RXADVANCE
2 Park Central Drive
Southborough, MA 01772

RxAdvance **Clinical Policy Title: Cysteamine oral (Cystagon, Procysbi)**
Policy Number: RxA.84
Drug(s) Applied: Cysteamine bitartrate (Cystagon®, Procysbi®)
Last Review Date: 04/2020
Line of Business: Commercial, HIM, Medicaid

Background

Cysteamine bitartrate (Cystagon®, Procysbi®) is a cysteine-depleting agent.
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.

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

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

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

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, medical justification supports inability to use Cystagon (e.g., contraindication to excipients in Cystagon);

3. Dose does not exceed 1.95 g per m^2 per day.

Approval duration:
HIM – 6 months
Medicaid – 6 months

II. Continued Therapy

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

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
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:
HIM – 12 months
Medicaid – 12 months

III. Appendices

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.

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.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy was established	01/2020	02/07/2020
Updated line of business, drug availability, and removed old policy reference	04/2020	05/21/2020