Original Effective Date: 08/01/2018
Current Effective Date: 12/17/2025
Last P&T Approval/Version: 10/29/2025
Next Review Due By: 10/2026
Policy Number: C15418-A

Penicillamine (Depen, Cuprimine), Trientine (Cuvrior, Syprine)

PRODUCTS AFFECTED

Cuprimine (penicillamine), Cuvrior (trientine), Depen Titratabs (penicillamine), penicillamine, Syprine (trientine), trientine

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:
Wilson's disease, Cystinuria, Rheumatoid arthritis

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. WILSON'S DISEASE:
1. Documented diagnosis of Wilson's disease
   AND
2. (a) Documentation diagnosis confirmed by genetic testing confirming biallelic pathogenic ATP7B mutations (in either symptomatic or asymptomatic members) [DOCUMENTATION REQUIRED]

OR

(b) Documentation of THREE of the following diagnostic features: Presence of Kayser-Fleisher rings, Serum ceruloplasmin (CPN) less than 20 mg/dL, 24-hour urine Copper greater than 40 mcg, Liver biopsy with copper dry weight greater than 250 mcg/g [DOCUMENTATION REQUIRED]

AND

3. FOR TRIENTINE REQUESTS: Documented treatment failure, serious side effects or clinical contraindication to ALL of the following: generic penicillamine tablets AND generic penicillamine capsules

   AND

   FOR BRAND CUVRIOR AND SYPRINE REQUESTS: Documented treatment failure, serious side effects or clinical contraindication to ALL of the following: generic penicillamine tablets AND generic penicillamine capsules AND generic trientine

   AND
4. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal (e.g., urinary copper excretion) [DOCUMENTATION REQUIRED]

   AND
5. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications topenicillamine include: Women who are breastfeeding, Patients with a history of penicillamine-related aplastic anemia or agranulocytosis should not be restarted on penicillamine. Contraindications to trientine include: hypersensitivity to the product.]

B. CYSTINURIA (PENICILLAMINE ONLY):

1. Documented diagnosis of Cystinuria

   AND
2. Documented treatment failure, serious side effects or clinical contraindication to a trial (30 days) of urinary alkalization therapy with potassium citrate

   AND
3. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal (e.g., cystine concentration, urine pH, cystine crystal visualization by urinalysis) [DOCUMENTATION REQUIRED]

   AND
4. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications topenicillamine include: Women who are breastfeeding, Patients with a history of penicillamine-related aplastic anemia or agranulocytosis should not be restarted on penicillamine.]

C. RHEUMATOID ARTHRITIS (PENICILLAMINE ONLY):

1. Documented diagnosis of severe active rheumatoid arthritis

   AND
2. Documentation of treatment failure, serious side effects or clinical contraindication to a 3-month trial of at least TWO of the following DMARDs: Hydroxychloroquine, Leflunomide, Methotrexate, Sulfasalazine

   AND
3. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal (e.g., joint involvement and quality) [DOCUMENTATION REQUIRED]

   AND
4. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications topenicillamine include: Women who are pregnant or breastfeeding, Patients with a history of penicillamine-related aplastic anemia or agranulocytosis should not be restarted on penicillamine, and Penicillamine should not be administered to rheumatoid arthritis patients with a history or other

evidence of renal insufficiency.]

CONTINUATION OF THERAPY:
A. FOR ALL INDICATIONS:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
   AND
3. Documentation of disease stabilization, improvement in clinical signs and symptoms, improvement in functionality, and/or improvement compared to baseline activity (For Wilson's disease treatment goals should include, but not limited to an increase in urinary copper excretion from baseline (should be in the range of 200 to 500 mcg. For Cystinuria, goals should be to lower the cystine concentration to below 243mg/L and raise urine pH to above 7 in a 24-hour urine or a decrease in persistence of cystine crystals visualized by urinalysis. For rheumatoid arthritis, decrease in swollen, tender joints.)

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of therapy: 12 months

PRESCRIBER REQUIREMENTS:
WILSON'S DISEASE: Prescribed by or in consultation with a board-certified gastroenterologist, hepatologist or liver transplant specialist.
CYSTINURIA: Prescribed by or in consultation with a board-certified nephrologist
RHEUMATOID ARTHRITIS: Prescribed by or in consultation with a board-certified rheumatologist.
[If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
Wilson's Disease: Cuvrior: 18 years of age and older; Other agents: No restriction
Cystinuria: No restriction
Rheumatoid Arthritis: 18 years of age and older

QUANTITY:
WILSON'S DISEASE: Penicillamine: maximum dose: 2,000 mg/day, Syprine, Trientine: maximum dose: 2,000 mg/day; Cuvrior: maximum dose: 3,000 mg/day
CYSTINURIA: maximum dose: 4,000 mg/day
RHEUMATOID ARTHRITIS: maximum 1,500 mg/day

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:
Chelating Agents

FDA-APPROVED USES:
Cuprimine, Depen (penicillamine): indicated in the treatment of Wilson's disease, cystinuria, and in patients with severe, active rheumatoid arthritis who have failed to respond to an adequate trial of conventional

therapy.
Available evidence suggests that Cuprimine/Depen is not of value in ankylosing spondylitis

Syprine (trientine hydrochloride): indicated in the treatment of patients with Wilson's disease who are intolerant of penicillamine.

Cuvrior (trientine tetrahydrochloride): indicated for the treatment of adult patients with stable Wilson's disease who are de-coppered and tolerant to penicillamine

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
None

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of penicillamine and trientine are considered experimental/investigational and therefore, will follow Molina's Off-Label policy. Contraindications to penicillamine include: Women who are pregnant except for treatment of Wilson's disease or certain cases or cystinuria, breastfeeding, Patients with a history of penicillamine-related aplastic anemia or agranulocytosis should not be restarted on penicillamine, and Penicillamine should not be administered to rheumatoid arthritis patients with a history or other evidence of renal insufficiency. Contraindications to trientine include: hypersensitivity to the product.

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
N/A	N/A

AVAILABLE DOSAGE FORMS:
Clovique CAPS 250MG

Cuprimine CAPS 250MG
Cuvrior TABS 300MG
Depen Titratabs TABS 250MG
penicillAMINE CAPS 250MG
penicillAMINE TABS 250MG
Syprine CAPS 250MG
Trientine HCl CAPS 250MG
Trientine HCl CAPS 500MG

REFERENCES

1. Depen (penicillamine) tablet [prescribing information]. Somerset, NJ: Meda Pharmaceuticals Inc.; July 2023.
2. Cuprimine (penicillamine) capsule [prescribing information]. Telangana India: Suven Pharmaceuticals Limited; October 2020.
3. Syprine (trientine) capsule [prescribing information]. Steinbach, Canada: Bausch Health Companies; September 2020.
4. Cuvrior (trientine tetrahydrochloride) tablets [prescribing information]. Chicago, IL: Orphalan; January 2024.
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SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy References	Q4 2025
REVISION- Notable revisions: Coding/Billing Information Template Update ANNUAL REVIEW COMPLETED- No coverage criteria changes with this annual review.	Q4 2024

REVISION- Notable revisions: Products Affected Diagnosis Required Medical Information Age Restrictions Quantity FDA-Approved Uses Available Dosage Forms References	Q4 2023
REVISION- Notable revisions: Products Affected Required Medical Information Continuation of Therapy Prescriber Requirements Contraindications/Exclusions/Discontinuation Available Dosage Forms References	Q4 2022
Q2 2022 Established tracking in new format	Historical changes on file