BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 3/31/14**
SECTION: DRUGS	**LAST REVIEW DATE: 3/15/18**
	LAST CRITERIA REVISION DATE: 3/15/18
	ARCHIVE DATE:

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.

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.**

CYSTARAN™ (cysteamine hydrochloride) ophthalmic solution (cont.)

Description:

Cystaran (cysteamine hydrochloride) ophthalmic solution is a cystine-depleting agent indicated for the treatment of corneal cystine crystal accumulation in patients with cystinosis.

Cystaran (cysteamine hydrochloride) ophthalmic solution is available in a 15 mL bottle that should be stored in a freezer until needed for use. Each week one new bottle should be removed from the freezer and allowed to thaw, this should be done 24 hours prior to using. Once thawed it must be discarded in seven days, even if there is medication left in the bottle. This process is repeated every seven days. The dose is one drop each eye every waking hour.

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 or classic infantile cystinosis (NC) 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
        - 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 are able to exit lysosomes thereby reducing intracellular cystine content and cystine crystal accumulation

Cystaran (cysteamine)

Medication class:
Anticystine Agent, Ophthalmic Agent

FDA-approved indication(s):
- A cystine-depleting agent for the treatment of corneal cystine crystal accumulation in patients with cystinosis

Recommended Dose:
- Place 1 drop in each eye every waking hour

Maximum dosage
- Not stated

Available Dosage Forms:
- 0.44% ophthalmic solution in a 15 mL bottle (if 15 drops = 1 mL, then have 225 drops/bottle)
  - If have a person sleeps 8 hours, then have 16 hours of application
  - One drop each eye = 32 drops in the 16 hours
  - One 15 mL bottle will last about 7 days
  - Package label says to discard bottle after 1 week of use, the discard date is 7 days from the day the bottle is thawed, the medication is only stable for 1 week after thawing

Warnings, Precautions, and other Clinical Information:
- Benign intracranial hypertension (or pseudotumor cerebri) when used with oral cysteamine

Criteria:

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

1. Original diagnosis made by an eye specialist
2. Individual has medical record documentation of a confirmed diagnosis of cystinosis
3. Individual has medical record documentation of corneal cystine crystals

Initial approval duration: Up to 4 bottles of 15ml/month or 60ml/30days x 6 months

CYSTARAN™ (cysteamine hydrochloride) ophthalmic solution (cont.)

- **Criteria for continuation of coverage (renewal request):** Cystaran (cysteamine hydrochloride) ophthalmic solution is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

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

  2. Individual has been adherent with the medication

  Renewal duration: Up to 4 bottles of 15ml/month or 60ml/30days x 12 months

Resources:

Refer to package insert for complete dosing information.

Cystaran™ (cysteamine hydrochloride) ophthalmic solution. Package Insert reference ID 3198343 revised by manufacturer on 10-2012. Accessed 11-01-2013, 03-19-2015, 02-08-2016, 02-24-2017

UpToDate: Cystinosis. Current through Jan 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/cystinosis?search=cysteamine&source=search_result&selectedTitle=5~12&usage_type=default&display_rank=5

UpToDate: Cystine stones. Current through Dec 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/cystine-stones?search=cystinuria&source=search_result&selectedTitle=1~30&usage_type=default&display_rank=1

Gahl WA, Thoene JG, and Schneider JA. Cystinosis. NEJM 2002; 347 (2): 111-121.

Nesterova G and Gahl WA. Cystinosis: The evolution of a treatable disease. Pediatr Nephrol 2012 Aug 18. DOI 10.1007/s00467-012-2242-5.

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

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Office notes, labs, and medical testing relevant to the request that show medical justification are required.