**Medication Policy Manual**

**Policy No:** dru311

**Topic:** Procysbi®, cysteamine delayed-release

**Date of Origin:** August 1, 2013

**Committee Approval Date:** November 10, 2017

**Next Review Date:** November 2018

**Effective Date:** December 1, 2017

**IMPORTANT REMINDER**

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medication policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

**Description**

Cysteamine delayed-release (DR) capsule (Procysbi) is an oral medication used for the chronic management of nephropathic cystinosis.
Policy/Criteria

I. Most contracts require prior authorization approval of cysteamine DR (Procysbi) prior to coverage. Cysteamine DR (Procysbi) may be considered medically necessary in patients when criteria A and B below are met.

   A. Documentation of a diagnosis of nephropathic cystinosis.

   AND

   B. Treatment with cysteamine IR (Cystagon®) was ineffective, not tolerated, or is contraindicated.

II. Administration, Quantity Limitations, and Authorization Period

   A. Regence Pharmacy Services considers cysteamine DR (Procysbi) to be a self-administered medication.

   B. Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

III. Cysteamine DR (Procysbi) is considered investigational when used for all other conditions, including, but not limited to:

   A. Acetaminophen toxicity

   B. HIV infection

   C. Infantile neuronal ceroid lipofuscinosis

   D. Non-alcoholic fatty liver disease (NAFLD)

   E. Non-alcoholic steatohepatitis (NASH)

Position Statement

Summary

- Cysteamine is a cystine-depleting agent used for the chronic management of nephropathic cystinosis, a rare genetic disease characterized by abnormal cellular accumulation of cystine.

- Cysteamine DR (Procysbi) is a delayed-release formulation of cysteamine IR (Cystagon). It is dosed twice daily vs. four times daily. It is unclear if the potential additional adherence benefit of cysteamine DR (Procysbi) justifies the substantial (100 times) increase in cost.

- Among these cystine-depleting medications, cysteamine IR (Cystagon) is the best value for members and has the longest track record of clinical experience.

- The safety and effectiveness of cysteamine DR (Procysbi) in conditions other than nephropathic cystinosis have not been established.
Background
- Cystinosis is a rare, genetic lysosomal storage disease that is characterized by the abnormal cellular accumulation of cystine, resulting in a buildup of cystine crystals in various tissues including corneas, kidneys, liver, pancreas, muscles, and brain. If left untreated, affected patients often die in childhood. [1,2]
- Cysteamine is a cystine-depleting agent which lowers the cystine content of cells in patients with cystinosis. Although not curative, use of oral cysteamine is the standard of care and has improved long-term complications and survival in patients with cystinosis. [1-3]

Clinical Efficacy
NEPHROPATHIC CYSTINOSIS
Cysteamine DR (Procysbi) is comparable to cysteamine IR (Cystagon) in the chronic management of nephropathic cystinosis; however, there is no evidence that one is more efficacious than another.

- A randomized, active-controlled crossover trial reported cysteamine DR (Procysbi) was non-inferior to cysteamine IR (Cystagon) in the chronic management of cystine levels in 43 patients with cystinosis. [4]
  * Patients in the trial were on stable therapy with cysteamine IR (Cystagon) at the time of enrollment. Cysteamine DR (Procysbi) dosages were adjusted up to 100% of the cysteamine IR (Cystagon) dose.
  * The primary endpoint, white blood cell (WBC) cystine level, is considered a clinically relevant for nephropathic cystinosis and the standard target of therapy. Control of WBC cystine level has been linked to slowing of renal deterioration. [2]
  * The trial was too short to assess impact of cysteamine DR (Procysbi) on adherence or kidney function.
- There is no evidence that cysteamine DR (Procysbi) is more efficacious than the better value cysteamine IR (Cystagon).

INVESTIGATIONAL CONDITIONS
- Acetaminophen Toxicity
  * Although not evaluated with cysteamine DR (Procysbi), cysteamine IR (Cystagon) has been evaluated in the prevention of hepatotoxicity associated with acetaminophen toxicity. A systematic review concluded that while cysteamine IR (Cystagon) may be efficacious in limiting hepatotoxicity, other agents (such as acetylcysteine) are more effective and less toxic. [5] There is no direct evidence that cysteamine DR (Procysbi) is safe and effective for this use.
- Other Uses
  * Cysteamine DR (Procysbi) is currently being studied in a variety of other conditions including infantile neuronal ceroid lipofuscinosis, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), and treatment of HIV infection. [6, 7]
  * Cysteamine DR (Procysbi) is considered investigational in these conditions due to lack of conclusive data.
**Safety**

- The safety profiles of cysteamine DR (Procysbi) and cysteamine IR (Cystagon) are similar. There is no reliable evidence that one is safer than another.

- The most common adverse reactions of cysteamine DR (Procysbi) reported with an incidence of at least 5% include: vomiting, abdominal pain, anorexia, breath and skin odor, diarrhea, fatigue, dizziness, and rash. [8]

- Additional rare, but serious adverse reactions include Ehlers-Danlos like syndrome (skin and bone lesions), gastrointestinal bleeding, leukopenia, and benign intracranial hypertension. [8]

- There is no evidence that cysteamine DR (Procysbi) is better tolerated than cysteamine IR (Cystagon). In the pivotal trial, a higher incidence of adverse reactions was reported in patients taking cysteamine DR (Procysbi) than cysteamine IR (Cystagon). The majority of these adverse reactions were gastrointestinal in nature. [4, 8]

**Dosing**

- The total daily dose of cysteamine DR (Procysbi) is 1.3 g/m² administered in two equally divided dosages, every 12 hours. [8]

- The dose may be increased to 1.95 g/m²/day if the goal of therapy has not been achieved. Goals of therapy include: [8]
  * WBC cystine level < 1 nmol ½ cystine/mg protein.
  * Plasma cysteamine concentration > 0.1 mg/L.

- Although the twice-daily dosing of cysteamine DR (Procysbi) may be preferred over the four-times-daily dosing of cysteamine IR (Cystagon), there is no evidence that the morbidity/mortality associated with nephropathic cystinosis is improved with cysteamine DR (Procysbi). It is, therefore, unclear if the potential additional adherence benefit of cysteamine DR (Procysbi) justifies the substantial increase in cost.

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References

1. Niaudet P. Cystinosis. In: UpToDate, Mattoo, TK (ed), UpToDate, Waltham, MA, 2014.

Revision History

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