Generic Name: N/A

Applicable Drugs: Sildenafil (Revatio®), Tadalafil (Adcirca®, Alyq®, Tadliq®) Ambrisentan (Letairis®), Bosentan (Tracleer®), Macitentan (Opsumit®), Macitentan-Tadlafil (Opsynvi®) Riociguat (Adempas®), Selexipag (Uptravi®), Sotatercept-csrk (Winrevair TM), Epoprostenol (Flolan®, Veletri®), Treprostinil(Remodulin®, Tyvaso®, Tyvaso DPI®, Orenitram®), Iloprost (Ventavis®), Sildenafil (generic), Tadalafil (generic), Ambrisentan (generic), Bosentan (generic), Epoprostenol solution (generic), Teprostinil solution (generic)

Preferred Sildenafil (generic), Tadalafil (generic), Ambrisentan (generic), Bosentan (generic), Epoprostenol solution (generic), Teprostinil solution (generic)

Non-preferred: Sildenafil (Revatio®), Tadalafil (Adcirca®, Alyq®, Tadliq®) Ambrisentan (Letairis®), Bosentan (Tracleer®), Macitentan (Opsumit®), Macitentan-Tadlafil (Opsynvi®) Riociguat (Adempas®), Selexipag (Uptravi®), Sotatercept-csrk (Winrevair TM), Epoprostenol (Flolan®, Veletri®), Treprostinil(Remodulin®, Tyvaso®, Tyvaso DPI®, Orenitram®), Iloprost (Ventavis®)

Date of Origin: 5/20/2024

Date Last Reviewed / Revised: N/A

PRIOR AUTHORIZATION CRITERIA

(May be considered medically necessary when criteria I-III are met)

I. Documented diagnosis of pulmonary hypertension (WHO groups 1-4) AND requested medication is used for an FDA-approved indication, or use is supported by current clinical practice guidelines. Refer to Table 1 for medication specific criteria. Must meet A, B or C diagnosis.

A. WHO Group I (Pulmonary Arterial Hypertension)
   i. Documented diagnosis of Pulmonary Arterial Hypertension (PAH)
   ii. Classification of World Health Organization (WHO) PAH Group I - idiopathic, heritable, drug-induced, connective-tissue disease–associated, or after shunt correction.
   iii. Documentation of right heart catheterization demonstrating 1 through 3:
      1. Mean pulmonary artery pressure (mPAP) ≥ 20 mmHg
      2. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
      3. Pulmonary vascular resistance (PVR) > 2 Wood units
   iv. WHO functional class II to IV symptoms. Refer to appendix.
   v. Failed response to calcium channel blocker (CCB) or not candidate for CCB due to negative vasoreactivity testing

B. WHO Group 3 (Pulmonary Hypertension Associated with Lung Diseases and/or Hypoxia)
   i. Documentation of diagnostic tests (echocardiogram, computerized tomography imaging, right heart catheterization, ventilation/perfusion scan, Single-photon emission computed tomography)
   ii. Documentation of right heart catheterization demonstrating 1 through 3:
      1. Mean pulmonary artery pressure (mPAP) ≥ 20 mmHg

2. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
3. Pulmonary vascular resistance (PVR) > 2 Wood units

C. WHO Group 4 (Chronic Thromboembolic Pulmonary Hypertension (CTEPH))
   i. Documentation of diagnosis of CTEPH (Echocardiogram, computed tomography pulmonary angiography)
   ii. Documentation of right heart catheterization demonstrating 1 through 3:
      1. Mean pulmonary artery pressure (mPAP) ≥ 20 mmHg
      2. Pulmonary capillary wedge pressure (PCWP) ≤ 15 mmHg
      3. Pulmonary vascular resistance (PVR) > 2 Wood units
   iii. Documented pulmonary hypertension after surgical treatment with pulmonary endarterectomy OR inoperable CTEPH

II. The medication is prescribed by or in consultation with a cardiologist or pulmonologist.

III. Refer to plan document for the list of preferred products. If requested agent is not listed as a preferred product, must have a documented failure, intolerance, or contraindication to the preferred product(s).

EXCLUSION CRITERIA

- Co-administration with drugs or conditions not recommended per the FDA package labeling or current clinical practice guidelines.
- Medication specific treatment exclusion as noted in Table 1.

OTHER CRITERIA

Table 1

Agents	Medication Specific Criteria	Dosing Limits
Phosphodiesterase 5 inhibitors (PDE5i): Sildenafil (Revatio®) Tadalafil (Adcirca®, Alyq®, Tadliq®)	Indication: • PAH (WHO group 1) Criteria: • WHO FC I-IV • Treatment naïve or in combination with ERA or PCA • Sildenafil may be used in pediatrics • Sildenafil may be used in pregnancy (category B) • Brand name contingent on trial & failure, or contraindication to generic PDE5i (e.g. sildenafil, tadalafil Exclusion: • Taking nitrates or riociguat • CrCl <30 ml/min, HD, PD • Severe hepatic impairment (Child pugh class C)	Sildenafil: Max of 80 mg three times per day (270 tabs per 30 days) Tadalafil: Max of 40 mg daily (30 tablets for 30 days)

	• Aortic/mitral valve disease, life threatening arrhythmias, hypotension (<90/50 mmHg), uncontrolled hypertension, left ventricular dysfunction, pericardial constriction, cardiomyopathy, symptomatic coronary artery disease • Hereditary degenerative retinal disorders • Peptic ulcer disease • Pulmonary veno-occlusive disease	
Endothelin Receptor Antagonists (ERA): Ambrisentan (Letairis®) Bosentan (Tracleer®), Macitentan (Opsumit®)	Indication: • PAH (WHO group 1) Criteria: • Treatment naïve or in combination with PDE5i or PCA • Enrolled in REMS program • Bosentan may be used in pediatrics • Brand name contingent on trial & failure, or contraindication to generic ERA (e.g. ambrisentan, bosentan) Exclusion: • Pregnancy • Drug interactions: cyclosporine or glyburide medication • Pulmonary veno-occlusive disease • Hepatotoxicity • PH-idiopathic pulmonary fibrosis (Ambrisentan)	Ambrisentan: Max 10 mg daily (30 tablets per 30 days) Bosentan: Max 125 mg two times per day (60 tablets per 30 days) Macitentan: Max 10 mg daily (30 tablets per 30 days)
Macitentan-Tadlafil (Opsynvi®)	Indication: • PAH (WHO group 1) Criteria: • WHO FC II-III • Enrolled in REMS program • Trial and failure, or contraindication to generic ERA (e.g. ambrisentan, bosentan) in combination with generic PDE5i (e.g. sildenafil, tadalafil) Exclusion: • Pregnancy • Drug interactions • Pulmonary veno-occlusive disease • Hepatotoxicity • Taking nitrates or riociguat • CrCl <30 ml/min, HD, PD • Severe hepatic impairment (Child pugh class C) • Aortic/mitral valve disease, life threatening arrhythmias, hypotension (<90/50 mmHg), uncontrolled hypertension, left ventricular dysfunction, pericardial constriction,	Max of 10/40 mg daily (30 tablets per 30 day)

	cardiomyopathy, symptomatic coronary artery disease • Hereditary degenerative retinal disorders	
Soluble guanylate cyclase (sGC) stimulator: Riociguat (Adempas®)	Indication: • PAH (WHO group 1) • CTEPH (WHO group 4) Criteria for WHO group 1 • Enrolled in REMS program • Trial and failure, or contraindication to generic ERA (e.g. ambrisentan, bosentan) in combination with generic PDE5i (e.g. sildenafil, tadalafil) Criteria for WHO group 4 • WHO FC III-IV • Enrolled in REMS program Exclusion: • Drug interactions (strong CYP and P-p/BCRP inhibitors) • PDE-5 inhibitor concomitant use • CrCl <15 ml/min or on dialysis • Severe hepatic impairment • Pregnancy • Bleeding	Max of 2.5 mg three time a day (up to 90 tablets for 30 days)
Prostacyclin Receptor Agonist (PRA): Selexipag (Uptravi®)	Indication: • PAH (WHO group 1) Criteria: • Trial and failure, or contraindication to generic ERA (e.g. ambrisentan, bosentan) in combination with generic PDE5i (e.g. sildenafil, tadalafil) Exclusion: • Pregnancy • Monotherapy • Egfr <15, dialysis • Severe hepatic impairment • Pulmonary veno-occlusive disease • Drug interactions (CYP2C8 strong inhibitors)	Max 1600 mg twice a day (60 tablets per 30 days)
Prostacyclin Analogue (PCA): Epoprostenol (Flolan®, Veletri®) Treprostinil(Remodulin®, Tyvaso®, Tyvaso DPI®, Orenitram®)	Indication: • PAH (WHO group 1) • PH-ILD (DPI, Inhaler solution) (WHO group 3) • CTEPH (WHO group 4) Criteria for WHO group 1 • IV/SC PCA ○ Trial and failure, or contraindication to generic ERA (e.g. ambrisentan, bosentan) in combination with generic PDE5i (e.g. sildenafil, tadalafil)	Epoprostenol (IV): 16-30 ng/kg/min Iloprost: 5 mcg 6-9 times per day (540 ampules per month) Treprostinil DPI/solution: 48 to 64 mcg four times per day (120 cartridges

Iloprost (Ventavis®)	○ Brand name contingent on trial & failure, or contraindication to generic PCA (e.g. epoprostenol, treprostinil) • Oral Treprostinil (Orenitram ®) – meet all the following criteria: ○ Trial and failure, or contraindication to TWO of the following as either monotherapy or combination therapy: generic ERA (e.g. ambrisentan, bosentan), generic PDE5i (e.g. sildenafil, tadalafil), Riociguat, or generic PCA (e.g. epoproestenol, treprostinil) ○ Documented trial or contraindication of DPI or solution for nebulizer ○ Trial and failure, or contraindication of PRA (e.g. selexipag) • May be used in pediatrics ○ IV/SC Treprostinil >16 years ○ Iloprost ○ Epoprostenol (IV) • May be used in pregnancy ○ Epoprostenol (category B) ○ Treprostinil (category B) ○ Iloprost (category C) Criteria for WHO group 3 • Documented Interstitial lung disease related PH • Inhaled Treprostinil may be considered Criteria for WHO group 4 • WHO FC III-IV • SC Treprostinil may be considered Exclusion: • Severe hepatic impairment (oral)	per month or 30 ampules per month) Teprostinil (oral): max tolerated dose (120 mg total daily dose) (720 tablets per 30 days) Teprostinil (IV/SC): 25-60 mcg/kg/min
Sotatercept-csrk (Winrevair™)	Indication: • PAH (WHO group 1) Criteria: • WHO class II-III • Trial and failure, or contraindication to THREE of the following as combination therapy: generic ERA (e.g. ambrisentan, bosentan), generic PDE5i (e.g. sildenafil, tadalafil). and generic PCA (e.g. epoproestenol, treprostinil) • Documented baseline platelets (>50,000/mm3) Exclusion: • Treatment naïve	0.3 to 0.7 mg/kg every 3 weeks

	• During treatment; Erythrocytoisis (Hgb increases >2g/dL from previous dose and is above ULN, increases >4g/dL from baseline or increases >2g /dL above upper limit of normal) • Thrombocytopenia/bleeding • Pregnancy	
PAH: Pulmonary arterial hypertension		

QUANTITY / DAYS SUPPLY RESTRICTIONS

- Requested quantities not exceeding dosing limits listed in Table 1.

APPROVAL LENGTH

- **Authorization:** 12 months
- **Re-Authorization:** An updated letter of medical necessity or progress notes showing current medical necessity criteria are met and that the medication is effective

APPENDIX

Appendix 1. WHO Classification of Pulmonary Hypertension

Group	Diagnosis
1.1	Idiopathic PAH
1.2	Heritable PAH
1.3	PAH associated with Drugs and Toxins
1.4	PAH associated with: • Connective tissue disorder • HIV infection • Portal hypertension • Congenital heart disease • Schistosomiasis
1.5	PAH with features of venous/capillary (PVOD/PCH) involvement
1.6	Persistent pulmonary hypertension of the newborn
2.1	Heart Failure • With preserved ejection fraction • With reduced or mildly reduced ejection fraction
2.2	Valvular heart disease
2.3	Congenital/acquired cardiovascular conditions leading to post-capillary PH
3.1	Obstructive lung disease or emphysema
3.2	Restrictive lung disease
3.3	Lung disease with mixed restrictive/obstructive pattern
3.4	Hypoventilation syndromes
3.5	Hypoxia without lung disease (e.g. high altitude

3.6	Developmental lung disorders
4.1	Chronic thrombo-embolic PH (CTEPH)
4.2	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 arterial stenoses, and hydatidosis
5.1	Haematological disorders • Inherited and acquired chronic hemolytic anemia and chronic myeloproliferative disorders
5.2	Systemic disorders
5.3	Metabolic disorders • glycogen storage diseases and Gaucher disease
5.4	Chronic renal failure with or without hemodialysis
5.5	Pulmonary tumor thrombotic microangiopathy
5.6	Fibrosing mediastinitis

Appendix 2. WHO Functional Classification

Class	Description
WHO-FC I	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
WHO-FC II	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
WHO-FC III	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
WHO-FC IV	Patients with PH with an inability to carry out any physical activity without symptoms. These patients manifest signs of right HF. Dyspnea and/or fatigue may even be present at rest. Discomfort is increased by any physical activity

Appendix 3. Issues for Consideration

PDE5i

- May be used in combination with ERA in those without cardiopulmonary^ comorbidities
- May be monotherapy in those with cardiopulmonary^ comorbidities

ERA

- Without cardiopulmonary^ comorbidities (all risk categories) – may be combination therapy with PDE5i or PCA
- Cardiopulmonary^ comorbidities (all risk categories)- may be monotherapy

Riociguat

- In patients with IPAH/HPAH/DPAH who present at intermediate–low risk of death while receiving ERA/PDE5i therapy, switching from PDE5i to riociguat may be considered

Selexipag

- Should not be used in combination for treatment naïve individuals
- In patients with PAH (Group 1) who present at intermediate–low risk of death while receiving ERA/PDE5i therapy, the addition of selexipag should be considered

PCA

  - In patients with PAG (Group 1) who present at intermediate–high or high risk of death while receiving ERA/PDE5i therapy, the addition of IV/SC prostacyclin analogues should be considered

The following are not recommended:

- For treatment naïve - Initial combination with oral triple-combination therapy
- Riociguat in combination with a PDE5i
- Bosentan in combination with sildenafil

In patients with inoperable CTEPH, a combination of sGC/PDE5i, ERA or parenteral prostacyclin analogues may be considered

Investigational Use:

- WHO Groups 2-5 therapies largely to be considered investigational
  - PH associated with left heart diseases (WHO group 2)
  - PH associated with lung diseases and/ or hypoxemia (including chronic obstructive pulmonary disease) (WHO group 3)
  - PH due to chronic thrombotic and/or embolic disease (WHO group 4)
  - Miscellaneous group (sarcoidosis, histiocytosis X and lymphangiomatosis) (WHO group 5)

^Cardiopulmonary comorbidities are conditions associated with an increased risk of left ventricular diastolic dysfunction, and include obesity, hypertension, diabetes mellitus, and coronary heart disease; pulmonary comorbidities may include signs of mild parenchymal lung disease and are often associated with a low DLCO (<45% of the predicted value)

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DISCLAIMER: Medication Policies are developed to help ensure safe, effective and appropriate use of selected medications. They offer a guide to coverage and are not intended to dictate to providers how to practice medicine. Refer to Plan for individual adoption of specific Medication Policies. Providers are expected to exercise their medical judgement in providing the most appropriate care for their patients.