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5.55.003

Section:	Prescription Drugs	**Effective Date:**	July 1, 2024
Subsection:	Genitourinary Agents	**Original Policy Date:**	May 14, 2021
Subject:	Tiopronin	**Page:**	1 of 4

Last Review Date: June 13, 2024

Tiopronin

Description

Thiola (tiopronin) and Thiola EC (tiopronin delayed release tablets)

Background
Cystinuria is an autosomal recessive disorder in which the kidney, due to a genetic defect in the cystine transporter, is unable to reabsorb cystine in the proximal tubule, resulting in urinary hyperexcretion of amino acids cystine, ornithine, lysine, and arginine. Of these, only cystine is relatively insoluble at normal urinary pH, leading to stone formation when cystine concentration rises above the solubility limit. The goal of treatment in cystinuria is to prevent recurrence of stones by decreasing urinary cystine concentrations to below the solubility limit (< 250 mg/L) or increasing the solubility of cystine. Tiopronin is a reducing agent that undergoes thiol-disulfide exchange with cystine to form tiopronin-cystine disulfide, which is more water soluble than cystine. As a result, the amount of sparingly soluble cystine in the urine is decreased and the formation of kidney stone is reduced (1-3).

Regulatory Status
FDA-approved indication: Tiopronin is a reducing and complexing thiol indicated, in combination with high fluid intake, alkali, and diet modification, for the prevention of cystine stone formation in adults and pediatric patients 20 kg and greater with severe homozygous cystinuria, who are not responsive to these measures alone (2-3).

Urinary cystine levels should be measured 1 month after initiation of treatment with tiopronin and every 3 months thereafter (2-3).

There is no well-established maximum dose for the approved indication according to the prescribing information (2-3).

The safety and effectiveness of tiopronin in pediatric patients have been established (2-3).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Tiopronin may be considered **medically necessary** if the conditions indicated below are met.

Tiopronin may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnosis

Patient must have the following:

Severe Homozygous Cystinuria

AND ALL of the following:

1. Diagnosis confirmed by genetic testing
2. Used for prevention of cystine stones
3. Pretreatment baseline cystine levels have been or will be obtained
4. Prescriber agrees to monitor cystine levels 1 month after initiation of treatment and every 3 months thereafter
5. Used in combination with high fluid intake, alkali, and diet modification
6. Pediatric patients must weigh at least 20 kg

Prior–Approval *Renewal* Requirements

Diagnosis

Patient must have the following:

Homozygous Cystinuria

AND ALL of the following:

1. Patient has experienced decrease in urinary cystine levels and cystine stone formation compared to pretreatment baseline
2. Prescriber agrees to monitoring cystine levels every 3 months
3. Used in combination with high fluid intake, alkali, and diet modification
4. Pediatric patients must weigh at least 20 kg

Policy Guidelines

Pre–PA Allowance

None

Prior–Approval Limits

Duration 12 months

Prior–Approval *Renewal* Limits

Same as above

Rationale

Summary

Tiopronin is a reducing agent that undergoes thiol-disulfide exchange with cystine to form tiopronin-cystine disulfide, which is more water soluble than cystine. As a result, the amount of sparingly soluble cystine in the urine is decreased and the formation of kidney stone is reduced. The safety and effectiveness of tiopronin in pediatric patients have been established (2-3).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Tiopronin while maintaining optimal therapeutic outcomes.

References

1. Goldstein, Boss, and David S Goldfarb. “Early Recognition and Management of Rare Kidney Stone Disorders.” *Urologic Nursing*, U.S. National Library of Medicine, 2017, www.ncbi.nlm.nih.gov/pmc/articles/PMC5764757/. Accessed on April 20, 2023.
2. Thiola [package insert]. San Diego, CA. Mission Pharmacal Company. March 2021.
3. Thiola EC [package insert]. San Diego, CA. Mission Pharmacal Company. June 2019.

Policy History

Date	Action
May 2021	Addition to PA
September 2021	Annual review and reference update
December 2022	Annual review. Changed policy number to 5.55.003
June 2023	Annual review and reference update
June 2024	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 13, 2024 and is effective on July 1, 2024.