

## PRIOR AUTHORIZATION POLICY

**POLICY:** Metabolic Disorders – Cysteamine (Oral) Products

- Cystagon (cysteamine bitartrate capsules – Mylan Pharmaceuticals)
- Procysbi (cysteamine bitartrate delayed-release capsule, delayed release granules – Raptor Therapeutics Inc.)

**DATE REVIEWED:** 03/11/2020

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### OVERVIEW

Cystagon and Procysbi are cystine-depleting agent indicated for the management of nephropathic cystinosis in adults and children.<sup>1-2</sup> Note that Procysbi is indicated specifically in patients who are 1 year of age and older.<sup>1</sup> Therapy with a cysteamine product should be initiated promptly once the diagnosis is confirmed (i.e., increased white blood cell cystine concentration). Cystagon needs to be administered four times daily, whereas Procysbi (a delayed-release formulation of cysteamine) is given once every 12 hours.<sup>1-2</sup> For patients who are unable to swallow capsules, both products have instructions for opening the capsules and administering in food and/or liquids.

### Disease Overview

Cystinosis is a very rare autosomal recessive inborn error of metabolism in which the transport of cystine out of lysosomes is abnormal.<sup>3-5</sup> As a result of deficient or absent cystinosin (which normally transports cystine out of the lysosome), cystine accumulates within lysosomes and forms crystals in many tissues, including the kidneys, liver, bone marrow, pancreas, muscle, rectal mucosa, brain and eye. Diagnosis is confirmed by measuring cystine levels in polymorphonuclear leukocytes.<sup>6</sup> Molecular genetic testing identifies a characteristic mutation of the *CTNS* gene. Prenatal diagnosis is possible (i.e., by elevation of cystine in amniotic fluid or chorionic villi). Patients with cystinosis also experience growth failure and rickets, and cystine deposits in the cornea cause photophobia.<sup>3-5</sup> Over time, most organs are damaged. Cysteamine products are aminothiols that act as cystine-depleting agents.

### POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of cysteamine oral products (Cystagon and Procysbi). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with cysteamine oral products (Cystagon and Procysbi) as well as the monitoring required for adverse events and long-term efficacy, approval requires cysteamine oral products (Cystagon and Procysbi) to be prescribed by or in consultation with a physician who specializes in the condition being treated.

**Automation:** None.

### RECOMMENDED AUTHORIZATION CRITERIA

Coverage of cysteamine oral products (Cystagon and Procysbi) is recommended in those who meet the following criteria:

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### FDA-Approved Indications

1. **Cystinosis, Nephropathic.** Approve for 1 year if the patient meets the following criteria (A, B, and C):
  - A) According to the prescriber, the diagnosis was confirmed by one of the following (i or ii):
    - i. Genetic testing confirmed a mutation of the *CTNS* gene; OR
    - ii. White blood cell cystine concentration above the upper limit of the normal reference range for the reporting laboratory.  
Note: The methods used for measuring cystine vary among individual laboratories and depend upon the assay method used by the individual laboratory; values obtained from using different assay methods may not be interchangeable; AND
  - B) The patient will not be using Cystagon and Procysbi concurrently; AND
  - C) The medication is prescribed by or in consultation with a nephrologist or a metabolic disease specialist (or specialist who focuses in the treatment of metabolic diseases).

### CONDITIONS NOT RECOMMENDED FOR APPROVAL

Cysteamine oral products (Cystagon and Procysbi) have not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions.

1. **Concomitant Therapy with Cystagon and Procysbi.** There are no data available to support concomitant use.
2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

### REFERENCES

1. Procysbi [prescribing information]. Lake Forest, IL: Horizon Pharma; May 2019.
  2. Cystagon [prescribing information]. Morgantown, WV: Mylan Pharmaceuticals, Inc.; January 2019.
  3. Wilmer MJ, Schoeber JP, van den Heuvel LP, Levtchenko EN. Cystinosis: practical tools for diagnosis and treatment. *Pediatr Nephrol.* 2011; 26(2): 205–215.
  4. 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.
  5. Gahl WA, Thoene JG, Schneider JA, et al. NIH Conference. Cystinosis: progress in a prototypic disease. *Ann Int Med.* 1988;109:557-569.
  6. National Organization for Rare Disorders (NORD). Cystinosis. Accessed on February 25, 2020. Available at: <https://rarediseases.org/rare-diseases/cystinosis/>.
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