

**Clinical Policy: Cysteamine oral (Cystagon, Procysbi)**

Reference Number: CP.PHAR.155

Effective Date: 02.16

Last Review Date: 05.22

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

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

**Description**

Cysteamine bitartrate (Cystagon<sup>®</sup>, Procysbi<sup>®</sup>) is a cysteine-depleting agent.

**FDA Approved Indication**

Cystagon and Procysbi are indicated for the treatment of nephropathic cystinosis. Cystagon is indicated for both children and adults, while Procysbi is indicated for patients 1 year of age and older.

**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 Cystagon and Procysbi are **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria****A. Nephropathic Cystinosis (must meet all):**

1. Diagnosis of nephropathic cystinosis confirmed by one of the following (a, b, or c):
  - a. Increased leukocyte cystine concentration (normal concentration: < 0.2 nmol half-cystine/mg protein);
  - b. Cystinosis, lysosomal cystine transporter gene mutation;
  - c. Corneal crystals on slit lamp examination;
2. If Procysbi is requested, member must use Cystagon, unless contraindicated or clinically significant adverse effects are experienced;
3. Dose does not exceed 1.95 g per m<sup>2</sup> per day.

**Approval duration: 6 months**

**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. Nephropathic Cystinosis (must meet all):**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;

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2. Member is responding positively to therapy as evidenced by improvement in the leukocyte cystine concentration within the past 3 months;
3. If request is for a dose increase, new dose does not exceed 1.95 g per m<sup>2</sup> per day.

**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.

**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 policy – 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*

FDA: Food and Drug Administration

WBC: white blood cell

*Appendix B: Therapeutic Alternatives*

Not applicable

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): hypersensitivity to penicillamine or cysteamine.
- Boxed warning(s): none reported.

*Appendix D: General Information*

A clinical trial compared Cystagon and Procysbi in 43 (40 pediatric and 3 adult) patients with nephropathic cystinosis. Prior to randomization, patients were to be on a stable dose of Cystagon administered every six hours. This trial demonstrated that at steady-state, Procysbi administered every 12 hours was non-inferior to Cystagon administered every 6 hours with respect to the depletion of white blood cell (WBC) cystine concentrations. The least-square mean value of WBC cystine was  $0.52 \pm 0.06$  nmol  $\frac{1}{2}$  cystine/mg protein after 12 hours under Procysbi and  $0.44 \pm 0.06$  nmol  $\frac{1}{2}$  cystine/mg protein after 6 hours under Cystagon; a difference of  $0.08 \pm 0.03$  nmol  $\frac{1}{2}$  cystine/mg protein (95.8% Confidence Interval = 0.01 to 0.15). The goal of cysteamine therapy is to lower WBC cystine levels.

**V. Dosage and Administration**

Indication	Dosing Regimen	Maximum Dose
Cystagon	Initial: 1/4 to 1/6 of the maintenance dose Recommended maintenance dose: For age < 12 years: 1.30 g/m <sup>2</sup> /day given in four divided doses For age ≥ 12 years: 2.0 g/day in four divided doses	1.95 g/m <sup>2</sup> /day
Procysbi	Cysteamine-naïve patients: Initial: 1/4 to 1/6 of the maintenance dose Recommended maintenance dose: 1.3 g/m <sup>2</sup> /day given in two divided doses  Switching from Cystagon: the starting total daily dose of Procysbi is equal to the previous total daily dose of Cystagon. Divide the total daily dose by two and administer every 12 hours.	1.95 g/m <sup>2</sup> /day

**VI. Product Availability**

Drug	Availability
Cystagon	Capsule: 50 mg, 150 mg
Procysbi	Delayed-release capsule: 25 mg, 75 mg Delayed-release oral granule packet: 75 mg, 300 mg

**VII. References**

1. Cystagon Prescribing Information. Morgantown, WV: Mylan Pharmaceuticals Inc.; January 2019. <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f495b76d-96c6-48e5-8fa3-30a4336628eb>. Accessed February 21, 2022.
2. Procysbi Prescribing Information. Lake Forest, IL: Horizon Pharma USA, Inc.; February 2022. Available at <http://www.procysbi.com>. Accessed February 21, 2022.
3. Kleta R, Kaskel F, Dohil R, et al. First NIH/Office of Rare Diseases conference on cystinosis: past, present, and future. *Pediatr Nephrol*. 2005;20:452-454.
4. Bendavid C, Kleta R, Long R, et al. FISH diagnosis of the common 57-kb deletion in CTNS causing cystinosis. *Hum Genet*. November 2004;115(6):501-514.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Q2 2018 annual review: no significant changes; HIM added; age restriction removed; added requirement of a prior trial of Cystagon for all Procysbi requests; added specific parameters for documenting a positive response to therapy, for reauthorization; references reviewed and updated.	02.25.18	05.18
2Q 2019 annual review: no significant changes; references reviewed and updated.	02.28.19	05.19

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2020 annual review: no significant changes; references reviewed and updated.	02.05.20	05.20
Added Commercial line of business per October SDC and prior clinical guidance.	10.08.20	
2Q 2021 annual review: no significant changes; revised Procysbi’s Cystagon requirement to “must use” language; revised HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	02.28.21	05.21
2Q 2022 annual review: no significant changes; WCG.CP.PHAR.155 retired and approval durations consolidated to 6 month initial and 12 months for continued therapy; references reviewed and updated.	02.21.22	05.22

**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

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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.

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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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