure (PCWP) ≤ to 15 mm Hg at rest AND
- Pulmonary Vascular Resistance (PVR) ≥ 3 wood units (WU)

4. Progress notes including relevant diagnostic test results (including Right Heart Catheterization) are required on all new and recertification requests.

(Note: Refer to Adempas below for Policy Criteria when prescribed for a diagnosis of CTEPH)

Drug Specific Criteria:

ambrisentan, bosentan, sildenafil, tadalafil (generic products) – Rx benefit
Drug Criteria: sildenafil (generic for Revatio), **tadalafil** (generic for Adcirca), **ambrisentan** (generic for Letairis), **bosentan** (generic for Tracleer) **AND tadalafil/ambrisentan in combination** will be approved as oral advanced therapy for PAH when the Clinical Policy Criteria (on Page 2) have been met. Additional drug information: • **ambrisentan**: is an endothelin receptor antagonist (ERA) indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] group 1) to improve exercise ability and delay clinical worsening a. FDA approved for age ≥ 18 years b. Dosing guidelines: Maximum dose of Letairis / ambrisentan is 10mg once a day. c. See "Combination Therapy" below for recommendations regarding the use of Letairis / ambrisentan and tadalafil • **bosentan**: is an endothelin receptor antagonist (ERA) indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] group 1) • in adults with WHO-FC II, III, or IV symptoms to improve exercise ability and to decrease clinical deterioration • in pediatric patients ≥3 years of age with idiopathic or congenital PAH to improve pulmonary vascular resistance (PVR), resulting in an improvement in exercise ability a. FDA approved for age ≥ 3 years of age. A trial of sildenafil or tadalafil is not required for pediatric patients between 3 to 18 years of age. b. Dosing guidelines: Maximum dose of Tracleer / bosentan is 125mg twice a day. • **sildenafil**: is a phosphodiesterase-5 enzyme inhibitor (PDE5) indicated for treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] group 1) in adults to improve exercise ability and delay clinical worsening a. FDA approved for age ≥ 18 years. The use of Sildenafil, especially long-term use, is not recommended in children. After 2 years of treatment, increased mortality seen in a long-term (median treatment exposure, 3.8 years) study at higher doses (20 to 80 mg [depending upon weight] 3 times/day). b. Dosing guidelines: Maximum dose of sildenafil is 80mg three times per day. Doses above FDA approval will require documentation of a trial of the lower FDA approved dose which was shown to be ineffective c. The use of sildenafil and nitrates concurrently is contraindicated and therefore will not be covered. d. Sildenafil (generic Revatio) will NOT be authorized for a diagnosis of erectile dysfunction as there are FDA approved medications for this diagnosis • **tadalafil**: is a phosphodiesterase-5 enzyme inhibitor (PDE5) indicated for treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] group 1) to improve exercise ability a. FDA approved for age ≥ 18 years b. Dosing guidelines: Maximum dose of tadalafil is 40mg once a day. Doses above FDA approval will require documentation of a trial of the lower FDA approved dose which was shown to be

ineffective.
   c. See "Combination Therapy" below for recommendations regarding the use of tadalafil and Letairis / ambrisentan.
   d. The use of tadalafil and nitrates concurrently is contraindicated and therefore will not be covered.
   e. Tadalafil (generic Adcirca) will not be authorized for a diagnosis of erectile dysfunction as there are FDA approved medications for this diagnosis.

- **Ambrisentan and tadalafil** - Combination therapy:
  In October 2015, the FDA approved the combination of Letairis / ambrisentan in combination with Adcirca / tadalafil to treat patients with PAH (WHO Group 1) to reduce the risks of disease progression and hospitalization for worsening PAH, and to improve exercise ability. This approval was based on the results of the Ambition trial in which participants were started on combination therapy as initial treatment and demonstrated less clinical failure than those that were started on monotherapy of either drug. Based on this, a combination regimen of tadalafil and ambrisentan will be authorized as initial advanced therapy for those with a confirmed diagnosis of WHO Group 1 PAH.

- Alternative combination regimens:
  Other combination therapy regimens have been studied for the treatment of PAH with mixed results (such as macitentan + sildenafil; riociguat + bosentan; selexipag +ERA and/or PDE5i). The goal of combination therapy should be to maximize efficacy, while minimizing toxicity. For WHO Functional Class III or IV PAH patients with unacceptable clinical status despite established PAH-specific monotherapy, alternative combination therapy regimens (combining drugs with different mechanisms of action) can be considered. Combination therapy should only be attempted by those with the expertise to monitor such high-risk individuals.

Adcirca, Letairis, Revatio, Tracleer (brand name products) - Rx benefit

Drug Criteria: The following brand name medications Adcirca (tadalafil), Letairis (ambrisentan), Revatio (sildenafil), Tracleer (bosentan) will be approved as initial oral advanced therapy when the Clinical Policy Criteria (on Page 2) AND the following additional drug criteria have been met (1 and 2):

1. The patient has had a trial of the equivalent generic product confirmed in clinical progress notes or pharmacy claims history; AND
2. The prescribing physician provides supporting clinical rationale why the patient is unable to take the generic product (such as an intolerance to an inactive ingredient contained in the generic product that is not found in the brand name product).

Opsumit – Rx benefit

Drug Criteria: Opsumit (macitentan) for a diagnosis of PAH will be approved as oral advanced therapy when the Clinical Policy Criteria (on Page 2) AND the following drug criteria have been met:

1. The patient has had an adequate trial of at least one of the following oral *preferred* generic products with evidence of severe intolerance or drug failure / disease progression despite these treatments:
   a. PDE5 inhibitor: sildenafil or tadalafil
   b. ERA: ambrisentan, bosentan

Additional Drug Information:

- **Opsumit** (macitentan): is an endothelin receptor antagonist (ERA) indicated for treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] group 1) to delay disease progression
  a. FDA approved for age ≥ 18 years

b. Dosing guidelines: Maximum dose of Opsumit (macitentan) is 10mg once a day

Adempas – Rx benefit

Drug Criteria for PAH diagnosis: Adempas (riociguat) for a diagnosis of PAH will be approved as oral advanced therapy when the Clinical Policy Criteria (on Page 2) AND the following drug criteria have been met:

1. The patient has had an adequate trial of at least one of the following oral generic *preferred* products with evidence of severe intolerance or drug failure / disease progression despite these treatments:
   a. PDE5 inhibitor: sildenafil or tadalafil
   b. ERA: ambrisentan, bosentan

Drug Criteria for CTEPH diagnosis: Adempas (riociguat) for a diagnosis of chronic thromboembolic pulmonary hypertension (CTEPH) will be approved as oral advanced therapy when the following criteria have been met:

1. The medication must be prescribed by a cardiologist or pulmonologist experienced in the treatment of CTEPH; AND
2. The patient must have a diagnosis of World Health Organization (WHO) Group 4 CTEPH; AND
3. The diagnosis must be confirmed by Right Heart Catheterization (RHC) AND ventilation/perfusion scintigraphy (V/Q scan) or pulmonary angiogram (or both); AND
4. Right Heart Catheterization must confirm the diagnosis of pulmonary hypertension:
   - Mean pulmonary artery pressure (mPAP) of ≥ to 25 mmHg at rest **AND**
   - Pulmonary capillary wedge pressure (PCWP) ≤ to 15 mm Hg at rest; AND
5. The patient must have recurrent or persistent disease after surgical intervention OR
6. Inoperable disease determined by V/Q scan and/or pulmonary angiography in consultation with an experienced pulmonary thromboendarterectomy center.
7. Progress notes including relevant diagnostic test results (including Right Heart Catheterization and V/Q scan or pulmonary angiography) are required.

Additional Drug Information:

- **Adempas** (riociguat): is a soluble guanylate cyclase (sGC) stimulator indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO group 1) to improve exercise capacity, improve WHO functional class, and delay clinical worsening in adults **AND** treatment of persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) (World Health Organization [WHO] group 4)
  a. FDA approved for age ≥ 18 years
  b. Dosing guidelines: Maximum dose of Adempas (riociguat) is 2.5mg three times a day, however active smokers may require a titration above this based on increased drug metabolism.

Orenitram (treprostinil), Uptravi (selexipag) – Rx benefit

Orenitram and Uptravi are not recommended as first- or second-line PAH treatments according to the 6th World Symposium on Pulmonary Hypertension and updated CHEST (American College of Chest Physicians) guidelines.

Drug Criteria: Orenitram (treprostinil) or Uptravi (selexipag) for a diagnosis of PAH will be approved as oral advanced therapy for PAH when the Clinical Policy Criteria (on Page 2) and the following drug criteria have been met:

1. The patient has had an adequate trial of TWO oral therapies from two different classes (a, b or c) alone or in combination or has evidence of severe intolerance or rapid disease progression despite these treatments:
   a. PDE5 inhibitor: sildenafil or tadalafil
   b. ERA: ambrisentan, bosentan or Opsumit

c. Adempas (riociguat); AND

2. Past treatment with a prostacyclin (Flolan, Veletri, epoprostenol, Tyvaso, Remodulin, treprostinil or Ventavis) will also be taken into consideration if used as one of two previous therapies.

Additional Drug Information:

- **Orenitram** (treprostinil): is a prostacyclin vasodilator indicated for treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] group 1) in patients with WHO functional class II to III symptoms to delay disease progression and to improve exercise capacity.
    a. FDA approved for age ≥ 18 years
    b. Dosing guidelines: The recommended starting dose of Orenitram is 0.25 mg twice daily (BID) with food, taken approximately 12 hours apart or 0.125 mg three times daily (TID) with food, taken approximately 8 hours apart. Increase the dose to the highest tolerated dose. There is no FDA approved maximum dose of oral Orenitram (treprostinil), but the maximum dose allowed within the clinical trials was 16mg twice a day.

- **Uptravi** (selexipag): is a prostacyclin receptor agonist indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group I) to delay disease progression and reduce the risk of hospitalization for PAH
    a. FDA approved for age ≥ 18 years
    b. Dosing guidelines: Maximum dosing of Uptravi (selexipag) is 1,600 mcg twice daily

epoprostenol, Flolan, **Remodulin**, **treprostinil, Veletri**, **Ventavis (medical benefit) and Tyvaso (Rx benefit)**

Prostacyclins are generally not recommended as first- or second-line PAH treatments according to the 6th World Symposium on Pulmonary Hypertension and updated CHEST (American College of Chest Physicians) guidelines except in certain clinical scenarios noted below.

Drug Criteria: New starts of generic epoprostenol for IV infusion, Flolan (epoprostenol – IV infusion), Veletri (epoprostenol – IV infusion), Ventavis (iloprost – inhalation), generic treprostinil for IV/SC infusion, Remodulin (treprostinil – IV/SC infusion), or Tyvaso (treprostinil - inhalation) for a diagnosis of PAH will be approved as advanced therapy for PAH when the Clinical Policy Criteria (on Page 2) and the following drug criteria have been met:

1. The patient has had an adequate trial of TWO oral therapies from two different classes (a, b or c) alone or in combination with evidence of unacceptable or deteriorating clinical status despite these treatments:
    a. PDE5 inhibitor: sildenafil or tadalafil
    b. ERA: ambrisentan, bosentan or Opsumit
    c. Adempas (riociguat); AND

2. Past treatment with a prostacyclin (Flolan, Veletri, epoprostenol, Tyvaso, Remodulin, treprostinil or Ventavis) will also be taken into consideration if used as one of two previous therapies; OR

3. Patients with World Health Organization Functional Class (WHO-FC) III symptoms and evidence of rapidly progressing disease or other markers of poor clinical prognosis may require treatment with IV/SC or inhaled prostacyclin as initial or secondary therapy; OR

4. Patients with World Health Organization Functional Class (WHO-FC) IV symptoms may require continuous treatment with IV/SC prostacyclin as initial therapy according to treatment guidelines from the 6th World Symposium on Pulmonary Hypertension (WSPH).
    (IV prostacyclins include: Flolan/Veletri/epoprostenol and Remodulin/treprostinil)
    (SC prostacyclins include: Remodulin/treprostinil)

Additional Drug Information:

- **Flolan, Veletri and generic epoprostenol for IV infusion**: prostacyclin vasodilator indicated for treatment of pulmonary arterial hypertension (PAH) (World Health Organization group 1) to improve exercise capacity.
    a. FDA approved for age ≥ 18 years
    b. Dosing guidelines: There is no FDA approved maximum dose

- **Remodulin** and generic treprostinil for IV/SC infusion: is a prostacyclin vasodilator indicated for treatment of pulmonary arterial hypertension (PAH) (World Health Organization group 1) to diminish symptoms associated with exercise; to diminish the rate of clinical deterioration in patients with PAH requiring transition from epoprostenol.
    a. FDA approved for age ≥ 18 years
    b. Dosing guidelines: There is no FDA approved maximum dose

- **Tyvaso** (treprostinil – inhalation): is a prostacyclin vasodilator indicated for treatment of pulmonary arterial hypertension (World Health Organization group 1) to improve exercise ability
    a. FDA approved for age ≥ 18 years
    b. Dosing guidelines: Maximum dose is 54mcg (or 9 inhalations) FOUR times per day

- **Ventavis** (iloprost – inhalation): is a prostacyclin vasodilator indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] group I) in patients with New York Heart Association (NYHA) class III or IV symptoms to improve exercise tolerance, symptoms, and diminish clinical deterioration
    a. FDA approved for age ≥ 18 years
    b. Dosing guidelines: Maximum dose is 45 mcg/day (5 mcg 9 times per day)

Exclusion Criteria:

1. Advanced therapies for treatment of Pulmonary Arterial Hypertension have not been approved by the FDA for WHO Group 2 – 5 pulmonary hypertension (except for Adempas for Group 4 CTEPH) and therefore are excluded from coverage for these diagnoses:
    - Group 2: PH due to left heart disease (LHD) is characterized by PH associated with an elevated left atrial pressure (e.g., mean LA pressure >14 mmHg) resulting in pulmonary venous hypertension (i.e., post-capillary PH). Defined hemodynamically as a mean pulmonary arterial pressure (mPAP) > 20 mmHg and a PCWP > 15 mmHg and normal or reduced cardiac output.
    - Group 3: PH due to chronic lung disease and/or hypoxemia
    - Group 4: PH due to chronic thromboembolic pulmonary hypertension
    - Group 5: PH due to unclear multifactorial mechanisms (e.g., sickle cell disease)
2. Conditions considered investigational will not be covered. Conditions considered investigational due to lack of peer-reviewed literature for which efficacy or safety data is not yet available include, but are not limited to:
    - Ischemic vascular diseases
    - Congestive heart failure
    - Chronic obstructive pulmonary disease

Policy guidelines:

1. Unless otherwise stated within the individual drug criteria, approval time periods are listed in the table below
2. Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition. Such

documentation may include progress notes, imaging or laboratory findings, and other objective or subjective measures of benefit which support that continued use of the requested product is medically necessary. Also, ongoing use of the requested product must continue to reflect the current policy's preferred formulary [Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e.; generics or other guideline-supported treatment options)] and the requested dose must continue to meet FDA approved or off-label/guideline supported dosing

Line of Business	Rx Initial approval	Rx Continued approval	Medical Initial approval	Medical Recert
Medicaid Managed Care (MMC) / Child Health Plus (CHP)	2 years	2 years	6 months	12 months
Commercial / Exchange	2 years	2 years	Outpatient Hospital – 6 months	Outpatient Hospital – 6 months
			Home Care or Office Based – 2 years	Home Care or Office Based – 2 years
Medicare	Already defined in policies	Already defined in policies	Outpatient Hospital – 6 months	Outpatient Hospital – 6 months

3. Prior authorization is contract dependent.
4. This policy is applicable to drugs that are included on a specific drug formulary (RX benefit only). If a drug referenced in this policy is non-formulary, please reference the Coverage Exception Evaluation Policy for All Lines of Business Formularies policy for review guidelines.
5. Supportive documentation of previous drug use must be submitted for any criterion that requires the trial of a preferred agent, if the preferred drug is not found in claims history.
6. Dose and frequency should be in accordance with the FDA label or recognized compendia (for off label uses). When services are performed in excess of established parameters, they may be subject to review for medical necessity.
7. For contracts where Insurance Law § 4903(c-1), and Public Health Law § 4903(3-a) are applicable, if trial of *preferred* drug(s) is the only criterion that is not met for a given condition, and one of the following circumstances can be substantiated by the requesting provider, then trial of the *preferred* drug(s) will not be required.
    - The required prescription drug(s) is (are) contraindicated or will likely cause an adverse reaction or physical or mental harm to the member;
    - The required prescription drug is expected to be ineffective based on the known clinical history and conditions and concurrent drug regimen;
    - The required prescription drug(s) was (were) previously tried while under the current or a previous health plan, or another prescription drug or drugs in the same pharmacologic class or with the same mechanism of action was (were) previously tried and such prescription drug(s) was (were) discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event;
    - The required prescription drug(s) is (are) not in the patient's best interest because it will likely cause a significant barrier to adherence to or compliance with the plan of care, will likely worsen a comorbid condition, or will likely decrease the ability to achieve or maintain reasonable functional ability in performing daily activities;
    - The individual is stable on the requested prescription drug. The medical profile of the individual (age, disease state, comorbidities), along with the rational for deeming stability as it relates to standard medical practice and evidence-based practice protocols for the disease

state will be taken into consideration.

- The above criteria are not applicable to requests for brand name medications that have an AB rated generic. We can require a trial of an AB-rated generic equivalent prior to providing coverage for the equivalent brand name prescription drug.

CODES:
Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.
Codes may not be covered under all circumstances. Please read the policy and guidelines statements carefully
Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.
Code Key: Experimental/Investigational = (E/I), Not medically necessary / appropriate = (NMN).

HCPCS	
J1325	Flolan, Veletri, epoprostenol
J3285	Remodulin, treprostinil
J7686	Tyvaso (treprostinil, inhalation solution)
Q4074	Ventavis (iloprost, inhalation)

Appendix A :

Pulmonary Hypertension (PH) WHO Classification	
Group 1	PAH (pulmonary arterial hypertension)
Group 2	PH due to left heart disease
Group 3	PH due to lung disease and/or hypoxemia
Group 4	CETPH (chronic thromboembolic pulmonary hypertension)
Group 5	PH due to unclear multifactorial mechanisms

Comprehensive Clinical Classification of Pulmonary Hypertension

1. PAH – Group 1 Pulmonary Arterial Hypertension

1.1 Idiopathic PAH
1.2 Heritable PAH
1.2.1 *BMPR2*
1.2.2 *ALK-1, ENG, SMAD9, CAV1, KCNK3*
1.2.3 Unknown
1.3 Drug and toxin induced
1.4 Associated with:
1.4.1 Connective tissue disease
1.4.2 HIV infection
1.4.3 Portal hypertension
1.4.4 Congenital heart diseases
1.4.5 Schistosomiasis

1'. Pulmonary veno-occlusive disease and/or pulmonary capillary hemangiomatosis

1'.1 Idiopathic
1'.2 Heritable
1'.2.1 *EIF2AK4* mutation
1'.2.2 Other mutations
1'.3 Drugs, toxins, and radiation induced
1'.4 Associated with:
1'.4.1 Connective tissue disease
1'.4.2 HIV infection

1". Persistent pulmonary hypertension of the newborn

2. Group 2 - Pulmonary hypertension because of left heart disease

2.1 Left ventricular systolic dysfunction
2.2 Left ventricular diastolic dysfunction
2.3 Valvular disease
2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies

3. Group 3 - Pulmonary hypertension because of lung diseases and/or hypoxia

3.1 COPD
3.2 Interstitial lung disease
3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
3.4 Sleep-disordered breathing
3.5 Alveolar hypoventilation disorders
3.6 Chronic exposure to high altitude
3.7 Developmental lung diseases

4. Group 4 - Chronic thromboembolic pulmonary hypertension

4.1 Chronic thromboembolic pulmonary hypertension
4.2 Other pulmonary artery obstructions
4.2.1 Angiosarcoma
4.2.2 Other intravascular tumors
4.2.3 Arteritis
4.2.4 Congenital pulmonary arteries

5. Group 5 - Pulmonary hypertension with unclear multifactorial mechanisms

5.1 Hematologic disorders: chronic hemolytic anemia, myeloproliferative disorders, splenectomy
5.2 Systemic disorders: sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis
5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
5.4 Others: tumoral

Appendix B:

New York Heart Association Functional Classification	
Class 1	Ordinary physical activity does not cause symptoms
Class 2	Comfortable at rest, ordinary physical activity causes symptoms
Class 3	Comfortable at rest, less than ordinary activity (ADLs) causes symptoms
Class 4	Symptoms at rest

Appendix C:

World Health Organization Functional Classification of Patients With PH	
Class 1	Patients with PH but without resulting limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain, or near syncope.
Class 2	Patients with PH resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity causes undue dyspnea or fatigue, chest pain, or near syncope.
Class 3	Patients with PH resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary activity causes undue dyspnea or fatigue, chest pain, or near syncope
Class 4	Patients with PH with inability to carry out any physical activity without symptoms. These patients manifest signs of right-sided heart failure. Dyspnea and/or fatigue may even be present at rest. Discomfort is increased by any physical activity

UPDATES:

Date:	Revision
2/19/2020	Revised
11/19/2019	Reviewed
3/26/2019	Revised
10/1/2018	Revised
4/19/18	Revised
9/26/17	Revised
4/20/17	Reviewed
1/2016,	Revised
8/2014	Revised
6/2014	Revised
12/2013	Revised
8/2013	Revised
7/2013	Revised
2/2011	Revised
6/2005	Created

References:

In addition to the full FDA approved prescribing information for each individual drug, the following references have been utilized in creating this policy and specific drug criteria:

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