Clinical Policy: Trientine (Cuvrior, Syprine)

Reference Number: CP.PHAR.438
Effective Date: 12.01.18
Last Review Date: 11.26
Line of Business: Commercial, HIM/ICHRA, Medicaid Revision Log

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

Description

Trientine tetrahydrochloride (Cuvrior™) and trientine hydrochloride (Syprine®) are chelating agents.

FDA Approved Indication(s)

Cuvrior is indicated for the treatment of adult patients with stable Wilson's disease who are de-coppered and tolerant to penicillamine.

Syprine is indicated for the treatment of patients with Wilson's disease who are intolerant of penicillamine.

Limitation(s) of use: Unlike penicillamine, Syprine is not recommended in cystinuria or rheumatoid arthritis. Syprine is not indicated for treatment of biliary cirrhosis.

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 Cuvrior, Syprine, and trientine hydrocholoride are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Wilson's Disease (must meet all)**:**

1. Diagnosis of Wilson's disease;
2. One of the following (a or b):
   a. Cuvrior: Age ≥ 18 years;
   b. Syprine: Age ≥ 6 years;
3. Failure of generic penicillamine (*generic of Depen® is preferred*) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
4. Member meets one of the following, unless contraindicated or clinically significant adverse effects are experienced (a or b):*
   a. Failure of generic trientine hydrocholoride;
   b. For Illinois HIM requests only: If request is for brand Syprine, then member must use generic trientine hydrocholoride;

**Prior authorization may be required for generic trientine hydrocholoride*

5. Dose does not exceed one of the following (a or b):
   a. Cuvrior (both i and ii):
      i. 3,000 mg per day;
      ii. 10 tablets per day;
   b. Syprine (i or ii):
      i. Age > 12 years: 2,000 mg per day;
      ii. Age ≤ 12 years: 1,500 mg per day.

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 12 months or duration of request, whichever is less

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/ICHRA) 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/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) 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/ICHRA, 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/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Wilson's Disease (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 a dose increase, new dose does not exceed one of the following (a or b):
   a. Cuvrior (both i and ii):
      i. 3,000 mg per day;
      ii. 10 tablets per day;
   b. Syprine (i or ii):
      i. Age > 12 years: 2,000 mg per day;
      ii. Age ≤ 12 years: 1,500 mg per day.

Approval duration:
Medicaid/HIM/ICHRA – 12 months
Commercial – 12 months or duration of request, whichever is less

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/ICHRA) 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/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) 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/ICHRA, 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/ICHRA, 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, CP.PMN.53 for Medicaid, and HIM.PA.154 for health insurance marketplace/ICHRA, or evidence of coverage documents;
B. Biliary cirrhosis;
C. Cystinuria;
D. Rheumatoid arthritis.

IV. Appendices/General Information
Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
penicillamine (Depen, Cuprimine®)	**Wilson's disease** 250 mg PO QID initially; adjust to achieve urinary copper excretion 0.5-1 mg/day	Wilson's disease: 2 g/day (750 mg/day if pregnant)

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Trientine hydrocholoride (Syprine)	**Wilson's disease** Age ≤ 12 years: 500-750 mg/day PO in divided doses two, three, or four times daily Age > 12 years: 750-1,250 mg/day PO in divided doses two, three, or four times daily	Age ≤ 12 years: 1,500 mg/day Age > 12 years: 2,000 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hypersensitivity
- Boxed warning(s): none reported

Appendix D: General Information

- Clinical experience with Syprine is limited, and alternate dosing regimens have not been well-characterized; all endpoints in determining an individual patient's dose have not been well defined.
- Syprine and penicillamine cannot be considered interchangeable.
- The absence of a sulfhydryl moiety renders Syprine incapable of binding cystine and, therefore, it is of no use in cystinuria. In 15 patients with rheumatoid arthritis, Syprine was reported not to be effective in improving any clinical or biochemical parameter after 12 weeks of treatment.
- The differences in the FDA-approved indications for Cuvrior and Syprine are due to differing clinical trial design. The clinical trial supporting the Syprine FDA application was conducted in patients with Wilson's disease intolerant of penicillamine, while the clinical trial for Cuvrior was performed in stable de-coppered Wilson's disease patients who were tolerant to penicillamine. In the latter trial, Cuvrior was compared to and found to be non-inferior to penicillamine.
- There are currently no clinical data that investigate any differences in either efficacy or safety of different trientine salts in patients either tolerant or intolerant to penicillamine. Once the trientine salt is broken down in the gut, the active moiety of trientine is the same for both salts.

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Cuvrior*	300 mg up to 3,000 mg PO BID. Refer to the prescribing information for detail on switching from penicillamine or other trientine products to Cuvrior	3,000 mg/day
Syprine	Age ≤ 12 years: 500-750 mg/day PO in divided doses two, three, or four times daily Age > 12 years: 750-1,250 mg/day PO in divided doses two, three, or four times daily	Age ≤ 12 years: 1,500 mg/day Age > 12 years: 2,000 mg/day

**Cuvrior is not substitutable on a milligram-per-milligram basis with other trientine products*

VI. Product Availability

Drug Name	Product Availability
Cuvrior	Tablet: 300 mg
Syprine	Capsule: 250 mg

VII. References

1. Cuvrior Prescribing Information. Chicago, IL: Orphalan; June 2025. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f73feeae-62ad-401e-b9f7-5cb269127750. Accessed July 13, 2026.
2. Syprine Prescribing Information. Bridgewater, NJ: Bausch Health Companies Inc; September 2020. Available at: https://pi.bauschhealth.com/globalassets/BHC/PI/Syprine-PI.pdf. Accessed July 13, 2026.
3. Roberts EA and Schilsky ML. AASLD practice guidelines: Diagnosis and treatment of Wilson disease: an update. Hepatol. 2008; 47(6): 2089-2111.
4. European Association for the Study of the Liver. EASL clinical practice guidelines: Wilson's disease. J Hepatol. 2012; 56(3): 671-685.
5. European Association for the Study of the Liver. EASL-ERN Clinical Practice Guidelines on Wilson's disease. J Hepatol. 2025 Feb 22:S0168-8278(24)02706-5. doi: 10.1016/j.jhep.2024.11.007.
6. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2026. Available at: https://www.clinicalkey.com/pharmacology/. Accessed July 23, 2026.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2022 annual review: no significant changes; references reviewed and updated. Template changes applied to other diagnoses/indications.	06.23.22	11.22
4Q 2023 annual review: added redirection requirement of generic trientine hydrochloride to initial approval criteria; references reviewed and updated.	06.28.23	11.23
4Q 2024 annual review: for continued therapy, revised to "No COC" standard template language; references reviewed and updated.	07.15.24	11.24
4Q 2025 annual review: added trientine hydrocholoride to medically necessary statement as generic trientine hydrocholoride also requires prior authorization; for initial therapy, extended approval duration from 6 months to 12 months for Medicaid and HIM; revised step therapy to require generic trientine hydrocholoride for brand Syprine requests for IL HIM per IL HB 5395; references reviewed and updated.	07.10.25	11.25
4Q 2026 annual review: no significant changes; added ICHRA line of business; references reviewed and updated.	07.13.26	11.26

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

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.

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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.

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