Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	NA

Prostacyclins for Pulmonary Arterial Hypertension

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

Medications	Quantity limit
Flolan (epoprostenol sodium) Remodulin (treprostinil) Veletri (epoprostenol)	N/A
Tyvaso (treprostinil) Ventavis (iloprost)	May be subject to quantity limit

APPROVAL CRITERIA

Epoprostenol Agents (Flolan, Veletri)

Requests for continuous **intravenous** infusion of epoprostenol (Flolan, Veletri) may be approved if the following criteria are met:

I. Individual has a diagnosis of pulmonary arterial hypertension (PAH) confirmed by right-heart catheterization showing all of the following (Hoeper, 2013; Ivy, 2013; Abman, 2015):
   A. Mean pulmonary artery pressure (mPAP) greater than or equal to 25 mm Hg at rest; **AND**
   B. 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**
   C. Pulmonary vascular resistance (PVR) greater than 3 Wood units;

AND

II. Individual demonstrated an unfavorable acute response to vasodilators (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) (Badesch, 2007; McLaughlin, 2009); **OR**

III. Individual demonstrated a favorable acute response to vasodilators but has become refractory to or is unable to tolerate therapeutic doses of calcium channel blockers;

AND

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	NA

IV. Individual has World Health Organization (WHO) Group I PAH (idiopathic PAH, PAH associated with connective tissue disorders, PAH associated with congenital heart defects, and all Group 1 subtypes);

AND

V. Individual has New York Heart Association Functional Class III or IV symptoms.

Continuous **intravenous** infusion epoprostenol (Flolan, Veletri) may **not** be approved for the following:

I. All other indications not included above; **OR**
II. Individual with WHO Group II-V pulmonary hypertension; **OR**
III. Individual demonstrated a favorable acute response to vasodilators at cardiac catheterization (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) and is deemed appropriate by the treating physician for a trial of calcium channel blocker treatment; **OR**
IV. Individuals with heart failure due to severe left ventricular systolic dysfunction.

Remodulin (treprostinil)

Requests for continuous **subcutaneous** infusion of Remodulin (treprostinil) may be approved if the following criteria are met:

I. Individual has a diagnosis of pulmonary arterial hypertention (PAH) confirmed by right-heart catheterization showing all of the following (Hoeper, 2013; Ivy, 2013; Abman, 2015):
   A. Mean pulmonary artery pressure (mPAP) greater than or equal to 25 mm Hg at rest; **AND**
   B. 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**
   C. Pulmonary vascular resistance (PVR) greater than 3 Wood units;

AND

II. Individual demonstrates an unfavorable acute response to vasodilators (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

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	NA

oxide, intravenous epoprostenol or intravenous adenosine) (Badesch, 2007; McLaughlin, 2009);

OR

III. Individual demonstrated a favorable acute response to vasodilators but has become refractory to or is unable to tolerate therapeutic doses of calcium channel blockers;

AND

IV. Individual has World Health Organization (WHO) Group I PAH (idiopathic PAH, PAH associated with connective tissue disorders, PAH associated with congenital heart defects, and all Group 1 subtypes);

AND

V. Individual has New York Heart Association Functional Class II, III or IV symptoms.

Requests for continuous **intravenous** infusion of Remodulin (treprostinil) may be approved if the following criteria are met:

I. Individual has a diagnosis of pulmonary arterial hypertension (PAH) confirmed by a right-heart catheterization showing all of the following (Hoeper, 2013; Ivy, 2013; Abman, 2015):
   A. Mean pulmonary artery pressure (mPAP) greater than or equal to 25 mm Hg at rest; **AND**
   B. 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**
   C. Pulmonary vascular resistance (PVR) greater than 3 Wood units;

AND

II. Individual demonstrated an unfavorable acute response to vasodilators (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) (Badesch, 2007; McLaughlin, 2009);

OR

III. Individual demonstrated a favorable acute response to vasodilators but has become refractory to or is unable to tolerate therapeutic doses of calcium channel blockers;

AND

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	NA

IV. Individual has World Health Organization (WHO) Group I PAH (idiopathic PAH, PAH associated with connective tissue disorders, PAH associated with congenital heart defects, including and all Group 1 subtypes);

AND

V. Individual has New York Heart Association Functional Class II, III or IV symptoms;

AND

VI. Individual has confirmed inability to tolerate treatment by subcutaneous infusion of Remodulin.

Continuous subcutaneous or **intravenous** infusion of Remodulin (treprostinil) may **not** be approved for the following:

I. All other indications not included above; **OR**
II. Individual with WHO Group II-V pulmonary hypertension; **OR**
III. Individual demonstrated a favorable acute response to vasodilators at cardiac catheterization (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) and is deemed appropriate by the treating physician for a trial of calcium channel blocker treatment.

Tyvaso (treprostinil) and Ventavis (iloprost)

Requests for **inhalation** therapy with Tyvaso (treprostinil) or Ventavis (iloprost) may be approved if the following criteria are met:

I. Individual has a diagnosis of pulmonary arterial hypertension (PAH) confirmed by a right-heart catheterization showing all of the following (Hoeper, 2013; Ivy, 2013; Abman, 2015):
   A. Mean pulmonary artery pressure (mPAP) greater than or equal to 25 mm Hg at rest; **AND**
   B. 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**
   C. Pulmonary vascular resistance (PVR) greater than 3 Wood units;

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	NA

AND

II. Individual demonstrated an unfavorable acute response to vasodilators (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) (Badesch, 2007; McLaughlin, 2009);
OR
III. Individual demonstrated a favorable acute response to vasodilators but has become refractory to or is unable to tolerate therapeutic doses of calcium channel blockers;

AND

IV. Individual has World Health Organization (WHO) Group I PAH (idiopathic PAH, PAH associated with connective tissue disorders, PAH associated with congenital heart defects, and all Group 1 subtypes);

AND

V. Individual has New York Heart Association Functional Class III or IV symptoms.

Inhalation therapy with Tyvaso (treprostinil) or Ventavis (iloprost) may **not** be approved for the following:

I. All other indications not included above; **OR**
II. Individual with WHO Group II-V pulmonary hypertension; **OR**
III. Individual demonstrated a favorable acute response to vasodilators at cardiac catheterization (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) and is deemed appropriate by the treating physician for a trial of calcium channel blocker treatment.

New York Heart Association (NYHA) Functional Classification for Heart Failure Symptoms
Class I: No limitation with ordinary physical activity **Class II:** Slight limitation with fatigue, dyspnea, palpitations, or angina resulting from ordinary physical activity

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	NA

Class III: Marked limitation; symptomatic with less than ordinary activity
Class IV: Symptoms present while at rest

World Health Organization (WHO) – group classification of pulmonary hypertension (PH) (CHEST 2019)			
1.	Pulmonary arterial hypertension (PAH)		
	1.1	Idiopathic PAH	
	1.2	Heritable PAH	
		1.2.1	*BMPR2*
		1.2.2	*ALK-1, ENG, SMAD9, CAV1, KCNK3*
		1.2.3	Unknown
	1.3	Drug and toxin induced	
	1.4	Associated with	
		1.4.1	Connective tissue disease
		1.4.2	HIV infection
		1.4.3	Portal hypertension
		1.4.4	Congenital heart disease
		1.4.5	Schistosomiasis
1'.	Pulmonary veno-occlusive disease and/or pulmonary capillary hemangiomatosis		
	1'.1	Idiopathic	
	1'.2	Heritable	

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	NA

		1’.2.1	*EIF2AK4* mutation
		1’.2.2	Other mutations
	1’.3	Drugs, toxins, and radiation induced	
	1’.4	Associated with:	
		1’.4.1	Connective tissue disease
		1’.4.2	HIV infection
1’’.	Persistent pulmonary hypertension of the newborn		
2.	Pulmonary hypertension because of left heart diseases		
	2.1	Left ventricular systolic dysfunction	
	2.2	Leftventriculary diastolic dysfunction	
	2.3	Valvular disease	
	2.4	Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies	
3.	Pulmonary hypertension because of lung diseases and/or hypoxemia		
	3.1	Chronic obstructive pulmonary disease (COPD)	
	3.2	Interstitial lung disease	
	3.3	Other pulmonary disease with mixed restrictive and obstructive pattern	
	3.4	Sleep-disordered breathing	
	3.5	Alveolar hypoventilation disorders	
	3.6	Chronic exposure to high altitude	

Market Applicability							
Market	**DC**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	NA

	3.7	Developmental lung diseases	
4.	Chronic thrombotic pulmonary hypertension		
	4.1	Chronic thromboembolic pulmonary hypertension	
	4.2	Other pulmonary artery obstructions	
		4.2.1	Angiosarcoma
		4.2.2	Other intravascular tumors
		4.2.3	Arteritis
		4.2.4	Congenital pulmonary arteries
5.	Pulmonary hypertension with unclear multifactorial mechanisms		
	5.1	Hematologic disorders: chronic hemolytic anemia, myeloproliferative disorders, splenectomy	
	5.2	Systemic disorders: sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis	
	5.3	Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders	
	5.4	Others: tumoral	

Key References:

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2. 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.
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4. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: January 13, 2020.

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**	**GA**	**KY**	**MD**	**NJ**	**NY**	**WA**
Applicable	X	X	X	X	X	X	NA

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