

## PHARMACY COVERAGE GUIDELINE

### **CYSTADROPS® (cysteamine hydrochloride)** **CYSTARAN™ (cysteamine hydrochloride)** **PROCYSBI® (cysteamine bitartrate)** **Generic Equivalent (if available)**

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#### **This Pharmacy Coverage Guideline (PCG):**

- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively “Service”) is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider’s judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member’s benefit plan; and
- Is subject to change as new information becomes available.

#### **Scope**

- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

#### **Instructions & Guidance**

- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The “Criteria” section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member’s benefit plan.
- The “Description” section describes the Service.
- The “Definition” section defines certain words, terms or items within the policy and may include tables and charts.
- The “Resources” section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at [www.azblue.com/pharmacy](http://www.azblue.com/pharmacy). You must fully complete the [request form](#) and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to [Pharmacyprecert@azblue.com](mailto:Pharmacyprecert@azblue.com).

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#### **Criteria:**

### **CYSTADROPS (cysteamine hydrochloride)** **CYSTARAN (cysteamine hydrochloride)**

- **Criteria for initial therapy:** Cystadrops (cysteamine hydrochloride), Cystaran (cysteamine hydrochloride) and/or generic equivalent (if available) is considered **medically necessary** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient’s diagnosis or is in consultation with an Ophthalmologist or Optometrist

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- Individual has a confirmed diagnosis of corneal cystine crystal deposits due to cystinosis
- Individual has medical record documentation of **ONE** of the following:
  - Demonstration of corneal cystine crystal deposits by slit lamp examination
  - Elevated cystine content of peripheral blood leukocytes or fibroblasts
  - Detection of a pathologic *CTNS* gene variant
- If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))
- Cystadrops and Cystaran will not be used concurrently

#### **Initial approval duration:**

**Cystadrops:** Up to 4 bottles of 5 mL/month x 6 months  
**Cystaran:** Up to 4 bottles of 15 mL/month x 6 months

- **Criteria for continuation of coverage (renewal request):** Cystadrops (cysteamine hydrochloride), Cystaran (cysteamine hydrochloride) and/or generic equivalent (if available) is considered **medically necessary** and will be approved when **ALL** the following criteria are met (**samples are not considered for continuation of therapy**):

- Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Ophthalmologist or Optometrist
- Individual has documentation of positive clinical response to therapy defined as **BOTH** of the following:
  - Reduction in cystine crystal formation in the structures of the eye
  - Reduced symptoms of photophobia, visual impairment, or foreign body sensation
- Individual has been adherent with the medication
- If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))
- Cystadrops and Cystaran will not be used concurrently

#### **Renewal duration:**

**Cystadrops:** Up to 4 bottles of 5 mL/month x 6 months  
**Cystaran:** Up to 4 bottles of 15 mL/month x 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

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### CYSTADROPS® (cysteamine hydrochloride) CYSTARAN™ (cysteamine hydrochloride) PROCYSBI® (cysteamine bitartrate) Generic Equivalent (if available)

1. Off-Label Use of Non-Cancer Medications
2. Off-Label Use of Cancer Medications

### PROCYSBI (cysteamine bitartrate)

➤ **Criteria for initial therapy:** Procysbi (cysteamine bitartrate) delayed release and/or generic equivalent (if available) are considered **medically necessary** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Nephrologist or Pediatrician or Specialist in Inborn Errors of Metabolism
2. Individual is 1 year of age or older
3. Individual has a confirmed diagnosis of nephropathic cystinosis (classic infantile cystinosis)
4. Individual has medical record documentation of **ONE** of the following:
  - a. Demonstration of corneal cystine crystal deposits by slit lamp examination
  - b. Elevated cystine content of peripheral blood leukocytes or fibroblasts
  - c. Detection of a pathologic *CTNS* gene variant
5. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))
6. Individual has documented failure, contraindication per FDA label, intolerance or is not a candidate for Cystagon (cysteamine bitartrate) immediate release capsules
7. Procysbi and Cystagon will not be used concurrently
8. Individual does **NOT** have the FDA-label contraindication of a serious hypersensitivity reaction, including anaphylaxis, to penicillamine or cysteamine

**Initial approval duration:** 12 months

➤ **Criteria for continuation of coverage (renewal request):** Procysbi (cysteamine bitartrate) delayed release and/or generic equivalent (if available) are considered **medically necessary** and will be approved when **ALL** the following criteria are met (**samples are not considered for continuation of therapy**):

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Nephrologist or Pediatrician or Specialist in Inborn Errors of Metabolism
2. Individual has documentation of positive clinical response to therapy defined as the following:

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- a. WBC cystine concentrations are in the target range (must have used same assay method)
  - b. Serum creatinine or creatinine clearance is stable or improved over baseline
3. Individual has been adherent with the medication
  4. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))
  5. Procysbi and Cystagon will not be used concurrently
  6. Individual has not developed any contraindications or other significant adverse drug effects that may exclude continued use as follows:
    - a. Contraindications as listed in the criteria for initial therapy section
    - b. Significant adverse effect such as:
      - i. Severe skin rash such as erythema multiforme bullosa or toxic epidermal necrolysis
      - ii. Fibrosing colonopathy, including colonic stricture formation
      - iii. Persistent or progressive central nervous system symptoms
      - iv. Leukopenia and elevated phosphatase
      - v. Benign intracranial hypertension (pseudotumor cerebri) and/or papilledema

**Renewal duration:** 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**
  2. **Off-Label Use of Cancer Medications**
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### **Description:**

Cystadrops (cysteamine hydrochloride) and Cystaran (cysteamine hydrochloride) ophthalmic solution are cystine-depleting agents indicated for the treatment of corneal cystine crystal accumulation in patients with cystinosis. Cysteamine acts as a cystine-depleting agent by converting cystine to cysteine and cysteine-cysteamine complexes and reduces corneal cystine crystal accumulation. These compounds are then able to exit lysosomes thereby reducing intracellular cystine content.

Procysbi (cysteamine bitartrate) delayed release capsule and delayed-release pellets are cystine depleting agents that lower the cystine content of cells in adult and pediatric patients 1 years of age and older with nephropathic cystinosis.

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Another available agent is Cystagon (cysteamine bitartrate) capsule, a cystine depleting agent which lowers the cystine content of cells in patients with cystinosis. It is indicated for the management of nephropathic cystinosis in children and adults. Each capsule contains 50 mg or 150 mg of cysteamine free base as cysteamine bitartrate. Cystagon (cysteamine bitartrate) is given every 6 hours.

Cystinuria is a different disorder from cystinosis. It is a genetic disorder with impaired proximal tubular reabsorption of filtered cystine, resulting in increased urinary cystine excretion and cystine kidney stones.

Cysteamine, an aminothioliol, within lysosomes participates in a thiol-disulfide interchange reaction converting cystine into cysteine and cysteine-cysteamine mixed disulfide, both of which can exit the lysosome in patients with cystinosis.

Cystinosis is a rare autosomal recessive disorder involving abnormal lysosomal storage of the amino acid cysteine. It is due to a defect in the membrane transport protein, cystinosin. An inborn error of metabolism causes abnormal transport of cystine out of lysosomes leading to accumulation of cystine and formation of crystals that damage various organs that includes eyes, kidney, liver, pancreas, muscles, brain, white blood cells, thyroid, and other tissues and organs.

Cystine is derived from protein degradation within the lysosomes and is normally transported through the lysosomal membrane to the cytosol. The defect in the transport system leads to cellular accumulation of poorly soluble cysteine crystals.

Cystinosis is caused by a mutation in *CTNS* gene located on chromosome 17p13 that encodes for cystinosin, a lysosomal membrane protein. There are three distinct types of cystinosis.

Nephropathic cystinosis (NC) or classic infantile cystinosis is the most severe form, it usually appears between 3-6 months of age. It is the most common cause of Fanconi syndrome (FS) in pediatric patients, but it also affects eyes, liver, pancreas, thyroid, brain, and other organs. About 95% of cystinosis patients have the nephropathic form. In the nephropathic form, accumulation of cystine and formation of crystals damage various organs, especially the kidney, leading to renal tubular FS and progressive glomerular failure, with end stage renal failure and need for transplantation.

The intermediate (adolescent) form of cystinosis has all the manifestations of the nephropathic form, but its onset is generally around the time of adolescence, typically 8 years of age. It is usually a milder form of the disease with a markedly slower rate of progression.

Non-nephropathic or ocular cystinosis (adult) is characterized only by corneal crystals and photophobia. Accumulation of crystals starts in cornea, leads to photophobia, blepharospasms, and increases risk of glaucoma over time. The diagnosis is made by demonstration of cystine corneal crystal by the slit lamp examination. Corneal cysteine crystals do not dissolve with oral cysteamine therapy but does respond to administration of cysteamine eye drops. Ocularly administered cysteamine should be prescribed to prevent corneal deposits, because the oral formulation does not reach the cornea due to absent corneal vascularization.

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#### **Definitions:**

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting  
[MedWatch Forms for FDA Safety Reporting | FDA](#)

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#### **Resources:**

Cystadrops (cysteamine hydrochloride) ophthalmic 0.37% solution product information, revised by Recordati Rare Diseases, Inc. 08-2020. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed June 27, 2025.

Cystaran (cysteamine hydrochloride) ophthalmic 0.44% solution product information, revised by Leadiant Biosciences, Inc. 04-2025. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed June 27, 2025.

Cystagon (cysteamine bitartrate) cap product information, revised by Mylan Pharmaceuticals, Inc. 08-2021. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed September 09, 2025.

Procysbi (cysteamine bitartrate) delayed-release cap and delayed-release pellets product information, revised by Horizon Therapeutics USA, Inc. 12-2024. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed June 27, 2025.

Niaudet P. Cystinosis. In: UpToDate, Mattoo TK, Kremen J (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Literature current through August 2025. Topic last updated March 26, 2024. Accessed September 09, 2025.

Golfarb DS, Ferraro PM, Sas DJ, Baum MA. Cystinuria and cysteine stones. In: UpToDate, Preminger GM, Lam AQ (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Literature current through August 2025. Topic last updated July 14, 2025. Accessed September 09, 2025.