Pulmonary Arterial Hypertension Prior Authorization with Quantity Limit Program Summary

This program applies to Medicaid.

The BCBS MN Step Therapy Supplement also applies to this program for Medicaid.

For injectable agents refer to BCBSMN medical policy.

Requests for an oral liquid form of a drug must be approved if BOTH of the following apply:

1) the indication is FDA approved AND

2) the patient is using an enteral tube for feeding or medication administration

POLICY REVIEW CYCLE

Effective Date	Date of Origin
06-01-2024	02-15-2017

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Adcirca® (tadalafil) Tablets^	Treatment of pulmonary arterial hypertension (PAH) (*WHO Group 1) 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%)	* – WHO = World Health Organization ^- generic available	1
Adempas® (riociguat) Tablets	Treatment of adults with persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH), (*WHO Group 4) after surgical treatment, or inoperable CTEPH, to improve exercise capacity and WHO functional class Treatment of adults with pulmonary arterial hypertension (PAH), (*WHO Group 1), to improve exercise capacity, WHO functional class and to delay clinical worsening. Efficacy was shown in patients on 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%)	* – WHO = World Health Organization	2
Letairis® (ambrisentan) Tablets^	Treatment of pulmonary arterial hypertension (PAH) (*WHO Group 1): • To improve exercise ability and delay clinical worsening. • 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%)	* – WHO = World Health Organization ^- generic available	3

Agent(s)	FDA Indication(s)	Notes	Ref#
Liqrev® (sildenafil) Oral suspension	Treatment of pulmonary arterial hypertension (PAH) (*WHO Group 1) in adults to improve exercise ability and delay clinical worsening.	* – WHO = World Health Organization	24
Opsumit® (macitentan) Tablets	Treatment of pulmonary arterial hypertension (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 2 years. 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%)	* – WHO = World Health Organization	4
Opsynvi® (macitentan-tadalafil) Tablets	Chronic treatment of pulmonary arterial hypertension (PAH) (*WHO Group 1) in adults of WHO functional class (FC) II-III Individually, macitentan reduces the risk of clinical worsening events and hospitalization, and tadalafil improves exercise ability	* – WHO = World Health Organization	28
Orenitram® (treprostinil) Tablets	Treatment of pulmonary arterial hypertension (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%).	* – WHO = World Health Organization	5
Revatio® (sildenafil citrate) Tablets^ Oral solution^ Injection solution	Treatment of pulmonary arterial hypertension (PAH) (*WHO Group 1) in adults to improve exercise ability and delay clinical worsening. Treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) in pediatric patients 1 to 17 years of age to improve exercise ability and, in pediatric patients too young to perform standard exercise testing, pulmonary hemodynamics thought to underly improvements in exercise. Limitation of use: Adding sildenafil to bosentan therapy does not result in any beneficial effect on exercise capacity.	* – WHO = World Health Organization ^- generic available	6
Tadliq® (tadalafil) Oral suspension	Treatment of pulmonary arterial hypertension (PAH) (*WHO Group 1) 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%)	* – WHO = World Health Organization	23
Tracleer® (bosentan) Tablets film coated^ Tablets for suspension	Treatment of pulmonary arterial hypertension (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 3 years and older with idiopathic or congenital PAH to improve pulmonary vascular resistance	* – WHO = World Health Organization ^- generic available	7

Agent(s)	FDA Indication(s)	Notes	Ref#
	(PVR), which is expected to result in an improvement in exercise ability.		
Tyvaso®, Tyvaso DPI™ (treprostinil) Inhalation solution Inhalation powder	Treatment of pulmonary arterial hypertension (PAH) (*WHO Group 1) 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%). 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 PDE 5 inhibitor). The controlled clinical experience was limited to 12 weeks in duration. Treatment of pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO group 3) to improve exercise ability. The study establishing effectiveness included patients with etiologies of idiopathic interstitial pneumonia (IIP) inclusive of idiopathic pulmonary fibrosis (IPF), combined pulmonary fibrosis and emphysema (CPFE), and WHO group 3 connective tissue disease.	* – WHO = World Health Organization	8,22
Uptravi® (selexipag) Tablets Powder for injection	Treatment of pulmonary arterial hypertension (PAH, *WHO Group 1) to delay disease progression and reduce the risk of hospitalization for PAH. Effectiveness was established in a long-term study in PAH patients with WHO Functional Class II-III symptoms. Patients had idiopathic and heritable PAH (58%), PAH associated with connective tissue disease (29%), PAH associated with congenital heart disease with repaired shunts (10%)	* – WHO = World Health Organization	9
Ventavis® (iloprost) Inhalation solution	Treatment of pulmonary arterial hypertension (PAH) (*WHO Group 1) to improve 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%)	* – WHO = World Health Organization	10
Winrevair™ (sotatercept-csrk) Subcutaneous injection	Treatment of pulmonary arterial hypertension (PAH) (*WHO Group 1) in adults to improve exercise ability, improve WHO functional class (FC) and reduce the risk of clinical worsening events	* – WHO = World Health Organization	27

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Pulmonary Hypertension	The World Health Organization (WHO) has classified pulmonary hypertension (PH) based upon etiology into the following five groups:(15) • Group 1 - Pulmonary arterial hypertension (PAH) • Group 2 – PH due to left heart disease

	• 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 Group 1, also known as pulmonary arterial hypertension (PAH), is defined by a pre-capillary pattern in the invasive hemodynamic evaluation, characterized by a mean pulmonary arterial pressure (mPAP) greater than 20 mmHg with a normal pulmonary capillary wedge pressure (i.e., less than or equal to 15 mmHg) and a pulmonary vascular resistance greater than or equal to 3 Wood units, in the absence of pulmonary parenchymal or thromboembolic disease. Group 1 can occur in isolation or in association with clinical conditions, as noted in the following subcategories: idiopathic, heritable, drug/toxin induced, association with other diseases (i.e., connective tissue disease, HIV infection, portal hypertension, congenital heart diseases, schistosomiasis), long-term responders to calcium channel blockers, with overt features of venous/capillaries (pulmonary veno-occlusive disease [PVOD]/pulmonary capillary haemangiomatosis [PCH]), and persistent PH of the newborn syndrome.(15) Group 3 is pulmonary hypertension (PH) due to lung disease and/or hypoxia. PH associated with chronic lung disease is linked with reduced functional status and worse outcomes. There are seven subgroups within WHO group 3, one of which is ILD associated PH (WHO group 3.2). Right heart catheterization (RHC) is the gold standard for the diagnosis of PH associated with lung disease. WHO group 3 PH is distinguished from WHO group 1 based on the presence of an FVC less than 70% predicted and extensive parenchymal changes on CT. Prior to starting PAH therapy for the treatment of PH associated with lung disease, the patient's underlying lung disease should be optimally treated according to current guidelines.(21) Group 4 is due to chronic thrombotic and/or embolic disease including chronic thromboembolic pulmonary hypertension (CTEPH). CTEPH is characterized pathologically by organized thromboembolic material and altered by vascular remodeling initiated or potentiated by a combination of defective angiogenesis, impaired fibrinolysis and endothelial dysfunction. These changes lead to PH, defined as a mean pulmonary arterial pressure greater than 20 mmHg, pulmonary capillary wedge pressure less than or equal to 15 mmHg, and pulmonary vascular resistance greater than or equal to 3 Woods units. The hemodynamic changes occur in the presence of multiple chronic/organized occlusive thrombi/emboli in the elastic pulmonary arteries (main, lobar, segmental, subsegmental) after at least 3 months of effective anticoagulation. Ventilation/perfusion scan planar images combined with a confirmatory CT pulmonary angiography remain the preferred diagnostic tests for CTEPH despite advances in computed tomography (CT) and magnetic resonance (MR). CT and MR can be used in conjunction with the preferred diagnostic tests to identify complications of the disease but should not be solely relied upon due to concerns of false-positive cases mimicking CTEPH. The 6th World Symposium on Pulmonary Hypertension (WSPH) recommends all patients diagnosed with CTEPH start with lifelong anticoagulation therapy. WSPH notes that antiplatelet therapy is not an alternative to anticoagulation in patients with CTEPH. Pulmonary endarterectomy (PEA) remains the first line treatment option for CTEPH. WSPH notes that the best treatment is uncertain for patients that may be technically operable but may not benefit from endarterectomy due to comorbidities. Targeted medical therapy is initiated in those patients that are inoperable or those with persistent/recurrent PH following PEA.(12,17) The diagnosis of PAH requires right heart catheterization (RHC) to demonstrate a mPAP greater than 20 mmHg at rest and a pulmonary vascular resistance greater than

	or equal to 3 Wood units. Several additional criteria to exclude the remaining categories of PH must also be met:(14,15,19) • Mean pulmonary capillary wedge pressure less than or equal to 15 mmHg (to exclude PH due to left heart disease [i.e., group 2 PH]) • Chronic lung diseases and other causes of hypoxemia are mild or absent (to exclude PH owing to chronic lung disease or hypoxemia [i.e., group 3 PH]) • Venous thromboembolic disease is absent (to exclude chronic thromboembolic PH [i.e., group 4 PH]) • Certain miscellaneous disorders are absent, including systemic disorders (e.g., sarcoidosis), hematologic disorders (e.g., myeloproliferative diseases), and metabolic disorders (e.g., glycogen storage disease). The purpose is to exclude PH with unclear multifactorial mechanisms (group 5 PH). World Health Organization (WHO) Functional Classification of Patients with Pulmonary Hypertension include the following:(20) • Class I: Patients with PH without resulting limitation of physical activity. Ordinary physical activity does not cause undue dyspnea, fatigue, chest pain, or near syncope. • Class II: Patients with PH having slight limitation of physical activity. No discomfort at rest, but ordinary physical activity causes increased dyspnea, fatigue, chest pain, or near syncope. • Class III: Patients with PH having marked limitation of physical activity. No discomfort at rest, but less than ordinary activity causes increased dyspnea, fatigue, chest pain, or near syncope. • Class IV: Patients with PH unable to carry out any physical activity without symptoms and may have signs of right ventricular failure. Dyspnea and/or fatigue may be present at rest, with increased discomfort by any physical activity. The 6th symposium on PAH also included recommendations for pediatric patients with PH. The 2019 guidelines and the 2015 American Heart Association and American Thoracic Society guidelines note that the definition of PAH in pediatric patients mirrors the adult definition. The guidelines also recommend the same diagnostic testing and algorithm as adult patients, with the inclusion of a full shunt evaluation during RHC to rule out congenital heart disease.(13,18)
Treatment Guidelines	Guidelines recommend that patients be referred to a PAH expert center for diagnosis confirmation and management. Current treatment strategies are based on the severity of newly diagnosed patients, assessed by a risk stratification approach. The risk stratification takes clinical, exercise, right ventricular function, and hemodynamic parameters, and combines them to define a low, intermediate, or high-risk status according to patients expected 1-year mortality. The risk stratification includes the following factors:(11,13,14,20) Initial Assessment Tool: **Determinates of prognosis (estimated 1-** / **Low Risk** / **Less than 5%** / **Intermediate Risk** / **5-20%** / **High Risk** / **Greater than 20%**

year mortality)			
Clinical signs of right heart failure	Absent	Absent	Present
Progression of symptoms and clinical manifestations	No	Slow	Rapid
Syncope	No	Occasional during heavy exercise, or occasional orthostatic in stable patient	Repeated with little or regular physical activity
WHO functional class	I-II	III	IV
6-minute walking distance	greater than 440 meters	165-440 meters	less than 165 meters
Cardiopulmonary exercise testing	Peak VO_2 greater than 15 ml/min/kg (greater than 65% pred.) VE/VCO_2 slope less than 36	Peak VO_2 11–15 ml/min/kg (35–65% pred.) VE/VCO_2 slope 36–44	Peak VO_2 less than 11 ml/min/kg (less than 35% pred.) VE/VCO_2 slope greater than 44
N-terminal pro-brain natriuretic peptide (NT-proBNP) plasma levels	BNP less than 50 ng/l NT-proBNP less than 300 ng/l	BNP 50–800 ng/l NT-proBNP 300–1100 ng/l	BNP greater than 800 ng/l NT-proBNP greater than 1100 ng/l
Echocardiography	RA area less than 18 cm^2 TAPSE/sPAP greater than 0.32 mm/mmHg No pericardial effusion	RA area 18–26 cm^2 TAPSE/sPAP 0.19–0.32 mm/mmHg minimal pericardial effusion	RA area greater than 26 cm^2 TAPSE/sPAP less than 0.19 mm/mmHg Moderate to large pericardial effusion
cMRI	RVEF greather than 54% SVI greater than 40 mL/m^2 RVESVI less than 42 mL/m^2	RVEF 37–54% SVI 26–40 mL/m^2 RVESVI 42–54 mL/m^2	RVEF less than 37% SVI less than 26 mL/m^2 RVESVI greater than 54 mL/m^2
Hemodynamics	RAP less than 8 mmHg	RAP 8–14 mmHg	RAP greater than 14 mmHg

	CI greater than or equal to 2.5 L/min/m^2 SVI greater than 38 mL/m^2 SvO_2 greater than 65%	CI 2.0–2.4 L/min/m^2 SVI 31–38 mL/m^2 SvO_2 60–65%	CI less than 2.0 L/min/m^2 SVI less than 31 mL/m^2 SvO_2 less than 60%

6MWD, 6-minute walking distance; BNP, brain natriuretic peptide; CI, cardiac index; cMRI, cardiac magnetic resonance imaging; CPET, cardiopulmonary exercise testing; HF, heart failure; NT-proBNP, N-terminal pro-brain natriuretic peptide; PAH, pulmonary arterial hypertension; pred., predicted; RA, right atrium; RAP, right atrial pressure; sPAP, systolic pulmonary arterial pressure; SvO2, mixed venous oxygen saturation; RVESVI, right ventricular end-systolic volume index; RVEF, right ventricular ejection fraction; SVI, stroke volume index; TAPSE, tricuspid annular plane systolic excursion; VE/VCO2, ventilatory equivalents for carbon dioxide; VO2, oxygen uptake; WHO-FC, World Health Organization functional class.

Follow-up Assessment Tool:

Determinants of prognosis	Low Risk	Intermediate–low risk	Intermediate–high risk	High risk
Points assigned	1	2	3	4
WHO-FC	I or IIa	-	III	IV
6MWD, m	Greater than 44	320-440	165-319	Less than 165
BNP or NT-proBNP,a ng/L	Less than 50 Less than 300	50-199 300-649	200-800 650-1100	Greater than 800 Greater than 1100

6MWD, 6-minute walking distance; BNP, brain natriuretic peptide; NT-proBNP, N-terminal pro-brain natriuretic peptide; WHO-FC, World Health Organization functional class.
Risk is calculated by dividing the sum of all grades by the number of variables and rounding to the next integer.
aWHO-FC I and II are assigned 1 point as both are associated with good long-term survival.

The 6th World Symposium on Pulmonary Hypertension evidence-based treatment algorithm for adults includes the following recommendations:(11,16)

- Treatment Naïve patients:
  - Head-to-head comparisons among different compounds are not available, no evidence-based first line treatment can be proposed for initial monotherapy, if monotherapy is chosen.
  - Vasoreactive patients (only idiopathic PAH, heritable PAH, or drug induced PAH):
    - High dose calcium channel blockers (CCB) that have been progressively titrated
    - Response should be evaluated after 3 to 6 months
    - Adequate treatment response is defined as WHO-FC I/II with sustained hemodynamic improvement after at least 1 year on CCBs alone
    - Patients without an adequate response to high dose CCBs should be treated with approved PAH medications according to non-vasoreactive treatment strategy. In some cases, the combination of CCB with approved PAH is required.
  - Non-vasoreactive patients:

	▪ Low or intermediate risk: Treat with initial oral combination therapy with an endothelin receptor antagonist (ERA) and a phosphodiesterase type-5 (PDE5) inhibitor: ambrisartan plus tadalafil, macitentan plus tadalafil, or other ERA and PDE5 inhibitor ▪ High risk: Initial combination therapy (an ERA and a PDE5 inhibitor) plus IV prostacyclin with epoprostenol having the strongest recommendation • Response should be evaluated after 3 to 6 months: o Low risk at follow up: continue therapy with structured follow up until risk progression o Intermediate risk: Triple sequential combination therapy or double combination therapy in case initial monotherapy was chosen ▪ Macitentan plus sildenafil, riociguat plus bosentan, selexipag plus ERA and/or PDE5 have the highest levels of recommendations and evidence ▪ Referral for lung transplant should also be considered o High risk: maximal medical therapy including an IV prostacyclin (epoprostenol or treprostinil) is recommended and listing for lung transplant o If still at intermediate or high risk after second treatment step (3 to 6 months after change in therapy), maximal medical therapy (triple therapy including a SC or IV prostacyclin [IV preferred for high risk]) is recommended and listing for lung transplant ▪ Intermediate-risk status on double combination therapy with an ERA and a PDE5 or riociguat, the addition of selexipag should be considered ▪ Triple combination therapy including selexipag who remain in the intermediate-risk group or progress to high risk, substitution with SC or IV prostacyclin should be considered • Transitioning patients from one PAH-specific therapy to another might be considered for a number of reasons, but transitioning patients that have an extraordinary response to therapy and desire to transition to less invasive therapy is not recommended except in rare circumstances and under close expert care The 2022 European Society of Cardiology (ESC) and the European Respiratory Society (ERS) guidelines recommend a risk-based, goal-orientated treatment approach in patients with PAH. Risk stratification at diagnosis is done using a three-strata model and follow-up a four strata model. The recommended treatment algorithm for non-vasoreactive patients or patients unresponsive to CCB is as follows:(11) • Initial treatment: o Patients without cardiopulmonary comorbidities (e.g., obesity, hypertension, diabetes): ▪ Low or intermediate prognosis risk: Treat with oral combination therapy with an endothelin receptor antagonist (ERA) and a phosphodiesterase type-5 (PDE5) inhibitor: ambrisentan plus tadalafil, macitentan plus tadalafil, or other ERA and PDE5 combination ▪ High prognosis risk: Treat with oral combination therapy with an endothelin receptor antagonist (ERA) plus a phosphodiesterase type-5 (PDE5) inhibitor and IV/SC prostacyclin analogue o Patients with cardiopulmonary comorbidities (all prognosis risk categories) ▪ Oral monotherapy with PDE5 inhibitors or ERA • Response should be evaluated after 3 to 6 months: o Patients without cardiopulmonary comorbidities: ▪ Low risk at follow up: continue therapy

- Intermediate to low risk: add prostacyclin receptor agonist (PRA) (selexipag), OR, switch from PDE5 inhibitor to soluble guanylate cyclase stimulator(sGCs) (riociguat)
- Intermediate to high or high risk: add IV/SC prostacyclin analogue (epoprostenol or treprostinil) and/or evaluate for lung transplant. If adding IV/SC prostacyclin analogue is unfeasible, adding selexipag or switching from PDE5 inhibitor to riociguat may be considered

- Patients with cardiopulmonary comorbidities:
  - Individualized therapy. Patients that present at intermediate or high risk of death while receiving PDE5 inhibitors or ERA monotherapy, treatment based on individual basis

The 6th World Symposium on Pulmonary Hypertension pragmatic treatment algorithm in pediatrics includes the following recommendations:(11,18)

- Treatment with targeted PAH therapies in children is almost exclusively based on experience and data from adult studies, due to the lack of pediatric clinical trials
- Therapeutic strategy is based on risk stratification and treatment response, extrapolated from that in adults, but adapted for age
- Patients with a positive vasoreactive response should be initiated on high-dose oral CCBs and continued if there is sustained and improved response.
- Recommend vasoreactive patients remain on CCBs in addition to targeted PAH therapies
- Non-vasoreactive patients or those with failed or non-sustained response should undergo risk stratification to determine therapy. Pediatric risk stratification is as follows:

Determinates of Risk	**Low Risk**	**High Risk**
Clinical signs of right heart failure	No	Yes
Progression of symptoms	No	Yes
6-minute walking distance (greater than 6 years of age)	greater than 350 meters	less than 350 meters
Growth	Normal	Failure to thrive
WHO functional class	I, II	III, IV
N-terminal pro-brain natriuretic peptide plasma levels	Minimally elevated	Significantly elevated, Rising level
Echocardiography	NA	RA/RV enlargement Reduced LV size Increased RV/LV ratio Reduced TAPSE Low RV FAC Pericardial effusion

Hemodynamics	Systemic CI greater than 3.0 L/min/m^2 Systemic venous saturation greater than 65% Acute vasoreactivity	Systemic CI less than 2.5 L/min/m^2 mRAP greater than 10 mmHg PVRI greater than 20 WU/m^2 Systemic venous saturation less than 60% PACI less than 0.85 ml/mmHg/m^2

RV: right ventricle; WHO: World Health Organization; RA: right atrium; LV: left ventricle; FAC: fractional area change; TAPSE: tricuspid annular plane systolic excursion; CI: cardiac index; mRAP: mean right atrial pressure; PVRI: pulmonary vascular resistance index; WU: Wood Units; PACI: pulmonary arterial compliance index.

- Low prognosis risk: oral monotherapy with either an ERA (i.e., bosentan, ambrisentan) or a PDE5 inhibitor (i.e., sildenafil, tadalafil) is recommended
  - Early combination therapy should be considered in children that deteriorate on either ERA or PDE5 therapy
  - Remain low risk despite deterioration: addition of inhaled prostacyclin may be beneficial
- High prognosis risk: IV epoprostenol or treprostinil are recommended, with early consideration of lung transplantation in patients with deteriorating high-risk features
- In cases of insufficient response to recommended therapy or when drugs are not available, a Potts shunt, balloon atrial septostomy (BAS) or lung transplant may be considered in patients with severe pulmonary hypertension

The American College of Chest Physicians (CHEST) guideline (2019) states:(20)

- WHO FC II [treatment naïve and not a candidate for or failure to calcium channel blocker (CCB) therapy]:
  - Combination with ambrisentan and tadalafil
  - Patients unable to tolerate or unwilling to take combination therapy: monotherapy with an ERA or PDE5 inhibitor (listed in order of recommendation level and alphabetically)
    - Ambrisentan, sildenafil, bosentan, macitentan, tadalafil, riociguat
  - Parenteral or inhaled prostanoids should not be used as initial or second line therapy

- WHO FC III [treatment naïve, not a candidate for or failure to calcium channel blocker (CCB) therapy, and no evidence of rapid progression of their disease or poor prognosis]:
  - Combination with ambrisentan and tadalafil

	○ Patients unable to tolerate or unwilling to take combination therapy: monotherapy with an ERA or PDE5 inhibitor (listed in order of recommendation level and alphabetically) ▪ Ambrisentan, bosentan, sildenafil, macitentan, tadalafil, riociguat • WHO FC III [treatment naïve with evidence of rapid progression of their disease, or other markers of a poor clinical prognosis]: ○ Initial treatment with IV or SC prostanoid ○ There is no recommendation for patients unwilling to manage PAH with IV or SC prostanoid, so may consider addition of inhaled or oral prostanoid • WHO FC III [who have evidence of progression of their disease, and/or markers of poor clinical prognosis despite treatment with one or two classes of oral agents]: addition of a parenteral or inhaled prostanoid ○ Suggest the addition of inhaled prostanoid (i.e., treprostinil, iloprost) in patients that remain symptomatic on stable and appropriate doses of an ERA or PDE5 inhibitor • WHO FC IV [treatment naïve]: monotherapy with a parenteral prostanoid agent • WHO FC IV [treatment naïve and unable/or do not desire parenteral prostanoid therapy]: an inhaled prostanoid in combination with an ERA and PDE5 inhibitor • WHO FC III or IV [with unacceptable or deteriorating clinical status despite established PAH pharmacotherapy]: a second or third class of PAH therapy should be started • Due to insufficient evidence, recommendations cannot be made for or against the use of selexipag • There is no evidence to support the use of oral treprostinil as add-on or combination therapy The AHA/ATS guidelines for the treatment of pediatric pulmonary hypertension state:(13) • Oral therapy in children with lower-risk PAH is recommended and should include either a PDE5 inhibitor or an ERA • A goal-targeted therapy approach in which PAH-specific drugs are added progressively to achieve specified therapeutic targets can be useful • Intravenous and subcutaneous prostacyclin or its analogs should be initiated without delay for patients with higher-risk PAH The Chest guideline recognizes that there is still a lack of head-to-head comparisons of pharmacologic agents for the treatment of PAH, and because of their differing burdens and risks to patients, it is recommended that drug therapy be chosen on the basis of a methodical evaluation of disease severity and the risk for further short-term deterioration. The optimal method of evaluation has not been studied. No one agent can be definitively recommended preferentially. Additionally, it notes that adding a second class of PAH therapy for patients whose clinical status remains unacceptable despite established PAH-specific monotherapy requires that the clinician assess whether the patient has received an adequate trial of the initial monotherapy. At present, this assessment combines evaluation of the duration of monotherapy, the expected response to the monotherapy, the observed response to the monotherapy, and the patient's severity of illness and pace of decline. Unacceptable clinical status will vary for individual patients and clinicians, but symptomatic limitation of desired physical activities usually guides these decisions.(20)
Efficacy of Winrevair (sotatercept)	The safety and efficacy of sotatercept was evaluated in the STELLAR trial. This was a multicenter, double-blinded, randomized phase three trial. Eligible adult patients had symptomatic PAH Group 1 confirmed by right heart catheterization (RHC)

	and classified as WHO FC II or III. Patients were on stable background therapy for at least 90 days. Background PAH therapy refers to combination therapy consisting of drugs from two or more of the following drug classes: an endothelin-receptor antagonist (ERA), a phosphodiesterase 5(PDE5) inhibitor, a soluble guanylate cyclase stimulator, and/or a prostacyclin analogue or receptor agonist. Excluded criteria included: pregnancy or breastfeeding, uncontrolled systemic hypertension of greater than 160/100 mmHg, and baseline systolic blood pressure under 90 mmHg.(25-26) Patients were randomly assigned in a 1:1 ratio to receive subcutaneous sotatercept (starting dose, 0.3 mg per kilogram of body weight; target dose, 0.7 mg per kilogram) or placebo every 3 weeks. The primary end point was the change from baseline at week 24 in the 6-minute walk distance. There were nine secondary end points: multicomponent improvement, change in pulmonary vascular resistance (PVR), change in N-terminal pro–B-type natriuretic peptide (NT-proBNP) level, improvement in WHO FC, time to death or clinical worsening event, French risk score, and changes in the Pulmonary Arterial Hypertension–Symptoms and Impact (PAH-SYMPACT), Cardiopulmonary Symptoms, and Cognitive/Emotional Impacts domain scores. All were assessed at week 24 except time to death or clinical worsening, which was assessed when the last patient completed the week 24 visit. (25-26) A total of 163 patients were assigned to receive sotatercept and 160 to receive placebo. The median change from baseline at week 24 in the 6-minute walk distance was 34.4 m (95% confidence interval [CI], 33.0 to 35.5) in the sotatercept group and 1.0 m (95% CI, −0.3 to 3.5) in the placebo group. The first eight secondary end points were significantly improved with sotatercept as compared with placebo, whereas the PAH-SYMPACT Cognitive/Emotional Impacts domain score was not. Adverse events that occurred more frequently with sotatercept than with placebo included epistaxis, dizziness, telangiectasia, increased hemoglobin levels, thrombocytopenia, and increased blood pressure.(25-26)
Safety	**Adcirca(1), Tadliq(23)** Tadalafil has the following contraindications: • Concurrent use (regular or intermittent) of organic nitrates in any form • Do not use Adcirca in patients who are using a Guanylate Cyclase (GC) stimulator, such as riociguat • History of known serious hypersensitivity reaction to tadalafil (Adcirca, Cialis, or Tadliq) **Adempas(2)** Riociguat has the following contraindications: • Pregnancy • Co-administration with nitrates or nitric oxide donors (e.g., amyl nitrite) in any form • Concomitant use with specific phosphodiesterase (PDE) inhibitors (e.g., sildenafil, tadalafil, vardenafil) or nonspecific PDE inhibitors (e.g., dipyridamole, theophylline) • Concomitant use with other soluble guanylate cyclase (sGC) stimulators • Pulmonary hypertension associated with idiopathic interstitial pneumonias (PH-IIP) Boxed warnings include:

	• Do not administer Adempas to a pregnant female because it may cause fetal harm. Adempas was consistently shown to have teratogenic effects when administered to animals. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus. • Females of reproductive potential: exclude pregnancy before the start of treatment, monthly during treatment, and 1 month after stopping treatment. To prevent pregnancy, females of reproductive potential must use effective forms of contraception during treatment and for one month after stopping treatment. **Letairis(3)** Ambrisentan has the following contraindications: • Pregnancy • Idiopathic pulmonary fibrosis (including IPF patients with pulmonary hypertension [WHO group 3]) Boxed warnings include: • Do not administer Letairis to a pregnant female because it may cause fetal harm. Letairis is very likely to produce serious birth defects if used by pregnant females, as this effect has been seen consistently when it is administered to animals. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus. • Exclude pregnancy before the initiation of treatment with Letairis. Females of reproductive potential must use acceptable methods of contraception during treatment with Letairis and for one month after treatment. Obtain monthly pregnancy tests during treatment and 1 month after discontinuation of treatment. **Opsumit(4)** Macitentan has the following contraindications: • Pregnancy • History of hypersensitivity reaction to macitentan or any component of the product Boxed warnings include: • Do not administer Opsumit to a pregnant female because it may cause fetal harm. Opsumit was consistently shown to have teratogenic effects when administered to animals. If Opsumit is used during pregnancy, advise the patient of the potential risk to a fetus. • Females of reproductive potential: Exclude pregnancy before the start of treatment, monthly during treatment, and 1 month after stopping treatment.

	Prevent pregnancy during treatment and for one month after stopping treatment by using acceptable methods of contraception. **Opsynvi(28)** Macitentan-tadalafil has the following contraindications: • Pregnancy • History of hypersensitivity reaction to macitentan, tadalafil or any component of the product • Concomitant organic nitrates • Concomitant guanylate cyclase (GC) stimulators Boxed warnings include: • Do not administer Opsynvi to a pregnant female because it may cause fetal harm. Macitenan was consistently shown to have teratogenic effects when administered to animals. If Opsynvi is used during pregnancy, advise the patient of the potential risk to a fetus. • Females of reproductive potential: Exclude pregnancy before the start of treatment, monthly during treatment, and 1 month after stopping treatment. Prevent pregnancy during treatment and for one month after stopping treatment by using acceptable methods of contraception. • For all female patients, Opsynvi is available only through a restricted program called Macitentan-Containing Products Risk Evaluation and Mitigation Strategy (REMS). **Orenitram(5)** Treprostinil tablets have the following contraindication: • Severe hepatic impairment (Child-Pugh Class C) **Revatio(6) Liqrev (24)** Sildenafil has the following contraindications: • Concomitant use of organic nitrates in any form, either regularly or intermittently • Concomitant use of riociguat • Known hypersensitivity to sildenafil or any component of the tablet, injection, or oral suspension **Tracleer(7)** Bosentan has the following contraindications:

	• Pregnancy • Use with cyclosporine A • Use with glyburide • Hypersensitivity to bosentan or any component of the product Boxed warnings include: *Hepatotoxicity* In clinical studies, Tracleer caused at least 3-fold upper limit of normal (ULN) elevation of liver aminotransferases (ALT and AST) in about 11% of patients, accompanied by elevated bilirubin in a small number of cases. Because these changes are a marker for potential serious hepatotoxicity, serum aminotransferase levels must be measured prior to initiation of treatment and then monthly. In the post marketing period, in the setting of close monitoring, rare cases of unexplained hepatic cirrhosis were reported after prolonged (greater than 12 months) therapy with Tracleer in patients with multiple comorbidities and drug therapies. There have also been reports of liver failure. The contribution of Tracleer in these cases could not be excluded. In at least one case, the initial presentation (after greater than 20 months of treatment) included pronounced elevations in aminotransferases and bilirubin levels accompanied by nonspecific symptoms, all of which resolved slowly over time after discontinuation of Tracleer. This case reinforces the importance of strict adherence to the monthly monitoring schedule for the duration of treatment and the treatment algorithm, which includes stopping Tracleer with a rise of aminotransferases accompanied by signs or symptoms of liver dysfunction. Elevations in aminotransferases require close attention. Tracleer should generally be avoided in patients with elevated aminotransferases (greater than 3 × ULN) at baseline because monitoring for hepatotoxicity may be more difficult. If liver aminotransferase elevations are accompanied by clinical symptoms of hepatotoxicity (such as nausea, vomiting, fever, abdominal pain, jaundice, or unusual lethargy or fatigue) or increases in bilirubin greater than or equal to 2 × ULN, treatment with Tracleer should be stopped. There is no experience with the reintroduction of Tracleer in these circumstances. *Embryo-Fetal Toxicity* Tracleer is likely to cause major birth defects if used by pregnant females based on animal data. Therefore, pregnancy must be excluded before the start of treatment with Tracleer. Throughout treatment and for one month after stopping Tracleer, females of reproductive potential must use two reliable methods of contraception unless the patient has an intrauterine device (IUD) or tubal sterilization, in which case no other contraception is needed. Hormonal contraceptives, including oral, injectable, transdermal, and implantable contraceptives should not be used as the sole means of contraception because these may not be effective. **Uptravi(9)**

	Selexipag has the following contraindications: • Hypersensitivity to the active substance or to any of the excipients • Concomitant use of a strong CYP2C8 inhibitor (e.g., gemfibrozil) **Winrevair (27)** Sotatercept-csrk has no contraindications

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POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Letairis	ambrisentan tab	10 MG ; 5 MG	M ; N ; O ; Y	O ; Y		
Tracleer	bosentan tab ; bosentan tab for oral susp	125 MG ; 32 MG ; 62.5 MG	M ; N ; O ; Y	N ; O ; Y		
Ventavis	iloprost inhalation solution	10 MCG/ML ; 20 MCG/ML	M ; N ; O ; Y	N		
Opsumit	macitentan tab	10 MG	M ; N ; O ; Y	N		
Opsynvi	macitentan-tadalafil tab	10-20 MG ; 10-40 MG	M ; N ; O ; Y	N		
Adempas	riociguat tab	0.5 MG ; 1 MG ; 1.5 MG ; 2 MG ; 2.5 MG	M ; N ; O ; Y	N		
Uptravi	selexipag tab	1000 MCG ; 1200 MCG ; 1400 MCG ; 1600 MCG ; 200 MCG ; 400 MCG ; 600 MCG ; 800 MCG	M ; N ; O ; Y	N		
Uptravi titration pack	selexipag tab therapy pack	200 & 800 MCG	M ; N ; O ; Y	N		
Revatio	sildenafil citrate for suspension	10 MG/ML	M ; N ; O ; Y	O ; Y		
Liqrev	sildenafil citrate oral susp	10 MG/ML	M ; N ; O ; Y	N		
Revatio	sildenafil citrate tab	20 MG	M ; N ; O ; Y	O ; Y		
Winrevair	sotatercept-csrk for subcutaneous soln kit	2 x 45 MG ; 2 x 60 MG ; 45 MG ; 60 MG	M ; N ; O ; Y	N		
Tadliq	tadalafil oral susp	20 MG/5ML	M ; N ; O ; Y	N		
Adcirca ; Alyq	tadalafil tab	20 MG	M ; N ; O ; Y	O ; Y		
Orenitram ; Orenitram titration kit m	treprostinil diolamine tab er ; treprostinil tab er titr	0.125 & 0.25 &1 MG ; 0.125 & 0.25 MG ;	M ; N ; O ; Y	N		

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
	pk (mo ; treprostinil tab er titr pk(mo	0.125 MG ; 0.25 MG ; 1 MG ; 2.5 MG ; 5 MG				
Tyvaso dpi titration kit	Treprostinil Inh Powd	16 & 32 & 48 MCG	M ; N ; O ; Y	N		
Tyvaso dpi institutional ; Tyvaso dpi maintenance ki	Treprostinil Inh Powder	16 MCG	M ; N ; O ; Y	N		
Tyvaso dpi institutional ; Tyvaso dpi maintenance ki	Treprostinil Inh Powder	32 MCG	M ; N ; O ; Y	N		
Tyvaso dpi institutional ; Tyvaso dpi maintenance ki	Treprostinil Inh Powder	48 MCG	M ; N ; O ; Y	N		
Tyvaso dpi institutional ; Tyvaso dpi maintenance ki	Treprostinil Inh Powder	64 MCG	M ; N ; O ; Y	N		
Tyvaso dpi maintenance ki	Treprostinil Inh Powder	112 x 32MCG & 112 x48MCG	M ; N ; O ; Y	N		
Tyvaso dpi titration kit	Treprostinil Inh Powder	112 x 16MCG & 84 x 32MCG	M ; N ; O ; Y	N		
Tyvaso ; Tyvaso refill ; Tyvaso starter	Treprostinil Inhalation Solution 0.6 MG/ML	0.6 MG/ML	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Adcirca ; Alyq	tadalafil tab	20 MG	60	Tablets	30	DAYS			
Adempas	riociguat tab	0.5 MG ; 1 MG ; 1.5 MG ; 2 MG ; 2.5 MG	90	Tablets	30	DAYS			
Letairis	ambrisentan tab	10 MG ; 5 MG	30	Tablets	30	DAYS			
Liqrev	sildenafil citrate oral susp	10 MG/ML	244	mLs	30	DAYS			
Opsumit	macitentan tab	10 MG	30	Tablets	30	DAYS			
Opsynvi	macitentan-tadalafil tab	10-20 MG	30	Tablets	30	DAYS			
Opsynvi	macitentan-tadalafil tab	10-40 MG	30	Tablets	30	DAYS			
Orenitram titr kit Month 1	Treprostinil tab er Mo 1 titr kit	0.125 & 0.25 MG	1	Pack	180	DAYS			
Orenitram titr kit Month 2	Treprostinil tab er Mo 2 titr kit	0.125 & 0.25 MG	1	Pack	180	DAYS			
Orenitram titr kit Month 3	Treprostinil tab er Mo 3 titr kit	0.125 & 0.25 &1 MG	1	Pack	180	DAY			
Revatio	sildenafil citrate for suspension	10 MG/ML	2	Bottles	30	DAYS			
Revatio	sildenafil citrate tab	20 MG	90	Tablets	30	DAYS			
Tadliq	Tadalafil Oral Susp	20 MG/5ML	300	mLs	30	DAYS			
Tracleer	bosentan tab	125 MG ; 62.5 MG	60	Tablets	30	DAYS			

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Tracleer	bosentan tab for oral susp	32 MG	120	Tablets	30	DAYS			
Tyvaso	treprostinil inhalation solution	0.6 MG/ML	7	Packages	28	DAYS			66302020603
Tyvaso dpi institutional ; Tyvaso dpi maintenance ki	Treprostinil Inh Powder	16 MCG	112	Cartridges	28	DAYS			
Tyvaso dpi institutional ; Tyvaso dpi maintenance ki	Treprostinil Inh Powder	32 MCG	112	Cartridges	28	DAYS			
Tyvaso dpi institutional ; Tyvaso dpi maintenance ki	Treprostinil Inh Powder	48 MCG	112	Cartridges	28	DAYS			
Tyvaso dpi institutional ; Tyvaso dpi maintenance ki	Treprostinil Inh Powder	64 MCG	112	Cartridges	28	DAYS			
Tyvaso dpi maintenance ki	Treprostinil Inh Powder	112 x 32MCG & 112 x48MCG	224	Cartridges	28	DAYS			
Tyvaso dpi titration kit	Treprostinil Inh Powd	16 & 32 & 48 MCG	252	Cartridges	180	DAYS			
Tyvaso dpi titration kit	Treprostinil Inh Powder	112 x 16MCG & 84 x 32MCG	196	Cartridges	180	DAYS			
Tyvaso refill	treprostinil inhalation solution	0.6 MG/ML	1	Kit	28	DAYS			66302020602
Tyvaso starter	treprostinil inhalation solution	0.6 MG/ML	1	Kit	180	DAYS			66302020604
Tyvaso starter	treprostinil inhalation solution	0.6 MG/ML	1	Kit	180	DAYS			66302020601
Uptravi	selexipag tab	1000 MCG ; 1200 MCG ; 1400 MCG ; 1600 MCG ; 200 MCG ; 400 MCG ; 600 MCG ; 800 MCG	60	Tablets	30	DAYS			
Uptravi	selexipag tab	200 MCG	140	Tablets	180	DAYS			66215060214
Uptravi	selexipag tab	200 MCG	60	Tablets	30	DAYS			66215060206
Uptravi titration pack	selexipag tab therapy pack	200 & 800 MCG	1	Package	180	DAYS			
Ventavis	iloprost inhalation solution	10 MCG/ML ; 20 MCG/ML	270	Ampules	30	DAYS			
Winrevair	sotatercept-csrk for subcutaneous soln kit	45 MG	1	Kit	21	DAYS			
Winrevair	sotatercept-csrk for subcutaneous soln kit	60 MG	1	Kit	21	DAYS			

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Winrevair	sotatercept-csrk for subcutaneous soln kit	2 x 45 MG	1	Kit	21	DAYS			
Winrevair	sotatercept-csrk for subcutaneous soln kit	2 x 60 MG	1	Kit	21	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Adcirca ; Alyq	tadalafil tab	20 MG	Medicaid
Adempas	riociguat tab	0.5 MG ; 1 MG ; 1.5 MG ; 2 MG ; 2.5 MG	Medicaid
Letairis	ambrisentan tab	10 MG ; 5 MG	Medicaid
Liqrev	sildenafil citrate oral susp	10 MG/ML	Medicaid
Opsumit	macitentan tab	10 MG	Medicaid
Opsynvi	macitentan-tadalafil tab	10-20 MG ; 10-40 MG	Medicaid
Orenitram ; Orenitram titration kit m	treprostinil diolamine tab er ; treprostinil tab er titr pk (mo ; treprostinil tab er titr pk(mo	0.125 & 0.25 &1 MG ; 0.125 & 0.25 MG ; 0.125 MG ; 0.25 MG ; 1 MG ; 2.5 MG ; 5 MG	Medicaid
Revatio	sildenafil citrate for suspension	10 MG/ML	Medicaid
Revatio	sildenafil citrate tab	20 MG	Medicaid
Tadliq	tadalafil oral susp	20 MG/5ML	Medicaid
Tracleer	bosentan tab ; bosentan tab for oral susp	125 MG ; 32 MG ; 62.5 MG	Medicaid
Tyvaso ; Tyvaso refill ; Tyvaso starter	Treprostinil Inhalation Solution 0.6 MG/ML	0.6 MG/ML	Medicaid
Tyvaso dpi institutional ; Tyvaso dpi maintenance ki	Treprostinil Inh Powder	64 MCG	Medicaid
Tyvaso dpi institutional ; Tyvaso dpi maintenance ki	Treprostinil Inh Powder	48 MCG	Medicaid
Tyvaso dpi institutional ; Tyvaso dpi maintenance ki	Treprostinil Inh Powder	32 MCG	Medicaid
Tyvaso dpi institutional ; Tyvaso dpi maintenance ki	Treprostinil Inh Powder	16 MCG	Medicaid
Tyvaso dpi maintenance ki	Treprostinil Inh Powder	112 x 32MCG & 112 x48MCG	Medicaid
Tyvaso dpi titration kit	Treprostinil Inh Powd	16 & 32 & 48 MCG	Medicaid
Tyvaso dpi titration kit	Treprostinil Inh Powder	112 x 16MCG & 84 x 32MCG	Medicaid
Uptravi	selexipag tab	1000 MCG ; 1200 MCG ; 1400 MCG ; 1600 MCG ; 200 MCG ; 400 MCG ; 600 MCG ; 800 MCG	Medicaid
Uptravi titration pack	selexipag tab therapy pack	200 & 800 MCG	Medicaid
Ventavis	iloprost inhalation solution	10 MCG/ML ; 20 MCG/ML	Medicaid
Winrevair	sotatercept-csrk for subcutaneous soln kit	2 x 45 MG ; 2 x 60 MG ; 45 MG ; 60 MG	Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Adcirca ; Alyq	tadalafil tab	20 MG	Medicaid

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Adempas	riociguat tab	0.5 MG ; 1 MG ; 1.5 MG ; 2 MG ; 2.5 MG	Medicaid
Letairis	ambrisentan tab	10 MG ; 5 MG	Medicaid
Liqrev	sildenafil citrate oral susp	10 MG/ML	Medicaid
Opsumit	macitentan tab	10 MG	Medicaid
Opsynvi	macitentan-tadalafil tab	10-40 MG	Medicaid
Opsynvi	macitentan-tadalafil tab	10-20 MG	Medicaid
Orenitram titr kit Month 1	Treprostinil tab er Mo 1 titr kit	0.125 & 0.25 MG	Medicaid
Orenitram titr kit Month 2	Treprostinil tab er Mo 2 titr kit	0.125 & 0.25 MG	Medicaid
Orenitram titr kit Month 3	Treprostinil tab er Mo 3 titr kit	0.125 & 0.25 &1 MG	Medicaid
Revatio	sildenafil citrate for suspension	10 MG/ML	Medicaid
Revatio	sildenafil citrate tab	20 MG	Medicaid
Tadliq	Tadalafil Oral Susp	20 MG/5ML	Medicaid
Tracleer	bosentan tab	125 MG ; 62.5 MG	Medicaid
Tracleer	bosentan tab for oral susp	32 MG	Medicaid
Tyvaso	treprostinil inhalation solution	0.6 MG/ML	Medicaid
Tyvaso dpi institutional ; Tyvaso dpi maintenance ki	Treprostinil Inh Powder	48 MCG	Medicaid
Tyvaso dpi institutional ; Tyvaso dpi maintenance ki	Treprostinil Inh Powder	64 MCG	Medicaid
Tyvaso dpi institutional ; Tyvaso dpi maintenance ki	Treprostinil Inh Powder	16 MCG	Medicaid
Tyvaso dpi institutional ; Tyvaso dpi maintenance ki	Treprostinil Inh Powder	32 MCG	Medicaid
Tyvaso dpi maintenance ki	Treprostinil Inh Powder	112 x 32MCG & 112 x48MCG	Medicaid
Tyvaso dpi titration kit	Treprostinil Inh Powd	16 & 32 & 48 MCG	Medicaid
Tyvaso dpi titration kit	Treprostinil Inh Powder	112 x 16MCG & 84 x 32MCG	Medicaid
Tyvaso refill	treprostinil inhalation solution	0.6 MG/ML	Medicaid
Tyvaso starter	treprostinil inhalation solution	0.6 MG/ML	Medicaid
Tyvaso starter	treprostinil inhalation solution	0.6 MG/ML	Medicaid
Uptravi	selexipag tab	200 MCG	Medicaid
Uptravi	selexipag tab	200 MCG	Medicaid
Uptravi	selexipag tab	1000 MCG ; 1200 MCG ; 1400 MCG ; 1600 MCG ; 200 MCG ; 400 MCG ; 600 MCG ; 800 MCG	Medicaid
Uptravi titration pack	selexipag tab therapy pack	200 & 800 MCG	Medicaid
Ventavis	iloprost inhalation solution	10 MCG/ML ; 20 MCG/ML	Medicaid
Winrevair	sotatercept-csrk for subcutaneous soln kit	2 x 60 MG	Medicaid
Winrevair	sotatercept-csrk for subcutaneous soln kit	2 x 45 MG	Medicaid
Winrevair	sotatercept-csrk for subcutaneous soln kit	60 MG	Medicaid
Winrevair	sotatercept-csrk for subcutaneous soln kit	45 MG	Medicaid

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent(s)** will be approved when ONE of the following is met: 1. ALL of the following:

Module	Clinical Criteria for Approval
	A. ONE of the following: 1. BOTH of the following: A. The requested agent is eligible for continuation of therapy AND ONE of the following: **Target Agents Eligible for Continuation of Therapy** All target agents are eligible for continuation of therapy 1. The patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days **OR** 2. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed **AND** B. The patient has an FDA labeled indication for the requested agent and route of administration **OR** 2. The patient has a diagnosis of chronic thromboembolic pulmonary hypertension (CTEPH), WHO Group 4 and ALL of the following: A. The requested agent is Adempas **AND** B. The patient's diagnosis has been confirmed by a ventilation-perfusion scan and a confirmatory selective pulmonary angiography **AND** C. The patient has a mean pulmonary artery pressure of greater than 20 mmHg **AND** D. The patient has a pulmonary capillary wedge pressure less than or equal to 15 mmHg **AND** E. The patient has a pulmonary vascular resistance greater than or equal to 3 Wood units **AND** F. ONE of the following: 1. The patient is NOT a candidate for surgery **OR** 2. The patient has had a pulmonary endarterectomy AND has persistent or recurrent disease **AND** G. The patient will NOT be using the requested agent in combination with a PDE5 inhibitor (e.g., tadalafil [Adcirca or Cialis] or sildenafil [Revatio or Viagra]) **OR** 3. The patient has a diagnosis of pulmonary arterial hypertension (PAH), WHO Group 1 and ALL of the following: A. The patient's diagnosis has been confirmed by right heart catheterization (medical records required) **AND** B. The patient's mean pulmonary arterial pressure is greater than 20 mmHg **AND** C. The patient has a pulmonary capillary wedge pressure less than or equal to 15 mmHg **AND** D. The patient has a pulmonary vascular resistance greater than or equal to 3 Wood units **AND** E. The patient's World Health Organization (WHO) functional class is II or greater **AND** F. If the requested agent is sotatercept, then BOTH of the following: 1. The patient has been stable on background PAH therapy for at least 90 days (Please note: Background therapy refers to combination therapy consisting of drugs from two or more of the following drug classes: ERA, PDE5i, soluble guanylate cyclase stimulator, and/or prostacyclin analogue or receptor agonist) **AND** 2. The patient is not pregnant or planning to become pregnant while on therapy with the requested agent **AND** G. If the requested agent is Adcirca, Adempas, Revatio, sildenafil, or tadalafil, the patient will NOT be using the requested agent in combination with a PDE5 inhibitor (e.g., tadalafil [Adcirca or Cialis] or sildenafil [Revatio or Viagra]) **AND**

Module	Clinical Criteria for Approval
	H. If the requested agent is NOT sotatercept, then ONE of the following: 1. The requested agent will be utilized as monotherapy **OR** 2. The requested agent will be utilized as dual therapy that consists of an endothelin receptor antagonist (ERA) plus phosphodiesterase 5 inhibitor (PDE5i) as initial therapy **OR** 3. The requested agent will be utilized for add-on therapy to existing monotherapy (dual therapy) [except combo requests for endothelin receptor antagonist (ERA) plus phosphodiesterase 5 inhibitor (PDE5i) for dual therapy], and BOTH of following: A. The patient has unacceptable or deteriorating clinical status despite established PAH pharmacotherapy **AND** B. The requested agent is in a different therapeutic class **OR** 4. The requested agent will be utilized for add-on therapy to existing dual therapy (triple therapy) and ALL of the following: A. The patient is WHO functional class III or IV **AND** B. ONE of the following: 1. A prostanoid has been started as one of the agents in the triple therapy **OR** 2. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to ALL prostanoids **AND** C. The patient has unacceptable or deteriorating clinical status despite established PAH pharmacotherapy **AND** D. All three agents in the triple therapy are from a different therapeutic class **OR** 5. The requested agent will be utilized as part of triple therapy in a treatment naive patient AND both of the following: A. The patient is WHO functional class IV **AND** B. The 3 agents being utilized consist of: endothelin receptor antagonist (ERA) plus PDE5i plus prostanoid **OR** 4. The patient has a diagnosis of pulmonary hypertension associated with interstitial lung disease (PH-ILD, WHO group 3) AND ALL of the following: A. The requested agent is Tyvaso **AND** B. The patient's diagnosis has been confirmed by right heart catheterization (medical records required) **AND** C. The patient's mean pulmonary arterial pressure is greater than 20 mmHg **AND** D. The patient has a pulmonary capillary wedge pressure less than or equal to 15 mmHg **AND** E. The patient has a pulmonary vascular resistance greater than or equal to 3 Wood units **AND** F. The patient has an FVC less than 70% of predicted **AND** G. The patient has extensive parenchymal changes on computed tomography (CT) **AND** H. BOTH of the following: 1. The patient is currently treated with standard of care therapy for ILD (e.g., Ofev) **AND** 2. The patient will continue standard of care therapy for ILD (e.g., Ofev) **OR** 5. The patient has another FDA approved indication for the requested agent **AND** B. If the patient has an FDA labeled indication, then ONE of the following:

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	1. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** 2. There is support for using the requested agent for the patient's age for the requested indication **AND** C. ONE of the following: 1. The requested agent is a preferred agent in the Minnesota Medicaid Preferred Drug List (PDL) **OR** 2. The request is for a non-preferred agent in the Minnesota Medicaid Preferred Drug List (PDL) and ONE of the following: A. The patient is currently being treated with the requested agent and is experiencing a positive therapeutic outcome AND the prescriber provides documentation that switching the member to a preferred drug is expected to cause harm to the member or that the preferred drug would be ineffective **OR** B. The patient has tried and had an inadequate response to two preferred chemically unique agents within the same drug class in the Minnesota Medicaid Preferred Drug List (PDL) as indicated by BOTH of the following: 1. ONE of the following: A. Evidence of a paid claim(s) **OR** B. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) **AND** 2. ONE of the following: A. The required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event **OR** B. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over the prerequisite/preferred agent(s) **OR** C. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to the preferred agents within the same drug class in the Minnesota Medicaid Preferred Drug List (PDL) that is not expected to occur with the requested agent **OR** D. The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR** E. The prescriber has submitted documentation supporting the use of the non-preferred agent over the preferred agent(s) **AND** D. The prescriber is a specialist in the area of the patient's diagnosis (e.g., cardiologist, pulmonologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** E. The patient does NOT have any FDA labeled contraindications to the requested agent **OR** 2. If the request is for an oral liquid form of a medication, then BOTH of the following: A. The patient has an FDA approved indication **AND** B. The patient uses an enteral tube for feeding or medication administration **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation**

Module	Clinical Criteria for Approval
	Target Agent(s) will be approved when ONE of the following is met: 1. ALL of the following: A. The patient has been previously approved for the requested agent through the plan's Prior Authorization process [NOTE: Patients not previously approved for the requested agent will require initial evaluation review] **AND** B. The patient has had clinical benefit with the requested agent (e.g., stabilization, decreased disease progression) (medical records required) **AND** C. If the requested agent is Tyvaso for a diagnosis of pulmonary hypertension associated with interstitial lung disease (PH-ILD, WHO group 3), then the patient will continue standard of care therapy for ILD (e.g., Ofev) **AND** D. If the requested agent is sotatercept for a diagnosis of pulmonary arterial hypertension (PAH), the patient will continue to use background PAH therapy (Please note: Background therapy refers to combination therapy consisting of drugs from two or more of the following drug classes: ERA, PDE5i, soluble guanylate cyclase stimulator, and/or prostacyclin analogue or receptor agonist) **AND** E. The prescriber is a specialist in the area of the patient's diagnosis (e.g., cardiologist, pulmonologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** F. The patient does NOT have any FDA labeled contraindications to the requested agent **OR** 2. If the request is for an oral liquid form of a medication, then BOTH of the following: A. The patient has an FDA approved indication **AND** B. The patient uses an enteral tube for feeding or medication administration **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity Limit for the Target Agent(s) will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **OR** 3. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** C. There is support for therapy with a higher dose for the requested indication **Length of Approval**: 12 months