Clinical Policy Title:	selexipag
Policy Number:	RxA.290
Drug(s) Applied:	Uptravi®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

Selexipag (Uptravi®) is a prostacyclin receptor agonist. It is indicated for the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to delay disease progression and reduce the risk of hospitalization for PAH.

Effectiveness was established in a long-term study in PAH patients with WHO Functional Class II-III symptoms. Patients had idiopathic and heritable PAH (58%), PAH associated with connective tissue disease (29%), and PAH associated with congenital heart disease with repaired shunts (10%).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
selexipag (Uptravi®)	PAH	200 mcg PO twice daily, increased at weekly intervals to highest tolerated dose up to 1,600 mcg twice daily	3,200 mcg/day

Dosage Forms

- Tablets: 200 mcg, 400 mcg, 600 mg, 800 mg, 1,000 mcg, 1,200 mcg, 1,400 mcg, 1,600 mcg

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. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administer by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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. Age ≥ 18 years;
4. 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 vasoreactivity testing;
   b. Contraindication or clinically significant adverse effects to calcium channel blockers are experienced;
5. Dose does not exceed 3,200 mcg per day (if request is for titration, provider must submit a titration plan).

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Pulmonary Arterial Hypertension (must meet all):
1. Member is 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 3,200 mcg per day (if request is for titration, provider must submit a titration plan).

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FC: functional class
FDA: Food and Drug Administration
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 (Adalat® CC, Procardia®, Procardia XL®)	60 mg PO once daily; may increase to 120 to 240 mg/day	240 mg/day
diltiazem (Dilt-XR®, Cardizem® CD, Cartia XT®, Tiazac®, Taztia XT®, Cardizem® LA, Matzim® LA)	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):
  - Concomitant use with strong CYP2C8 inhibitors.

- Boxed Warning(s):
  - None.

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 PH-targeted 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	Prostacyclin* pathway agonist	Prostacyclin	epoprostenol	Veletri (IV) Flolan (IV) Flolan generic (IV)

Mechanism of Action	Drug Class	Drug Subclass	Drug	Brand/Generic Formulations
arterial pressure through vasodilation	*Member of the prostanoid class of fatty acid derivatives.*	Synthetic prostacyclin analog	treprostinil	Orenitram® (oral tablet) Remodulin® (IV) Tyvaso® (inhalation)
			iloprost	Ventavis® (inhalation)
		Non-prostanoid prostacyclin receptor (IP receptor) agonist	selexipag	Uptravi® (oral tablet)
	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)
			tadalafil	Adcirca® (oral tablet)
		Guanylate cyclase stimulant (sGC)	riociguat	Adempas® (oral tablet)

References

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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Policy title table was updated. 2. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 3. Approval duration was updated to include months in initial approval as well as in clinical therapy criteria. 4. QD was updated with once daily in document. 5. All brand drugs were updated to have "®" for consistency. 6. References were updated.	07/23/2020	09/14/2020
Policy was reviewed: 1. Initial approval criteria I.A.3 was added to consider patient age. 2. Initial approval criteria I.A.4a was updated to change term "vasodilator" to "vasoreactivity" for accuracy. 3. Clinical policy section standard verbiage was updated to include "The provision of provider samples…". 4. Continued therapy criteria II.A.1 was rephrased to "Member is currently receiving medication…". 5. Appendix B for therapeutic alternatives standard verbiage updated. Also brand Afeditab® CR was removed	04/02/2021	06/10/2021

due to discontinuation. 6. References were updated.		