Clinical Policy Title:	cysteamine bitartrate
Policy Number:	RxA.84
Drug(s) Applied:	Cystagon®, Procysbi®
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Cysteamine bitartrate is a cysteine-depleting agent. Cystagon® and Procysbi® are indicated for the treatment of corneal cystine crystal accumulation in patients with nephropathic cystinosis in children and adults.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
cysteamine bitartrate (Cystagon®)	Nephropathic cystinosis	Initial: One-fourth (1/4) to one-sixth (1/6) of the maintenance dose Recommended maintenance dose: For ages less than 12 years of age: 1.3 g/m^2/day given in four divided doses. For ages 12 years and older (and over 110 lb): 2 g/day in four divided doses	1.95 g/m^2/day
cysteamine bitartrate (Procysbi®)		Initial: One-fourth (1/4) to one-sixth (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

Dosage Forms

- Cystagon®:
  - Immediate release capsules: 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 is less than 0.2 nmol half-cystine/mg protein);
   b. Cystinosin, lysosomal cystine transporter gene mutation;
   c. Corneal crystals on slit lamp examination;
2. Prescribed by or in consultation with a nephrologist or metabolic disease specialist;
3. Member is 1 year of age or older;
4. If Procysbi® is requested, medical justification supports inability to use Cystagon® (e.g., contraindication to excipients in Cystagon®);
5. Cystagon® and Procysbi® are not being used concomitantly;
6. Dose does not exceed 1.95 g per m^2 per day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

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

1. Member is 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; and
3. If request is for a dose increase, new dose does not exceed 1.95 g per m^2 per day.

Approval Duration
Commercial: 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 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.; January 2019. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f495b76d-96c6-48e5-8fa3-30a4336628eb. Accessed January 21, 2021.
2. Procysbi® Prescribing Information. Novato, CA: Raptor Pharmaceuticals, Inc.; February 2020. Available at https://www.hzndocs.com/PROCYSBI-Prescribing-Information.pdf. Accessed January 21, 2021.
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. Wilmer MJ, Schoeber JP, van den Heuvel LP, Levtchenko EN. Cystinosis: practical tools for diagnosis and treatment. Pediatr Nephrol. 2011; 26(2): 205–215.
6. Tsilou E, Zhou M, Gahl W, et al. Ophthalmic manifestations and histopathology of infantile nephropathic cystinosis: Report of a case and review of the literature. Surv Ophthalmol. 2007; 52(1): 97–105.
7. Gahl WA, Thoene JG, Schneider JA, et al. NIH Conference. Cystinosis: progress in a prototypic disease. Ann Int Med. 1988; 109: 557-569.
8. National Organization for Rare Disorders (NORD). Cystinosis. Accessed on February 25, 2020. Available at: https://rarediseases.org/rare-diseases/cystinosis/. Accessed January 21, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy was established	01/2020	02/07/2020
Updated line of business, drug availability, and removed old policy reference	4/2020	05/20/2020
Policy was reviewed and updated. 1. Clinical policy title and lines of business updated. 2. Commercial approval duration was updated for initial and Continued approval criteria. 3. Initial criteria for approval and duration of approval updated. 4. Continued therapy criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance…". 5. References updated.	01/21/2021	03/09/2021