

Clinical Policy: Riociguat (Adempas)

Reference Number: CP.PHAR.195

Effective Date: 03/16

Last Review Date: 03/17

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for riociguat (Adempas®).

Policy/Criteria

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

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: Refer to CP.PHAR.57 - Global Biopharm Policy.

II. Continued Approval

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 CP.PHAR.57 - Global Biopharm Policy.

Background*Description/Mechanism of Action:*

Adempas (riociguat) is a tablet for oral administration. Riociguat is a stimulator of soluble guanylate cyclase (sGC), an enzyme in the cardiopulmonary system and the receptor for nitric oxide (NO). When NO binds to sGC, the enzyme catalyzes synthesis of the signaling molecule cyclic guanosine monophosphate (cGMP). Intracellular cGMP plays an important role in regulating processes that influence vascular tone, proliferation, fibrosis and inflammation. Pulmonary hypertension is associated with endothelial dysfunction, impaired synthesis of nitric oxide and insufficient stimulation of the NO-sGC-cGMP pathway. Riociguat has a dual mode of action. It sensitizes sGC to endogenous NO by stabilizing the NO-sGC binding. Riociguat also directly stimulates sGC via a different binding site, independently of NO. Riociguat stimulates the NO-sGC-cGMP pathway and leads to increased generation of cGMP with subsequent vasodilation. The active metabolite (M1) of riociguat is 1/3 to 1/10 as potent as riociguat.

Formulations:

Adempas oral tablets: 0.5 mg, 1 mg, 1.5 mg, 2 mg, 2.5 mg

FDA Approved Indications:

Adempas is a soluble guanylate cyclase (sGC) stimulator/oral tablet formulation indicated for:

- Treatment of adults with pulmonary arterial hypertension (PAH), (WHO Group 1), to improve exercise capacity, WHO functional class and to delay clinical worsening.
 - Efficacy was shown in patients on Adempas monotherapy or in combination with endothelin receptor antagonists or prostanoids. Studies establishing effectiveness included predominately patients with WHO functional class II–III and etiologies of idiopathic or heritable PAH or PAH associated with connective tissue diseases.
- 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.

Appendices**Appendix A: Abbreviation Key**

- FC: functional classification
- NYHA: New York Heart Association
- PAH: pulmonary arterial hypertension
- PH: pulmonary hypertension
- 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 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 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	Prostacyclin	Epoprostenol	Velettri (IV) Flolan (IV) Flolan generic (IV)	
	<i>*Member of the prostanoid class of fatty acid derivatives.</i>	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	Selective receptor antagonist	Ambrisentan	Letairis (oral tablet)	
			Nonselective dual action receptor antagonist	Bosentan	Tracleer (oral tablet)
				Macitentan	Opsummit (oral tablet)

Mechanism of Action	Drug Class	Drug Subclass	Drug	Brand/Generic Formulations
	Nitric oxide-cyclic guanosine monophosphate enhancer	Phosphodiesterase type 5 inhibitor	Sildenafil	Revatio (IV, oral tablet, oral suspension)
			Tadalafil	Adcirca (oral tablet)
		Guanylate cyclase stimulant (sGC)	Riociguat	Adempas (oral tablet)

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
N/A	

Reviews, Revisions, and Approvals	Date	Approval Date
Policy split from CP.PHAR.33.PAH and converted to new template. Criteria: added specialist requirement; removed echocardiogram as an option for confirming a PH diagnosis –added requirement of right heart catheterization for PAH WHO Group 4 (CTEPH); removed hard stop after 3 months of therapy. Appendices removed: 1) examples of calcium channel blocker contraindications; 2) nitrate therapy examples; 3) PAH definition.	02/16	03/16
Age restriction removed. FC II added to the prostanoid class of PH drugs. Safety criteria were removed unless they 1) represent contraindications or black box warnings not covered by a REMS program, and 2) provide specific lab/imaging parameters that must be met prior to initiation of therapy. An efficacy statement was added to the continuation criteria. Initial and continuation durations increased to 6 and 12 months respectively. Appendices covering PH groups, functional class and therapies reorganized.	03/17	03/17

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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

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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.

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Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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