

MEDICATION COVERAGE POLICY



PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

| | | | |
|----------------|------------------------|------------------------|---------------------------|
| POLICY: | Pulmonary Hypertension | P&T DATE: | 3/11/2025 |
| CLASS: | Respiratory Disorders | REVIEW HISTORY: | 12/22, 12/21, 9/20, 5/19, |
| LOB: | MCL | (month/year) | 5/18, 12/16, 11/15, 5/13 |

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the Health Plan of San Joaquin/Mountain Valley Health Plan (Health Plan) Pharmacy and Therapeutic Advisory Committee.

Effective 1/1/2022, the Pharmacy Benefit is regulated by Medi-Cal Rx. Please visit <https://medi-calrx.dhcs.ca.gov/home/> for portal access, formulary details, pharmacy network information, and updates to the pharmacy benefit.

All medical claims require that an NDC is also submitted with the claim. If a physician administered medication has a specific assigned CPT code, that code must be billed with the correlating NDC. If there is not a specific CPT code available for a physician administered medication, the use of unclassified CPT codes is appropriate when billed with the correlating NDC.

OVERVIEW

The purpose of this coverage policy is to review the available agents (Table 1) and distinguish where the medications may be billed to. For agents listed for coverage under the medical benefit, this coverage is specific to outpatient coverage only (excludes emergency room and inpatient coverage).

Table 1: Available Pulmonary Hypertension Agents (Current as of 11/2024)

| CPT code | Generic Name (Brand Name) | Available Strengths | Pharmacy Benefit | Outpatient Medical Benefit (Restrictions) |
|---------------------------------------|---|---|------------------|---|
| Calcium Channel Blockers (CCB) | | | | |
| Dihydropyridine: | | | | |
| -- | Amlodipine (Norvasc) Dose range for PAH: 20 – 30 mg qd | Tablets: 2.5 mg, 5 mg, 10 mg | Yes | No |
| -- | Nifedipine (Adalat CC, Afeditab CR, Nifediac CC, Nifedical XL, Procardia XL) Dose range for PAH: 180 – 240 mg qd | IR capsules: 10 mg, 20 mg 24 Hour ER Tablets: 30 mg, 60 mg, 90 mg XL Tablets: 30 mg, 60 mg, 90 mg | Yes | No |
| Non-Dihydropyridine: | | | | |
| -- | Diltiazem (Cardizem, Cardizem CD, Cardizem LA, Cartia XT, Dilacor XR, Dilt-XR, Martizem LA, Tiazac XC) Dose range for PAH: 720 – 960 mg qd | CD Capsules: 120 mg, 180 mg, 240 mg, 300mg, 360 mg XR capsules: 120 mg, 180 mg, 240 mg 12 Hour ER Capsules: 60 mg, 90 mg, 120 mg 24 Hour ER Capsules: 120 mg, 180 mg, 240 mg, 300 mg, 360 mg, 420 mg IR Tablets: | Yes | No |

| | | | | |
|--|--|--|-----|--------------------------|
| | | 30mg, 60 mg, 90 mg, 120 mg ER Tablets: 180 mg, 240 mg, 300 mg, 360 mg Cardizem LA Tablets: 120 mg Cartia XT Capsules: 120 mg, 180 mg, 240 mg, 300 mg Taztia XT Capsules: 120 mg, 180 mg, 240 mg, 360 mg Matzim LA Tablets: 180 mg, 240 mg | | |
| Phosphodiesterase-5 Inhibitors (PDE-5i) | | | | |
| S0090 | Sildenafil (Revatio) Dose range for PAH: 20 mg every 8 hours, up to 80 mg every 8 hours | Tablets: 20 mg, Intravenous solution: 10 mg/12.5 mL | Yes | Yes, for IV only |
| -- | Tadalafil (Adcirca) | Tablets: 5 mg, 20 mg | Yes | No |
| Endothelin Receptor Antagonists (ERA) | | | | |
| -- | Bosentan (Tracleer) | Tablets: 62.5 mg, 125 mg Tablet, Dispersible: 32 mg | Yes | No |
| -- | Ambrisentan (Letairis) | Tablets: 5 mg, 10 mg | Yes | No |
| -- | Macitentan (Opsumit) | Tablets: 10 mg | Yes | No |
| -- | Macitentan and tadalafil (Opsynvi) | Tablets: 10-20 mg, 10-40 mg | Yes | No |
| Prostanoids | | | | |
| J1325 | Epoprostenol (Flolan, Veletri) | IV Solution: 0.5mg, 1.5mg | Yes | Yes (PA) |
| Q4074 | Iloprost Tromethamine (Ventavis) | Inhalation Solution: 10 mcg/mL, 20 mcg/mL | Yes | No |
| J3285 for SQ or IV use | Treprostinil (Orenitram; Remodulin; Tyvaso) | Remodulin (IV or SQ): 1 mg/mL, 2.5 mg/mL, 5 mg/mL, 10 mg/mL Orenitram ER tablets: 0.125mg, 0.25 mg, 1 mg, 2.5mg, 5 mg Tyvaso Inhalation: Starter Kit (includes nebulizer). Refill Kit | Yes | Yes, for IV/SQ only (PA) |
| -- | Riociguat (Adempas) | Tablets: 0.5 mg, 1 mg, 1.5 mg, 2 mg, 2.5 mg | Yes | No |
| -- | Selexipag (Uptravi) | Tablets: 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1,000 mcg, 1,200 mcg, 1,400 mcg, 1,600 mcg, 200 mcg- 800mcg Therapy Pack Solution (reconstituted): 1800 mcg | Yes | Yes, for IV only (PA) |

| Activin Receptor Ligand Trap | | | | |
|------------------------------|-------------------------------------|---|-----|----|
| -- | Sotatercept-csrk (Winrevair) | Subcutaneous injection kit: 2 x 45 mg, 2 x 60 mg | Yes | No |

PA=prior authorization, IV=intravenous, SQ=Subcutaneous, IR=Immediate-release, XL, XR, XT=Extended-release, LA=Long-acting

Clinical Justification:

Diagnosis of Pulmonary Hypertension requires Right Heart Catheterization (RHC)⁵. Following the current pulmonary arterial hypertension (PAH) recommendations, Health Plan has set RHC and vasoreactivity test as a part of the requirements and restricts medications based on clinical evidence. Calcium channel blockers (CCB) are the preferred agents in patients who can tolerate them, and who have shown good response during right heart catheterization, unless contraindicated. Drugs are restricted based on World Health Organization (WHO) Functional Class (FC) and patient's prior use of PAH medications. Endothelin Receptor Antagonists (ERA) are not benign drugs. They are teratogenic, can potentially cause liver function test (LFT) elevations in patients who take them chronically, and can cause fluid retention. Sildenafil is widely available and relatively benign, thus carries few restrictions, while intravenous prostanoids carry significant risk, and should not be used unless all other therapeutic agents have been exhausted. Although the 2019 American College of Chest Physicians (CHEST) Guidelines suggest Ambrisentan and Tadalafil as an initial therapy for WHO FC II and III, this is a weak recommendation resulting from borderline clinically significant improvement in 6-min walk distance (6MWD), no change in WHO FC, variabilities of end points in clinical trial and studies; the guidelines do not prefer one regimen over the other in this treatment group.

The 2022 European Society of Cardiology and European Respiratory Society (ESC/ERS) Guidelines for Pulmonary Hypertension also indicate similar treatment strategies for idiopathic, heritable, drug-associated, or connective tissue disease-associated pulmonary arterial hypertension, stratified based on risk level.

Medications (e.g. Winrevair) that may be self-administered per their respective package inserts will be excluded from the medical benefit.

EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for agents with medical benefit restrictions. This coverage criteria has been reviewed and approved by the Health Plan Pharmacy & Therapeutics (P&T) Advisory Committee. For agents that do not have established prior authorization criteria, Health Plan will make the determination based on Medical Necessity criteria as described in Health Plan Medical Review Guidelines (UM06).

Phosphodiesterase-5 Inhibitors (PDE-5i): Sildenafil, Tadalafil

Sildenafil (Revatio) IV

- ☐ **Coverage Criteria:** Reserved for patients with WHO FC II-IV with: (-) vasoreactivity test **OR** (+) vasoreactivity test and dose optimized Calcium Channel Blocker (CCB) for 3 months.
- ☐ **Limits:** None
- ☐ **Required Information for Approval:** Basic criteria as listed above plus all of the following: clinical documentation of inadequate response to dose optimized CCB for 3 months evidenced by worsening of symptoms (i.e. decline in 6MWD) and pharmacy fill history.

Prostanoids: Epoprostenol, Iloprost, Treprostinil

Epoprostenol (Flolan, Velettri), Treprostinil (Remodulin)

- ☐ **Coverage Criteria:**
 - [1] WHO FC IV **OR**
 - [2] Inadequate response to dose optimized PDE-5i and Endothelin Receptor Antagonists (ERA) for 3 months for (-) vasoreactive patients **OR**
 - [3] Inadequate response to dose optimized Calcium Channel Blocker (CCB) plus Phosphodiesterase-5 Inhibitors (PDE-5i) AND Endothelin Receptor Antagonists (ERA) for 3 months for (+) vasoreactivity test **OR**
 - [4] Patients with clinical evidence of Right Ventricle (RV) failure or moderate to rapid rate of progression of symptoms/disease

- ☐ **Limits:** None
- ☐ **Required Information for Approval:** Basic criteria as listed above, clinical documentation of inadequate response evidenced by worsening of symptoms (i.e. decline in 6MWD), and pharmacy fill history or clinical evidence of Right Ventricle (RV) failure or moderate to rapid rate of progression of symptoms/disease

Treprostinil Inhalation (Tyvaso)

- ☐ **Coverage Criteria:** WHO FC III AND one of the following:
 - [1] Inadequate response to dose optimized Phosphodiesterase-5 Inhibitors (PDE-5i) and Endothelin Receptor Antagonists (ERA) for 3 months for (-) vasoreactive patients **OR**
 - [2] Inadequate response to dose optimized Calcium Channel Blocker (CCB) plus Phosphodiesterase-5 Inhibitors (PDE-5i) AND Endothelin Receptor Antagonists (ERA) for 3 months for (+) vasoreactive patients **OR**
 - [3] Contraindication to Phosphodiesterase-5 Inhibitors (PDE-5i), Riociguat and Endothelin Receptor Antagonists (ERA).
- ☐ **Limits:** None
- ☐ **Required Information for Approval:** Basic criteria as listed above, clinical documentation of inadequate response evidenced by worsening of symptoms (i.e. decline in 6MWD), and pharmacy fill history +/- documentation of the nature of contraindication

Prostacyclin IP Receptor Agonist: Selexipag (Uptravi)

Selexipag (Uptravi)

- ☐ **Coverage Criteria:** WHO FC III to IV AND one of the following:
 - [1] Inadequate response to dose optimized Phosphodiesterase-5 Inhibitors (PDE-5i) and Endothelin Receptor Antagonists (ERA) for 3 months for (-) vasoreactive patients **OR**
 - [2] Inadequate response to dose optimized Calcium Channel Blocker (CCB) plus Phosphodiesterase-5 Inhibitors (PDE-5i) AND Endothelin Receptor Antagonists (ERA) for 3 months for (+) vasoreactivity test **OR**
 - [3] Contraindication to PDE-5i, Riociguat, and Endothelin Receptor Antagonists (ERA).
- ☐ **Limits:** None
- ☐ **Required Information for Approval:** Basic criteria plus specific coverage criteria clinical documentation of inadequate response evidenced by worsening of symptoms (i.e. decline in 6MWD), and pharmacy fill history +/- documentation of the nature of contraindication.

REFERENCES

1. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, Brida M, et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Respir J*. (2022) 43:3618–731. 10.1183/13993003.00879-20228
2. Sitbon O., Channick R., Chin KM, et al. Selexipag for the Treatment of Pulmonary Arterial Hypertension. *N Engl J Med* 2015; 373:2522-33
3. Galiè N, Humbert M, Vachiery JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J*. 2016; 37(1):67-119.
4. Whelton PK, Carey RM, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults, Journal of the American College of Cardiology (2017), doi: 10.1016/j.jacc.2017.11.006
5. Hoeper MM et al. Definitions and diagnosis PH. *JACC* 2013; 62:D42-50.
6. Burger C, Pulmonary Hypertension Guidelines 5th World Symposium. *Am Coll Cardiol* 2009; 53:1573-1619.
7. Galiè N et al. Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J* 2009; 30:2493-537.
8. Gaile N, Corris PA, Frost A, et al. Updated treatment algorithm of pulmonary arterial hypertension. *J AM Coll Cardiol* 2013;62:D60-72

9. McLaughlin V, Badesch D, Barst R, et. al. ACCF/AHA 2009 Expert consensus document on pulmonary hypertension: a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association. *Circulation*. 2009;119:2250 –2294.
10. Galie N, Barbera J, Frost A, et al. Initial use of Ambrisentan plus Tadalafil in Pulmonary Arterial Hypertension. August 27, 2015 *N Engl J Med* 2015; 373:834-844 DOI: 10.1056/NEJMoa1413687
11. Taichman D., Ornelas J., Chung L., et al. Pharmacologic Therapy for Pulmonary Arterial Hypertension in Adults CHEST Guideline and Expert Panel Report. *CHEST* 2014; 146 (2): 449 – 475
12. Falk J., Phillip K., and Schwarz R., The emergence of oral tadalafil as a once-daily treatment for pulmonary arterial hypertension. *Vasc Health Risk Manag*. 2010; 6: 273–280.
13. Lajoie AC, Lauzière G, Lega J., et. al., Combination therapy versus monotherapy for pulmonary arterial hypertension: a meta-analysis. *Lancet Respir Med*. 2016 Apr;4(4):291-305. doi: 10.1016/S2213-2600(16)00027-8. Epub 2016 Feb 27.
14. Galie N, Brundage BH, Ghofrani HA., et. al., Pulmonary Arterial Hypertension and Response to Tadalafil (PHIRST) Study Group. Possible blunting effect of Bosentan on Tadalafil due to Drug drug interactions -- Tadalafil therapy for pulmonary arterial hypertension. *Circulation*. 2009 Jun 9; 119(22):2894-903.
15. J Klinger, C Elliot, D Levine et al., Therapy for Pulmonary Arterial Hypertension in Adults Update of the CHEST Guideline and Expert Panel Report. *CHEST* 2019; 155(3):565-586.
16. Galie N, McLaughlin VV, Rubin LJ, et al. An overview of the 6th World Symposium on Pulmonary Hypertension. *Eur Respir J* 2019; 53: 1802148 [https://doi.org/10.1183/13993003.02148-2018].
17. Simonneau G, Montani D, Celermajer DS, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. *Eur Respir J* 2019;53:1801913.
18. Frost A, Badesch D, Gibbs JSR, et al. Diagnosis of pulmonary hypertension. *Eur Respir J* 2019; 53: 1801904 [https://doi.org/10.1183/13993003.01904-2018].
19. Galie N, Channick RN, Frantz RP, et al. Risk stratification and medical therapy of pulmonary arterial hypertension. *Eur Respir J* 2019; 53 1801889 [https://doi.org/10.1183/13993003.01889-2018].
20. WINREVAIR™ (sotatercept-csrk) [prescribing information]. Rahway, JK: Merck & Co, Inc.; March 2024.

REVIEW & EDIT HISTORY

| Document Changes | Reference | Date | P&T Chairman |
|-------------------------|--|-------------|-----------------------------------|
| Creation of Policy | PAH Class Review 5-21-2013.docx | 5/2013 | Jonathan Szkotak, PharmD BCACP |
| Update Policy | Drug Class Review – Respiratory disorders – Pulmonary Hypertension 2015-11.docx | 11/2015 | Johnathan Yeh, PharmD |
| Update Policy | HPSJ Coverage Policy – Respiratory disorders – Pulmonary Hypertension 2016-12.docx | 12/2016 | Johnathan Yeh, PharmD |
| Update Policy | HPSJ Coverage Policy – Respiratory disorders – Pulmonary Hypertension 2018-05.docx | 5/2018 | Johnathan Yeh, PharmD |
| Update Policy | HPSJ Coverage Policy – Respiratory disorders – Pulmonary Hypertension 2019-05.docx | 5/2019 | Matthew Garrett, PharmD |
| Review of Policy | Pulmonary Hypertension | 9/2020 | Matthew Garrett, PharmD |
| Review of Policy | Pulmonary Hypertension | 12/2021 | Matthew Garrett, PharmD |
| Review of Policy | Pulmonary Hypertension | 12/2022 | Matthew Garrett, PharmD |
| Review of Policy | Pulmonary Hypertension | 01/2024 | Matthew Garrett, PharmD |
| Review of Policy | Pulmonary Hypertension | 03/2025 | Matthew Garrett, PharmD |

Note: All changes are approved by the Health Plan P&T Committee before incorporation into the utilization policy