BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 3/31/2014**
SECTION: DRUGS	**LAST REVIEW DATE: 11/18/2021**
	LAST CRITERIA REVISION DATE: 11/18/2021
	ARCHIVE DATE:

CYSTADROPS® (cysteamine hydrochloride) ophthalmic solution
CYSTARAN™ (cysteamine hydrochloride) ophthalmic solution

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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CYSTADROPS® (cysteamine hydrochloride) ophthalmic solution
CYSTARAN™ (cysteamine hydrochloride) ophthalmic solution

Criteria:

- **Criteria for initial therapy:** Cystadrops (cysteamine hydrochloride) or Cystaran (cysteamine hydrochloride) ophthalmic solution is considered ***medically necessary*** and will be approved when **ALL** of 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

  2. Individual has medical record documentation of a confirmed diagnosis of cystinosis

  3. Individual has medical record documentation of corneal cystine crystal deposits

  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) or Cystaran (cysteamine hydrochloride) ophthalmic solution is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Ophthalmologist or Optometrist

  2. Individual's condition has responded while on therapy
     a. Response is defined as:
        i. Reduction in cystine crystal formation in the structures of the eye
        ii. Reduced symptoms of photophobia, visual impairment, or foreign body sensation

  3. Individual has been adherent with the medication

  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:

  1. **Off-Label Use of a Non-cancer Medications**

  2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

CYSTADROPS® (cysteamine hydrochloride) ophthalmic solution
CYSTARAN™ (cysteamine hydrochloride) ophthalmic solution

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.

Background:

- 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
        - Diagnosis is by demonstration of cystine corneal crystal by the slit lamp examination

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- Corneal cysteine crystals do not dissolve with oral cysteamine therapy but does respond to administration of cysteamine eye drops
- Administration of cysteamine acts as a cystine-depleting agent by converting cystine to cysteine and cysteine-cysteamine complexes
- These compounds are then able to exit lysosomes thereby reducing intracellular cystine content and cystine crystal accumulation

Resources:

Cystadrops (cysteamine hydrochloride) ophthalmic 0.37% solution product information, revised by Recordati Rare Diseases, Inc. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed September 14, 2021.

Cystaran (cysteamine hydrochloride) ophthalmic 0.44% solution product information, revised by Leadiant Biosciences, Inc. 05-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed September 14, 2021.

Niaudet P. Cystinosis. In: UpToDate, Mattoo TK, Kim MS (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed September 14, 2021.