

## Clinical Policy: Riociguat (Adempas)

Reference Number: CP.PHAR.195

Effective Date: 03.16

Last Review Date: 02.22

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

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

### Description

Riociguat (Adempas<sup>®</sup>) is a soluble guanylate cyclase stimulator.

### FDA Approved Indication(s)

Adempas is indicated for the treatment of:

- Adults with persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH), (World Health Organization [WHO] Group 4) after surgical treatment, or inoperable CTEPH, to improve exercise capacity and WHO functional class
- 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 (61%) or PAH associated with connective tissue diseases (25%)

### Policy/Criteria

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

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

#### I. Initial Approval Criteria

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

1. Diagnosis of PAH or CTEPH;
2. Prescribed by or in consultation with a cardiologist or pulmonologist;
3. Member meets one of the following:
  - a. For PAH: Failure of a calcium channel blocker (*see Appendix B*), unless member meets one of the following (i or ii):
    - i. Inadequate response or contraindication to acute vasodilator testing;
    - ii. Contraindication or clinically significant adverse effects to calcium channel blockers are experienced;
  - b. For CTEPH: Disease is inoperable or persistent (i.e., suboptimal surgical outcome);
4. Dose does not exceed 7.5 mg (3 tablets) per day (*members who smoke may require higher doses*).

**Approval duration:**

**Medicaid/HIM** – 6 months

**Commercial** – Length of Benefit

**B. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**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. If request is for a dose increase, new dose does not exceed 7.5 mg (3 tablets) per day (*members who smoke may require higher doses*).

**Approval duration:**

**Medicaid/HIM** – 12 months

**Commercial** – 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 6 months (whichever is less);** or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

CTEPH: chronic thromboembolic  
pulmonary hypertension

FC: functional class

FDA: Food and Drug Administration

NYHA: New York Heart Association

PAH: pulmonary arterial hypertension

PH: pulmonary hypertension

WHO: World Health Organization

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.*

<b>Drug Name</b>	<b>Dosing Regimen</b>	<b>Dose Limit/ Maximum Dose</b>
nifedipine (Adalat <sup>®</sup> CC, Afeditab <sup>®</sup> CR, Procardia <sup>®</sup> , Procardia XL <sup>®</sup> )	60 mg PO QD; may increase to 120 to 240 mg/day	240 mg/day
diltiazem (Dilacor XR <sup>®</sup> , Dilt-XR <sup>®</sup> , Cardizem <sup>®</sup> CD, Cartia XT <sup>®</sup> , Tiazac <sup>®</sup> , Taztia XT <sup>®</sup> , Cardizem <sup>®</sup> LA, Matzim <sup>®</sup> LA)	720 to 960 mg PO QD	960 mg/day
amlodipine (Norvasc <sup>®</sup> )	20 to 30 mg PO QD	30 mg/day

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s):
  - Pregnancy
  - Nitrates and nitric oxide donors
  - Phosphodiesterase inhibitors
  - Pulmonary hypertension associated with idiopathic interstitial pneumonitis
- Boxed warning(s): embryo-fetal toxicity (REMS program)

*Appendix D: 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)*

<b>Treatment Approach*</b>	<b>FC</b>	<b>Status at Rest</b>	<b>Tolerance of Physical Activity (PA)</b>	<b>PA Limitations</b>	<b>Heart Failure</b>
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	II	Comfortable at rest	Slight limitation	Ordinary PA causes undue dyspnea or	

Treatment Approach*	FC	Status at Rest	Tolerance of Physical Activity (PA)	PA Limitations	Heart Failure
with PH-targeted therapy - see Appendix F**				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  <i>*Member of the prostanoid class of fatty acid derivatives.</i>	Prostacyclin	Epoprostenol	Velettri (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)

Mechanism of Action	Drug Class	Drug Subclass	Drug	Brand/Generic Formulations
		Guanylate cyclase stimulant (sGC)	Riociguat	Adempas (oral tablet)

#### V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
PAH	1 mg PO TID, increased by 0.5 mg every 2 weeks as tolerated to 2.5 mg TID	7.5 mg/day
CTEPH		

#### VI. Product Availability

Tablets: 0.5 mg, 1 mg, 1.5 mg, 2 mg, 2.5 mg

#### VII. References

- Adempas Prescribing Information. Whippany, NJ: Bayer HealthCare Pharmaceuticals, Inc.; September 2021. Available at: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2021/204819s015lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/204819s015lbl.pdf). Accessed November 9, 2021.
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- Yaghi S, Novikov A, Trandafirescu T. Clinical update on pulmonary hypertension. *J Investig Med*. 2020; 0:1-7. doi:10.1136/jim-2020-001291.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q18 annual review: Policies combined for commercial, HIM and Medicaid; No significant changes from previous corporate approved policy; Medicaid/HIM: removed WHO/NYHA classifications from initial criteria since specialist is involved in care; References reviewed and updated.	11.21.17	02.18
1Q 2019 annual review: no significant changes; references reviewed and updated.	11.20.18	02.19
1Q 2020 annual review: no significant changes; added max quantity per day; references reviewed and updated.	11.26.19	02.20
1Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	10.12.20	02.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	11.09.21	02.22

**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.

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