Market Applicability															
Market	**DC**	**FL & FHK**	**FL MMA**	**FL LTC**	**GA**	**KS**	**KY**	**LA**	**MD**	**NJ**	**NV**	**NY**	**TN**	**TX**	**WA**
Applicable	X	X	NA	NA	X	NA	X	X	X	X	X	X	NA	NA	NA

*FHK- Florida Healthy Kids

Prostacyclins for Pulmonary Arterial Hypertension

CG-DRUG-82

Override(s)	Approval Duration
Prior Authorization Quantity Limit	1 year

Medications	Line of Business Criteria Applies	Quantity limit
Flolan (epoprostenol sodium) Remodulin (treprostinil) Veletri (epoprostenol)	AGP, VA MCD	N/A
Tyvaso (treprostinil) Ventavis (iloprost)	All MCD	May be subject to quantity limit

APPROVAL CRITERIA

Diagnostic Criteria for adult and pediatric Pulmonary Arterial Hypertension (PAH):

Right heart catheterization which shows a mean pulmonary artery pressure (mPAP) greater than or equal to 25 mm Hg at rest; a pulmonary capillary wedge pressure (PCWP), mean pulmonary artery wedge pressure (PAWP), left atrial pressure, or left ventricular end-diastolic pressure (LVEDP) less than or equal to 15 mm Hg; and a pulmonary vascular resistance (PVR) greater than 3 Wood units (ACCF/AHA Hoeper, 2013; Ivy, 2013; AHA/ATS Abman, 2015).

Criteria for Vasodilator Response:

A favorable response is defined as a fall in mPAP of at least 10 mm Hg to an absolute mPAP of less than 40 mm Hg without a decrease in cardiac output, when challenged with inhaled nitric oxide, intravenous epoprostenol or intravenous adenosine.

I. Continuous intravenous infusion of epoprostenol sodium (prostacyclin, PGI2, Veletri, Flolan) **may be approved** as treatment for individuals who meet **all** of the following criteria:
   - Meets the diagnostic criteria for PAH (above); **AND**
   - Demonstrates an unfavorable acute response to vasodilators; **AND**
   - Meets one of the following selection criteria with New York Heart Association functional Class III or IV symptoms:

Market Applicability															
Market	**DC**	**FL & FHK**	**FL MMA**	**FL LTC**	**GA**	**KS**	**KY**	**LA**	**MD**	**NJ**	**NV**	**NY**	**TN**	**TX**	**WA**
Applicable	X	X	NA	NA	X	NA	X	X	X	X	X	X	NA	NA	NA

*FHK- Florida Healthy Kids

World Health Organization (WHO) Group I idiopathic pulmonary arterial hypertension including all subtypes of WHO Group I PAH; **or**
Pulmonary hypertension associated with connective tissue disorders (e.g., scleroderma, systemic sclerosis, etc.); **or**
Pulmonary hypertension associated with congenital heart defects.

II. Continuous **subcutaneous infusion** of **treprostinil sodium (Remodulin) may be approved** as a treatment for individuals who meet **all** of the following criteria:
- Meets the diagnostic criteria for PAH (above); **AND**
- Demonstrates an unfavorable acute response to vasodilators; **AND**
- Meets one of the following selection criteria with New York Heart Association functional Class II, III, or IV symptoms:

  World Health Organization (WHO) Group I idiopathic pulmonary arterial hypertension including all subtypes of WHO Group I PAH; **or**
  Pulmonary hypertension associated with connective tissue disorders (e.g. scleroderma, systemic sclerosis, etc.); **or**
  Pulmonary hypertension associated with congenital heart defects.

III. Continuous **intravenous infusion** of **treprostinil sodium (Remodulin) may be approved** for treatment of individuals who meet criteria for treprostinil treatment above when there is a documented inability to tolerate treatment by subcutaneous infusion.

IV. **Inhalation therapy** with **iloprost (Ventavis) Inhalation Solution or Tyvaso Inhalation Solution* (treprostinil)** may be approved as a treatment for individuals who meet **all** of the following criteria:
- Meets the diagnostic criteria for PAH above; **AND**
- Demonstrates an unfavorable acute response to vasodilators; **AND**
- Meets one of the following selection criteria with New York Heart Association (NYHA) Functional Class III or IV symptoms:

  World Health Organization (WHO) Group I idiopathic pulmonary arterial hypertension including all subtypes of WHO Group I PAH; **or**
  Pulmonary hypertension associated with connective tissue disorders (e.g., scleroderma, systemic sclerosis, etc.); **or**
  Pulmonary hypertension associated with congenital heart defects.

***FDA approved labeling for Tyvaso (treprostinil) inhalation solution states for use in the treatment of pulmonary arterial hypertension (WHO Group I) in individuals with NYHA Class III symptoms, to increase walk distance (FDA, 2009).

Market Applicability															
Market	**DC**	**FL & FHK**	**FL MMA**	**FL LTC**	**GA**	**KS**	**KY**	**LA**	**MD**	**NJ**	**NV**	**NY**	**TN**	**TX**	**WA**
Applicable	X	X	NA	NA	X	NA	X	X	X	X	X	X	NA	NA	NA

*FHK- Florida Healthy Kids

V. Continuous infusion of **epoprostenol or treprostinil may be approved** for individuals with severe pulmonary arterial hypertension refractory to medical therapy with calcium channel blockers.

World Health Organization (WHO) - functional classification for pulmonary arterial hypertension
Class I: no limitation of clinical activity; ordinary physical activity does not cause dyspnea or fatigue; **Class II:** slight limitation in physical activity; ordinary physical activity produces dyspnea, fatigue, chest pain, or near-syncope; no symptoms at rest; **Class III:** marked limitation of physical activity; less than ordinary physical activity produces dyspnea, fatigue, chest pain, or near-syncope; no symptoms at rest; **Class IV:** unable to perform any physical activity without symptoms; dyspnea and/or fatigue present at rest; discomfort increased by any physical activity (Rich, 1998).

World Health Organization (WHO) – group classification of pulmonary hypertension (PH)			
1.	Pulmonary arterial hypertension (PAH)		
	1.1.	Idiopathic (IPAH)	
	1.2.	Familial (FPAH)	
	1.3.	Associated with (APAH):	
		1.3.1.	Connective tissue disorder
		1.3.2.	Congenital systemic-to-pulmonary shunts
		1.3.3.	Portal hypertension
		1.3.4.	HIV infection

Market Applicability															
Market	**DC**	**FL & FHK**	**FL MMA**	**FL LTC**	**GA**	**KS**	**KY**	**LA**	**MD**	**NJ**	**NV**	**NY**	**TN**	**TX**	**WA**
Applicable	X	X	NA	NA	X	NA	X	X	X	X	X	X	NA	NA	NA

*FHK- Florida Healthy Kids

		1.3.5.	Drugs and toxins
		1.3.6.	Other (thyroid disorders, glycogen storage disease, Gaucher's disease, hereditary hemorrhagic telangiectasia, hemoglobinopathies, chronic myeloproliferative disorders, splenectomy)
	1.4.	Associated with significant venous or capillary involvement	
		1.4.1.	Pulmonary veno-occlusive disease (PVOD)
		1.4.2.	Pulmonary capillary hemangiomatosis (PCH)
	1.5.	Persistent pulmonary hypertension of the newborn (PPHN)	
2.	Pulmonary hypertension associated with left heart diseases		
	2.1.	Left-sided atrial or ventricular heart disease	
	2.2.	Left-sided valvular heart disease	
3.	Pulmonary hypertension associated with respiratory diseases and/or hypoxemia (including COPD)		
	3.1.	Chronic obstructive pulmonary disease	
	3.2.	Interstitial lung disease	
	3.3.	Sleep disordered breathing	
	3.4.	Alveolar hypoventilation disorders	
	3.5.	Chronic exposure to high altitude	
	3.6.	Developmental abnormalities	
4.	Pulmonary hypertension due to chronic thrombotic and/or embolic disease (CTEPH)		

Market Applicability															
Market	**DC**	**FL & FHK**	**FL MMA**	**FL LTC**	**GA**	**KS**	**KY**	**LA**	**MD**	**NJ**	**NV**	**NY**	**TN**	**TX**	**WA**
Applicable	X	X	NA	NA	X	NA	X	X	X	X	X	X	NA	NA	NA

*FHK- Florida Healthy Kids

	4.1.	Thromboembolic obstruction of proximal pulmonary arteries
	4.2.	Thromboembolic obstruction of distal pulmonary arteries
	4.3.	Nonthrombotic pulmonary embolism (tumor, parasites, foreign material)
5.	Miscellaneous	
	Sarcoidosis, histiocytosis X, lymphangiomatosis, compression of pulmonary vessels (adenopathy, tumor, fibrosing mediastinitis).	

<u>May not</u> be approved for the following:

Use of epoprostenol, treprostinil or iloprost **<u>may not</u> be approved** as treatment for individuals appropriate for treatment with calcium channel blockers:

- Individuals who demonstrate a favorable acute hemodynamic response to vasodilators at cardiac catheterization who are deemed appropriate by the treating physician for a trial of calcium channel blocker treatment, **or**
- Individuals who demonstrated a favorable acute hemodynamic response to vasodilators but have not become refractory to, or unable to, tolerate therapeutic doses of calcium channel antagonists.

Continuous intravenous infusion of treprostinil sodium (Remodulin) **<u>may not</u> be approved** *for treatment of individuals when inability to tolerate treatment by subcutaneous infusion has not been documented.*

The use of epoprostenol, treprostinil, or iloprost **<u>may not</u> be approved** for all other applications in the absence of WHO Group I PAH including those with WHO Group II to V pulmonary hypertension and for other causes of pulmonary hypertension, including, but not limited to, left ventricular failure, left sided valvular heart disease, chronic pulmonary diseases, and alveolar hypoventilation syndromes.

State Specific Mandates

This policy does not apply to health plans or member categories that do not have pharmacy benefits, nor does it apply to Medicare. Note that market specific restrictions or transition-of-care benefit limitations may apply.

Market Applicability															
Market	**DC**	**FL & FHK**	**FL MMA**	**FL LTC**	**GA**	**KS**	**KY**	**LA**	**MD**	**NJ**	**NV**	**NY**	**TN**	**TX**	**WA**
Applicable	X	X	NA	NA	X	NA	X	X	X	X	X	X	NA	NA	NA

*FHK- Florida Healthy Kids

State name	Date effective	Mandate details (including specific bill if applicable)
N/A	N/A	N/A

Key References:

1. Abman SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: guidelines from the American Heart Association and American Thoracic Society. Circulation. 2015; 132(21):2037-2099.
2. American Hospital Formulary Service® (AHFS). AHFS Drug Information 2014®. Bethesda, MD: American Society of Health-Systems Pharmacists®, 2014.
3. Badesch BD, Abman SH, Simonneau G, et al. Medical therapy for pulmonary arterial hypertension: updated ACCP evidence-based clinical practice guidelines. Chest. 2007; 131(6):1917-1928.
4. Barst RJ, Gibbs JS, Ghofrani HA, et al. Updated evidence based treatment algorithm in pulmonary arterial hypertension. J Am Coll Cardiol. 2009; 54(Suppl 1):S78-84.
5. Epoprostenol sodium. In: DrugPoints® System (electronic version). Truven Health Analytics, Greenwood Village, CO. Updated December 30, 2017. Available at: http://www.micromedexsolutions.com. Accessed on December 31, 2017.
6. Fleming T, Lindenfeld J, Lipicky R, et al. Report from the 93rd Cardiovascular and Renal Drugs Advisory Committee Meeting, August 9-10, 2001. Circulation. 2001; 104(15):1742.
7. Flolan [Product Information], Research Triangle Park, NC, GlaxoSmithKline; March 29, 2011. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2011/020444s018lbl.pdf. Accessed on December 31, 2017.
8. Galie N, Corris PA, Frost A, et al. Updated treatment algorithm of pulmonary arterial hypertension. J Am Coll Cardiol. 2013; 62(25 Suppl):D60-72.
9. Galiè N, Humbert M, Vachiery JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Pediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). Eur Heart J. 2016; 37(1):67-119.
10. Hoeper MM, Bogaard HJ, Condliffe R, et al. Definitions and Diagnosis of Pulmonary Hypertension. J Am Coll Cardiol. 2013; 62(suppl 25):D42- D50. Available at: http://www.onlinejacc.org/content/62/25_Supplement/D42. Accessed on December 30, 2017.
11. Iloprost inhalation solution. In: DrugPoints System (electronic version). Truven Health Analytics, Greenwood Village, CO. Updated December 30, 2017. Available at: http://www.micromedexsolutions.com. Accessed on December 31, 2017.
12. Ivy DD, Abman SH, Barst RJ, et al. Pediatric Pulmonary Hypertension. J Am Coll Cardiol. 2013; 62(suppl 25):D117- D126. Available from: http://www.onlinejacc.org/content/62/25_Supplement/D117. Accessed on December 30, 2017.
13. McCrory DC, Coeytaux RR, Schmit KM, et al. Pulmonary arterial hypertension: screening, management, and treatment [Internet]. Comparative Effectiveness Review No. 117. (Prepared by the Duke Evidence based Practice Center under Contract No. 290-2007-10066-I.). AHRQ Publication No. 13-EHC087-EF. Rockville (MD): Agency for Healthcare Research and Quality (US); 2013 April.
14. McLaughlin VV, Archer SL, Badesch DB, 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. J Am Coll Cardiol. 2009; 53:1573-1619. Available at: http://circ.ahajournals.org/content/119/16/2250.full.pdf+html. Accessed on December 31, 2017.
15. National Institutes of Health (NIH). National Heart Lung and Blood. Patient Registry for Primary Pulmonary Hypertension (PPH Registry). Ann Intern Med. 1987; 107:216-223; Ann Intern Med. 1991; 115:343-349. Last updated June 23, 2005. Available at: https://biolincc.nhlbi.nih.gov/studies/pphreg/?q=Pulmonary%20hypertension. Accessed on December 31, 2017.
16. Paramothayan NS, Lasserson TJ, Wells AU, Walters EH. Prostacyclin for pulmonary hypertension in adults. Cochrane Database Syst Rev. 2005; (2):CD002994.

This policy does not apply to health plans or member categories that do not have pharmacy benefits, nor does it apply to Medicare. Note that market specific restrictions or transition-of-care benefit limitations may apply.

Market Applicability															
Market	**DC**	**FL & FHK**	**FL MMA**	**FL LTC**	**GA**	**KS**	**KY**	**LA**	**MD**	**NJ**	**NV**	**NY**	**TN**	**TX**	**WA**
Applicable	X	X	NA	NA	X	NA	X	X	X	X	X	X	NA	NA	NA

*FHK- Florida Healthy Kids

17. Pohar R, Clark M, Spry C. Drugs for pulmonary arterial hypertension: a systematic review of the clinical-effectiveness of combination therapy. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2009.
18. Rich S, Rubin LJ, Abenhaim L, et al. Executive summary from the World Health Organization world symposium on primary pulmonary hypertension 1998. World Health Organization. Evian, France: 1998; 6-10.
19. Remodulin [Product Information], Research Triangle Park, NC. United Therapeutics Corporation; September 26, 2013. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/021272s020lbledt.pdf. Accessed on December 31, 2017.
20. Simonneau G, Galie N, Rubin LJ, et al. Clinical classification of pulmonary hypertension. J Am Coll Cardiol. 2004; 43(12 Suppl S):5S-12S.
21. Simonneau G, Gatzoulis MA, Adatia I, et al. Updated clinical classification of pulmonary hypertension. J Am Coll Cardiol. 2013; 62(25 Suppl):D34-41.
22. Simonneau G, Robbins IM, Beghetti M, et al. Updated classification of pulmonary hypertension. J Am Coll Cardiol 2009; 54(1 suppl):S43-54.
23. Taichman DB, Ornelas J, Chung L, et al. American College of Chest Physicians (ACCP). Pharmacologic therapy for pulmonary arterial hypertension in adults: CHEST Guideline and Expert Panel Report. Chest. 2014; 146 (2): 449-475.
24. Treprostinil. In: DrugPoints System (electronic version). Truven Health Analytics, Greenwood Village, CO. Updated December 30, 2017. Available at: http://www.micromedexsolutions.com. Accessed on December 31, 2017.
25. Tyvaso [Product Information], Research Triangle Park, NC. United Therapeutics Corporation; Updated October 2017. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/022387s015lbl.pdf. Accessed on December 31, 2017.
26. Veletri [Product Information], Actelion Pharmaceuticals US, Inc. South San Francisco, CA; July, 2016. Available at: https://www1.actelion.us/documents/us/product-documentation/veletri-(epoprostenol-for-injection)-prescribing-information.pdf. Accessed on December 31, 2017.
27. Ventavis [Product Information], Actelion Pharmaceuticals US, Inc. South San Francisco, CA; Updated October 2017. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/021779s018lbl.pdf Accessed on December 31, 2017.

This policy does not apply to health plans or member categories that do not have pharmacy benefits, nor does it apply to Medicare. Note that market specific restrictions or transition-of-care benefit limitations may apply.