

PHARMACY POLICY STATEMENT

North Carolina Marketplace

DRUG NAME	Cuvrior (trientine tetrahydrochloride)
BENEFIT TYPE	Pharmacy
STATUS	Prior Authorization Required

Cuvrior, approved by the FDA in 2022, is a copper chelator indicated for the treatment of adult patients with stable Wilson's disease who are de-coppered and tolerant to penicillamine. It eliminates absorbed copper from the body by forming a stable complex that is then eliminated through urinary excretion. It also chelates copper in the intestinal tract, reducing copper absorption.

Wilson's disease is a genetic disorder of copper metabolism leading to copper accumulation in the liver, brain, and corneas. It is caused by mutations in the intracellular copper-transporting ATP7B gene. Symptoms can include hepatic, neurologic, and/or psychiatric manifestations. The first phase of treatment is to remove existing copper that has accumulated using a chelator, D-penicillamine (Depen or Cuprimine), or trientine (Syprine). Trientine has fewer side effects. Unlike Cuvrior, Syprine is indicated in patients who do not tolerate penicillamine. The second phase of treatment focuses on preventing further copper accumulation.

Cuvrior was approved based on results of the phase 3 CHELATE trial in which it was found to be noninferior to penicillamine for the primary outcome that measured serum non-ceruloplasmin copper (NCC) at 6 months.

Cuvrior (trientine tetrahydrochloride) will be considered for coverage when the following criteria are met:

Wilson's Disease

For **initial** authorization:

1. Member is at least 18 years of age; AND
2. Medication is prescribed by or in consultation with a hepatologist or gastroenterologist; AND
3. Member has a diagnosis of Wilson's disease confirmed by at least one of the following (a, b, or c):
 - a) Genetic test results showing mutation on both alleles of *ATP7B* gene
 - b) Documentation of a Leipzig score of 4 or greater
 - c) At least 2 of the following:
 - i) Kayser-Fleischer rings identified on slit-lamp exam
 - ii) Serum ceruloplasmin (CPN) level < 20 mg/dL
 - iii) 24-hour urinary copper excretion (UCE) > 40 mcg/24 hours
 - iv) Liver biopsy (hepatic copper content 250 mcg/g or greater); AND
4. Member tolerates penicillamine and has been adequately controlled with treatment as evidenced by at least one of the following:
 - a) NCC level of 25 to 150 mcg/L
 - b) UCE 200 to 500 mcg/24 hours; AND
5. Cuvrior will not be used in combination with penicillamine or any other trientine product. (Current penicillamine use must be discontinued).
6. **Dosage allowed/Quantity limit:** 300 mg to 3,000 mg per day in divided doses (twice daily). (QL: 280 tablets per 28 days)

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:

1. Chart notes must document continued stability/normalization of at least one of the following:
 - a) NCC level
 - b) 24-hour UCE; AND
2. Member is clinically stable (e.g., stable hepatic, neurologic, psychiatric exam/labs).

If all the above requirements are met, the medication will be approved for an additional 12 months.

CareSource considers Cuvrior (trientine tetrahydrochloride) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
08/16/2022	New policy for Cuvrior created.
11/21/2024	Updated AASLD reference. Updated trial reference. Added biallelic genetic confirmation as a stand-alone diagnostic option and removed from combined listing. Removed uncontrolled liver disease exclusion. Removed duration from adequate control on penicillamine.

References:

1. Cuvrior [prescribing information]. Orphan; 2022.
2. Schilsky ML, Czlonkowska A, Zuin M, et al. Trientine tetrahydrochloride versus penicillamine for maintenance therapy in Wilson disease (CHELATE): a randomised, open-label, non-inferiority, phase 3 trial. *Lancet Gastroenterol Hepatol*. 2022;7(12):1092-1102. doi:10.1016/S2468-1253(22)00270-9
3. European Association for Study of Liver. EASL Clinical Practice Guidelines: Wilson's disease. *J Hepatol*. 2012;56(3):671-685. doi:10.1016/j.jhep.2011.11.007
4. Socha P, Janczyk W, Dhawan A, et al. Wilson's Disease in Children: A Position Paper by the Hepatology Committee of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition. *J Pediatr Gastroenterol Nutr*. 2018;66(2):334-344. doi:10.1097/MPG.0000000000001787
5. Saroli Palumbo C, Schilsky ML. Clinical practice guidelines in Wilson disease. *Ann Transl Med*. 2019;7(Suppl 2):S65. doi:10.21037/atm.2018.12.53
6. Schilsky ML, Roberts EA, Bronstein JM, et al. A multidisciplinary approach to the diagnosis and management of Wilson disease: Executive summary of the 2022 Practice Guidance on Wilson disease from the American Association for the Study of Liver Diseases. *Hepatology*. 2023;77(4):1428-1455. doi:10.1002/hep.32805

Effective date: 07/01/2025

Revised date: 11/21/2024