Clinical Policy: Cysteamine (Cystagon, Procysbi)

Reference Number: WA.PHAR.21
Effective Date: 01//2018
Last Review Date: 01/2020, 01/2021 Revision Log
Line of Business: Medicaid

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(s)

Cystagon and Procysbi are indicated for the treatment of nephropathic cystinosis. Cystagon is indicated for both children and adults, which Procysbi is indicated for patients 1 year or 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 (normal concentration: < 0.2 nmol half-cystine/mg protein);
   b. Cystinosin, lysosomal cystine transporter gene mutation;
   c. Corneal crystals on slit lamp examination;
2. If Procysbi is requested, all of the following are met (a and b):
   a. Age ≥ 1 year;
   b. If Procysbi is requested, patient must have a contraindication for Cystagon that is not present in Procysbi (e.g. contraindication to excipients in Cystagon) or provide evidence supporting increased efficacy or safety for Procysbi over Cystagon.
      i. Coverage of Procysbi will not be authorized for dosing convenience.
3. Dose does not exceed 1.95 g/m^2/day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by improvement in the leukocyte cysteine concentration within the past 3 months. In addition, if Procysbi is requested, must provide documentation that patient did not respond positively to an adequate dose and duration of Cystagon. Coverage of Procysbi will not be authorized for dosing convenience.
3. If request is for a dose increase, new dose does not exceed 1.95 g/m^2/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 CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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.PHAR.57 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: 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 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 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^2/day

VI. Product Availability

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

VII. References

1. Cystagon Prescribing Information. Morgantown, WV: Mylan Pharmaceuticals Inc.; https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f495b76d-96c6-48e5-8fa3-30a4336628eb. Accessed January 12, 2018.
2. Procysbi Prescribing Information. Novato, CA: Raptor Pharmaceuticals, Inc.; December 2017. Available at http://www.procysbi.com. Accessed January 12, 2018.
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
Policy split from CP.PHAR.48 LSD Policy converted to new template	01.16	02.16
Age restriction removed. Additional diagnostic criteria added. Reasons to discontinue added to continuation criteria. Positive response to therapy added. Background section converted to new template.	12.16	02.17
Policy converted to newer template. Age restriction added. Reasons to discontinue removed from continuation criteria.	09.05.17	11.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Age restriction for Procysbi updated to reflect new FDA approved age range. Added requirement of a prior trial of Cystagon for all Procysbi requests.	01.12.18	
Annual Review- No Changes	01.09.2019	01.09.2019
Annual Review- No Changes	01.03.2020	01.14.2020
Updated initial criteria in IA2b to state, "If Procysbi is requested, patient must have a contraindication for Cystagon that is not present in Procysbi (e.g. contraindication to excipients in Cystagon) or provide evidence supporting increased efficacy or safety for Procysbi over Cystagon." Also added Procysbi will not be authorized for dosing convenience. Updated continuation criteria in IIA2 to state, "Member is responding positively to therapy as evidenced by improvement in the leukocyte cysteine concentration within the past 3 months. In addition, if Procysbi is requested, must provide documentation that patient did not respond positively to an adequate dose and duration of Cystagon." Also added Procysbi will not be authorized for dosing convenience.	12.29.2020	01.12.2021

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.

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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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