Clinical Policy: Macitentan (Opsumit)

Reference Number: CP.CPA.107
Effective Date: 11.16.16
Last Review Date: 11.17 Revision Log
Line of Business: Medicaid – Medi-Cal

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Macitentan (Opsumit®) is an endothelin receptor antagonist.

FDA approved indication
Opsumit® is indicated for the treatment of Pulmonary Arterial Hypertension (PAH, WHO Group I) to delay disease progression.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Opsumit is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of Pulmonary Arterial Hypertension (WHO Group 1);
2. Dose does not exceed 10 mg/day.

Approval duration: Length of Benefit

B. Other diagnoses/indications

1. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. Dose does not exceed 10 mg/day.

Approval duration: Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or

2. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.PHAR.57 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviations/Acronym Key

PAH: pulmonary arterial hypertension
PH: pulmonary hypertension
IPAH: idiopathic pulmonary arterial hypertension
WHO: World Health Organization
REMS: Risk Evaluation and Mitigation Strategy

Appendix B: General Information

- 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). Opsumit also reduced hospitalization for PAH.
- In light of potential teratogenic risks (pregnancy category X), for all female patients, Opsumit is available only through a restricted program called the Opsumit Risk Evaluation and Mitigation Strategy (REMS). Male patients are not enrolled in the REMS. Further information is available at www.OPSUMITREMS.com or 1-866-228-3546. Information on Opsumit certified pharmacies or wholesale distributors are available through Actelion Pathways at 1-866-228-3546.
- WHO classifies patients into 5 groups based on etiologies of pulmonary hypertension:
  - Group 1 PAH: sporadic idiopathic pulmonary arterial hypertension (IPAH), heritable IPAH, PAH caused by diseases of the pulmonary arterioles and drug and toxin-induced PAH.
  - Group 2 PH: due to cardiac origin.
  - Group 3 PH: due to severe lung diseases or hypoxemia.
  - Group 4 PH: Chronic Thromboembolic Pulmonary Hypertension (CTEPH).
  - Group 5 PH: miscellaneous, unclear causes.

Appendix C: Therapeutic Alternatives

Drug	Dosing Regimen	Dose Limit/Maximum Dose
Flolan®, Veletri® (epoprostenol)*	Initiate chronic infusion rate at 2 ng/kg/min continuous IV infusion via central venous catheter and increase in increments of 2 ng/kg/min every 15 min until dose-limiting pharmacological effects are elicited or until an	Titrate as needed and tolerated, avoid abrupt withdrawal. Should dose-limiting effects occur, reduce infusion rate by 2 ng/kg/min every 15 minutes.

Drug	Dosing Regimen	Dose Limit/Maximum Dose
	intolerance limit is established or further increases are not clinically warranted.	
sildenafil citrate* (Revatio®)	Tablets and Oral Suspension: 5 mg or 20 mg PO TID taken approximately 4 to 6 hours apart. Injection: 2.5 mg or 10 mg IV bolus TID	Tablets: 20 mg PO TID Injection: 10 mg IV bolus TID
Remodulin® (treprostinil)*	Initiate at 1.25 ng/kg/min SC continuous infusion (undiluted) or IV continuous infusion (diluted). The infusion rate should be increased in increments of 1.25 ng/kg/min per week for the first four weeks then 2.5 ng/kg/min per week for the remaining duration of infusion depending on clinical response. Avoid abrupt discontinuation. Transition from Flolan: Initial Remodulin dose is 10% of the current Flolan dose. Dose should be increased as Flolan dose is decreased.	40 ng/kg/min. Titrate as tolerated. Avoid abrupt withdrawal.
Orenitram™ (treprostinil)*	Initial dosage: 0.25 mg PO BID or 0.125 mg PO TID. Increase by 0.25 or 0.5 mg PO BID or 0.125 mg PO TID every 3 to 4 days to achieve optimal clinical response. Maximum studied dose was 21 mg PO BID.	21 mg PO BID
Tracleer® (bosentan)	Initiate: 62.5 mg PO BID for 4 weeks. Maintenance: up to125 mg PO BID (if body wt.< 40 kg and age > 12 y/o initial and maintenance is 62.5 mg PO BID)	125 mg PO BID

Drug	Dosing Regimen	Dose Limit/Maximum Dose
Ventavis® (iloprost)*	1.5 – 5 mcg inhaled PO 6 to 9 times per day (no more than every two hours) ***Do not initiate therapy in patients with systolic blood pressure (SBP) below 85 mmHg****	45 mcg (5 mcg nine times per day)
Letairis® (ambrisentan)	5 to 10 mg PO QD	10 mg PO QD
Tyvaso® (treprostinil)*	Initial dosage: Inhale 3 breaths PO (18 mcg) per treatment session. If 3 breaths are not tolerated, reduce to 1 or 2 breaths. Administer in 4 separate treatment sessions each day approximately four hours apart, during waking hours. Dosage should be increased by an additional 3 breaths at approximately 1-2 week intervals, if tolerated. Titrate to target maintenance dosage of 9 breaths (54 mcg) per treatment session.	9 breaths (54 mcg) QID
Adcirca® (tadalafil)*	40 mg PO QD	40 mg PO QD
Adempas® (riociguat)*	1 mg PO TID If hypotension is a problem, may initiate at 0.5 mg PO TID; Increase by 0.5 mg every 2 weeks as tolerated up to a max dose of 2.5 mg PO TID.	2.5 mg PO TID

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.
*Requires Prior Authorization

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Pulmonary arterial hypertension	10 mg PO QD Doses higher than 10 mg once daily have not been	10 mg/day

	studied in patients with PAH and are not recommended.	

VI. Product Availability

Tablet: 10 mg

VII. References

1. Opsumit Prescribing Information. South San Francisco, CA: Actelion Pharmaceuticals US, Inc.;October 2013. Available at: www.Opsumit.com. Accessed January 11, 2017.
2. Opsumit Drug Monograph. Clinical Pharmacology. Accessed January 11, 2017. http://www.clinicalpharmacology-ip.com
3. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed January11, 2017.
4. Opsumit. American Hospital Formulary Service Drug Information.Available at: http://www.medicinescomplete.com/mc/ahfs/current/.Accessed January 11, 2017.
5. The Classification of Pulmonary Arterial Hypertension. Updated2006. Available at http://www.medscape.org/viewarticle/544175. Accessed January 12, 2016.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Minor changes to verbiage and grammar. References updated.	01.11.17	11.17

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.