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Subject: Pulmonary Hypertension Drug Therapy

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Pulmonary hypertension (PH) is a hemodynamic state defined by a resting mean pulmonary artery pressure at or above 25 mmHg. Because this definition is based on hemodynamic criteria, PH can be the result of a variety of disease of different causes. The World Health Organization (WHO) divides PH into five groups (Table 4) organized based on the cause of the condition and treatment options; it should be noted that while together all groups are called pulmonary hypertension, group 1 is called pulmonary arterial hypertension (PAH) and groups 2 through 5 are called pulmonary hypertension. The WHO functional classification (WHO-FC) of PH (Table 5) is a modification of the New York Heart Association functional class (Table 6).

Pharmacologic treatment of PAH is aimed primarily at vasodilation and includes calcium channel blockers, prostacyclin analogues (epoprostenol, iloprost, treprostinil), endothelin receptor antagonists (ambrisentan, bosentan), and phosphodiesterase-5 (PDE-5) inhibitors (sildenafil, tadalafil). Children with idiopathic PAH typically respond well to calcium channel blockers and are treated similarly to adults.

POSITION STATEMENT:

Comparative Effectiveness

The Food and Drug Administration has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of pulmonary hypertension drug therapy **meets the definition of medical necessity** when **ALL** of the product specific criteria outlined in Table 1 are met.

Continuation of pulmonary hypertension drug therapy **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue in the past two years, **OR** the member has previously met all product specific initiation criteria
2. Treatment is prescribed or supervised by a cardiologist or pulmonologist with the following exception:
    a. Indication for use is treatment of digital ulcers in members with systemic sclerosis
3. Member meets all product specific criteria outlined in Table 2

Table 1

Initation criteria for use of pulmonary hypertension drug therapy	
Product *Brand*	**Criteria**
Ambrisentan *Letairis®*	Use is a **medical necessity** for the treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) if **ALL** criteria are met: 1. Diagnosis is confirmed by right-heart cardiac catheterization 2. Member exhibits WHO-FC II or III symptoms (Table 5) 3. Member has not responded adequately to conventional therapy or is not a candidate for conventional therapy (e.g., calcium channel blockers, diuretics, oxygen therapy, anticoagulants, digoxin) 4. Prescribed by a cardiologist or pulmonologist a. Member is not concomitantly taking another endothelin receptor antagonist (e.g. bosentan) 5. Dosage does not exceed 10 mg daily Approval duration: 1 year
Bosentan *Tracleer® tablets, Tracleer® tablets for oral suspension*	Use is a **medical necessity** for either of the following indications if **ALL** criteria are met: 1. Treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) a. Diagnosis is confirmed by right-heart cardiac catheterization b. Member exhibits WHO-FC II, III or IV symptoms (Table 5) c. Member has not responded adequately to conventional therapy or is not a candidate for conventional therapy (e.g., calcium channel blockers, diuretics, oxygen therapy, anticoagulants, digoxin) d. Prescribed by a cardiologist or pulmonologist i. Member is not concomitantly taking another endothelin receptor antagonist (e.g. ambrisentan)

	e. Dosage does not exceed 125 mg twice daily i. Treatment of digital ulcers in members with systemic sclerosis Approval duration: 1 year
Sildenafil citrate *Revatio® Tablets, Revatio® Oral Suspension, Revatio IV®*	Use is a **medical necessity** for the treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) if **ALL** criteria are met: 1. Diagnosis is confirmed by right-heart cardiac catheterization 2. Member exhibits WHO-FC II or III symptoms (Table 5) 3. Member has not responded adequately to conventional therapy or is not a candidate for conventional therapy (e.g., calcium channel blockers, diuretics, oxygen therapy, anticoagulants, digoxin) 4. Prescribed by a cardiologist or pulmonologist 5. Member is not concomitantly taking another phosphodiesterase 5 (PDE-5) inhibitor (e.g. tadalafil) 6. Member is not concomitantly taking riociguat (Adempas) 7. Member meets **ALL** criteria for requested formulation: a. Sildenafil citrate tablet (generic) i. Dosage does not exceed 20 mg three times a day b. Revatio® Tablets, Revatio® Oral Suspension: i. Member has tried and had intolerable adverse effects to generic sildenafil – specific intolerance to generic sildenafil and rationale for use of brand Revatio must be provided in addition to **BOTH** of the following: 1. Completed Medwatch reporting form (FDA 3500) - https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda 2. Completed Naranjo Adverse Drug reaction probablility scale - https://livertox.nih.gov/Naranjoassessment.pdf ii. Dosage does not exceed 20 mg three times a day c. Revatio IV®: i. Member has a contraindication or is temporarily unable to take oral sildenafil citrate therapy ii. Dosage does not exceed 10 mg IV three times a day Approval duration: 1 year
Tadalafil *Adcirca®*	Use is a **medical necessity** for the treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) if **ALL** criteria are met: 1. Diagnosis is confirmed by right-heart cardiac catheterization 2. Member exhibits WHO-FC II or III symptoms (Table 5) 3. Member has not responded adequately to conventional therapy or is not

	a candidate for conventional therapy (e.g., calcium channel blockers, diuretics, oxygen therapy, anticoagulants, digoxin) 4. Prescribed by a cardiologist or pulmonologist 5. Member is not concomitantly taking another phosphodiesterase 5 (PDE-5) inhibitor (e.g. sildenafil citrate) 6. Member is not concomitantly taking riociguat (Adempas) 7. Member has an inadequate response, contraindication, or intolerance to generic sildenafil citrate 8. For brand Adcirca only: Member has tried and had intolerable adverse effects to generic tadalafil – specific intolerance to generic tadalafil and rationale for use of brand Adcirca must be provided in addition to BOTH of the following: a. Completed Medwatch reporting form (FDA 3500) - https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda b. Completed Naranjo Adverse Drug reaction probablility scale - https://livertox.nih.gov/Naranjoassessment.pdf 9. Dosage does not exceed 40 mg daily Approval duration: 1 year
Iloprost inhalation solution *Ventavis*®	Use is a **medical necessity** for the treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) if **ALL** criteria are met: 1. Diagnosis is confirmed by right-heart cardiac catheterization 2. Member exhibits WHO-FC III or IV symptoms (Table 5) 3. Member has not responded adequately to conventional therapy or is not a candidate for conventional therapy (e.g., calcium channel blockers, diuretics, oxygen therapy, anticoagulants, digoxin) 4. Prescribed by a cardiologist or pulmonologist 5. Member is not concomitantly being treated with another inhaled prostacyclin (e.g. treprostinil inhalation solution) 6. Dosage does not exceed 45 mcg daily (5 mcg 9 times per day) Approval duration: 1 year
Treprostinil inhalation solution *Tyvaso*®	Use is a **medical necessity** for the treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) if **ALL** criteria are met: 1. Diagnosis is confirmed by right-heart cardiac catheterization 2. Member exhibits WHO-FC III symptoms (Table 5) 3. Member has not responded adequately to conventional therapy or is not a candidate for conventional therapy (e.g., calcium channel blockers, diuretics, oxygen therapy, anticoagulants, digoxin) 4. Prescribed by a cardiologist or pulmonologist 5. Member is not concomitantly being treated with another inhaled prostacyclin (e.g. iloprost)

	6. Dosage does not exceed 9 breaths (54 mcg) 4 times daily Approval duration: 1 year
Treprostinil injection *Remodulin*®	Use is a **medical necessity** for the treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) if **ALL** criteria are met: 1. Diagnosis is confirmed by right-heart cardiac catheterization 2. Member exhibits WHO-FC II-IV symptoms (Table 5) 3. Member has not responded adequately to conventional therapy or is not a candidate for conventional therapy (e.g., calcium channel blockers, diuretics, oxygen therapy, anticoagulants, digoxin) 4. Prescribed by a cardiologist or pulmonologist Approval duration: 1 year
Treprostinil oral tablets *Orenitram*™	Use is a **medical necessity** for the treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) if **ALL** criteria are met: 1. Diagnosis is confirmed by right-heart cardiac catheterization 2. Member exhibits WHO-FC II or III symptoms (Table 5) 3. Member has not responded adequately to conventional therapy or is not a candidate for conventional therapy (e.g., calcium channel blockers, diuretics, oxygen therapy, anticoagulants, digoxin) 4. Prescribed by a cardiologist or pulmonologist Approval duration: 1 year
Epoprostenol *Flolan*®*, Veletri*®	Use is a **medical necessity** for the treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) if **ALL** criteria are met: 1. Diagnosis is confirmed by right-heart catheterization 2. Member exhibits WHO-FC III or IV (Table 5) 3. Member has not responded adequately to conventional therapy or is not a candidate for conventional therapy (e.g., calcium channel blockers, diuretics, oxygen therapy, anticoagulants, digoxin) 4. Prescribed by a cardiologist or pulmonologist Approval duration: 1 year
Macitentan *Opsumit*®	Use is a **medical necessity** for the treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) if **ALL** criteria are met: 1. Diagnosis is confirmed by right-heart cardiac catheterization 2. Member exhibits WHO-FC II, III or IV symptoms (Table 5) 3. Member has not responded adequately to conventional therapy or is not a candidate for conventional therapy (e.g., calcium channel blockers, diuretics, oxygen therapy, anticoagulants, digoxin) 4. Prescribed by a cardiologist or pulmonologist 5. Member is not concomitantly taking another endothelin receptor

	antagonist (e.g. ambrisentan, bosentan) 6. Dosage does not exceed 10 mg daily Approval duration: 1 year
Riociguat *Adempas*®	Use is a **medical necessity** for either of the following indications if **ALL** criteria are met: 1. Treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) a. Diagnosis is confirmed by right-heart cardiac catheterization b. Member exhibits WHO-FC II, III or IV symptoms (Table 5) c. Member has not responded adequately to conventional therapy or is not a candidate for conventional therapy (e.g., calcium channel blockers, diuretics, oxygen therapy, anticoagulants, digoxin) d. Prescribed by a cardiologist or pulmonologist e. Member is not concomitantly taking a phosphodiesterase 5 (PDE-5) inhibitor (e.g. sildenafil citrate, tadalafil) f. Member is not concomitantly taking organic nitrates or nitric oxide donors (e.g., isosorbide mononitrate, isosorbide dinitrate, nitroglycerin) g. Dosage does not exceed 2.5 mg three times daily 2. Treatment of persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) (WHO Group 4; Table 4) a. Diagnosis is confirmed by right-heart cardiac catheterization b. Member has not responded adequately to surgical treatment (e.g., pulmonary endarterectomy) or is not a surgical candidate c. Prescribed by a cardiologist or pulmonologist d. Member is not concomitantly taking a phosphodiesterase 5 (PDE-5) inhibitor (e.g. sildenafil citrate, tadalafil) e. Member is not concomitantly taking organic nitrates or nitric oxide donors (e.g., isosorbide mononitrate, isosorbide dinitrate, nitroglycerin) f. Dosage does not exceed 2.5 mg three times daily Approval duration: 1 year
Selexipag *Uptravi*®	Use is a medical necessity for the treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) if ALL criteria are met: 1. Diagnosis is confirmed by right-heart cardiac catheterization 2. Member exhibits WHO-FC II or III symptoms (Table 5) 3. Member has not responded adequately to conventional therapy or is not a candidate for conventional therapy (e.g., calcium channel blockers, diuretics, oxygen therapy, anticoagulants, digoxin)

	4. Prescribed by a cardiologist or pulmonologist 5. Member is not concomitantly taking an oral, inhaled, or injectable prostacyclin analog (e.g. epoprostanol, iloprost, treprostinil) 6. Dosage does not exceed 3200 mcg daily Approval duration: 1 year

Table 2

Continuation criteria for use of pulmonary hypertension drug therapy	
Product Brand	**Criteria**
Ambrisentan *Letairis®*	Use is a medical necessity for the treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) if **ALL** criteria are met: 1. Member is not concomitantly taking another endothelin receptor antagonist (e.g. bosentan) 2. Dosage does not exceed 10 mg daily Approval duration: 1 year
Bosentan *Tracleer® tablets, Tracleer® tablets for oral suspension*	Use is a medical necessity for either of the following indications if **ALL** criteria are met: 1. Treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) a. Member is not concomitantly taking another endothelin receptor antagonist (e.g. ambrisentan) b. Dosage does not exceed 125 mg twice daily 2. Treatment of digital ulcers in patients with systemic sclerosis Approval duration: 1 year
Sildenafil citrate *Revatio® Tablets, Revatio® Oral Suspension, Revatio IV®*	Use is a medical necessity for the treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) if **ALL** criteria are met: 1. Member is not concomitantly taking another phosphodiesterase 5 (PDE-5) inhibitor (e.g. tadalafil) 2. Member is not concomitantly taking riociguat (Adempas) 3. Dosage does not exceed: a. Sildenafil citrate tablet (generic): 20 mg three times a day b. Revatio® Tablets, Revatio® Oral Suspension: 20 mg three times a day c. Revatio IV®: 10 mg IV three times a day Approval duration: 1 year
Tadalafil	Use is a medical necessity for the treatment of pulmonary arterial hypertension

Adcirca®	(WHO Group 1; Table 4) if **ALL** criteria are met: 1. Member is not concomitantly taking another phosphodiesterase 5 (PDE-5) inhibitor (e.g. sildenafil citrate) 2. Member is not concomitantly taking riociguat (Adempas) 3. Dosage does not exceed 40 mg daily Approval duration: 1 year
Iloprost inhalation solution *Ventavis*®	Use is a medical necessity for the treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) if **ALL** criteria are met: 1. Member is not concomitantly being treated with another inhaled prostacyclin (e.g. treprostinil inhalation solution) 2. Dosage does not exceed 45 mcg daily (5 mcg 9 times per day) Approval duration: 1 year
Treprostinil inhalation solution *Tyvaso*®	Use is a medical necessity for the treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) if **ALL** criteria are met: 1. Member is not concomitantly being treated with another inhaled prostacyclin (e.g. iloprost) 2. Dosage does not exceed 9 breaths (54 mcg) 4 times daily Approval duration: 1 year
Treprostinil injection *Remodulin*®	Use is a medical necessity for the treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) Approval duration: 1 year
Treprostinil oral tablets *Orenitram*™	Use is a medical necessity for the treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) Approval duration: 1 year
Epoprostenol *Flolan*®, *Veletri*®	Use is a medical necessity for the treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) Approval duration: 1 year
Macitentan *Opsumit*®	Use is a medical necessity for the treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) if **ALL** criteria are met: 1. Member is not concomitantly taking another endothelin receptor antagonist (e.g. ambrisentan, bosentan) 2. Dosage does not exceed 10 mg daily Approval duration: 1 year
Riociguat	Use is a medical necessity for either of the following indications if **ALL** criteria

Adempas®	are met: 1. Treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) a. Member is not concomitantly taking a phosphodiesterase 5 (PDE-5) inhibitor (e.g. sildenafil citrate, tadalafil) b. Member is not concomitantly taking organic nitrates or nitric oxide donors (e.g., isosorbide mononitrate, isosorbide dinitrate, nitroglycerin) c. Dosage does not exceed 2.5 mg three times daily 2. Treatment of persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) (WHO Group 4; Table 4) a. Member is not concomitantly taking a phosphodiesterase 5 (PDE-5) inhibitor (e.g. sildenafil citrate, tadalafil) b. Member is not concomitantly taking organic nitrates or nitric oxide donors (e.g., isosorbide mononitrate, isosorbide dinitrate, nitroglycerin) c. Dosage does not exceed 2.5 mg three times daily Approval duration: 1 year
Selexipag Uptravi®	Use is a medical necessity for the treatment of pulmonary arterial hypertension (WHO Group 1; Table 4) if **ALL** criteria are met: 1. Member is not concomitantly taking an oral, inhaled, or injectable prostacyclin analog (e.g. epoprostanol, iloprost, treprostinil) 2. Dosage does not exceed 3200 mcg daily Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

Consult product prescribing information for appropriate dosing.

PRECAUTIONS:

Specific precautions and warnings are highlighted in Table 3; however, it is strongly recommended that the prescriber refer to product-specific labeling for complete precautions and warnings.

Table 3

Precautions and warnings of pulmonary hypertension drug therapy	
Product	**Precautions/Warnings**
Ambrisentan *Letairis®*	Use is contraindicated with organic nitrates. Carefully consider whether underlying conditions (e.g., cardiovascular

	disease, impaired autonomic control of blood pressure, aortic stenosis) could be adversely affected by vasodilatory effects. Avoid use with CYP3A inhibitors, potent CYP3A inducers, and PDE5 inhibitors.
Bosentan *Tracleer® tablets, Tracleer® tablets for oral suspension*	Hepatotoxicity and teratogenicity are associated with use (Boxed Warning). Use with cyclosporine A or glyburide is contraindicated.
Sildenafil citrate *Revatio® Tablets, Revatio® Oral Suspension, Revatio IV®*	Use is contraindicated with organic nitrates. Carefully consider whether underlying conditions (e.g., cardiovascular disease, impaired autonomic control of blood pressure, aortic stenosis) could be adversely affected by vasodilatory effects.
Tadalafil *Adcirca®*	Use is contraindicated with organic nitrates. Carefully consider whether underlying conditions (e.g., cardiovascular disease, impaired autonomic control of blood pressure, aortic stenosis) could be adversely affected by vasodilatory effects.
Iloprost inhalation solution *Ventavis®*	Hypotension leading to syncope has been observed with use; do not administer if systolic blood pressure is below 85 mmHg.
Treprostinil inhalation solution *Tyvaso®*	Use has been associated with increases in bleeding risk, particularly in those receiving anticoagulants.
Treprostinil injection *Remodulin®*	Do not abruptly lower the dose or withdraw dosing.
Treprostinil oral tablets *Orenitram™*	Use is contraindicated in severe hepatic impairment. Do not abruptly discontinue dosing. Use has been associated with increases in bleeding risk, particularly in those receiving anticoagulants.
Epoprostenol *Flolan®, Veletri®*	Use is contraindicated in congestive heart failure and pulmonary edema. Do not abruptly lower the dose or withdraw dosing.
Macitentan *Opsumit®*	Teratogenicity is associated with use **(Boxed Warning)**.
Riociguat *Adempas®*	Teratogenicity is associated with use **(Boxed Warning)**. Use is contraindicated with nitrates, nitric oxide donors, and PDE inhibitors.
Selexipag Uptravi	Pulmonary edema in patients with pulmonary veno-occlusive disease. If confirmed, discontinue treatment

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding:

J1325	Injection, epoprostenol, 0.5 mg
J3285	Injection, treprostinil, 1 mg
J3490	Unclassified drugs (Revatio® injection)
J7686	Treprostinil, inhalation solution, FDA-approved final product, non-compounded, administered through DME, unit dose form, 1.74 mg
J8499	Prescription drug, oral, non-chemotherapeutic, Not Otherwise Specified (Tracleer®, Letairis®, Revatio® Tablets, Revatio® Oral Solution, sildenafil citrate, Adcirca®, Orenitram™, Opsumit®, Adempas®, Uptravi)

K0455	Infusion pump used for uninterrupted parenteral administration of medication, (e.g., epoprostenol or treprostinil
K0730	Controlled dose inhalation drug delivery system
Q4074	Iloprost, inhalation solution, FDA-approved final product, non-compound, administered through DME, unit dose form, up to 20 micrograms
S0155	Sterile dilutant for epoprostenol, 50 ml
S9347	Home infusion therapy, uninterrupted, long-term, controlled rate intravenous or subcutaneous infusion therapy (e.g., epoprostenol); administrative services, professional pharmacy services, care coordination and all necessary supplies and equipment (drugs and nursing visits coded separately), per diem

ICD-10 Diagnoses Codes That Support Medical Necessity:

I27.0	Primary pulmonary hypertension
I27.2	Other secondary pulmonary hypertension
I27.89	Other specified pulmonary heart diseases
M34.0	Progressive systemic sclerosis
M34.1	CR(E)ST syndrome
M34.9	Systemic sclerosis, unspecified

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT.**

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: BCBSF has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage Products The following Local Coverage Determination (LCD) was reviewed on the last guideline revised date: L33794 External Infusion Pumps, L33370 Nebulizers located at http://www.cgsmedicare.com.

DEFINITIONS:

WHO: World Health Organization

NYHA: New York Heart Association

RELATED GUIDELINES:

None applicable.

OTHER:

Table 4: WHO Clinical Classification of Pulmonary Hypertension

WHO Group	Description
1	Pulmonary arterial hypertension (PAH) • Idiopathic (IPAH) • Familial (FPAH) Associated with (APAH) • Connective tissue disease • Congenital systemic-to-pulmonary shunts • Portal hypertension • HIV infection • Drugs and toxins • Other (thyroid disorders, glycogen storage disease, Gaucher's disease, hereditary haemorragic telangiectasia, haemoglobinopathies, myeloproliferative disorders, splenectomy) Associated with significant venous or capillary involvement • Pulmonary veno-occlusive disease (PVOD) • Pulmonary capillary haemangiomatosis (PCH) • Persistent pulmonary hypertension of the newborn (PPHN)
2	Pulmonary hypertension associated with left heart diseases • Left-sided atrial or ventricular heart disease • Left-sided valvular heart disease.
3	Pulmonary hypertension associated with respiratory diseases and/or hypoxemia • Chronic obstructive pulmonary disease • Interstitial lung disease • Sleep disordered breathing • Alveolar hypoventilation disorders • Chronic exposure to high altitude • Developmental abnormalities.
4	Pulmonary hypertension due to chronic thrombotic and/or embolic disease • Thromboembolic obstruction of proximal pulmonary arteries • Thromboembolic obstruction of distal pulmonary arteries • Non-thrombotic pulmonary embolism (tumor, parasites, foreign material).
5	Miscellaneous group (e.g. sarcoidosis, histiocytosis X, compression of pulmonary vessels (adenopathy, tumor, fibrosing mediastinitis) and lymphangiomatosis)

Table 5: WHO Functional Class (WHO-FC) of Pulmonary Hypertension

WHO-FC	Description
I	Individuals with pulmonary hypertension but without resulting limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain, or near syncope.
II	Individuals with pulmonary hypertension 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.
III	Individuals with pulmonary hypertension 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.
IV	Individuals with pulmonary hypertension with inability to carry out any physical activity without symptoms. These individuals manifest signs of right heart failure. Dyspnea and/or fatigue may be present even at rest. Discomfort is increased by any physical activity.

Table 6: New York Heart Association Functional Classification of Heart Failure

Class	Description
I	No limitation of physical activity. Ordinary physical activity does not cause symptoms of heart failure (undue fatigue, palpitations, and dyspnea).
II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in symptoms of heart failure.
III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms of heart failure.
IV	Unable to carry out any physical activity without symptoms of heart failure or symptoms of heart failure at rest.

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 6/12/19.

GUIDELINE UPDATE INFORMATION:

11/15/09	New Medical Coverage Guideline.
01/01/10	Annual HCPCS coding update: added HCPCS code Q4074.
07/15/10	Review and revision to guideline; consisting of moving NYHA New York Heart Association Classification to the bullet criteria for coverage. Updated list of conservative therapy drugs. Updated precautions section to include warning regarding concomitant organic nitrate use with PDE-5 inhibitors and enhanced hypotension. Updated PAH classification tables and HCPCS coding section.
01/01/11	Revision; consisting of updating coding.
07/15/11	Review and revision to guideline; consisting of the addition of Revatio IV and WHO Group 1 comment to Flolan/epoprostenol.
07/15/12	Review and revision to guideline; consisting of updates precautions and position statement. Revisions to the position statement for Remodulin to include NYHC II-IV as per prescribing information, updated Flolan, et al to remove specific reference to scleroderma as it is included in the connective tissue disease spectrum for WHO Group I PAH, removed comments regarding improved exercise tolerance.
09/15/12	Revision to guideline; consisting of clarification of continuation criteria.
10/15/12	Revision to guideline; consisting of adding addition criteria for Revatio®.
03/15/13	Revision to guideline; consisting of updating dosage limits for Tracleer, Revatio PO, IV, Adcirca, Ventavis and Tyvaso. Added step for Revatio PO and Adcirca for generic sildenafil citrate preferred. Added therapeutic duplication language for drugs in same class (e.g. Tracleer, Letaris). Added orphan drug designation for Tracleer. Updated Warnings, Updated ICD-9, ICD-10.
07/15/13	Review and revision to guideline; consisting of updating position statement to include generic sildenafil.
03/15/14	Revision to guideline; consisting of revising description, position statement, dosage/administration, precautions/warnings, references.
06/15/14	Revision to guideline; consisting of position statement, precautions/warnings, billing coding, references.

07/15/14	Review and revision to guideline; consisting of description and position statement
08/15/14	Revision to guideline; consisting of position statement.
07/15/15	Review and revision to guideline; consisting of updating references.
11/01/15	Revision: ICD-9 Codes deleted.
03/15/16	Revision; consisting of position statement and precautions/warnings.
07/15/16	Review and revision to guideline; consisting of position statement and coding.
04/01/17	Revision; consisting of position statement.
7/15/17	Review and revision to guideline; consisting of position statement.
11/15/17	Revision to guideline to include new bosentan formulation in position statement, dosing and administration, references.
07/15/18	Review and revision to guideline; consisting of references and position statement.
7/15/19	Review and revision to guideline; consisting of updating references and position statement.