

**Clinical Policy: Sildenafil (Revatio, Liqrev)**

Reference Number: CP.PHAR.197

Effective Date: 03.16

Last Review Date: 02.25

Line of Business: Commercial, HIM, Medicaid

[Coding Implications](#)[Revision Log](#)

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

**Description**

Sildenafil (Revatio<sup>®</sup>, Liqrev<sup>®</sup>) is a phosphodiesterase-5 inhibitor.

**FDA Approved Indication(s)**

Revatio and Liqrev are indicated:

- For the treatment of pulmonary arterial hypertension (PAH) (World Health Organization [WHO] Group 1) in adults to improve exercise ability and delay clinical worsening.

Revatio is additionally indicated:

- In pediatric patients 1 to 17 years old for the treatment of PAH (WHO Group 1) to improve exercise ability and, in pediatric patients too young to perform standard exercise testing, pulmonary hemodynamics thought to underly improvements in exercise.

**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 sildenafil, Revatio, and Liqrev are **medically necessary** when the following criteria are met:

**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. Age  $\geq$  1 year;
4. 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;
5. If request is for brands Revatio or Liqrev, member must use generic sildenafil, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed the following (a or b):
  - a. Adult: one of the following, in divided doses (i or ii):
    - i. 240 mg per day (oral formulation);
    - ii. 30 mg per day (intravenous formulation);
  - b. Pediatric: one of the following, in divided doses (i, ii, or iii):

- i. Body weight  $\leq$  20 kg: 30 mg per day (oral formulation);
- ii. Body weight  $>$  20 kg to  $<$  45 kg: 60 mg per day (oral formulation);
- iii. Body weight  $\geq$  45 kg: 120 mg per day (oral formulation).

**Approval duration:**

**Medicaid/HIM** – 6 months

**Commercial** – 12 months or duration of request, whichever is less

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**II. Continued Therapy**

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

1. Member meets one of the following (a or b):
  - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
  - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Member is responding positively to therapy;
3. If request is for brands Revatio or Liqrev, member must use generic sildenafil, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, new dose does not exceed the following (a or b):
  - a. Adult: one of the following, in divided doses (i or ii):
    - i. 240 mg per day (oral formulation);
    - ii. 30 mg per day (intravenous formulation);
  - b. Pediatric: one of the following, in divided doses (i, ii, or iii):
    - i. Body weight  $\leq$  20 kg: 30 mg per day (oral formulation);
    - ii. Body weight  $>$  20 kg to  $<$  45 kg: 60 mg per day (oral formulation);
    - iii. Body weight  $\geq$  45 kg: 120 mg per day (oral formulation).

**Approval duration:**

**Medicaid/HIM** – 12 months

**Commercial** – 12 months or duration of request, whichever is less

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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	PA: physical activity
FC: functional class	PAH: pulmonary arterial hypertension
FDA: Food and Drug Administration	PH: pulmonary hypertension
NYHA: New York Heart Association	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.*

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
nifedipine (Adalat <sup>®</sup> CC, Procardia XL <sup>®</sup> ) <sup>†</sup>	<u>Adult:</u> 30 mg PO QD; may increase to 60 to 120 mg BID  <u>Pediatric:</u>	<u>Adult:</u> 240 mg/day  <u>Pediatric:</u> 180 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	0.3 to 0.6 mg/kg/dose PO QD; may increase to 2 to 3 mg/kg/day	
diltiazem (Dilt-XR <sup>®</sup> , Cardizem <sup>®</sup> CD, Cartia XT <sup>®</sup> , Tiazac <sup>®</sup> , Cardizem <sup>®</sup> LA, Matzim <sup>®</sup> LA) <sup>†</sup>	<u>Adult:</u> 60 mg PO BID; may increase to 120 to 360 mg BID  <u>Pediatric:</u> 0.75 mg/kg/dose PO BID; may increase to 3 to 5 mg/kg/day	<u>Adult:</u> 720 mg/day  <u>Pediatric:</u> 360 mg/day
amlodipine (Norvasc <sup>®</sup> ) <sup>†</sup>	<u>Adult:</u> 5 mg PO QD; may increase to 15 to 30 mg/day  <u>Pediatric:</u> 0.1 to 0.3 mg/kg/dose PO QD; may increase to 2.5 to 7.5 mg/day	<u>Adult:</u> 30 mg/day  <u>Pediatric:</u> 10 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.

<sup>†</sup> Off-label

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s):
  - Use with organic nitrates or riociguat
  - History of hypersensitivity reaction to sildenafil or any component of the tablet, injection, or oral suspension
- Boxed warning(s): none reported

*Appendix D: Pulmonary Hypertension: WHO Classification*

- Group 1: PAH
- 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)*

Treatment Approach*	FC	Status at Rest	Tolerance of Physical Activity (PA)	PA Limitations	Heart Failure
Monitoring for progression of PH and treatment of co-	I	Comfortable at rest	No limitation	Ordinary PA does not cause undue dyspnea or fatigue, chest pain, or near syncope.	

Treatment Approach*	FC	Status at Rest	Tolerance of Physical Activity (PA)	PA Limitations	Heart Failure
existing conditions					
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  <i>*Member of the prostanoid class of fatty acid derivatives.</i>	Prostacyclin	Epoprostenol	Veletri (IV) Flolan (IV) Flolan generic (IV)
		Synthetic prostacyclin analog	Treprostinil	Orenitram (oral tablet) Remodulin (IV) Tyvaso (inhalation)
			Iloprost	Ventavis (inhalation)
	Endothelin receptor antagonist (ETRA)	Non-prostanoid prostacyclin receptor (IP receptor) agonist	Selexipag	Upravi (oral tablet)
		Selective receptor antagonist	Ambrisentan	Letairis (oral tablet)
			Nonselective dual action receptor antagonist	Bosentan
	Macitentan	Opsumit (oral tablet)		

Mechanism of Action	Drug Class	Drug Subclass	Drug	Brand/Generic Formulations
	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. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
PAH	<p><u>Adult:</u> Tablet and oral suspension: 20 mg to 80 mg PO TID Injection: 10 mg TID as an IV bolus</p> <p><u>Pediatric:</u> Tablet and oral suspension: Body weight ≤ 20 kg: 10 mg PO TID Body weight &gt; 20 kg to &lt; 45 kg: 20 mg PO TID Body weight ≥ 45 kg: 20 mg to 40 PO TID</p>	<p><u>Adult:</u> Tablet and oral suspension: 240 mg/day Injection: 30 mg/day</p> <p><u>Pediatric:</u> See dosing regimen</p>

## VI. Product Availability

- Tablet: 20 mg
- Oral suspension: 10 mg/mL (equivalent to 14 mg sildenafil citrate)
- Single-use vial: 10 mg/12.5 mL

## VII. References

1. Revatio Prescribing Information. Morgantown, WV: Viatrix Specialty LLC; January 2023. Available at: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2023/021845s025lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/021845s025lbl.pdf). Accessed November 7, 2024.
2. Liqrev Prescribing Information. Farmville, NC: CMP Pharma, Inc.; April 2023. Available at: [https://www.accessdata.fda.gov/drugsatfda\\_docs/label/2023/214952s000lbl.pdf](https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/214952s000lbl.pdf). Accessed November 7, 2024.
3. Clinical Pharmacology [database online]. Tampa, FL: Elsevier; 2024. URL: [www.clinicalkeys.com/pharmacology](http://www.clinicalkeys.com/pharmacology).
4. 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.
5. Klinger JR, Elliott CG, Levine DJ, et al. Therapy for pulmonary arterial hypertension in adults: update of the CHEST guideline and expert panel report. *CHEST*. 2019;155(3):565-586. doi: <https://doi.org/10.1016/j.chest.2018.11.030>.

6. Abman SH, Hansmann G, Archer SL, et al. Pediatric pulmonary hypertension: Guidelines from the American Heart Association and American Thoracic Society. *Circulation*. 2015 Nov 24; 132(21): 2037-99.
7. Kim NH, Delcroix M, Jenkins DP, et al. Chronic thromboembolic pulmonary hypertension. *J Am Coll Cardiol*. 2013; 62(25): Suppl D92-99.
8. Galiè N, Humbert M, Vachiary JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of Pulmonary Hypertension. *European Heart Journal*.  
Doi:10.1093/eurheartj/ehv317.
9. Simmonneau G, Montani D, Celermajer D, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. *Eur Respir J*. 2019; 53:1801913.
10. Sitbon O, Humber M, Jais X, et al. Long-term response to calcium channel blockers in idiopathic pulmonary arterial hypertension. *Circulation*. 2005;111(23);3105;11.
11. Yaghi S, Novikov A, Trandafirescu T. Clinical update on pulmonary hypertension. *J Investig Med*. 2020; 0:1-7. doi:10.1136/jim-2020-001291.
12. Humbert M, Kovacs G, Hoeper MM, et al. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. *European Heart Journal*, Volume 43, Issue 38, 7 October 2022, Pages 3618–3731, <https://doi.org/10.1093/eurheartj/ehac237>.

**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
J3490	Unclassified drugs
J8499	Prescription drug, oral, non-chemotherapeutic, Not Otherwise Specified
C9399	Unclassified drug or biologicals

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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; added generic redirection to initial and continued therapy; references reviewed and updated.	11.09.21	02.22
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less. Template changes applied to other diagnoses/indications and continued therapy section.	06.23.22	11.22
1Q 2023 annual review: no significant changes; references reviewed and updated.	11.15.22	02.23

Reviews, Revisions, and Approvals	Date	P&T Approval Date
RT4: updated PAH criteria to include newly FDA approved pediatric age expansion; updated adult PAH dosing per revised PI; updated HCPCS codes and Appendix B.	03.08.23	
RT4: added new oral suspension formulation Liqrev to policy	05.09.23	
1Q 2024 annual review: no significant changes; removed commercially unavailable branded products from Appendix B; references reviewed and updated.	10.03.23	02.24
1Q 2025 annual review: in Policy/Criteria, clarified criteria also applies to brand Revatio and Liqrev; in Appendix B per Clinical Pharmacology, removed commercially unavailable branded products and clarified drugs used for off-label indications; references reviewed and updated.	11.07.24	02.25

**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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