

Drug Policy

Policy:	Syprine (trientine hydrochloride) Cuvrior (trientine hydrochloride)	Annual Review Date: 07/18/2024 Last Revised Date: 07/18/2024
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OVERVIEW

Syprine and Cuvrior are chelating agents indicated for the treatment of patients with Wilson's disease (hepatolenticular degeneration). Syprine and Cuvrior may be used when treatment with penicillamine is no longer possible because of intolerable or life-endangering side effects. Syprine and Cuvrior are not indicated for use in patients with cystinuria, rheumatoid arthritis (RA), or biliary cirrhosis. In general, patients should remain under regular medical supervision while receiving Syprine or Cuvrior and patients (especially women) should be closely monitored for evidence of iron deficiency anemia. Controlled studies of Syprine and Cuvrior in pediatric patients are not available; however, it has been used in patients as young as 6 years with no adverse events (AEs).

POLICY STATEMENT

This policy involves the use of Syprine and Cuvrior. Prior authorization is recommended for pharmacy benefit coverage of Syprine and Cuvrior. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Syprine or Cuvrior as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Syprine or Cuvrior be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Syprine and Cuvrior are recommended in those who meet the following criteria:

Food and Drug Administration (FDA)-Approved Indications

1. **Wilson's Disease.** Approve for 1 year if the patient meets the following criteria (A, B, and C):
 - A) **Diagnosis of Wilson's disease is confirmed by ONE of the following (i or ii):**
 - i. Genetic testing results confirming biallelic pathogenic *ATP7B* mutations (in either symptomatic or asymptomatic individuals); OR
 - ii. Confirmation of at least two of the following (a, b, c, d):

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- a. Presence of Kayser-Fleischer rings;
 - b. Serum ceruloplasmin level < 20 mg/dL;
 - c. Liver biopsy findings consistent with Wilson's disease;
 - d. 24-hour urinary copper > 40 mcg/24 hours; AND
- B) Patient meets ONE of the following criteria (i, ii, iii, iv, v or vi):**
- i. Patient has tried one preferred penicillamine product and is intolerant to penicillamine therapy, according to the prescriber; OR
 - ii. Patient has clinical features indicating the potential for intolerance to penicillamine therapy, according to the prescriber; OR
Note: Specific clinical features include history of any renal disease, congestive splenomegaly causing severe thrombocytopenia, autoimmune tendency [documentation required]; OR
 - iii. Patient has a contraindication to penicillamine therapy, according to the prescriber [documentation required]; OR
 - iv. Patient has neurologic manifestations of Wilson's disease; OR
 - v. Patient is pregnant; OR
 - vi. Patient has been started on therapy with trientine (generic of Syprine) and, according to the prescriber, the patient has experienced inadequate efficacy or significant intolerance; AND
- C) The medication is prescribed by or in consultation with a gastroenterologist, hepatologist, or liver transplant physician.**

Initial Approval/ Extended Approval.

A) Initial Approval: 1 year (365 days)

B) Extended Approval: 1 year (365 days)

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Syprine and Cuvrior have not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

- 1. Biliary Cirrhosis.** Syprine and Cuvrior are not indicated for the treatment of biliary cirrhosis.
- 2. Cystinuria.** Syprine and Cuvrior are not recommended for use in patients with cystinuria. Unlike penicillamine, Syprine and Cuvrior do not contain a sulfhydryl moiety and therefore it is not capable of binding cysteine.
- 3. Rheumatoid Arthritis (RA).** Syprine and Cuvrior are not recommended for use in patients with RA. Per the prescribing information, Syprine and Cuvrior were not found to be effective in improving any clinical or biochemical parameter after 12 weeks of treatment of patients with RA.
- 4.** Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Syprine® capsules [prescribing information]. Bridgewater, NJ: Valeant Pharmaceuticals North America LLC; September 2020.
2. Weiss KH, Thurik F, Gotthardt DN, et al. Efficacy and safety of oral chelators in treatment of patients with Wilson Disease. *Clin Gastroenterol Hepatol*. 2013;11:1028-1035.
3. Roberts EA and Schilsky ML, "Diagnosis and Treatment of Wilson Disease: An Update. American Association for Study of Liver Diseases (AASLD)," *Hepatology*, 2008, 47(6):2089-111.