RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title:	trientine
Policy Number:	RxA.501
Drug(s) Applied:	Syprine®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Trientine (Syprine®) is a chelating agent. It 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
trientine (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

Dosage Forms

- Capsule: 250 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

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

1. Diagnosis of Wilson's disease;
2. Age ≥ 6 years;
3. Failure of penicillamine (*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
Commercial: 6 months
Medicaid: 6 months
HIM: 6 months

II. Continued Therapy Approval

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

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
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
Commercial: 12 months
Medicaid: 12 months
HIM: 12 months

III. Appendices

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	Maximum Dose
Depen®, Cuprimine® (penicillamine)	Wilson's disease: 250 mg PO four times daily; 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.

References

1. Syprine Prescribing Information. Bridewater, NJ: Valeant Pharmaceuticals: December 2016. Available at: www.syprine.com. Accessed September 7, 2020.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2016. Available at: http://www.clinicalpharmacology-ip.com/. Accessed September 7, 2020.
3. Palumbo CS, Schilsky ML. Clinical practice guidelines in Wilson disease. Ann Transl Med. Apr 2019; 7(Suppl 2): S65. doi: 10.21037/atm.2018.12.53. Accessed September 13, 2020.
4. Roberts EA, Schilsky ML. American Association for Study of Liver Diseases (AASLD) Diagnosis and treatment of Wilson disease: an update. Hepatology. 2008; 47: 2089-111. doi: 10.1002/hep.22261. Accessed September 13, 2020.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Policy title table was updated: Line of business policy applies was updated to all lines of business. 2. Continued therapy criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized by RxAdvance…”. 3. References were updated.	09/13/2020	12/7/2020