Clinical Policy: Tiopronin Delayed-Release (Thiola EC)

Reference Number: CP.PHAR.725
Effective Date: 06.01.23
Last Review Date: 12.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 health plans affiliated with Centene Corporation® 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. If request is for Thiola EC, member must use tiopronin delayed-release (generic Thiola EC), unless contraindicated or clinically significant adverse effects are experienced;
7. 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 (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid;or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Member is responding positively to therapy;
3. If request is for Thiola EC, member must use tiopronin delayed-release (generic Thiola EC), unless contraindicated or clinically significant adverse effects are experienced;
4. 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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business:

CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

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	P&T Approval Date
Policy created (adapted from CP.PCH.50, to be retired); added Medicaid line of business; references reviewed and updated.	03.11.25	05.25
Per SDC request, added requirement for Thiola EC requests that member must use tiopronin delayed-release (generic Thiola EC).	09.09.25	12.25

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.