Effective Date: 11/01/2016
Last P&T Approval/Version: 01/26/2022
Next Review Due By: 1/26/2023
Policy Number: C17185-A

Pulmonary Arterial Hypertension (PAH) IL Medicaid ONLY

PRODUCTS AFFECTED

Endothelin-Receptor Antagonists (ERAs)
Letairis (ambrisentan) Tracleer (bosentan) Opsumit (macitentan), ambrisentan, bosentan

Phosphodiesterase type 5 inhibitors (PDE-5 inhibitors)
Adcirca (tadalafil), ALYQ (tadalafil), Revatio (sildenafil), sildenafil, tadalafil

Soluble Guanylate Cyclase Stimulator
Adempas (riociguat)

Prostanoids/prostacyclin therapies
Epoprostenol, Flolan (epoprostenol for injection), Orenitram (treprostinil extended-release tablets), Remodulin (treprostinil injection),treprostinil, Tyvaso (treprostinil inhalation solution), Uptravi (selexipag), Veletri (epoprostenol for injection), Ventavis (iloprost)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.
This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive

DIAGNOSIS:
Pulmonary Hypertension, Chronic Thromboembolic Pulmonary Hypertension, Pulmonary hypertension associated with interstitial lung disease

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information

along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review

A. PULMONARY ARTERIAL HYPERTENSION:
   a. (a) The member has a diagnosis of PAH (WHO Group 1) confirmed by a right heart catheterization and results confirm all the following: Mean pulmonary arterial pressure (mPAP) >20 mm Hg at rest AND Pulmonary capillary wedge pressure (PCWP) <15 mm Hg AND Pulmonary vascular resistance (PVR) >3 Wood units
      OR
      (b) The member has a diagnosis of PAH (WHO Group 1) and has a contraindication to right heart catheterization due to: Infection at the insertion site, the presence of a right ventricular assist device, insertion during cardiopulmonary bypass, coagulopathy (international normalized ratio >1.5), thrombocytopenia (platelet count <50,000/microl), electrolyte disturbances (hypo- or hyper-kalemia, -magnesemia, -natremia, -calcemia), and severe acid- base disturbances (e.g., pH <7.2 or >7.5) which cannot be corrected or considered high-risk for pulmonary artery catherization
      AND
      (c) Member diagnosed by echocardiogram showing mPAP >20mm Hg or acute vasoreactivity test and other underlying causes of pulmonary hypertension has been ruled out
      AND
   b. Medication requested for treatment is consistent with its own FDA- labeled approved indicated WHO functional class
      AND
   c. FOR ORENITAM (TREPROSTINIL) and UPTRAVI (SELEXIPAG) ONLY:
      i. Member has tried or is currently receiving two oral therapies for PAH from two of the three following different categories (either alone or in combination) each for ≥ 60 days: one phosphodiesterase type 5 (PDE5) inhibitor, one endothelin receptor antagonist (ERA), OR Adempas (riociguat)
         OR
      ii. Member is receiving or has received in the past for PAH one prostacyclin therapy, or a prostacyclin receptor agonist for PAH.
      AND
   d. FOR ADCIRCA, ALYQ, REVATIO OR SILDENAFIL ONLY: The member will not be taking a PDE5 inhibitor at the same time as the requested therapy
      AND
   e. FOR REQUESTS FOR OPSUMIT (MACITENTAN): Documentation of a trial and failure or contraindication to Letairis (ambrisentan) and Tracleer (bosentan)
      AND
   f. IF THIS IS A NON-FORMULARY/NON-PREFERRED PRODUCT: Documentation of trial and failure or absolute contraindication to preferred formulary products in the same drug class

B. CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION (CTEPH)- ADEMPAS ONLY:
   a. Documentation member has been diagnosed as inoperable by a center specializing in CTEPH or pulmonary endarterectomy (PEA)
      OR
   b. Documentation member been diagnosed as recurrent or persistent CTEPH after PEA
      AND
   c. Adempas (riociguat) will NOT be administered with phosphodiesterase (PDE)-5 inhibitor or nitrates

C. PULMONARY HYPERTENSION ASSOCIATED WITH INTERSTITIAL LUNG DISEASE-TYVASO ONLY
   a. Documentation that member has a diagnosis of an interstitial lung disease [examples: Idiopathic pulmonary fibrosis (IPF) or pulmonary fibrosis (PF); Combined pulmonary fibrosis and emphysema (CPFE); Connective tissue disease (CTD)]
      AND
   b. Documentation that member has Group 3 pulmonary hypertension confirmed by
      i. Right heart catheterization and results confirm all the following: Mean pulmonary arterial pressure (mPAP) >25 mm Hg at rest AND Pulmonary capillary wedge pressure (PCWP) <15 mm Hg AND Pulmonary vascular resistance (PVR) >3 Wood units
         OR
      ii. The member has a diagnosis of pulmonary hypertension and has a contraindication to right heart catheterization due to: Infection at the insertion site, the presence of a right ventricular assist device, insertion during cardiopulmonary bypass, coagulopathy (international normalized ratio >1.5), thrombocytopenia (platelet count <50,000/microl), electrolyte disturbances (hypo- or hyper-kalemia, -magnesemia, -natremia, -calcemia), and severe acid- base disturbances (e.g., pH <7.2 or >7.5) which cannot be corrected or considered high-risk for pulmonary artery catherization AND Member diagnosed by echocardiogram showing mPAP >25 mm Hg or acute vasoreactivity test and other underlying causes of pulmonary hypertension has been ruled out
      AND
   c. Documentation of member's baseline 6-minute walk test

CONTINUATION OF THERAPY:

A. PULMONARY ARTERIAL HYPERTENSION:
   a. Documentation member is responding to therapy as demonstrated by ONE of the following: Improvement in Six Minute Walking Test or Exercise Capacity, Improvement in WHO Functional Class, decrease in mean pulmonary artery pressure (mPAP),or Increase in Cardiac Index
      AND
   b. Documentation member is NOT experiencing any adverse effects, drug toxicity or poor response to treatment

B. CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION (CTEPH) - ADEMPAS ONLY:
   a. Documentation that member's condition has nor progressed or worsened on therapy
      AND
   b. Adherence to therapy at least 85% of the time as verified by Prescriber and member's medication fill history (review Rx history for compliance)

C. PULMONARY HYPERTENSION ASSOCIATED WITH INTERSTITIAL LUNG DISEASE-TYVASO ONLY
   a. Documentation that member has had improvement in 6-minute walk test from baseline
      AND
   b. Adherence to therapy at least 85% of the time as verified by Prescriber and member's medication fill history (review Rx history for compliance)

DURATION OF APPROVAL:
Initial authorization: 12 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:
Letairis: No prescriber requirement
Other Agents: Prescribed by or in consultation with a board-certified cardiologist, pulmonologist, of physician affiliated at a center of expertise in the diagnosis of pulmonary arterial hypertension.
FOR ADEMPAS: prescriber has fulfilled the Adempas REMS requirements for certification

AGE RESTRICTIONS:
No requirement

QUANTITY:
Adcirca (tadalafil), Alyq (tadalafil) 20 mg tablet: 60 tabs per 30 days
Adempas (riociguat) 0.5 mg,1mg,1.5mg,2mg, or 2.5mg tablet: 90 tabs per 30 days
Letairis (ambrisentan) 5 mg or 10mg tablet: 30 tabs per 30 days
Opsumit (macitentan) 10 mg tablet: 30 tabs per 30 days
Orenitram (treprostinil): determine by tolerability, 90 tabs per 30 days
Revatio (sildenafil): 20 mg tablet 3 tablets per day OR 10 mg/mL oral suspension 2 bottles (224 mL)/30 days
Tracleer (bosentan) 62.5 mg or 125mg tablet: 60 tabs per 30 days
Tyvaso (inhaled treprostinil) 0.6 mg/mL System Starter Kit 1 kit/180 days or 0.6 mg/mL System Refill kit -1 package of 28 ampules/28 days or 4 pack Carton 7 packages of 4 ampules/28 days
Uptravi (selexipag) tablets: Titration pack 1 pack/180 days 200 mcg, 400 mcg, 600 mcg,800 mcg,1000 mcg,1200 mcg,1400 mcg or 1600 mcg tablet - 2 tablets per day
Ventavis (iloprost) 10 mcg/mL or 20 mcg/mL - 9 packages of 30 ampules/30 days

NOTE: For Uptravi tablets and Orenitram: authorizations may occur in small quantities per strength to allow for titration as prescribed

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

The recommendation is that inhalation medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.

The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-hospital facility-based location as per the Molina Health Care Site of Care program.
Note: Site of Care Utilization Management Policy applies for epoprostenol (generic for Flolan), Flolan (epoprostenol), Remodulin (treprostinil sodium), Tyvaso (treprostinil). For information on site of care, see Specialty Medication Administration Site of Care Coverage Criteria (molinamarketplace.com)

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral, Intravenous, Inhalation

DRUG CLASS:

FDA-APPROVED USES:

Adcirca (tadalafil): indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise ability.

Adempas (riociguat): indicated for: 1. Persistent/recurrent Chronic Thromboembolic Pulmonary Hypertension (CTEPH) (WHO Group 4) after surgical treatment or inoperable CTEPH to improve exercise capacity and WHO functional class; 2. Pulmonary Arterial Hypertension (PAH) (WHO Group 1) to improve exercise capacity, improve WHO functional class and to delay clinical worsening.

Flolan (epoprostenol): indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to improve exercise capacity.

Letairis (ambrisentan):indicated for the treatment ofadults with pulmonary arterial hypertension World Health Organization [WHO] Group 1.

Remodulin (treprostinil injection): indicated for treatment of pulmonary arterial hypertension (PAH; WHO Group 1) to diminish symptoms associated with exercise and for patients who require transition from epoprostenol, to reduce the rate of clinical deterioration.

Revatio (sildenafil): indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group I) in adults to improve exercise ability and delay clinical worsening.

Opsumit (macitentan): indicated for the treatment of pulmonary arterial hypertension (PAH, WHO Group I) to reduce the risks of disease progression and hospitalization for PAH

Orenitram (treprostinil extended-releasetablets): indicated for the treatment of pulmonary arterial hypertension (PAH) (WHO Group 1) to delay disease progression and to improve exercise capacity.

Tracleer (bosentan): indicated for the treatment of pulmonary arterial hypertension (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%).
- pediatric patients aged 3 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 (treprostinil inhalation solution): indicated for:

- Pulmonary arterial hypertension (PAH; WHO Group 1) to improve exercise ability. Studies establishing effectiveness predominately included patients with NYHA Functional Class III symptoms and etiologies of idiopathic or heritable PAH (56%) or PAH associated with connective tissue diseases (33%).
- Pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) to improve exercise ability.

Uptravi (selexipag): indicated for the treatment of pulmonary arterial hypertension (PAH) World Health Organization (WHO) Group 1 to delay disease progression and reduce the risk of hospitalization

Ventavis (iloprost): indicated for the treatment of PAH(World Health Organization [WHO] Group 1) to improve exercise tolerance, symptoms (NYHA Class), and lack of deterioration

COMPENDIAL APPROVED OFF-LABELED USES:
UpToDate, Micromedex, AHFS or Clinical Pharmacology

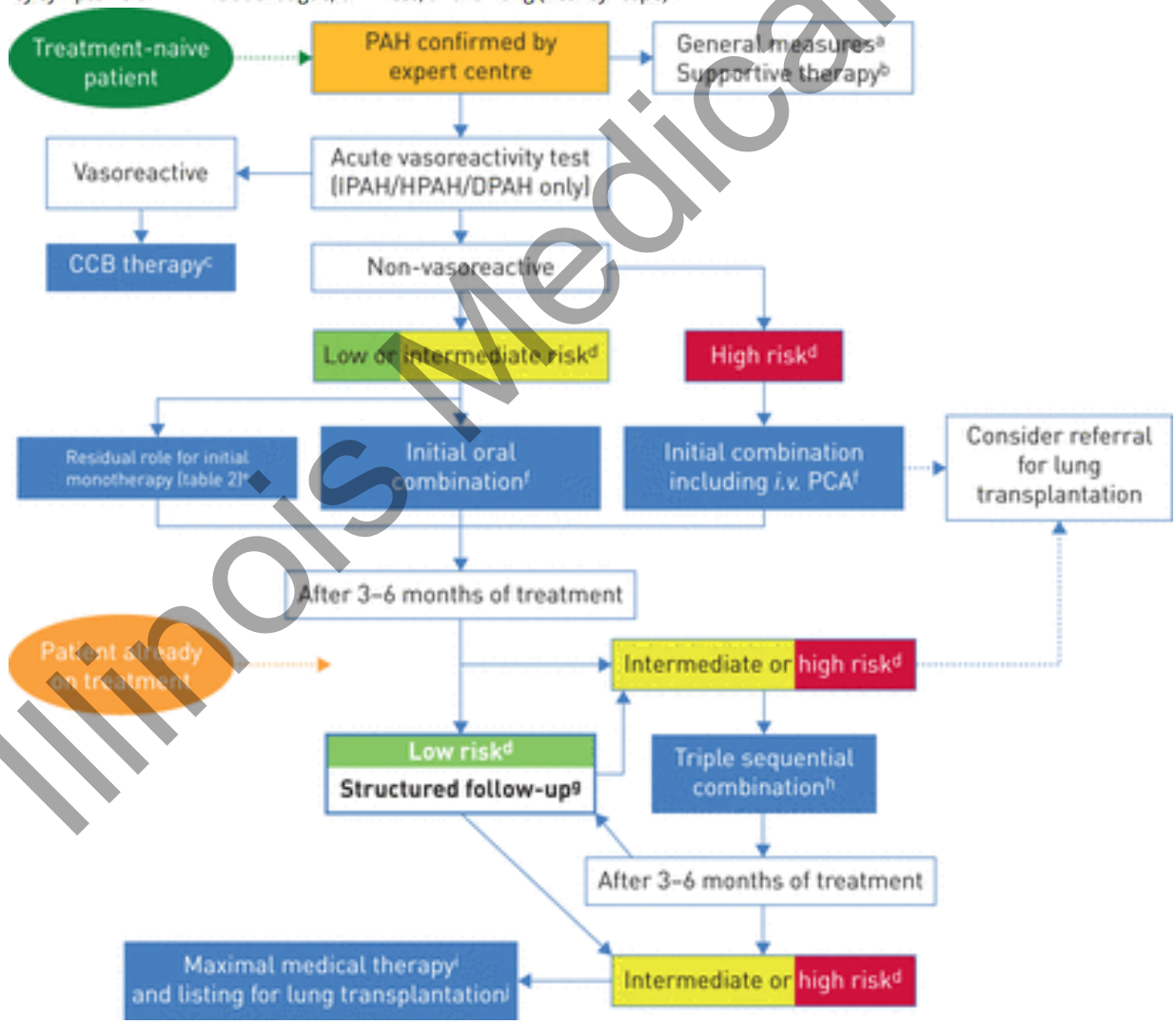
APPENDIX

APPENDIX:

World Health Organization (WHO) functional classification of pulmonary artery hypertension:

Class I	Persons with no symptoms[1], and for whom ordinary physical activity does not cause fatigue, palpitation, dyspnea, or angina pain
Class II	Persons who are comfortable at rest but who have symptoms[1] with ordinary physical activity
Class III	Persons who are comfortable at rest but have symptoms[1] with less-than-ordinary effort
Class IV	Persons who have symptoms[1] at rest

[1] Key symptoms of PAH include fatigue, dizziness, and fainting (near syncope)



Treatment algorithm. PAH: pulmonary arterial hypertension; IPAH: idiopathic PAH; HPAH: heritable PAH; DPAH: drug-induced PAH; CCB: calcium channel blocker; PCA: prostacyclin analogue; PH: pulmonary hypertension. [a]: 2015 ESC/ERS PH guidelines Table 16; [b]: 2015 ESC/ERS PH guidelinesTable 17; [c]: 2015 ESC/ERS PH guidelines Table 18; [d]: 2015 ESC/ERS PH guidelines Table 13; [e]: 2015 ESC/ERS PH guidelines Table 19; [f]: 2015 ESC/ERS PH guidelines Table 20; [g]: 2015 ESC/ERSPH guidelines Table 14; [h]: 2015 ESC/ERS PH guidelines Table 21; [i]: maximal medical therapy is considered triple combination therapy including a s.c. or an i.v. PCA (i.v. preferred in high-risk status); [j]: 2015 ESC/ERS PH guidelines

Risk stratification and medical therapy of pulmonary arterial hypertension
Nazzareno Galiè, Richard N. Channick, Robert P. Frantz, Ekkehard Grünig, Zhi Cheng Jing, OlgaMoiseeva, Ioana R. Preston, Tomas Pulido, Zeenat Safdar, Yuichi Tamura, Vallerie V. McLaughlinEuropean Respiratory Journal 2019 53: 1801889; DOI: 10.1183/13993003.01889-2018

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:

Adempas, a soluble guanylate cyclase (sGC) stimulator, is indicated for the treatment of adults with persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) [World Health Organization {WHO} Group 4] after surgical treatment, or inoperable CTEPH, to improve exercise capacity and WHO functional class. Adempas is also indicated for the treatment of adults with pulmonary arterial hypertension (PAH) [WHO Group 1], to improve exercise capacity, WHO functional class and to delay clinical worsening. Efficacy in WHO Group 1 PAH was established in patients receiving Adempas as monotherapy or in combination with endothelin receptor antagonists (ERAs) or prostanoids. Studies establishing effectiveness included mainly patients with WHO functional class II or III and etiologies of idiopathic or heritable PAH (61%) or PAH associated with connective tissue diseases (25%). The starting dose of Adempas is 1 mg three times daily (TID) and can be titrated to 2.5 mg TID.

Tracleer, Letairis and Opsumit are oral endothelin receptor antagonists (ERAs) that are used for the treatment of pulmonary arterial hypertension (PAH). Tracleer, which is given twice daily (BID), is indicated for the treatment of PAH (World Health Organization [WHO] Group 1) to improve exercise ability and decrease the rate of clinical worsening. Studies establishing the effectiveness included predominantly those with New York Heart Association (NYHA) Functional Class II to IV symptoms and etiologies of idiopathic or heritable PAH (60%), PAH associated with connective tissue diseases (21%), and PAH associated with congenital systemic-to-pulmonary shunts (18%). Patients with WHO Class II symptoms demonstrated reduction in the rate of clinical deterioration and a trend for improvement in walk distance. Physicians should consider if these benefits are sufficient to offset the risk of liver injury in WHO Class II patients, which may preclude future use as disease progression occurs. Letairis, which is given once daily (QD), is indicated for the treatment of PAH (WHO Group 1) to improve exercise ability and delay clinical worsening; it is also indicated for use in combination with Adcirca® (tadalafil tablets) to reduce the risks of disease progression and hospitalization for worsening PAH, and to improve exercise ability. Studies establishing effectiveness included predominantly those with WHO Functional Class II to III symptoms and etiologies of idiopathic or heritable PAH (60%) or PAH associated with connective tissue diseases (34%). Opsumit, which is given QD, is indicated for the treatment of PAH (WHO Group 1) to delay disease progression. Disease progression included: death, initiation of intravenous or subcutaneous prostanoids, or clinical worsening of PAH (decreased 6-minute walk distance, worsening PAH symptoms, and need for additional PAH treatment). Opsumit also reduced hospitalizations for PAH. All agents are in Pregnancy Category X and have a Boxed Warning regarding teratogenicity. Tracleer has a Boxed Warning regarding hepatotoxicity. All agents have a Boxed Warning regarding embryofetal toxicity

Risk Evaluation and Mitigation Strategies (REMS) Program Because of the risk of embryo-fetal toxicity and hepatotoxicity (Tracleer) associated with Tracleer, Letairis, Opsumit therapy, Tracleer, Letairis, Opsumit are available through a restricted program under the REMS. Under the REMS, only certified healthcare providers and pharmacies may prescribe and distribute Tracleer, Letairis, Opsumit.

Epoprostenol injection is a prostacyclin vasodilator. It is indicated for the treatment of pulmonary arterial hypertension (PAH) World Health Organization (WHO) Group 1 to improve exercise

capacity. Studies establishing the effectiveness predominately included patients with New York Heart Association (NYHA) Functional Class III to IV symptoms and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases. Several studies have noted beneficial effects with epoprostenol therapy. Epoprostenol is given by intravenous infusion through a central venous catheter.

Ventavis and Tyvaso are both inhaled prostacyclin vasodilators indicated for the treatment of pulmonary arterial hypertension (PAH). Ventavis, which is given six to nine times per day, is indicated for the treatment of PAH (World Health Organization [WHO] Group 1) to improve a composite endpoint consisting of exercise tolerance, symptoms (based on New York Heart Association [NYHA] Class), and lack of deterioration. Studies establishing effectiveness involved mainly patients with NYHA Functional Class III to IV symptoms and etiologies of idiopathic or heritable PAH (65%) or PAH associated with connective tissue diseases (23%). Tyvaso, which is given four times per day, is indicated for the treatment of PAH (WHO Group 1) to improve exercise ability. Studies establishing effectiveness mainly included those with NYHA Functional Class III symptoms and etiologies of idiopathic or heritable PAH (56%) or PAH associated with connective tissue diseases (33%). An updated treatment algorithm (2013) by the 2nd World Symposium on Pulmonary Hypertension (WSPH) states that patients with Functional Class II should be treated initially with oral therapies (e.g., Adempas® [riociguat tablets], sildenafil [Revatio® , generics {Note: brand name Revatio injection also available}], Adcirca® [tadalafil tablets], Opsumit® [macitentan tablets], Tracleer® [bosentan tablets], and Letairis® [ambrisentan tablets]). Ventavis and Tyvaso are recommended for patients in Functional Class III and IV. In situations of inadequate response, combination therapy (including double or triple therapy) is recommended.

Orenitram, an oral prostacyclin vasodilator, is indicated for the treatment of pulmonary arterial hypertension (PAH) World Health Organization (WHO) Group 1 to improve exercise capacity. The trial that established the efficacy of Orenitram included mainly patients with WHO functional class II to III symptoms. The prescribing information notes that Orenitram is probably most useful to replace subcutaneous, intravenous, or inhaled treprostinil, but this use requires further study. The recommended starting dose is 0.25 mg twice daily (BID) with food, taken approximately 12 hours apart. Dosing is individualized and titrated to response and tolerability; increase in increments of 0.25 to 0.5 mg BID every 3 to 4 days.

Revatio and Adcirca are phosphodiesterase type 5 (PDE5) inhibitors indicated for the treatment of pulmonary arterial hypertension (PAH). Revatio is indicated for PAH (World Health Organization [WHO] Group I) in adults to improve exercise ability and delay clinical worsening. The delay in clinical worsening was demonstrated when Revatio was added to background epoprostenol injection therapy (Flolan® [generic], Veletri®). Studies establishing its effectiveness were short-term (12 to 16 weeks) and included mainly patients with New York Heart Association (NYHA) Functional Class II to III symptoms and idiopathic etiology (71%) or associated with connective tissue disease (25%). A limitation of use is that adding Revatio to Tracleer® (bosentan tablets) does not result in any beneficial impact on exercise capacity. The recommended dose of Revatio is 5 mg or 20 mg three times daily (TID) given approximately 4 to 6 hours apart. In the clinical trial no, greater efficacy was achieved with the use of higher doses. Treatment with doses higher than 20 mg TID is not recommended. Revatio has a Warning regarding mortality with increasing doses in pediatric patients. In a long-term trial involving pediatric patients with PAH, an increase in mortality with increasing Revatio dose was noted. Deaths were first observed following about 1 year and causes

of death were usual of those with PAH. Revatio, especially chronic use, is not recommended in children. Adcirca is indicated for the treatment of PAH (WHO Group I) to improve exercise ability. Studies establishing effectiveness were mainly in patients with NYHA Functional Class II to III symptoms and etiologies of idiopathic or heritable PAH (61%) or PAH associated with connective tissue diseases (23%). The recommended dose is 40 mg once daily (QD). Dividing the dose (40 mg) over the course of the day is not recommended.

Remodulin is a prostacyclin vasodilator indicated for the treatment of pulmonary arterial hypertension (PAH) [World Health Organization {WHO} Group 1] to diminish symptoms associated with exercise. Studies establishing the effectiveness involved those with New York Heart Association (NYHA) Functional Class II to 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%). Remodulin may be administered via continuous subcutaneous (SC) infusion or continuous intravenous infusion. However, due to the risks associated with chronic indwelling central venous catheters, including serious blood stream infections, continuous intravenous infusion should be reserved for those intolerant of the SC, or in whom these risks are still considered acceptable. In those with PAH requiring transition from epoprostenol injection, Remodulin is indicated to diminish the rate of clinical deterioration. The risks and benefits of each agent should be considered carefully before transition.1 Several trials have shown benefits of Remodulin therapy.

Uptravi (selexipag), an oral prostacyclin receptor agonist, is indicated for the treatment of pulmonary arterial hypertension (PAH) World Health Organization (WHO) Group 1 to delay disease progression and reduce the risk of hospitalization. The trial that established the efficacy of selexipag included mainly patients with WHO functional class II to III symptoms. The recommended starting dose is 200 mcg twice daily (BID) and may be more tolerable when taken with food. Dosing is individualized and titrated to tolerability; increased in increments of 200 mcg weekly to up to 1600 mcg twice daily.
Those with moderated hepatic impairment should begin with 200 mcg and only dose once daily. Selexipag is not recommended to be used with those that have severe hepatic impairment. Selexipag is not to be chewed, crushed, or split.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of pulmonary arterial hypertension therapies are considered experimental/investigational and therefore will follow the Molina Healthcare, Inc. off-label policy. Contraindications to Adcirca (tadalafil) include concomitant use of organic nitrates or guanylate cyclase (GC) stimulators. Contraindications to Adempas (riociguat) include: pregnancy, use with nitrates or nitric oxide donors in any form, use with PDE inhibitors, patients with concomitant use of other soluble guanylate cyclase (sGC) stimulators, and pulmonary hypertension associated with idiopathic interstitial pneumonias (PH-IIP). Contraindications to Letairis (ambrisentan) include pregnancy and idiopathic pulmonary fibrosis. Contraindications to Tracleer (bosentan) includes pregnancy, use with cyclosporine, use with glyburide, and hypersensitivity. Contraindications to Opsumit (macitentan) include pregnancy. Contraindications to Orenitram (treprostinil) includes severe hepatic impairment (Child Pugh Class C). Contraindications to Flolan (epoprostenol sodium) include heart failure with reduced ejection fraction and hypersensitivity to Flolan and any of its ingredients. Contraindications to Revatio (sildenafil) include use with organic nitrates or riociguat

and history of hypersensitivity reaction to sildenafil or any component of the tablet, injection or oral suspension.

OTHER SPECIAL CONSIDERATIONS:

Treatment Guidelines The 6th World Symposium on Pulmonary Hypertension evidence-based treatment algorithm:

Initial approach

- After confirmation of the diagnosis of the treatment-naive PAH patient in an expert center, the suggested initial approach is the adoption of *general measures* and the initiation of *supportive therapy* (2015 ESC/ERS PH guidelines).
- *Acute vasoreactivity testing* should be performed to predict response to calcium channel blocker (CCBs) only in patients with IPAH, HPAH, and PAH associated with drugs and toxinuse. Vasoreactive patients (see the Task Force article by Simonneau *et al.* in this issue of the *European Respiratory Journal*) should be treated with *high doses (progressively titrated)of CCBs*; adequate response should be confirmed after 3–6 months of treatment (2015 ESC/ERS PH guidelines *Adequate treatment response to high doses of CCBs* is consideredWHO FC I/II with sustained hemodynamic improvement (same or better than achieved in the acute test) after at least 1 year on CCBs only. Vasoreactive patients without an adequate treatment response to high doses of CCBs should be treated with approved PAH medications according to the non-vasoreactive patients' treatment strategy.
- *Non-responders to acute vasoreactivity testing who are at low or intermediate risk* should be treated with *initial oral combination therapy with an ERA and a PDE5i* (2015 ESC/ERS PH guidelines
- Some specific PAH subsets in which the efficacy/safety ratio of initial combination therapy is not established should be treated with initial monotherapy.

Recommendations for initial monotherapy are reported in the 2015 ESC/ERS PH guidelines

- If initial monotherapy is chosen, as head-to-head comparisons among different compounds are not available, no evidence-based first-line monotherapy can be proposed. The choice of drug may depend on a variety of factors, including approval status, labelling, route of administration,side-effect profile, potential interaction with background therapies, patient preferences, comorbidities, physician experience and cost.
- *In non-vasoreactive and treatment-naive patients at high risk*, initial combination therapy including *i.v.* PCAs is recommended (2015 ESC/ERS PH guidelines). Intravenous epoprostenolreceives the strongest recommendation as it has reduced the 3-month rate of mortality in high-risk PAH patients also as monotherapy (2015 ESC/ERS PH guidelines). Alternative types of initial combination therapy may be considered (2015 ESC/ERS PH guidelines. Referral for lungtransplantation should also be considered.

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CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION

J1325	Injection, epoprostenol, 0.5 mg
J3285	Injection, treprostinil, 1 mg
J7686	Treprostinil, inhalation solution, fda-approved final product, non-compounded, administered through dme, unit dose form, 1.74 mg
Q4074	Iloprost, inhalation solution, fda-approved final product, non-compounded, administered through dme, unit dose form, up to 20 micrograms

AVAILABLE DOSAGE FORMS:

Adcirca TABS 20MG
Adempas TABS 0.5MG
Adempas TABS 1.5MG
Adempas TABS 1MG
Adempas TABS 2.5MG
Adempas TABS 2MG
Alyq TABS 20MG
Ambrisentan TABS 10MG
Ambrisentan TABS 5MG
Bosentan TABS 125MG
Bosentan TABS 62.5MG
Epoprostenol Sodium SOLR 0.5MG
Epoprostenol Sodium SOLR 1.5MG
Flolan SOLR 0.5MG
Flolan SOLR 1.5MG
Letairis TABS 10MG
Letairis TABS 5MG
Opsumit TABS 10MG
Orenitram TBCR 0.125MG
Orenitram TBCR 0.25MG
Orenitram TBCR 1MG
Orenitram TBCR 2.5MG
Orenitram TBCR 5MG
Remodulin SOLN 100MG/20ML
Remodulin SOLN 200MG/20ML
Remodulin SOLN 20MG/20ML
Remodulin SOLN 50MG/20ML
Revatio SOLN 10MG/12.5ML
Revatio SUSR 10MG/ML
Revatio TABS 20MG
Sildenafil Citrate SOLN 10MG/12.5ML
Sildenafil Citrate SUSR 10MG/ML
Sildenafil Citrate TABS 20MG
Tadalafil (PAH) TABS 20MG
Tracleer TABS 125MG
Tracleer TABS 62.5MG
Tracleer TBSO 32MG
Treprostinil SOLN 100MG/20ML
Treprostinil SOLN 200MG/20ML
Treprostinil SOLN 20MG/20ML
Treprostinil SOLN 50MG/20ML
Tyvaso SOLN 0.6MG/ML
Tyvaso Refill SOLN 0.6MG/ML
Tyvaso Starter SOLN 0.6MG/ML
Uptravi SOLR 1800MCG
Uptravi TABS 1000MCG
Uptravi TABS 1200MCG
Uptravi TABS 1400MCG
Uptravi TABS 1600MCG
Uptravi TABS 200MCG
Uptravi TABS 400MCG
Uptravi TABS 600MCG
Uptravi TABS 800MCG
Uptravi TBPK 200 & 800MCG
Veletri SOLR 0.5MG
Veletri SOLR 1.5MG
Ventavis SOLN 10MCG/ML
Ventavis SOLN 20MCG/ML

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