BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 3/16/17**
SECTION: DRUGS	**LAST REVIEW DATE: 3/15/18**
	LAST CRITERIA REVISION DATE: 3/15/18
	ARCHIVE DATE:

PROCYSBI® (cysteamine bitartrate) oral capsule, delayed release

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.**

PROCYSBI® (cysteamine bitartrate) oral capsule, delayed release (cont.)

Description:

Procysbi (cysteamine bitartrate) is a cystine-depleting agent indicated for the treatment of nephropathic cystinosis in adult and pediatric patients 2 years of age and older.

Procysbi (cysteamine bitartrate) delayed release capsule is a cysteine depleting agent that lowers the cystine content of cells in patients with nephropathic cystinosis. It is indicated for the treatment of nephropathic cystinosis in adult and pediatric patients 2 years of age and older. Each 25 mg delayed release capsule contains 74 mg cysteamine bitartrate, equivalent to 25 mg cysteamine. Each 75 mg delayed release capsule contains 221 mg cysteamine bitartrate, equivalent to 75 mg cysteamine. Procysbi (cysteamine bitartrate) is given every 12 hours.

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.

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

Procysbi (cysteamine bitartrate) delayed release

Medication class:
Anticystine Agent, Urinary Tract Product

FDA-approved indication(s):
- A cystine-depleting agent indicated for the treatment of nephropathic cystinosis in adults and pediatric patients 1 year of age and older

Recommended Dose:
- Dosing is weight based for initiation and maintenance (See tables)
- Dose is adjusted to achieve a therapeutic target white blood cell cystine concentration, values from different assay methods may not be interchangeable
    - When using the mixed leukocyte assay, the recommended target WBC cystine concentration is < 1 nmol ½ cystine/mg protein
- Doses are increased in 10% increments, round to the nearest dose that can be given with the available capsule strengths
- Capsules are to be swallowed whole, but label has instructions for opening capsule and administering with food or liquid
- For cysteamine-naïve patients start with a dose equal to 1/6th to 1/4th of the maintenance dose
    - The maintenance dose is 1.3 g/m^2 per day divided into two doses given every 12 hours
- Switching from immediate release cysteamine to Procysbi, the starting total daily dose of Procysbi is equal to the total daily dose of immediate release. The dose is divided by two and given every 12 hours

Maximum dosage
- 1.95 g/m^2 per day

Available Dosage Forms:
- 25 mg, 75 mg delayed release capsules
- The 25 mg strength is supplied as a bottle of 60 capsules & is dispensed in the original packaging only
- The 75 mg strength is supplied as a bottle of 250 capsules & is dispensed in the original packaging only
- Bottles are dispensed with a 4 month expiration date

Warnings and Precautions:
- Permanently discontinue in an individual who develops a severe skin rash such as erythema multiforme bullosa or toxic epidermal necrolysis from cysteamine bitartrate
- Permanently discontinue in an individual who develops benign intracranial hypertension (pseudotumor cerebri) and/or papilledema from cysteamine bitartrate

PROCYSBI® (cysteamine bitartrate) oral capsule, delayed release (cont.)

- Woman who is breast feeding an infant or child should stop breast feeding
- Drugs that contain bicarbonate or carbonate may cause premature release of cysteamine and increase the WBC cystine concentration
- Individuals should avoid alcohol when using Procysbi

Criteria:

- **Criteria for initial therapy:** Procysbi (cysteamine bitartrate) delayed release is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual is 1 years of age or older

  2. A confirmed diagnosis of nephropathic cystinosis

  3. Individual has failure, contraindication or intolerance to Cystagon (cysteamine bitartrate) immediate release capsules

  4. There are **NO** contraindications:
     - Contraindications include:
       - Hypersensitivity, including anaphylaxis, to penicillamine or cysteamine

  Initial approval duration: 12 months

- **Criteria for continuation of coverage (renewal request):** Procysbi (cysteamine bitartrate) delayed release is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual's condition responded while on therapy
     - Response is defined as:
       - WBC cystine concentrations are in the target range (must have used same assay method)
       - Serum creatinine or creatinine clearance is stable or improved over baseline

  2. Individual has been adherent with the medication

  3. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
     - Contraindications as listed in the criteria for initial therapy section
     - Significant adverse effect such as:
       - Severe skin rash such as erythema multiforme bullosa or toxic epidermal necrolysis
       - Benign intracranial hypertension (pseudotumor cerebri) and/or papilledema

  Renewal duration: 12 months

PROCYSBI® (cysteamine bitartrate) oral capsule, delayed release (cont.)

Resources:

Procysbi (cysteamine bitartrate). Package Insert. Revised by manufacturer 12-2017. Accessed 02-13-18.

Procysbi (cysteamine bitartrate). Package Insert. Revised by manufacturer 08-2015. Accessed 02-22-17.

Cystagon (cysteamine bitartrate). Package Insert. Revised by manufacturer 07-2007. Accessed 02-22-17.

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.

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

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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.

Incomplete forms or forms without the chart notes will be returned.

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