Clinical Policy: Cysteamine (Cystagon, Procysbi)

Reference Number: PA.CP.PHAR.155
Effective Date: 01/18
Last Review Date: 04/19 Revision Log

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
It is the policy of health plans affiliated with Pennsylvania Health and Wellness 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 any of the following:
   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, medical justification supports inability to use Cystagon (e.g., contraindication to excipients in Cystagon);
3. Dose does not exceed 1.95 g/m^2/day.

Approval duration: 6 months

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. Nephropathic Cystinosis (must meet all):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
2. Member is responding positively to therapy as evidenced by improvement in the leukocyte cystine concentration since starting treatment;
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 Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53

III. 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 ± 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.

IV. 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

V. Product Availability

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

VI. References

1. Cystagon Prescribing Information. Morgantown, WV: Mylan Pharmaceuticals Inc.; June 2018. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f495b76d-96c6-48e5-8fa3-30a4336628eb. Accessed February 28, 2019.
2. Procysbi Prescribing Information. Novato, CA: Raptor Pharmaceuticals, Inc.; December 2017. Available at http://www.procysbi.com. Accessed February 28, 2019.
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	Approval Date
Q2 2018 annual review: no significant changes; age restriction added; 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: references reviewed and updated	04/19	