Original Effective Date: 02/01/2020
Current Effective Date: 09/01/2024
Last P&T Approval/Version: 07/31/2024
Next Review Due By: 07/2025
Policy Number: C18004-A

Thiola (tiopronin)

PRODUCTS AFFECTED

Thiola (tiopronin)

COVERAGE POLICY

Coverage for services, procedures, medical devices, and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Severe homozygous cystinuria

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. PREVENTION OF CYSTINE STONE FORMATION DUE TO CYSTINURIA:
   1. Documented diagnosis of cystinuria
      AND
   2. Documentation diagnosis was confirmed by ONE or more of the following: (i) stone analysis showing cysteine, (ii) positive family history of cystinuria or (iii) identification of

pathognomonic hexagonal cystine crystals on urinalysis or (iv) positive cyanide-nitroprusside screen [DOCUMENTATION REQUIRED]
AND

3. Documentation member weighs at least 20 kg
AND
4. Documentation of baseline urinary cystine concentration > 500mg/day [DOCUMENTATION REQUIRED]
AND
5. Prescriber attests member has tried and failed* 30 days of compliance to increasing fluid intake, restricting sodium and protein intake
*NOTE: Failure is defined as inability to lower the urine cystine concentration to below 250 mg/L and to raise the urine pH to above 7 in a 24-hour urine (or, if the measurement is available, failure to lower the urinary supersaturation of cystine to below 1) OR Persistence of cystine crystals visualized by urinalysis, indicating that the urine is supersaturated with cystine
AND
6. Prescriber attests that member has tried and failed* or has a labeled contraindication to a 30-day trial of urinary alkalization with potassium citrate or potassium bicarbonate
*NOTE: Failure is defined as inability to lower the urine cystine concentration to below 250 mg/L and to raise the urine pH to above 7 in a 24-hour urine (or, if the measurement is available, failure to lower the urinary supersaturation of cystine to below 1) OR Persistence of cystine crystals visualized by urinalysis, indicating that the urine is supersaturated with cystine
AND
7. Prescriber attests that the member does NOT have history of agranulocytosis, aplastic anemia, or thrombocytopenia from previous Thiola use

CONTINUATION OF THERAPY:

A. PREVENTION OF CYSTINE STONE FORMATION DUE TO CYSTINURIA:
1. Adherence to therapy at least 85% of the time as verified by Prescriber and member's medication fill history (review Rx history for compliance)
AND
2. Documentation member has a positive response to therapy defined by: Urinary cystine concentration is <250 mg/L OR Reduction in cystine stone production [DOCUMENTATION REQUIRED]
AND
3. Prescriber attests member continues to increase fluid intake, restrict sodium and protein intake
AND
4. Prescriber attests to or clinical reviewer has found member has not developed any contraindications or other significant adverse drug effects that may exclude continued use such as: Hypersensitivity reaction, Agranulocytosis, a plastic anemia, thrombocytopenia, Renal complications of proteinuria or nephrotic syndrome, Goodpasture syndrome, Myasthenia gravis or myasthenic syndrome, Pemphigus-type reaction

DURATION OF APPROVAL:

Initial authorization: 3 months**,** Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a urologist or nephrologist. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

2 years of age and older

QUANTITY:

Thiola 100 mg: 900 tablets per 30 days

Thiola EC 100 mg: 900 tablets per 30 days
Thiola EC 300 mg: 300 tablets per 30 days

Maximum Quantity Limits – Usual maximum rarely exceeds 2,000 mg/day; literature reports up to 3,000 mg/day PO in some patients. Avoid doses greater than 50 mg/kg per day in pediatric patients.

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Urinary Stone Agents

FDA-APPROVED USES:
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

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Thiola/Thiola EC is an active reducing agent that undergoes thiol-disulfide exchange with cystine to form a mixed disulfide of tiopronin-cysteine; formation of this mixed disulfide reduces the amount of soluble cystine in the urine, thereby preventing cystine stone formation. According to the American Urologic Association (AUA) 2014 guidelines for the medical management of kidney stones, Thiola/Thiola EC is the recommended agent for the prevention of cystine stone formation in members with cystinuria who are unresponsive to increased fluid intake, alkali, and dietary modifications, or who have large, recurrent stone burdens.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Thiola/Thiola EC are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to Thiola/Thiola EC include hypersensitivity to tiopronin or any other component of the medication. Thiola/Thiola EC should only be used in members who are greater than or equal to 20 kg (44 lbs.) and in combination with high fluid intake, alkali, and dietary modifications. Pediatric members receiving greater than or equal to 50 mg/kg of tiopronin per day may be at increased risk for proteinuria; discontinue Thiola/Thiola EC in members who develop proteinuria. Once proteinuria has resolved, can consider resuming Thiola/Thiola EC at a lower dose.

OTHER SPECIAL CONSIDERATIONS:
Thiola/Thiola EC is dose adjusted to maintain a urinary cystine concentration below 250 mg/L. The recommended initial dosage in adult members is 800 mg/day; up to 3,000 mg/day has been reported in rare members. Consider a lower initial dose in members with history of severe toxicity to d- penicillamine.

The recommended initial dosage in pediatric members greater than or equal to 20 kg is 15 mg/kg/day; avoid dosages greater than 50 mg/kg/day in pediatric members due to risk of proteinuria. Thiola should be taken 1 hour before or 2 hours after meals. Thiola EC can be taken with or without food, however, it is important to keep consistency with regards to food. Thiola/Thiola EC cannot be crushed or chewed, and therefore cannot be used in pediatric members unable to swallow pills. Thiola/Thiola EC can decrease prolactin concentrations, which may decrease milk production in lactation; breastfeeding is not recommended.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Thiola EC TBEC 100MG
Thiola EC TBEC 300MG
Thiola TABS 100MG
Tiopronin TABS 100MG
Tiopronin TBEC 100MG
Tiopronin TBEC 300MG

REFERENCES

1. Thiola (tiopronin) [prescribing information]. San Antonio, TX: Mission Pharmacal; January 2021.
2. Thiola EC (tiopronin) [prescribing information]. San Antonio, TX: Mission Pharmacal; March 2021.
3. Pearle MS, Goldfarb DS, Assimos DG, et al. Medical Management of Kidney Stones (2014) Reviewed and Validity Confirmed 2019: AUA Guideline. Accessed May 2020. Available at: https://www.auanet.org/guidelines/kidney-stones- medical- management-guideline.
4. Eisner, B. H., Goldfarb, D. S., Baum, M. A., Langman, C. B., Curhan, G. C., Preminger, G. M., … Sur, R. L. (2020). Evaluation and medical management of patients with cystine nephrolithiasis: A consensus statement. Journal of Endourology, 34(11), 1103–1110. doi:10.1089/end.2019.0703
5. Servais, A., Thomas, K., Dello Strologo, L., Sayer, J. A., Bekri, S., Bertholet-Thomas, A., … Levtchenko, E. (2021). Cystinuria: Clinical Practice Recommendation. Kidney International, 99(1), 48–58. doi:10.1016/j.kint.2020.06.035

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Available Dosage Forms	Q3 2024
REVISION- Notable revisions: Required Medical Information Continuation of Therapy FDA-Approved Uses References	Q3 2023
REVISION- Notable revisions: Required Medical Information Age Restrictions References	Q3 2022
Q2 2022 Established tracking in new format	Historical changes on file