Clinical Policy: Cysteamine (Cystagon, Procysbi)

Reference Number: ERX.SPA.105
Effective Date: 10.01.16
Last Review Date: 05.22
Line of Business: Commercial, Medicaid

Revision Log

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, 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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, member must use Cystagon, unless contraindicated or clinically significant adverse effects are experienced;
3. Dose does not exceed 1.95 g per m^2 per day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 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 a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
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: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to ERX.PA.01 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 – ERX.PA.01 or evidence of coverage documents.

IV. 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.

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Cystagon	*Initial*: 1/4 or 1/6 of the maintenance dose *Maintenance*: age up to 12 years: 1.3 g/m^2/day given in 4 divided doses; 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 *Maintenance*: 1.3 g/m^2/day divided into 2 doses given every 12 hours; titrate as needed Patients switching from immediate-release cysteamine (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 Name	Availability
Cystagon	Capsule: 50 mg, 150 mg
Procysbi	Delayed-release capsule: 25 mg, 75 mg Delayed-release oral granule packet: 75 mg, 300 mg

VII. 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 February 21, 2022.
2. Procysbi Prescribing Information. Lake Forest, IL: Horizon Pharma USA, Inc.; February 2022. Available at http://www.procysbi.com. Accessed February 21, 2022.
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
2Q 2018 annual review: Removed age restriction for Procysbi; Added requirement of a prior trial of Cystagon for all Procysbi requests; References reviewed and updated.	02.25.18	05.18
2Q 2019 annual review: no significant changes; references reviewed and updated.	02.28.19	05.19
2Q 2020 annual review: no significant changes; references reviewed and updated.	02.05.20	05.20
2Q 2021 annual review: no significant changes; revised Procysbi's Cystagon requirement to "must use" language; references reviewed and updated.	02.28.21	05.21
2Q 2022 annual review: no significant changes; references reviewed and updated.	02.21.22	05.22

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.