CareSource Rx Innovations

PHARMACY POLICY STATEMENT
North Carolina Marketplace

DRUG NAME	Procysbi and Cystagon (cysteamine bitartrate); Cystaran and Cystadrops (cysteamine hydrochloride solution)
BENEFIT TYPE	Pharmacy
STATUS	Prior Authorization Required

Cysteamine bitartrate, approved by the FDA in 1994 as immediate release Cystagon and in 2013 as extended release Procysbi, is indicated for the treatment of nephropathic cystinosis.
Cystinosis is a rare inherited metabolic disease in which cystine builds up as damaging crystals in organs including the kidneys and eyes. It is caused by *CTNS* gene mutations that result in defective cystinosin transport protein that keeps cystine from effectively exiting lysosomes.
Manifestations can include Fanconi syndrome, renal failure, photophobia due to cystine deposits in the cornea, and endocrine disruption such as hypothyroidism or hypogonadism. Nephropathic (infantile) cystinosis is the most common and most severe type of cystinosis. The adult non-nephropathic ocular form affects the cornea only.
Cysteamine depletes white blood cell (WBC) cystine levels to slow the progression of disease manifestations such as end stage renal disease. Systemic cysteamine does not affect the cornea, thus cysteamine eye drops are indicated when corneal cystine crystals are present.
Cysteamine hydrochloride eye drops are supplied as Cystaran or Cystadrops. Cystadrops can be administered less frequently but has a higher incidence of side effects.

Cysteamine products will be considered for coverage when the following criteria are met:

Nephropathic Cystinosis (Procysbi or Cystagon)

For **initial** authorization:

1. Member must be 1 year of age or older if the request is for Procysbi (no limit for Cystagon); AND
2. Medication must be prescribed by or in consultation with a nephrologist or endocrinologist; AND
3. Member has a documented diagnosis of nephropathic cystinosis confirmed by an elevated WBC cystine concentration greater than 2 nmol ½ cystine/mg protein (lab report must include reference values) AND at least one of the following:
   a) *CTNS* gene mutation
   b) Presence of corneal crystals, as shown by slit lamp exam performed by an ophthalmologist; AND
4. If the request is for Procysbi, ALL the following that are applicable must be documented in chart notes:
   a) Inability to reach target cystine level (<1 nmol ½ cystine/mg protein) despite a minimum of 6 months of compliant therapy with Cystagon at max dose (or highest tolerated dose)
   b) If requesting switch from Cystagon due to intolerance, member must first attempt to temporarily stop therapy, then re-initiate at a lower dose and gradually increase to the proper dose
   c) If requesting switch from Cystagon due to GI side effects, member must also try taking with a proton pump inhibitor (e.g., omeprazole), in addition to attempting dose adjustment
   d) NOTE: Any other rationale for switching from Cystagon (aside from inefficacy or intolerance) will be considered on a case-by-case basis. In general, CareSource does not recognize frequency of dosing convenience or lack of adherence as being indicative of medical necessity.
5. **Dosage allowed/Quantity limit:** Refer to product label for initiation, titration, and adjustment details.

Cystagon: Every 6 hours orally
Procysbi: Every 12 hours orally
Max dose 1.95 g/m^2 /day

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:
1. Lab report must show decreased cystine levels from baseline; AND
2. Chart notes must show stabilized or improved signs and symptoms of disease or slowed progression (e.g., kidney function).

If all the above requirements are met, the medication will be approved for an additional 12 months.

Cystinosis (Cystaran or Cystadrops)

For **initial** authorization:
1. Medication must be prescribed by or in consultation with a nephrologist or ophthalmologist; AND
2. Member has a diagnosis of cystinosis confirmed by an elevated WBC cystine concentration 1 nmol ½ cystine/mg protein or greater; AND
3. Presence of corneal crystal deposits as evidenced by slit lamp exam.
4. **Dosage allowed/Quantity limit:**
   Cystaran: 1 drop in each eye, every waking hour
   Cystadrops: 1 drop in each eye, 4 times a day during waking hours
   QL: 4 bottles per 28 days

If all the above requirements are met, the medication will be approved for 3 months.

For **reauthorization**:
1. Chart notes have been provided to show improvement of signs and symptoms of disease (e.g., reduction of corneal cystine crystal accumulation, decreased severity of photophobia).

If all the above requirements are met, the medication will be approved for an additional 12 months.

CareSource considers cysteamine products not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
10/07/2020	New policy for Procysbi and Cystagon (cysteamine bitartrate), Cystaran and Cystadrops (cysteamine hydrochloride solution) created
08/09/2023	Transferred to new template. Added QL for eye drops. NC: Added endocrinology as a specialist. Elaborated on dosing information. Specified target cystine level. In renewal, changed “stabilized or decreased” cystine to “decreased.” Updated/added references.

References:

1. 2021 Georgia Code Title 33 – Insurance Chapter 20A - Managed Health Care Plans Article 2 - Patient's Right to Independent Review § 33-20A-31 Definitions. Justia US Law. Accessed April 25, 2023. https://law.justia.com/codes/georgia/2021/title-33/chapter-20a/article-2/section-33-20a-31/.
2. Procysbi (cysteamine bitartrate) [package insert]. Lake Forest, IL: Horizon Therapeutics USA, Inc.; 2022.
3. Cystagon (cysteamine bitartrate) [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc; 2021.
4. Wilmer MJ, Schoeber JP, van den Heuvel LP, Levtchenko EN. Cystinosis: practical tools for diagnosis and treatment. *Pediatr Nephrol*. 2011;26(2):205-215. doi:10.1007/s00467-010-1627-6
5. Elmonem MA, Veys KR, Soliman NA, Dyck MV, Heuvel LPVD, Levtchenko E. Cystinosis: a review. *Orphanet Journal of Rare Diseases*. April 2016. doi:10.1186/s13023-016-0426-y
6. Bäumner S, Weber LT. Nephropathic Cystinosis: Symptoms, Treatment, and Perspectives of a Systemic Disease. *Front Pediatr*. 2018;6:58. Published 2018 Mar 14. doi:10.3389/fped.2018.00058
7. Emma F, Nesterova G, Langman C, et al. Nephropathic cystinosis: an international consensus document. *Nephrol Dial Transplant*. 2014;29 Suppl 4(Suppl 4):iv87-iv94. doi:10.1093/ndt/gfu090
8. Nesterova G, Gahl WA. Cystinosis. 2001 Mar 22 [Updated 2017 Dec 7]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2020. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1400/
9. Bäumner S, Weber LT. Conversion from immediate- to extended-release cysteamine may decrease disease control and increase additional side effects. *Pediatric Nephrology*. 2017;32(7):1281-1282. doi:10.1007/s00467-017-3618-3
10. Langman CB, Barshop BA, Deschênes G, et al. Controversies and research agenda in nephropathic cystinosis: conclusions from a "Kidney Disease: Improving Global Outcomes" (KDIGO) Controversies Conference. *Kidney Int*. 2016;89(6):1192-1203. doi:10.1016/j.kint.2016.01.033
11. Langman CB, Greenbaum LA, Sarwal M, et al. A randomized controlled crossover trial with delayed-release cysteamine bitartrate in nephropathic cystinosis: effectiveness on white blood cell cystine levels and comparison of safety [published correction appears in Clin J Am Soc Nephrol. 2013 Mar 7;8(3):468]. *Clin J Am Soc Nephrol*. 2012;7(7):1112-1120. doi:10.2215/CJN.12321211
12. Cystaran (cysteamine hydrochloride solution) [package insert]. Gaithersburg, MD: Leadiant Biosciences, Inc.; 2022.
13. Cystadrops (cysteamine hydrochloride solution) [package insert]. Lebanon, NJ: Recordati Rare Diseases Inc.; 2020.
14. Kaur S, Sarma P, Kaur H, et al. Efficacy and safety of topical cysteamine in corneal cystinosis: a systematic review and meta- analysis. *American Journal of Ophthalmology*. September 2020. doi:10.1016/j.ajo.2020.07.052
15. Biswas S, Gaviria M, Malheiro L, Marques JP, Giordano V, Liang H. Latest Clinical Approaches in the Ocular Management of Cystinosis: A Review of Current Practice and Opinion from the Ophthalmology Cystinosis Forum. *Ophthalmol Ther*. 2018;7(2):307-322. doi:10.1007/s40123-018-0146-6.

Effective date: 01/01/2024
Revised date: 08/09/2023