Clinical Policy Title:	macitentan
Policy Number:	RxA.433
Drug(s) Applied:	Opsumit®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Macitentan (Opsumit®) is an endothelin receptor antagonist.

Opsumit® is indicated for treatment of pulmonary arterial hypertension (PAH) (World Health Organization (WHO) Group I) to delay disease progression. Disease progression included: death, initiation of intravenous (IV) or subcutaneous prostanoids, or clinical worsening of PAH (decreased 6-minute walk distance, worsened PAH symptoms and need for additional PAH treatment). It also reduced hospitalization for PAH.

Effectiveness was established in a long-term study in PAH patients with predominantly WHO Functional Class II-III symptoms treated for an average of 2 years. Patients were treated with Opsumit® monotherapy or in combination with phosphodiesterase-5 inhibitors or inhaled prostanoids. Patients had idiopathic and heritable PAH (57%), PAH caused by connective tissue disorders (31%), and PAH caused by congenital heart disease with repaired shunts (8%).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
macitentan (Opsumit®)	PAH	10 mg orally once daily	10 mg/day

Dosage Forms

- Tablet: 10 mg

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 administered 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. 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 10 mg per day.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving the medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 10 mg 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
WHO: World Health Organization
PAH: Pulmonary Arterial Hypertension
PH: Pulmonary Hypertension

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	Dose Limit/Maximum Dose
nifedipine (Adalat® CC, Procardia XL®)	60 mg orally 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)	240 to 720 mg orally once daily	720 mg/day
amlodipine (Norvasc®)	Initial: 2.5 mg orally once daily; increase cautiously and progressively up to the maximum tolerated dose	20 mg/day

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):

- Pregnancy.

- Boxed Warning(s):
  - Embryo-fetal toxicity.

APPENDIX D: General Information

- Obtain a pregnancy test in females of reproductive potential prior to Opsumit® treatment, monthly during treatment and one month after stopping Opsumit®. Initiate treatment with Opsumit® in females of reproductive potential only after a negative pregnancy test.
- 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 mechanism

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 co-existing 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 arterial pressure through vasodilation	Prostacyclin* pathway agonist *Member of the prostanoid class of fatty acid derivatives.	Prostacyclin	Epoprostenol	Veletri (IV) Flolan (IV) Flolan generic (IV)
		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

1. Opsumit® Prescribing Information. South San Francisco, CA: Actelion Pharmaceuticals, Inc.; May 2021. Available at: https://www.opsumit.com/ . Accessed June 25, 2021.
2. McLaughlin Vallerie V., Archer Stephen L., Badesch David B., et al. Accf/aha 2009 expert consensus document on pulmonary hypertension. Journal of the American College of Cardiology. 2009;53(17):1573-1619. Available at: https://www.jacc.org/doi/full/10.1016/j.jacc.2009.01.004 . Accessed June 30, 2021.
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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Policy title table was updated. 2. Dosing information was updated. 3. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 4. Appendices updated 5. References were updated.	07/20/2020	09/14/2020
Policy was reviewed: 1. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 2. Initial Approval Criteria I.A.2 was updated to remove "Member has documented proof of negative pregnancy test…". 3. Initial Approval Criteria and Continued Therapy Approval criteria were updated to remove HIM approval duration. 4. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 5. Appendix A was updated to include abbreviations WHO,PAH, and PH. 6. Therapeutic Alternatives verbiage was rephrased to "Below are suggested therapeutic alternatives based on clinical guidance..". 7. Appendix B: Therapeutic Alternatives was updated to remove brand-name drugs Afeditab CR, Procardia, and Dilacor XR. 8. Appendix B: Therapeutic Alternatives dosing regimen for amlodipine was updated from "20 to 30 mg PO once daily" to "Initial: 2.5 mg orally once daily;	06/25/2021	09/14/2021

increase cautiously and progressively up to the maximum tolerated dose…”. 9. Appendix B: Therapeutic Alternatives dosing regimen and maximum dose for diltiazem was updated from “720 to 960mg” to “240 to 720mg.” 10. Statement about drug listing format in Appendix B is updated to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 11. Appendix D was updated to include “Obtain a pregnancy test in females of reproductive potential prior…” 12. .References were reviewed and updated.		