Clinical Policy: Cysteamine (Cystagon, Procysbi)

Reference Number: PA.CP.PHAR.155
Effective Date: 01/2018
Last Review Date: 04/2023 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
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 PA Health & 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 (CTNS) 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/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 PA Health & 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 PA Health & 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
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.

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 Delayed-release oral granule packet: 75 mg, 300 mg

VI. 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 01, 2023.
2. Procysbi Prescribing Information. Lake Forest, IL: Horizon Pharma USA, Inc.; February 2020. Available at http://www.procysbi.com. Accessed January 10, 2023.
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	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.	02/2018	05.18
2Q 2019 annual review: references reviewed and updated	04/2019	
2Q 2020 annual review: references reviewed and updated	04/2020	
2Q 2021 annual review: no significant changes; revised Procysbi's Cystagon requirement to "must use" language; references reviewed and updated.	04/2021	
2Q 2022 annual review: references reviewed and updated.	04/2022	
2Q 2023 annual review: no significant changes; references reviewed and updated.	04/2023	