Medical Policy:
Pulmonary Arterial Hypertension (Remodulin, Tyvaso, Veletri, Ventavis)

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.164	January 12, 2024	

Definition

Pulmonary arterial hypertension (PAH) is a progressive disease characterized by elevated pressure in the vessels that carry blood between the heart and the lungs. This results in ventricular dysfunction, reduced exercise capacity, the potential for right sided heart failure, and even death.

Several mechanisms have been identified in the pathogenesis of PAH, leading to the development of four classes of medications to treat the disorder. Endothelin receptor antagonists (ERAs), phosphodiesterase-5 (PDE-5) inhibitors, prostacyclin analogs, and soluble guanylate cyclase (sGC) stimulators may be used as monotherapy, sequential combination therapy, or simultaneous combination therapy to treat PAH.

Remodulin (trepostinil), **Tyvaso** (treprostinil), **Veletri** (epoprostenol), **Ventavis** (iloprost) are prostacyclin analogs.

Remodulin is indicated for the treatment of pulmonary hypertension (WHO Group 1) to diminish symptoms associate with exercise; to diminish the rate of clinical deterioration in patients with PAH requiring transition from epoprostenol.

Tyvaso is indicated for the treatment of pulmonary arterial hypertension (WHO Group 1) to diminish symptoms associated with exercise. Tyvaso is also indicated for the treatment of pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) to improve exercise ability.

Veletri is indicated for the treatment of pulmonary hypertension (WHO Group 1) to improve exercise capacity.

Ventavis is indicated for the treatment of pulmonary hypertension (WHO Group 1) with NYHA class III or IV symptoms to improve a composite endpoint consisting of exercise tolerance, symptoms and lack of deterioration

New York Heart Association (NYHA) functional classification:
Class 1: No symptoms with ordinary physical activity.
Class 2: Symptoms with ordinary activity. Slight limitation of activity.
Class 3: Symptoms with less than ordinary activity. Marked limitation activity.
Class 4: Symptoms with any activity or event at rest

Length of Authorization

Coverage will be provided for 12 months and may be renewed.

Guideline

I. INITIAL APPROVAL CRITERIA

1. **Pulmonary Arterial Hypertension**:

Criteria for **Remodulin, Tyvaso, Veletri, and Ventavis**:

A. Patient has clinically diagnosed primary or secondary pulmonary arterial hypertension [defined as a mean pulmonary arterial pressure (mPAP) >25mm Hg at rest or >30mm Hg during exercise, with a normal pulmonary capillary wedge pressure(PCWP)]; **AND**
B. Patient exhibits Class III or IV symptoms (**Tyvaso, Veletri, and Ventavis** only); **OR**
C. Patient exhibits Class II to IV symptoms (**Remodulin** only); **AND**
D. Patient has had an intolerance to, or treatment failure of a calcium channel blocker after favorable response to acute vasoreactivity testing; **OR**
E. Failure to have a pulmonary vasodilator response to an acute challenge of a short acting vasodilator

II. RENEWAL CRITERIA

Documentation the patient is receiving clinical benefit to therapy.

Dosage/Administration

Indication	Dose
Pulmonary arterial hypertension (PAH)	**Remodulin:** 1.25 ng/kg/min (or 0.625 ng/kg/min if not tolerated or in patients with mild or moderate hepatic insufficiency); dose increase based on clinical response (increments of 1.25 ng/kg/min per week for the first 4 weeks of treatment, then 2.5 ng/kg/min per week for the remaining duration of the infusion). Transitioning from epoprostenol: • Initiate Remodulin at a recommended dose of 10% of the current epoprostenol dose • Decrease the dose of epoprostenol while simultaneously increasing the dose of

	Remodulin, based on response **Tyvaso:** Therapy should begin with 3 breaths of Tyvaso (18 mcg of treprostinil) per treatment session 4 times daily. If 3 breaths are not tolerated, reduce to 1 or 2 breaths and subsequently increase to 3 breaths, as tolerated. Dosage should be increased by an additional 3 breaths per treatment session, 4 times daily at approximately 1- to 2-week intervals. Studies establishing effectiveness in patients with PAH and PH-ILD have used target doses of 9 to 12 breaths per treatment session, 4 times daily. If adverse effects preclude titration to target dose, Tyvaso should be continued at the highest tolerated dose. **Veletri:** Initiate at 2 ng/kg/min. Increase infusion by 1- to 2-ng/kg/min increments every 15 minutes or longer until dose-limiting pharmacologic effects are elicited or until a tolerance limit to the drug is established. Epoprostenol must be infused via a central venous catheter. **Ventavis:** Initial, 2.5 mcg inhaled using the I-neb(R) ADD(R) System; if tolerated, increase dose to 5 mcg inhaled 6 to 9 times per day (no more than every 2 hours) during waking hours; MAX daily dose was 45 mcg (5 mcg 9 times per day) Do not initiate therapy in patients with systolic blood pressure below 85 mmHg

Applicable Procedure Codes

Code	Description
J3285	Injection, treprosinil, 1 mg, (Remodulin) 1 billable unit = 1 mg
J7686	Injection, treprosinil, 1 mg, (Tyvaso) 1 billable unit = 1 mg
J1325	Injection, epoprostenol, 0.5 mg (Veletri) 1 billable unit = 0.5 mg
Q4074	Inhalation solution, iloprost, (Ventavis) billable unit = up to 20 mcg

Applicable NDCs

Code	Description
66302-0110-xx	Remodulin; solution for injection 1 mg/mL – 20 mg injection
66302-0102-xx	Remodulin; solution for injection 2.5 mg/mL – 50 mg injection
66302-0105-xx	Remodulin; solution for injection 5 mg/mL – 100 mg injection
66302-0110-xx	Remodulin; solution for injection 10 mg/mL – 200 mg injection
66302-0120-xx	Remodulin; solution for injection 20 mg/mL – 400 mg injection
66302-0110-xx	Tyvaso vial; solution for injection
66215-0403-xx	Veletri single dose vial; lyophilized powder for solution 0.5 mg injection
66215-0402-xx	Veletri single dose vial; lyophilized powder for solution 1.5 mg injection
66215-0302-xx	Ventavis single dose vial; solution for inhalation

ICD-10 Diagnoses

Code	Description
I27.0	Primary pulmonary hypertension

I27.1	Kyphoscoliotic heart disease
I27.2	Other secondary pulmonary hypertension
I27.20	Pulmonary hypertension, unspecified
I27.21	Secondary pulmonary arterial hypertension
I27.83	Eisenmenger's syndrome
I27.89	Other specified pulmonary heart diseases
I27.9	Pulmonary heart disease, unspecified
M34.0	Progressive systemic sclerosis
M34.1	CR(E)ST syndrome
M34.9	Systemic sclerosis, unspecified

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	1/12/2024	Annual Review: Updated definitions and dosing chart.
EmblemHealth & ConnectiCare	5/19/2023	Annual Review: added NDC's: 66302-0102-xx, 66302-0105-xx, 66302-0110-xx, 66302-0120-xx, 66215-0402-xx. Added ICD-10 Codes: I27.1, I27.83, I27.89, I27.9, M34.0, M34.1, M34.9 Deleted codes I27.22, I27.23, I27.24, I29.29
EmblemHealth & ConnectiCare	10/13/2022	Transferred policy to new template
EmblemHealth & ConnectiCare	07/15/2019	Annual review

References

1. Product Information: REMODULIN® subcutaneous injection, intravenous injection, treprostinil subcutaneous injection, intravenous injection. United Therapeutics Corp (per FDA), Research Triangle Park, NC, 2018.
2. Product Information: TYVASO inhalation solution, treprostinil inhalation solution. United Therapeutics Corp., Research Triangle Park, NC, 2009.
3. Product Information: VELETRI intravenous powder for injection, epoprostenol intravenous powder for injection. Actelion Pharmaceuticals US, Inc., South San Francisco, CA, 2011.
4. Product Information: VENTAVIS(R) inhalation solution, iloprost inhalation solution. Actelion Pharmaceuticals US, Inc. (per Manufacturer), South San Francisco, CA, 2013.