cysteamine bitartrate (Cystagon®; Procysbi®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO118

Description

Cysteamine bitartrate (Cystagon; Procysbi) is a cystine-depleting agent that lowers cystine levels within cells.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit
cysteamine (Cystagon)	50 mg capsule	Nephropathic cystinosis	60 capsules/30 days
	150 mg capsule		120 capsules/30 days
cysteamine (Procysbi)	25 mg DR capsule		60 capsules/30 days
	75 mg DR capsule		*990 capsules/30 days

**Based on an average BSA of 1.9m²*

Initial Evaluation

I. Cysteamine bitartrate (Cystagon; Procysbi) may be considered medically necessary when the following criteria below are met:
   A. A diagnosis of **nephropathic cystinosis** when the following are met:
      1. Diagnosis has been confirmed with ONE of the following:
         i. Presence of corneal cysteine accumulation; **OR**
         ii. CTNS gene analysis; **OR**
         iii. Elevated intracellular cystine levels (>1nmol cystine/mg protein); **AND**
      2. **If Procysbi is requested**, documentation member has an intolerance, or contraindication to, Cystagon; **OR**
         i. Documentation of unavoidable non-adherence to cysteamine IR (Cystagon) that prevents the achievement of optimal white blood cell (WBC) cystine levels (<1 nmol ½ cystine per mg protein); **AND**
      3. Dose does not exceed 1.95 g per m^2 per day

II. Cysteamine bitartrate (Cystagon, Procysbi) is considered investigational when used for all other conditions.

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has exhibited improvement or stability of disease symptoms; **AND**
IV. Member is responding positively to therapy as evidenced by improvement in the leukocyte cystine concentration within the past 3 months; **AND**
V. If request is for a dose increase, new dose does not exceed 1.95 g per m^2 per day

Supporting Evidence

I. Cystinosis is a rare, multisystem genetic disorder caused by mutations within the CTNS gene on chromosome 17p13, which is characterized by the accumulation of cystine in different organs and tissues, increasing the potential for severe organ dysfunction. It is further classified into three forms known as nephropathic cystinosis, intermediate cystinosis and non-nephropathic (or ocular) cystinosis. Corneal cystine crystal accumulation may present in all three types of cystinosis. Therapy of cystinosis is comprised of the amelioration of symptoms, the administration of cysteamine, and renal transplantation for those who progress to end-stage renal disease (ESRD). Topical cysteamine is prescribed to prevent corneal deposits, because the oral formulation does not reach the cornea due to absent corneal vascularization.
II. Diagnosis of cystinosis is confirmed by elevated intraleukocyte cystine content, (i.e. measuring cystine levels in polymorphonuclear leukocytes), detection of CNTS gene mutation, or demonstration of cystine corneal crystals by the slit lamp examination.
III. The immediate-release preparation of cysteamine bitartrate is the most commonly used formulation. The dose should be progressively increased from 10 to 50 mg/kg per day (maximum dose of 1.95 gm/m2 per day), given in divided doses every six hours. Cystine levels are measured in white blood cells once a maintenance dose is reached; this is then followed by monitoring monthly for three months, quarterly for one year, and then twice a year. Blood sampling should be obtained six hours after taking a dose of cysteamine.
IV. The goal of cysteamine therapy is to lower WBC cystine levels to an optimal target level of less than 1 nmol half-cystine/mg protein.
V. Cysteamine bitartrate (Procysbi) is a delayed-release formulation of cysteamine bitartrate (Cystagon). The delayed-release (Procysbi) formulation is dosed twice daily, while the immediate release (Cystagon) is dosed four times daily. Currently, there is insufficient evidence to support an additional adherence benefit from taking cysteamine DR (Procysbi) when considered together with the extensive increase in cost (estimated 90x increase). Additionally, in the pivotal trial for cysteamine DR (Procysbi), there was a higher incidence of adverse reactions in patients taking the delayed release product compared to patients taking immediate-release cysteamine (Cystagon).

References

1. Cystagon [Prescribing Information]. Morgantown, WV: Mylan Pharmaceuticals Inc.; June 2018.
2. Procysbi [Prescribing Information]. Novato, CA: Raptor Pharmaceuticals, Inc.; December 2017.
3. UpToDate, Inc. Cystinosis. UpToDate [database online]. Waltham, MA. Last updated February 27, 2019 Available at: http://www.uptodate.com/home/index.html.
4. National Organization for Rare Disorders. Cystinosis. Available at: https://rarediseases.org/rare-diseases/cystinosis/

Policy Implementation/Update:

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Action and Summary of Changes	Date