Policy and Procedure	
PHARMACY PRIOR AUTHORIZATION POLICY AND CRITERIA ORPTCCAR023.1025	**CARDIOVASCULAR AGENTS** **PULMONARY HYPERTENSION** See Table A for Applicable Medications
Effective Date: 1/1/2026	**Review/Revised Date**: 08/02, 06/03, 06/04, 06/05, 04/06, 02/07, 04/08, 04/09, 04/10, 06/10, 12/10, 04/11, 02/12, 06/12, 10/12, 04/13, 10/13, 10/14, 12/14, 10/15, 09/16, 09/17, 08/18, 08/19, 07/20, 05/21, 08/21, 05/22, 10/22, 04/23, 04/24, 08/24, 05/25, 09/25 (MTW)
Original Effective Date: 08/02	**P&T Committee Meeting Date**: 08/02, 06/03, 06/04, 06/05, 04/06, 02/07, 04/09, 04/10, 06/10, 12/10, 04/11, 02/12, 06/12, 10/12, 04/13, 10/13, 12/14, 10/15, 10/16, 10/17, 09/18, 10/18, 10/19, 10/20, 06/21, 08/21, 06/22, 10/22, 06/23, 06/24, 08/24, 06/25, 10/25
Approved by: Oregon Region Pharmacy and Therapeutics Committee	

SCOPE:
Providence Health Plan and Providence Health Assurance as applicable (referred to individually as "Company" and collectively as "Companies").

APPLIES TO:
Commercial
Medicaid

POLICY CRITERIA:

COVERED USES:
1. Pulmonary arterial hypertension (PAH)
2. Chronic Thromboembolic Pulmonary Hypertension (CTEPH) for Adempas® only
3. Pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) for Tyvaso®/Tyvaso® DPI and Yutrepia® only

REQUIRED MEDICAL INFORMATION:
For patients initiating therapy, the following criteria must be documented:
1. Diagnosis of Pulmonary Hypertension (PH) confirmed by right heart catheterization as defined by both of the following:
    a. Mean pulmonary artery pressure (mPAP) greater than or equal to 20 mmHg at rest
    b. Pulmonary vascular resistance (PVR) greater than 3 Wood units (WU)
2. Patient has one of the following:
    a. World Health Organization (WHO) Group 1 classification, pulmonary arterial hypertension (PAH; defined by a pulmonary capillary wedge pressure [PCWP] or left ventricular end diastolic pressure [LVEDP] less than or equal to 15 mmHg) with WHO/New York Heart Association (NYHA) functional class as outlined below:
        i. Flolan®, Veletri®, Tyvaso®, Tyvaso® DPI and Ventavis: Class III or IV
        ii. Winrevair®: Class II or III
        iii. All other therapies: Class II, III, or IV

   b. For Adempas® only, WHO Group 4 classification CTEPH with WHO/New York Heart Association (NYHA) functional class II, III, or IV
   c. For Tyvaso®/Tyvaso® DPI only, WHO Group 3 classification PH-ILD
3. For Winrevair®:
   a. Patient is currently established on (for at least 90 days) at least two of the following, unless all are not tolerated or contraindicated:
      i. Endothelin receptor antagonist (ERA; such as bosentan, ambrisentan, or macitentan)
      ii. Phosphodiesterase-5 inhibitor (PDE5i; such as Revatio® [sildenafi] or Adcirca® [tadalafil]) OR a soluble guanylate cyclase stimulator (sGCs; such as Adempas®)
      iii. Prostacyclin analogue or receptor agonist (such as epoprostenol, Ventavis®, Uptravi®, treprostinil)
   b. Medication will be used as add-on therapy in combination with at least two other pulmonary arterial hypertension agents, unless all are not tolerated or contraindicated
   c. Platelet count greater than or equal to 50,000/mm^3
4. For sildenafil citrate oral suspension or parenteral injection (Revatio®) and selexipag parenteral injection (Uptravi®): Documentation of intolerance or allergy to excipient ingredients of all available tablets or other medical rationale provided for use of oral suspension/parenteral injection over tablets.
5. For Tyvaso® DPI: Documented medical rationale for use over Yutrepia®
6. For Tracleer® tablets for suspension: Documented medical rationale for requiring use of a suspension over generically available tablets

For patients established on therapy:
1. One of the following:
   a. Documentation of improvement or stabilization of disease (such as lack of disease progression, improvement in walk distance, reduced number of hospitalizations, improvement in WHO functional class)
   b. Documentation supporting continued use of the requested agent is provided

   Winrevair® only:
   a. Medication will be used as add-on therapy in combination with at least two other pulmonary arterial hypertension agents, unless not tolerated or contraindicated
   b. Platelet count greater than or equal to 50,000/mm^3

EXCLUSION CRITERIA:
- Heart failure caused by reduced left ventricular ejection fraction for epoprostenol (Flolan®, Veletri®)

- Pulmonary hypertension associated with idiopathic interstitial pneumonia for riociguat (Adempas®) only
- Idiopathic pulmonary fibrosis for ambrisentan (Letairis®) only

AGE RESTRICTIONS:
- Winrevair®: ages 18 years and older
- All others: N/A

PRESCRIBER RESTRICTIONS:
Prescribed by or in consultation with a pulmonologist or cardiologist

COVERAGE DURATION:
Winrevair®: Initial authorization will be approved for six months. Reauthorization will be approved for 12 months.

All others: Authorization will be approved until no longer eligible with the plan, subject to formulary or benefit changes.

QUANTITY LIMIT:
Selexipag (Uptravi®): two tablets per day
Winrevair®: one kit per twenty-one days
Ambrisentan (Letairis®): one tablet per day

Requests for indications that were approved by the FDA within the previous six (6) months may not have been reviewed by the health plan for safety and effectiveness and inclusion on this policy document. These requests will be reviewed using the New Drug and or Indication Awaiting P&T Review; Prior Authorization Request ORPTCOPS047.

Requests for a non-FDA approved (off-label) indication requires the proposed indication be listed in either the American Hospital Formulary System (AHFS), Drugdex, or the National Comprehensive Cancer Network (NCCN) and is considered subject to evaluation of the prescriber's medical rationale, formulary alternatives, the available published evidence-based research and whether the proposed use is determined to be experimental/investigational.

Coverage for Medicaid is limited to a condition that has been designated a covered line item number by the Oregon Health Services Commission listed on the Prioritized List of Health Care Services.

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

INTRODUCTION:
PAH is a chronic life-threatening disorder with several treatment options available. There are several medication classes available for the treatment of this disease, with

differing mechanisms of action. A definitive diagnosis of PAH is important for determining the most appropriate therapy for this disease.

FDA APPROVED INDICATIONS:
Adcirca® (tadalafil tablet): treatment of PAH (WHO Group 1) in adults to improve exercise ability.

- Studies establishing effectiveness included predominately patients with NYHA Functional Class II – III symptoms and etiologies of idiopathic or heritable PAH (61%) or PAH associated with connective tissue diseases (23%).

Adempas® (riociguat tablet):

- Chronic/recurrent-Thromboembolic Pulmonary Hypertension (CTEPH), (WHO Group 4) after surgical treatment, or inoperable CTEPH, to improve exercise capacity and WHO functional class.
- Treatment of adults with PAH (WHO Group 1), to improve exercise capacity, WHO functional class and to delay clinical worsening. 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 (61%) or PAH associated with connective tissue diseases (25%).

Flolan® (epoprostenol for infusion): treatment of PAH (WHO Group 1) in adults to improve exercise capacity.

- Trials establishing effectiveness included predominantly (97%) patients with New York Heart Association (NYHA) Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH (49%) or PAH associated with connective tissue diseases (51%).

Letairis® (ambrisentan tablets):

- Treatment of PAH (WHO Group 1) in adult patients to improve exercise ability and delay clinical worsening.
- Treatment of PAH (WHO Group 1) in combination with tadalafil to reduce the risks of disease progression and hospitalization for worsening PAH, and to improve exercise ability.
    - Studies establishing effectiveness included predominantly patients with WHO Functional Class II–III symptoms and etiologies of idiopathic or heritable PAH (60%) or PAH associated with connective tissue diseases (34%).

Opsumit® (macitentan tablets): treatment of PAH (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 two years. Patients were treated with macitentan monotherapy or in combination with phosphodiesterase-5 (PDE5) inhibitors or inhaled prostanoids. Patients had idiopathic and heritable PAH (57%), PAH caused by connective tissue disorders (31%), and PAH caused by congenital heart disease with repaired shunts (8%).

Orenitram® (treprostinil extended-release tablets): treatment of PAH (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 (66%) or PAH associated with connective tissue disease (26%).

Remodulin® (treprostinil for infusion):

- Treatment of PAH (WHO Group 1) to diminish symptoms associated with exercise.
    - Studies establishing effectiveness included patients with NYHA Functional Class II-IV symptoms and etiologies of idiopathic or heritable PAH (58%), PAH associated with congenital systemic-to-pulmonary shunts (23%), or PAH associated with connective tissue diseases (19%).
- In patients with PAH requiring transition from epoprostenol, Remodulin® is indicated to diminish the rate of clinical deterioration. Consider the risks and benefits of each drug prior to transition.

Revatio® (sildenafil citrate oral suspension, injection):

- Treatment of PAH (WHO Group 1) in adults to improve exercise ability and delay clinical worsening. The delay of clinical worsening was demonstrated when sildenafil was added to epoprostenol infusion therapy.
- Treatment of PAH (WHO group 1) in pediatric patients 1 to 17 years old to improve exercise ability and, in pediatric patients too young to perform standardized exercise testing, pulmonary hemodynamics though to underly improvements in exercise.

Tracleer® (bosentan tablets): treatment of PAH (WHO Group 1):

- In adults to improve exercise ability and to decrease clinical worsening.
    - Studies establishing effectiveness included predominantly patients with WHO Functional Class II-IV symptoms and etiologies of idiopathic or heritable PAH (60%), PAH associated with connective tissue diseases (21%), and PAH associated with congenital heart disease with left-to-right shunts (18%).

- In pediatric patients aged three 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® and Tyvaso® DPI (treprostinil solution for inhalation and treprostinil powder for inhalation):

- Treatment of PAH (WHO Group 1) in adults to improve exercise ability.
    - Studies establishing effectiveness included predominately patients with NYHA Functional Class III symptoms and etiologies of idiopathic or heritable PAH (56%) or PAH associated with connective tissue diseases (33%).
    - The effects diminish over the minimum recommended dosing interval of four hours; treatment timing can be adjusted for planned activities.
    - While there are long-term data on use of treprostinil by other routes of administration, nearly all controlled clinical experience with inhaled treprostinil has been on a background of bosentan (an endothelin receptor antagonist) or sildenafil (a phosphodiesterase type 5 inhibitor). The controlled clinical experience was limited to 12 weeks in duration.
- Pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) to improve exercise ability.
    - The study establishing effectiveness predominately included patients with etiologies of idiopathic interstitial pneumonia (IIP) (45%) inclusive of idiopathic pulmonary fibrosis (IPF), combined pulmonary fibrosis and emphysema (CPFE) (25%), and WHO Group 3 connective tissue disease (22%)

Uptravi® (selexipag tablets and vial): treatment of PAH (WHO Group I) 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 and etiologies of idiopathic and heritable PAH (58%), PAH associated with connective tissue disease (29%), or PAH associated with congenital heart disease with repaired shunts (10%).

Veletri® (epoprostenol for infusion): treatment of PAH (WHO Group 1) in adults to improve exercise ability.

- Studies establishing effectiveness included predominantly patients with NYHA Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.

Ventavis® (Iloprost for inhalation): treatment of PAH (WHO Group 1) in adults to a composite endpoint consisting of exercise tolerance, symptoms (NYHA Class), and lack of deterioration.

- Studies establishing effectiveness included predominately patients with NYHA Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH (65%) or PAH associated with connective tissue diseases (23%).

Winrevair® (sotatercept-csrk for injection): treatment of adults with pulmonary arterial hypertension (PAH, WHO Group 1) to increase exercise capacity, improve WHO functional class (FC) and reduce the risk of clinical worsening events.

Yutrepia® (treprostinil solution for inhalation and treprostinil powder for inhalation):
- Treatment of PAH (WHO Group 1) in adults to improve exercise ability.
    - Studies establishing effectiveness included predominately patients with NYHA Functional Class III symptoms and etiologies of idiopathic or heritable PAH (56%) or PAH associated with connective tissue diseases (33%).
    - The effects diminish over the minimum recommended dosing interval of four hours; treatment timing can be adjusted for planned activities.
    - While there are long-term data on use of treprostinil by other routes of administration, nearly all controlled clinical experience with inhaled treprostinil has been on a background of bosentan (an endothelin receptor antagonist) or sildenafil (a phosphodiesterase type 5 inhibitor). The controlled clinical experience was limited to 12 weeks in duration.
- Pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) to improve exercise ability.
    - The study establishing effectiveness predominately included patients with etiologies of idiopathic interstitial pneumonia (IIP) (45%) inclusive of idiopathic pulmonary fibrosis (IPF), combined pulmonary fibrosis and emphysema (CPFE) (25%), and WHO Group 3 connective tissue disease (22%)

POSITION STATEMENT:
Pulmonary Arterial Hypertension
- A right heart catheterization (RHC) is the gold standard used to confirm diagnosis of PAH which is defined as mPAP greater or equal to 20 mmHg, PCWP/LVEDP less than or equal to 15 mmHg, and PVR greater than 3 WU. The recent 2022 ESC/ERC Guidelines came out with a revised hemodynamic definition and suggest that PAH may be diagnosed in patients with mPAP greater than 20 mmHg and PVR greater than 2 WU[12]. Of note, the efficacy of drugs approved for PAH has only been demonstrated in patients with mPAP greater than or equal to 25 mmHg and PVR greater than 3 WU. CHEST 2019 and ESC/ERS 2022 Guidelines suggest acute vasoreactivity testing during RHC to identify candidates for high-dose calcium channel blocker (CCB), only in patients with idiopathic, heritable, or drug-induced PAH. A high-dose CCB trial of up to three to four

months is suggested for vaso-reactive patients without right-sided heart failure, prior to starting PAH-targeted therapy.

- After diagnosis, patients are classified based on symptomology. The World Health Organization functional class (WHO-FC) is one of the most highly used classification systems to help predict survival and direct therapy options. [2,3,4]
- There are four categories of PAH-specific therapies: endothelin pathway agents (endothelin receptor antagonists [ERA]), nitric oxide pathway agents (phosphodiesterase 5 inhibitor [PDE5 inhibitors] and soluble cGMP stimulators), agents that target the prostacyclin pathway (prostacyclin receptor agonists and prostacyclin derivatives) and the activin signaling inhibitor sotatercept (Winrevair®). The first three categories are all vasodilatory agents, and drugs that target the same pathway should not be used together.
- Phosphodiesterase type 5 (PDE-5) inhibitors and riociguat target the same chemical pathway (nitric oxide-mediated) and concomitant use is contraindicated. Oral treprostinil has an approved indication for monotherapy in WHO-FC II-III patients, but it did not improve 6MWD at 16 weeks when added to an endothelin receptor antagonist (ERA) and/or a PDE5 inhibitor in FREEDOM-C and FREEDOM C-2.[5,6] In GRIPHON[7], the primary composite endpoint of death from any cause or a complication related to PAH was lower in patients on selexipag, as a monotherapy or add-on therapy to ERA and/or PDE5 inhibitor, compared to placebo at 26 weeks and was found to be statistically significant (99% CI 0.46 to 0.78, $p<0.001$).
- In patients with pulmonary hypertension (PH) due to left heart disease (LHD), epoprostenol is contraindicated due to association of increased mortality rates reported in the FIRST trial. ERA use in patients with PH due to LHD should be avoided. A large study with bosentan, ENABLE, failed to show benefit and reported increased risk of early heart failure (HF) exacerbations due to fluid retention. Studies with other ERAs also indicated an upward trend in HF exacerbation and increased mortality.[8] More recently, a clinical trial explored the use of riociguat for treatment of PH due to idiopathic interstitial pneumonia. Patients experienced worsening of interstitial lung disease and more deaths occurred in the riociguat group, therefore FDA updated riociguat's contraindication to include idiopathic interstitial pneumonia.[9]
- Sotatercept-csrk for injection (Winrevair®) is a first-in-class activin signaling inhibitor therapy which improves the balance between the pro-proliferative and anti-proliferative signaling to modulate vascular proliferation. There is thought that this unique mechanism of action has the potential for disease modification, but this has not yet been proven in humans. The efficacy of sotatercept in combination with background standard of care therapies was compared to placebo in combination with background standard of care therapies in one phase 3 clinical trial of 323 adult individuals over a period of 24 weeks. Participants all had PAH (WHO Group 1) with WHO functional class of II or III, were on 1-3

stable background PAH therapies for at least 90 days, and continued background therapies throughout the trial. 96% of participants were on 2 or 3 background PAH therapies, and only 4% were on 1 background PAH therapy at baseline. Sotatercept resulted in a placebo-adjusted median increase in 6MWD of 40.8 m (95% CI: 28, 54; P <0.001). A subgroup analysis of patients on 1 background therapy at baseline did not demonstrate a significant difference compared to placebo in 6MWD, however due to the small size of this population in the trial definitive conclusions cannot be made. 8 out of 9 secondary endpoints were met for sotatercept. This includes an improvement from baseline by at least one WHO FC in 29% of sotatercept-treated participants compared to 14% in placebo-treated participants (P <0.001). Sotatercept resulted in 84% reduction in the occurrence of death from any cause or PAH clinical worsening events compared to placebo – Hazard ratio 0.16 (95% CI: 0.08, 0.35; P <0.001). Sotatercept carries a risk of erythrocytosis and severe thrombocytopenia. Platelets and hemoglobin must be monitored before each dose for the first 5 doses, longer if values are unstable, and periodically thereafter. Dose adjustments may be required. Sotatercept should not be initiated in patients with platelets less than 50,000/mm^3.

- Institute for Clinical and Economic Review (ICER): Sotatercept for Pulmonary Arterial Hypertension
  - Moderate certainty of a small to substantial net health benefit, with a high certainty of at least a small net health benefit, corresponding to an ICER Evidence Rating of B+
  - Health benefit price benchmark: $17,900 to $35,400 per year
  - At an assumed placeholder annual cost for sotatercept of $400,000 per year, the incremental cost-effectiveness ratio for sotatercept plus background therapy as compared to background therapy alone is $2,380,000 per QALY gained

Guideline Recommended Therapy

- Treatment recommendations come from the CHEST 2019 and ESC/ERS 2022 guidelines as well as the treatment algorithm for pulmonary hypertension from the 7th World Symposium on Pulmonary Hypertension. While the recommendations are largely the same, there are differences in how risk is assessed and categorized.
- Treatment-naïve PAH patients without symptoms (WHO FC I) are considered to have relatively low risk of mortality within one year. However, due to the progressive nature of PAH, patients should be closely monitored for symptoms including worsened dyspnea on exertion, fatigue, lower extremity edema, angina, and/or syncope. According to the CHEST guideline, treatment-naïve PAH patients with WHO-FC II to IV should be initiated on PAH-targeted medication(s). Combination therapy (employed sequentially or initially) may be used to delay

PAH disease progression and improve functional capacity. Due to the progressive nature of the disease, the benefit of combination therapy may outweigh risks. For treatment-naïve WHO-FC II and III patients, the initial combination of ambrisentan and tadalafil has been recommended to improve 6-minute walk distance (6MWD), based on limited evidence. Monotherapy may be considered if tolerance for combination therapy is a concern. For treatment-naïve patients with WHO-FC II or WHO-FC III patients without evidence of rapid disease progression (such as enlargement and/or decreased function of right ventricle on ECHO), monotherapy with an endothelin receptor antagonist (bosentan, ambrisentan, or macitentan), a phosphodiesterase type 5 inhibitor (sildenafil or tadalafil), riociguat, or an oral prostacyclin receptor agonist may be considered. Ambrisentan (Letairis®) is contraindicated in patients with idiopathic pulmonary fibrosis. For WHO-FC III patients with evidence of rapid disease progression or poor prognosis, a parenteral prostacyclin (IV epoprostenol, IV treprostinil, or SC treprostinil) may be considered. If patient is not a candidate for parenteral therapy, then an inhaled or oral prostacyclin pathway targeted therapy should be initiated (inhaled treprostinil, oral selexipag). For WHO-FC IV, parenteral prostacyclin initiation is recommended but if patient is not a candidate for parenteral therapy, then consider combination of inhaled prostacyclin with an oral PDE5 inhibitor and an endothelin receptor antagonist. For treatment-experienced patients who have not achieved adequate response to initial therapy, add on additional PAH therapy from another class.2,3,4 A large study evaluating the effect of epoprosetenol on survival in NYHA Class III and IV patients with congestive heart failure due to severe left ventricular systolic dysfunction was terminated after an interim analysis of 471 patients revealed a higher mortality in patients receiving epoprostenol plus conventional therapy than in those receiving conventional therapy alone. The chronic use of epoprostenol products (Flolan®, Veletri®) in patients with congestive heart failure due to severe left ventricular systolic dysfunction is therefore contraindicated.

- The 2022 ESC/ERS Guideline[12] published a new recommendation to assess risk at the time of diagnosis using a three-strata model (low, intermediate, and high risk), considering all available data, including hemodynamics. For patients with PAH, they recommend having a treatment goal of achieving and maintaining a low-risk profile on optimized medical therapy. Development of a treatment plan is then made based off the patient's risk. According to these guidelines, patients assigned low or intermediate risk should receive combination oral therapy with an endothelin receptor antagonist and a phosphodiesterase 5 inhibitor, and high-risk patients should be placed on this same therapy with the addition of a parenteral prostacyclin analogue. Of note, all drug approvals are based in part on WHO functional class, and these risk assessment models have not been used as an outcome to assess treatment in any PAH trial.

- The 7th World Symposium on Pulmonary Hypertension came out with a treatment algorithm for pulmonary hypertension in 2024[15]. This algorithm initially classifies PAH patients as high-risk or not high-risk. For those who are not high-risk, initial combination therapy with an ERA and a phosphodiesterase 5 inhibitor is recommended. For those who are considered high risk, an IV or subcutaneous prostacyclin pathway agent should be added. Follow-up should be done after 3-4 months (and frequently thereafter), using a four-strata risk assessment model. Low risk individuals should continue their initial therapy. Those who are intermediate-low risk should add on an activin-signaling inhibitor or an oral or inhaled prostacyclin pathway agent, and should consider switching their phosphodiesterase 5 inhibitor to a soluble cGMP stimulator (riociguat). If classified as intermediate-high risk, an IV or subcutaneous prostacyclin pathway agent or activin-signaling inhibitor should be added as a 3rd agent. For those who are classified as high-risk, an IV or subcutaneous prostacyclin pathway agent should be added if not already on (1st choice), or an activin-signaling inhibitor could be used instead. At subsequent follow-up visits, if an individual is persistently intermediate-high or high risk, they should receive maximal four drug therapy: an IV or subcutaneous prostacyclin pathway agent, an ERA, a phosphodiesterase 5 inhibitor, and an activin-signaling inhibitor.

Pulmonary Hypertension with Interstitial Lung Disease

- The FDA approval of treprostinil oral inhalation solution (Tyvaso®) for pulmonary hypertension associated with interstitial lung disease (WHO group 3 – PA due to lung disease) to improve exercise ability was based off a single randomized control trial of 326 patients. The majority of the trial patients had idiopathic interstitial pneumonia (including idiopathic pulmonary fibrosis), combined pulmonary fibrosis and emphysema (CPFE) or connective tissue disease. Tyvaso® resulted in an improvement (mean difference of 31 meters) in the 6-Minute Walk Distance (6MWD) test compared to placebo after 16 weeks. The mean baseline 6MWD was 260 meters. Individuals with a 6MWD less than 100 meters were excluded from the trial. Approximately 25% of patients were on background therapy of pirfenidone or nintedanib. Tyvaso® DPI is a new formulation of treprostinil for inhalation. Tyvaso® DPI is a dry powder for inhalation using a Tyvaso DPI Inhaler. It is supplied as single-dose plastic cartridges.

REFERENCE/RESOURCES:

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Report: Endorsed by: Pulmonary Hypertension Association (PHA). *CHEST.* 2019; 155(3):565-586
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14. Lin G, Whittington MD, Nikitin D, et al. Institute for Clinical and Economic Review. Sotatercept for pulmonary arterial hypertension. Final evidence report. January 8, 2024. Accessed May 7, 2025. https://icer.org/wp-

content/uploads/2023/05/PAH_Final-Evidence-Report_For-Publication_01082024.pdf

15. Chin KM, Gaine SP, Gerges C, et al. Treatment algorithm for pulmonary arterial hypertension. Eur Respir J. 2024 Oct 31;64(4):2401325. doi: 10.1183/13993003.01325-2024. PMID: 39209476; PMCID: PMC11525349.

TABLE A:

Class	Brand Name	Generic Name
Endothelin receptor antagonists	Tracleer®	bosentan tablet and dispersible tablet for oral suspension
	Letairis®	ambrisentan tablets
	Opsumit®	macitentan tablets*
Phosphodiesterase type-5 inhibitors	Revatio®	sildenafil citrate oral suspension and intravenous bolus injection
Soluble guanylate cyclase stimulant	Adempas®	riociguat tablet
Prostacyclin receptor agonist	Uptravi®	selexipag tablet and vial for intravenous infusion
Oral prostacyclin derivative	Orenitram®	treprostinil extended-release tablets
Inhaled prostacyclin derivatives	Tyvaso®, Tyvaso® DPI	treprostinil for inhalation
	Ventavis®	iloprost for inhalation
	Yutrepia®	treprostinil for inhalation
Parenteral prostacyclin derivatives	Veletri®	epoprostenol for continuous intravenous infusion
	Flolan®	epoprostenol for continuous intravenous infusion
	Remodulin®	treprostinil for continuous subcutaneous or intravenous infusion
Activin signaling inhibitor	Winrevair®	sotatercept-csrk for injection

* Opsynvi® (macitentan/tadalafil) is available for coverage as the two separate components used together. See "New medications and formulations without established benefit" policy (ORPTCOTH001)

TABLE B: BILLING GUIDELINES AND CODING:

CODES◊		
HCPCS CODE	**Coding Description**	**Brand Name**
J1325	Injection, epoprostenol, 0.5 mg	Flolan®
J3285	Injection, treprostinil, 1 mg	Remodulin®
C9399, J3490	Unclassified drugs or biologicals	Revatio® (IV)
J7686	Treprostinil, inhalation solution, fda-approved final product, non-compounded, administered through dme, unit dose form, 1.74 mg	Tyvaso®
C9399, J3490	Unclassified drugs or biologicals	Uptravi® (IV)
J1325	Injection, epoprostenol, 0.5 mg	Veletri®
C9399, J3590	Unclassified drugs or biologicals	Winrevair®
PHARMACY BENEFIT ONLY		
J8499	Prescription drug, oral, non-chemotherapeutic, nos	Opsumit® tablets
		Adempas® tablets
		Orenitram® tablets
		Tyvaso® DPI (inhalation powder) Yutrepia (inhalation powder)
ADMINISTRATION◊		
96365	Ther/proph/diag iv inf init	
96366	Ther/proph/diag iv inf addon	
96372	Ther/proph/diag inj sc/im	
94640	Airway inhalation treatment	
G0068	Adm of infusion drug in home	
G0088	Adm iv drug 1st home visit	

◊ Coding/Administration Notes:

• The above code list is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit.

• HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as “medically unlikely edits” (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.