Clinical Policy: Riociguat (Adempas)
Reference Number: HIM.PA.SP20
Effective Date: 05/17
Last Review Date:
Line of Business: Health Insurance Marketplace

Coding Implications
Revision Log

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

Description
Riociguat (Adempas®) is a soluble guanylate cyclase (sGC) stimulator.

FDA approved indication
Adempas is indicated:

- For the treatment of adults with pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) to improve exercise capacity, WHO functional class, and to delay clinical worsening
- For the treatment of adults with persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) (WHO Group 4) after surgical treatment or inoperable CTEPH to improve exercise capacity and WHO functional class

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

I. Initial Approval Criteria

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

1. Prescribed by or in consultation with a cardiologist or pulmonologist experienced in the diagnosis and treatment of pulmonary hypertension (PH);
2. Diagnosis of PH confirmed by right heart catheterization and classified as (a and b):
   a. WHO Group 1 or 4 (Appendix B):
      i. WHO Group 1: PAH (pulmonary arterial hypertension) and (a or b):
         a) Inadequate response or contraindication to acute vasodilator testing;
         b) Trial and failure of, or contraindication to, calcium channel blockers;
      ii. WHO Group 4: CTEPH (chronic thromboembolic pulmonary hypertension) that is inoperable or persistent (i.e., suboptimal surgical outcome);
   b. WHO/NYHA Functional Class II, III or IV (Appendix C);
3. Prescribed dose of Adempas does not exceed 2.5 mg three times daily (patients who smoke may require higher doses).

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to HIM.PHAR.21 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. Prescribed dose of Adempas does not exceed 2.5 mg three times daily (patients who smoke may require higher doses).

Approval duration: 12 months

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to HIM.PHAR.21 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

Approval duration: 12 months

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 – HIM.PHAR.21 or evidence of coverage documents

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CTEPH: chronic thromboembolic pulmonary hypertension
ETRA: endothelin receptor antagonist
FC: functional classification
IP receptor: prostacyclin receptor
NYHA: New York Heart Association
PAH: pulmonary arterial hypertension
PDE5: phosphodiesterase-5
PH: pulmonary hypertension
sGC: soluble guanylate cyclase
WHO: World Health Organization

Appendix B: 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 C: 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	I	Comfortable at rest	No limitation	Ordinary PA does not cause undue dyspnea or fatigue,	

Treatment Approach*	FC	Status at Rest	Tolerance of Physical Activity (PA)	PA Limitations	Heart Failure
treatment of co-existing conditions				chest pain, or near syncope.	
Advanced treatment of PH with PH-targeted therapy - see Appendix D**	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 D: 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) Tyvasco (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	Opsummit (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)

V. References

1. Adempas prescribing information. Whippany, NJ: Bayer HealthCare Pharmaceuticals, Inc.; January 2017. Available at http://labeling.bayerhealthcare.com/html/products/pi/Adempas_PI.pdf. Accessed February 10, 2017.
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 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.
3. 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.
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5. Kim NH, Delcroix M, Jenkins DP, et al. Chronic thromboembolic pulmonary hypertension. *J Am Coll Cardiol* 2013; 62(25): Suppl D92-99.
6. Rubin LJ and Hopkins W. Overview of pulmonary hypertension in adults. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at UpToDate.com. Accessed February 14, 2017.
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9. Fedullo PF. Clnical manifestations and diagnosis of chronic thromboembolic pulmonary hypertension. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at UpToDate.com. Accessed February 14, 2017.
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11. Fedullo PF. Chronic thromboembolic pulmonary hypertension: Surgical treatment. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at UpToDate.com. Accessed February 14, 2017.
12. Fedullo PF. Chronic thromboembolic pulmonary hypertension: Medical treatment. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at UpToDate.com. Accessed February 14, 2017.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	02/17	05/17

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.