RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title:	iloprost
Policy Number:	RxA.545
Drug(s) Applied:	Ventavis®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Iloprost (Ventavis®) is a synthetic prostacyclin analog.
It is indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to improve a composite endpoint consisting of exercise tolerance, symptoms (New York Heart Association [NYHA] Class), and lack of deterioration.
Studies establishing effectiveness included predominately patients with NYHA Functional Class III-IV symptoms and etiologies of idiopathic or heritable PAH (65%) or PAH associated with connective tissue diseases (23%).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Iloprost (Ventavis®)	PAH	6 to 9 doses INH per day with at least 2 hours between doses Starting dose: 2.5 mcg, titrated to 5 mcg if well tolerated Maintenance dose: 5 mcg	45 mcg/day

Dosage Forms

- Ampules (1mL each): 10 mcg/mL, 20 mcg/mL

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Pulmonary Arterial Hypertension (must meet all):

1. Diagnosis of PAH;
2. Prescribed by or in consultation with a cardiologist or pulmonologist;
3. Failure of a calcium channel blocker (*see Appendix B*), unless member meets one of the following (a or b):
   a. Inadequate response or contraindication to acute vasodilator testing;
   b. Contraindication or clinically significant adverse effects to calcium channel blockers are experienced;
4. Dose does not exceed 45 mcg per day.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Pulmonary Arterial Hypertension (must meet all)**:**

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 45 mcg per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FC: functional class
FDA: Food and Drug Administration
NYHA: New York Heart Association
PAH: pulmonary arterial hypertension
PH: pulmonary hypertension
WHO: World Health Organization

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
nifedipine (Procardia®, Procardia XL®)	60 mg PO once daily; may increase to 120 to 240 mg/day	240 mg/day
diltiazem (Cardizem®, Cardizem CD®, Cardizem LA®, Cartia XT®, Dilt-XR®, Matzim LA®, Tiazac®, Taztia XT®)	720 to 960 mg PO once daily	960 mg/day
amlodipine (Norvasc®)	20 to 30 mg PO once daily	30 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported

- Boxed Warning(s):
  - None reported

APPENDIX D: General Information
Pulmonary Hypertension: WHO Classification

- Group 1: PAH (pulmonary arterial hypertension)
- Group 2: PH due to left heart disease
- Group 3: PH due to lung disease and/or hypoxemia
- Group 4: CTEPH (chronic thromboembolic pulmonary hypertension)
- Group 5: PH due to unclear multifactorial mechanisms

APPENDIX E: Pulmonary Hypertension: WHO/NYHA Functional Classes (FC)

Treatment Approach	FC	Status at rest	Tolerance of Physical Activity(PA)	PA Limitations	Heart Failure
Monitoring for progression of PH and treatment of coexisting conditions	I	Comfortable at rest	No limitation	Ordinary PA does not cause undue dyspnea or fatigue, chest pain, or near syncope.	
Advanced treatment of PH with PHtargeted therapy *- see Appendix F***	II	Comfortable at rest	Slight limitation	Ordinary PA causes undue dyspnea or fatigue, chest pain, or near syncope.	
	III	Comfortable at rest	Marked limitation	Less than ordinary PA causes undue dyspnea or fatigue, chest pain, or near syncope.	
	IV	Dyspnea or fatigue may be present at rest	Inability to carry out any PA without symptoms	Discomfort is increased by any PA.	Signs of right heart failure

**PH supportive measures may include diuretics, oxygen therapy, anticoagulation, digoxin, exercise, pneumococcal vaccination. **Advanced treatment options also include calcium channel blockers.*

APPENDIX F: Pulmonary Hypertension: Targeted Therapies

Mechanism of Action	Drug Class	Drug Subclass	Drug	Brand/Generic Formulations
Reduction of pulmonary arterial pressure through vasodilation	Prostacyclin* pathway agonist **Member of the prostanoid class of fatty acid*	Prostacyclin	Epoprostenol	Veletri (IV) Flolan (IV) Flolan generic (IV)
		Synthetic prostacyclin analog	Treprostinil	Orenitram (oral tablet) Remodulin (IV)

	derivatives.			Tyvaso (inhalation)
		Non-prostanoid prostacyclin receptor (IP receptor) agonist	Iloprost	Ventavis® (inhalation)
	Endothelin receptor antagonist (ETRA)	Selective receptor antagonist	Ambrisentan	Letairis (oral tablet)
		Nonselective dual action receptor antagonist	Bosentan	Tracleer (oral tablet)
			Macitentan	Opsumit (oral tablet)
	Nitric oxide-cyclic guanosine monophosphate enhancer	Phosphodiesterase type 5 (PDE5) inhibitor	Sildenafil	Revatio (IV, oral tablet, oral suspension)
		Guanylate cyclase stimulant (sGC)	Tadalafil	Adcirca (oral tablet)
			Riociguat	Adempas (oral tablet)

References

1. Ventavis® Prescribing Information. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.; December 2019. Available at: https://www.4ventavis.com/pdf/Ventavis_PI.pdf. Accessed September 17, 2020.
2. 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. Accessed September 17, 2020.
3. Association - developed in collaboration with the American College of Chest Physicians, American Thoracic Society, Inc., and the Pulmonary Hypertension Association. J Am Coll Cardiol. 2009; 53(17): 1573-1619. Accessed September 17, 2020.
4. Taichman D, Ornelas J, Chung L, et. al. CHEST guideline and expert panel report: Pharmacologic therapy for pulmonary arterial hypertension in adults. Chest. 2014; 146 (2): 449-475. Accessed September 17, 2020.
5. Abman SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: Guidelines from the American Heart Association and American Thoracic Society. Circulation. 2015 Nov 24; 132(21): 2037-99. Accessed September 17, 2020.
6. Kim NH, Delcroix M, Jenkins DP, et al. Chronic thromboembolic pulmonary hypertension. J Am Coll Cardiol 2013; 62(25): Suppl D92-99. Accessed September 17, 2020.
7. Galiè N, Humbert M, Vachiery JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. Kardiol Pol. 2015;73(12):1127-206. doi: 10.5603/KP.2015.0242. Accessed September 17, 2020.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Policy title table was	9/17/2020	12/07/2020

updated: Line of business policy applies was updated to all lines of business. 2. Dosing information section was updated to clarify starting and maintenance dose. 3. Dosage forms section was updated to include ampule size as 1mL. 4. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 5. Commercial approval duration was updated from length of benefit to 6 months for initial approval and 12 months for continued approval criteria. 6. Appendix B for therapeutic alternatives was updated to remove discontinued drugs and standard verbiage. 7. References were updated.		