Preemptive policy: This is a P&T approved policy and can be used after the drug is FDA approved until it is superseded by an updated policy

CENTENE® Corporation

# Clinical Policy: Udenafil

Reference Number: CP.PHAR.557
Effective Date: FDA Approval Date
Last Review Date: 11.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Revision Log

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

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## Description

Udenafil is a long acting, highly selective phosphodiesterase type 5 (PDE5) inhibitor.

## FDA Approved Indication(s) [Pending]

Udenafil is indicated for the treatment of single ventricle heart disease (SVHD) in patients 12 years of age and older who have undergone Fontan palliation.

## 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® that udenafil is **medically necessary** when the following criteria are met:

### I. Initial Approval Criteria*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

**A. Single Ventricle Heart Disease** (must meet all)**:**

1. Diagnosis of SVHD;*
2. Prescribed by or in consultation with a cardiologist;
3. Age ≥ 12 years and ≤ 18 years at therapy initiation;*
4. Member has undergone Fontan palliation;*
5. Documentation of baseline peak oxygen consumption;*
6. Peak oxygen consumption > 50% of predicted for age and sex;*
7. Respiratory exchange ratio ≥ 1.10 at peak exercise during cardiopulmonary exercise test;*
8. At the time of request, member meets all of the following (a, b, and c):*
   a. No hospitalization for acute decompensated heart failure within the last 12 months;
   b. Member does not have a diagnosis of active protein losing enteropathy or plastic bronchitis within the last 3 years, or history of liver cirrhosis;
   c. Member does not have Fontan baffle obstruction, branch pulmonary artery or vein stenosis, severe ventricular dysfunction, or atrioventricular valve regurgitation assessed by echocardiography within the last six months;
9. Dose does not exceed 175 mg per day.*

**Approval duration: 6 months**

**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/ICHRA) 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/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) 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/ICHRA, 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/ICHRA, and CP.PMN.53 for Medicaid.

## II. Continued Therapy*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

**A. Single Ventricle Heart Disease** (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 as evidenced by, including but not limited to, improvement or maintenance of positive peak oxygen consumption compared to baseline;*
3. If request is for a dose increase, new dose does not exceed 175 mg per day.*

**Approval duration: 12 months**

**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/ICHRA) 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/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) 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/ICHRA, and CP.PMN.16 for Medicaid; or

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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/ICHRA, 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/ICHRA, and CP.PMN.53 for Medicaid or evidence of coverage documents;

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*
FDA: Food and Drug Administration
PDE5: phosphodiesterase type 5
SVHD: single ventricle heart disease

*Appendix B: Therapeutic Alternatives*
Not applicable

*Appendix C: Contraindications/Boxed Warnings [Pending]*
- Contraindication(s): pending
- Boxed warning(s): pending

*Appendix D: General Information*
- Single ventricle defects include:
  - Hypoplastic left heart syndrome (HLHS): Occurs when the left ventricle, mitral valve, aortic valve and aorta are all undersized.
  - Double outlet right ventricle: Occurs when both the aorta and the pulmonary artery come out of the right ventricle. This leaves the left ventricle underdeveloped.
  - Tricuspid atresia: A defect where the tricuspid valve fails to develop. This leads to an underdeveloped right ventricle.
  - Double inlet left ventricle: occurs when both of the upper chambers of the heart (atria) connect to the left ventricle. This results in an underdeveloped right ventricle.
- The FUEL trial (Fontan Udenafil Exercise Longitudinal) was a phase III clinical trial conducted at 30 centers. Participants were randomly assigned udenafil, 87.5 mg twice daily, or placebo in a 1:1 ratio. The primary outcome was the between-group difference in change in oxygen consumption at peak exercise. Secondary outcomes included between-group differences in changes in submaximal exercise at the ventilator anaerobic threshold, the myocardial performance index, the natural log of the reactive hyperemia index, and serum brain-type natriuretic peptide. Individuals between the ages of 12 and 18 years (inclusive) who had undergone the Fontan procedure, who were not receiving treatment with a PDE5 inhibitor, who were ≥ 40 kg, and who met the minimum height requirement for cycle ergometry (≥ 132 cm) were eligible for enrollment. To isolate the effect of udenafil on exercise performance, patients with severe ventricular dysfunction,

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with severe atrioventricular valve insufficiency, or with a prior clinical exercise test in which peak oxygen consumption was < 50% of predicted for age and sex, were excluded.

## V. Dosage and Administration [Pending]

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| SVHD* | 87.5 mg PO BID* | 175 mg/day* |

## VI. Product Availability [Pending]

Pending

## VII. References

1. Goldberg DJ, Zak V, Goldstein BH, et al. Results of the FUEL trial. American Heart Association. Published online February 25, 2020. doi: 10.1161/CIRCULATIONAHA.119.044352.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| 4Q 2022 annual review: no significant changes as the drug is not yet FDA-approved; references reviewed and updated. Template changes applied to other diagnosis/indications and continued therapy section. | 07.22.22 | 11.22 |
| 4Q 2023 annual review: no significant changes as the drug is not yet FDA-approved; references reviewed and updated. | 08.23.23 | 11.23 |
| 4Q 2024 annual review: no significant changes as the drug is not yet FDA-approved; references reviewed and updated. | 07.30.24 | 11.24 |
| 4Q 2025 annual review: no significant changes as the drug is not yet FDA-approved; references reviewed and updated. | 07.24.25 | 11.25 |
| 4Q 2026 annual review: added ICHRA line of business; no significant changes as the drug is not yet FDA-approved; references reviewed and updated. | 07.23.26 | 11.26 |

**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.

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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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

**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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