

## PRIOR AUTHORIZATION POLICY

- POLICY:** Metabolic Disorders – Tiopronin Products Prior Authorization Policy
- Thiola® (tiopronin tablets – Mission Pharmacal)
  - Thiola® EC (tiopronin delayed-release tablets – Mission Pharmacal)

**REVIEW DATE:** 09/16/2020

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### OVERVIEW

Thiola and Thiola EC are indicated, in combination with high fluid intake, alkali, and diet modification, for the prevention of cystine kidney stone formation in adults and pediatric patients  $\geq 20$  kg with severe homozygous cystinuria, who are not responsive to these measures alone.<sup>1,2</sup>

### Disease Overview

Cystinuria is an autosomal recessive disorder of abnormal cystine transport.<sup>3</sup> The estimated prevalence is 1:7,000 to 1:10,000 individuals in the US. Excessive undissolved cystine in the urine leads to formation of stones in the kidney, bladder, and/or ureter. Symptoms typically begin to manifest between 10 and 30 years of age, although elevated cystine excretion may be found in infancy. Diagnosis is made clinically based on quantitative urinary cystine assays; genetic testing is not routine as it does not change medical management.<sup>4</sup> Homozygotes exhibit urinary cystine excretion  $> 300$  to  $400$  mg/L/day, whereas heterozygotes have intermediate urinary cystine excretion. Treatment is directed at decreasing urinary cystine concentration (generally targeting a urine cystine  $< 250$  mg/L) and enhancing solubility.<sup>4,5</sup> Tiopronin products work by binding to cystine and increasing urinary solubility.<sup>4</sup>

### Guidelines

According to the American Urological Association guideline for medical management of kidney stones (2014), all patients with cystine kidney stones should be encouraged to drink large amounts of fluid to maintain low urinary cystine concentrations; often volumes of 4 liters per day are required.<sup>5</sup> Recommended dietary modifications include restriction of sodium and animal proteins. Alkalinization of urine is also used to improve cystine solubility. This can be achieved through increased fruit and vegetable intake and/or with medications such as potassium citrate. The guideline recommends tiopronin for patients with cystine kidney stones who are unresponsive to increased fluid intake, dietary modification, and urinary alkalinization. Captopril, another thiol agent, has not been shown to be effective for the prevention of recurrent cystine stones. D-penicillamine may be associated with more adverse events and is not preferred.

### POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of tiopronin products (Thiola, Thiola EC). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with tiopronin products, approval requires the requested medication to be prescribed by or in consultation with a physician who specializes in the condition being treated.

**Automation:** None

### RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Thiola or Thiola EC is recommended in those who meet the following criteria:

### **FDA-Approved Indications**

1. **Cystinuria.** Approve for 1 year if the patient meets the following criteria (A, B, and C):
  - A) Diagnosis of cystinuria has been confirmed based on laboratory testing (e.g., urinary cystine crystals present on microscopy, quantitative urine cystine assay); AND
  - B) According to the prescriber, the patient has had an inadequate response to high fluid intake, dietary modification, and urinary alkalization; AND
  - C) The medication is prescribed by, or in consultation with, a nephrologist, urologist, or physician who specializes in the treatment of cystinuria.

### **CONDITIONS NOT RECOMMENDED FOR APPROVAL**

Coverage of Thiola or Thiola EC is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

### **REFERENCES**

1. Thiola® [prescribing information]. San Antonio, TX: Mission Pharmacal; June 2019.
2. Thiola® EC [prescribing information]. San Antonio, TX: Mission Pharmacal; June 2019.
3. Cystinuria. National Organization for Rare Disorders. Updated 2020. Available at: <https://rarediseases.org/rare-diseases/cystinuria/>. Accessed on September 9, 2020.
4. Castro Pereira DJ, Schoolwerth AC, Pais VM. Cystinuria: current concepts and future directions. *Clin Nephrology*. 2015;83(3):138-146.
5. Pearle MS, Goldfarb DS, Assimos DG, et al.; American Urological Association. Medical management of kidney stones: AUA guideline. *J Urol*. 2014;192(2):316-24. Available at: <https://www.auajournals.org/doi/10.1016/j.juro.2014.05.006>. Accessed on September 9, 2020.