Cystine Depleting Agents

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 IR (Cystagon)	50 mg capsule	Nephropathic cystinosis	60 capsules/30 days
	150 mg capsule		1.95 g/m^2/day
cysteamine DR (Procysbi)	25 mg DR capsule		60 capsules/30 days
	75 mg DR capsule		1.95 g/m^2/day
	75 mg DR granule packet		1.95 g/m^2/day
	300 mg DR granule packet		1.95 g/m^2/day

Initial Evaluation

Cysteamine bitartrate IR (Cystagon) is the preferred cystine-depleting agent.

- **Patients must have failed, have contraindication to, or intolerance of cysteamine bitartrate IR (Cystagon) prior to the consideration of cysteamine bitartrate DR (Procysbi).**
  - There is no prior authorization required for cysteamine bitartrate IR (Cystagon) when used for nephropathic cystinosis unless requesting above the quantity limit noted above.

I. **Cysteamine bitartrate DR (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. Documentation member has an intolerance or contraindication to cysteamine bitartrate IR (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 requested 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 or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, 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 [e.g., reduction in leukocyte cystine concentration]; **AND**
IV. If request is for a dose increase, the 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 infantile (nephropathic) cystinosis, late-onset (juvenile) cystinosis, and adult (benign or ocular nonnephropathic) cystinosis. Corneal cystine crystal accumulation may be present in all three types of cystinosis. Treatment 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). Ophthalmic 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 *CTNS* gene mutation, or demonstration of cystine corneal crystals by the slit lamp examination.
III. The immediate-release preparation of cysteamine bitartrate (Cystagon) is the most 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. 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.

IV. The safety and efficacy of cysteamine bitartrate IR (Cystagon) was demonstrated in the National Collaborative Cysteamine Study (NCCS) which treated 94 children with nephropathic cystinosis with increasing doses of cysteamine HCl (mean dose 54 mg/kg/day) to attain white cell cystine levels of <2 nmol ½ cystine per mg protein 5 to 6 hours post-dose in comparison with an historical control group of 17 children who had been in the placebo group of a randomized placebo-controlled trial of ascorbic acid. The average median white cell cystine level attained during treatment in the NCCs was 1.7 ± 0.2 nmol ½ cystine per mg protein. Among cysteamine patients, glomerular function was maintained over time despite the longer period of treatment and follow-up (up to 5 years vs. 2 years with placebo).

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.; August 2021.
2. Procysbi [Prescribing Information]. Novato, CA: Raptor Pharmaceuticals, Inc.; February 2022.
3. UpToDate, Inc. Cystinosis. UpToDate [database online]. Waltham, MA. Last updated March 11, 2022. 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:

Action and Summary of Changes	Date
Removed PA for cysteamine bitartrate (Cystagon) in favor of RDx edit programming. Adjusted policy to reflect programming change. Updated supporting evidence.	02/2024
Addition of Procysbi granule packets	04/2020
Policy created	11/2019