PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 3/16/2017
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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

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. 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 years of age or older

  3. A confirmed diagnosis of nephropathic cystinosis

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

  5. There are **NO** contraindications:
     a. Contraindications include:
        i. 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 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's condition responded while on therapy
     a. Response is defined as:
        i. WBC cystine concentrations are in the target range (must have used same assay method)
        ii. Serum creatinine or creatinine clearance is stable or improved over baseline

  3. Individual has been adherent with the medication

  4. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
     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. Benign intracranial hypertension (pseudotumor cerebri) and/or papilledema
        iii. Ehlers-Danlos-like syndrome skin and bone lesions
        iv. Persistent or progressive central nervous system symptoms

  Renewal duration: 12 months

PROCYSBI® (cysteamine bitartrate) oral capsule, delayed release

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.

Cysteamine, an aminothiol, 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.

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 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

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- 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

Resources:

Procysbi (cysteamine bitartrate) delayed release capsule & granule product information, revised by Horizon Therapeutics USA, Inc. 02-2020, at DailyMed http://dailymed.nlm.nih.gov accessed January 27, 2021.

Cystagon (cysteamine bitartrate) capsule product information, revised by Mylan Pharmaceuticals, Inc. 01-2019, at DailyMed http://dailymed.nlm.nih.gov accessed January 27, 2021.

Niaudet P. Cystinosis. In: UpToDate, Mattoo TK, Kim MS (Eds), UpToDate, Waltham MA.: UpToDate Inc. http://uptodate.com. Accessed on January 27, 2021.