Clinical Policy: Tiopronin Delayed-Release (Thiola EC)

Reference Number: PA.CP.PHAR.725
Effective Date: 05/2025
Last Review Date: 04/2025

Description
Delayed-release tiopronin (Thiola® EC) is a reducing and cystine-binding thiol.

FDA Approved Indication(s)
Thiola EC is 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.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Thiola EC and tiopronin delayed-release formulations are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Severe Homozygous Cystinuria (must meet all)**:**

1. Diagnosis of severe homozygous cystinuria;
2. Prescribed for the prevention of cystine stone formation;
3. Body weight ≥ 20 kg;
4. Provider attestation that tiopronin is prescribed in combination with all the following preventative measures (a, b, and c):
   a. High fluid intake;
   b. Urinary alkalization (e.g., potassium citrate, citric acid);
   c. Dietary modification (*see Appendix D*);
5. Provider attestation that member has had prior failure or inadequate response to preventative measures alone (e.g., high fluid intake, urinary alkalization, and dietary modification) (*see Appendix D*);
6. Dose does not exceed any of the following (a or b):
   a. Adult: 3,000 mg per day;
   b. Pediatric: 50 mg/kg per day.

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Severe Homozygous Cystinuria (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed any of the following (a or b):
   a. Adult: 3,000 mg/day;
   b. Pediatric: 50 mg/kg per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hypersensitivity to tiopronin or any component of Thiola EC
- Boxed warning(s): none reported

Appendix D: General Information
Per the 2019 American Urological Association Medical Management of Kidney Stones guideline, the following are examples of preventative measures for cysteine stone formation:

- Increasing fluid intake to achieve urine volume > 2.5 liters per day
- Limit sodium intake and consume 1,000-1,200 mg per day of dietary calcium
- Limited intake of non-dairy animal protein
- Limit intake of oxalate rich foods (e.g., spinach, rhubarb, rice bran, buckwheat, almonds, and miso)
- Urinary alkalization (potassium citrate/citric acid)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Prevention of cystine stones formation in severe homozygous cystinuria	Adults: 800 mg PO daily, administered in 3 divided doses	Adults: 3,000 mg/day* **Usual adult dose rarely exceeds 2,000 mg/day*
	Pediatric: 15 mg/kg/day PO, administered in 3 divided doses	Pediatric: 50 mg/kg/day or adult dose, whichever is less

VI. Product Availability

Tablets: 100 mg, 300 mg

VII. References

1. Thiola EC Prescribing Information. San Antonio, TX: Mission Pharmacal Company. March 2021. Available at www.thiolaec.com. Accessed January 14, 2025.
2. Thiola EC Monograph. Clinical Pharmacology. Available at: www.clinicalkeys.com/pharmacology. Accessed February 24, 2023.
3. American Urological Association. Medical Management of Kidney Stones (2019). Available at: www.auanet.org/guidelines-and-quality/guidelines/kidney-stones-medical-mangement-guideline#x2870. Accessed February 29, 2024.
4. Servais A, Thomas K, Dello Strologo L, et al. Cystinuria: clinical practice recommendation. Kidney International. 2021;99:48-58. https://doi.org/10.1016/ j.kint.2020.06.035.
5. Azer SM, Goldfarb DS. A summary of current guidelines and future directions for medical management and monitoring of patients with cystinuria. Healthcare. 2023;11:674. https://doi.org/10.3390/healthcare11050674.

Reviews, Revisions, and Approvals	Date
Policy created	04/2025