Clinical Policy: Trientine (Syprine)

Reference Number: CP.PHAR.438
Effective Date: 12.01.18
Last Review Date: 02.22
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Trientine (Syprine®) is a chelating agent.

FDA Approved Indication(s)

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 Syprine is **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. 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. Dose does not exceed one of the following (a or b):
   a. Age > 12 years: 2,000 mg per day;
   b. Age ≤ 12 years: 1,500 mg per day.

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, CP.PMN.53 for Medicaid, and HIM.PA.154 for health insurance marketplace.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
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. Age > 12 years: 2,000 mg per day;
   b. Age ≤ 12 years: 1,500 mg per day.

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

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, CP.PMN.53 for Medicaid, and HIM.PA.154 for health insurance marketplace.

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, 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; adjust to achieve urinary copper excretion 0.5-1 mg/day	Wilson's disease: 2 g/day (750 mg/day if pregnant)

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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
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

VI. Product Availability

Capsule: 250 mg

VII. References

1. Syprine Prescribing Information. Bridewater, NJ: Bausch Health Companies Inc: September 2020. Available at: www.syprine.com. Accessed July 14, 2021.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at: http://www.clinicalpharmacology-ip.com/.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created: adapted from previously approved corporate policy CP.CPA.312; no significant changes from previously approved corporate policy; added HIM line of business; added cystinuria and rheumatoid arthritis as diagnoses not covered; references reviewed and updated.	08.07.18	11.18
4Q 2019 annual review: added Medicaid line of business; references reviewed and updated.	08.26.19	11.19
4Q 2020 annual review: no significant changes; references reviewed and updated.	08.03.20	11.20
4Q 2021 annual review: no significant changes; references for HIM line of business off-label use revised from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	07.15.21	11.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	10.18.21	02.22

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.

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.