Clinical Policy: Cysteamine oral (Cystagon, Procysbi)

Reference Number: CP.PHAR.155
Effective Date: 02.16
Last Review Date: 05.25
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®, Procysbi®) 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® 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 above the upper limit of the normal reference range for the reporting laboratory (e.g., reported in units of nmol half-cystine/mg protein, methods used vary among individual laboratories and depend upon the assay method used; values obtained from using different assay methods may not be interchangeable);
   b. Cystinosin, lysosomal cystine transporter (CTNS) gene mutation;
   c. Corneal crystals on slit lamp examination;
2. Prescribed by or in consultation with a nephrologist or a metabolic disease specialist experienced in management of nephropathic cystinosis (e.g., endocrinologist or urologist);
3. If Procysbi is requested, member must use Cystagon, unless contraindicated or clinically significant adverse effects are experienced;
4. Request is not for combination use of Procysbi and Cystagon;
5. Dose does not exceed 1.95 g per m^2 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) 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. Nephropathic Cystinosis (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 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^2 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) 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 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
CTNS: cystinosin, lysosomal cystine transporter
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 ± 0.06 nmol ½ cystine/mg protein after 12 hours under Procysbi and 0.44 ± 0.06 nmol ½ cystine/mg protein after 6 hours under Cystagon; a difference of 0.08 ± 0.03 nmol ½ 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^2/day given in four divided doses For age ≥ 12 years: 2.0 g/day in four divided doses	1.95 g/m^2/day
Procysbi	Cysteamine-naïve patients: Initial: 1/4 to 1/6 of the maintenance dose Recommended maintenance dose: 1.3 g/m^2/day given in two divided doses	1.95 g/m^2/day

Indication	Dosing Regimen	Maximum Dose
	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.	

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.; August 2021. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f495b76d-96c6-48e5-8fa3-30a4336628eb. Accessed January 16, 2025.
2. Procysbi Prescribing Information. Lake Forest, IL: Horizon Pharma USA, Inc.; February 2022. Available at http://www.procysbi.com. Accessed January 16, 2025.
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.
5. Elmonem MA, Veys KR, Soliman NA, et. al. Cystinosis: a review. Orphanet J Rare Dis. 2016 Apr 22; 11: 47.
6. Veys KR, Elmonem MA, Arcolino FO, et. al. Nephropathic cystinosis: an update. Curr Opin Pediatr. 2017 Apr; 29 (2): 168-178.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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
Template changes applied to other diagnoses/indications and continued therapy section.	09.30.22	
2Q 2023 annual review: no significant changes; references reviewed and updated.	01.10.23	05.23
2Q 2024 annual review: added requirement that request is not for combination use of Procysbi and Cystagon for initial criteria; for	01.08.24	05.24

Reviews, Revisions, and Approvals	Date	P&T Approval Date
diagnostic confirmation by leukocyte cystine concentration, clarified this must be above the upper limit of the normal reference range for the reporting laboratory; references reviewed and updated.		
2Q 2025 annual review: added prescriber requirement for nephrologist or a metabolic disease specialist experienced in management of nephropathic cystinosis (e.g., endocrinologist or urologist); references reviewed and updated.	01.16.25	05.25

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.

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.