PRIOR AUTHORIZATION POLICY

POLICY: Chelating Agents – Trientine Prior Authorization Policy
- Syprine® (trientine hydrochloride capsules – Bausch Health, generic)

REVIEW DATE: 11/02/2022

OVERVIEW

Trientine, a metal chelator, is indicated for the treatment of patients with **Wilson's disease** who are intolerant of penicillamine.[1] Trientine and penicillamine are not interchangeable; trientine should be used when treatment with penicillamine is no longer possible because of intolerable or life-endangering side effects. Trientine is not indicated for use in patients with cystinuria, rheumatoid arthritis, or biliary cirrhosis.

Disease Overview

Wilson's disease is an inherited disorder in which alterations in cellular copper processing and impaired biliary excretion lead to copper accumulation.[3-5] Copper initially builds up in the liver and eventually is released into the bloodstream and deposited into other organs (e.g., brain, kidneys, and cornea). Lifelong pharmacologic therapy is the mainstay of treatment for Wilson's disease; without treatment, most patients will die from liver disease or progressive neurologic disease. Liver transplantation is reserved for severe or resistant cases. In patients with Wilson's disease, penicillamine acts as a general metal chelator and promotes urinary copper excretion.

Guidelines

The American Association for the Study of Liver Diseases (AASLD) provides guidelines for the diagnosis and management of Wilson's disease (2008).[3] Diagnosis of Wilson's disease is endorsed by conducting genetic testing confirming biallelic pathogenic *ATP7B* mutations or confirmation of at least two clinical features associated with Wilson's disease (Kayser-Fleischer rings, serum ceruloplasmin level < 20 mg/dL, liver biopsy, 24-hour urinary copper > 40 mcg/24 hours). The AASLD recommends a chelating agent (penicillamine or trientine) for initial treatment for symptomatic patients. For the treatment of presymptomatic patients or those on maintenance therapy, chelating agents and zinc are both treatment options.

The European Association for the Study of the Liver (EASL) also published a clinical practice guideline for the treatment of Wilson's disease (2012).[5] Like the AASLD, the EASL acknowledges that numerous studies have demonstrated the effectiveness of penicillamine. A chelating agent (penicillamine or trientine) is the recommended initial treatment of symptomatic patients, and again, a chelating agent or zinc may be used for the treatment of presymptomatic patients or patients established on maintenance therapy. In patients with neurological disease established on maintenance therapy either a chelating agent or zinc may be used; zinc may have a role as first-line therapy in these patients. If zinc is used, careful monitoring of transaminases is needed, with changing to chelators if these laboratory parameters are increasing.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of trientine. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with trientine as well as the monitoring required for adverse events and long-term efficacy, approval requires trientine to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of trientine is recommended in those who meet the following criteria:

FDA-Approved Indication

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 (TWO of a, b, c, and d):
       - **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 penicillamine product and is intolerant to penicillamine therapy, according to the prescriber; OR
       Note: Examples of penicillamine products are Cuprimine (penicillamine capsules, generic), Depen (penicillamine tablets, generic).
     - **ii.** Patient has clinical features indicating the potential for intolerance to penicillamine therapy, according to the prescriber; OR
       Note: Specific clinical features include of any renal disease, congestive splenomegaly causing severe thrombocytopenia, autoimmune tendency.
     - **iii.** Patient has a contraindication to penicillamine therapy, according to the prescriber; 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 (Syprine, generic).
   - **C)** The medication is prescribed by or in consultation with a gastroenterologist, hepatologist, or liver transplant physician.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of trientine is not recommended in the following situations:

1. **Biliary Cirrhosis.** Trientine is not indicated for the treatment of biliary cirrhosis.[1]

2. **Cystinuria.** Trientine is not recommended for use in patients with cystinuria.[1] Unlike penicillamine, trientine does not contain a sulfhydryl moiety and therefore it is not capable of binding cysteine.

3. **Rheumatoid Arthritis.** Trientine is not recommended for use in patients with rheumatoid arthritis.[1] Per the prescribing information, trientine was not found to be effective in improving any clinical or biochemical parameter after 12 weeks of treatment of patients with rheumatoid arthritis.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Syprine® capsules [prescribing information]. Bridgewater, NJ: Bausch Health; 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, Schilsky MI. AASLD Practice Guidelines: Diagnosis and treatment of Wilson Disease: an update. *Hepatology*. 2008;47(6):2089-2111.
4. European Association for Study of the Liver (EASL) clinical practice guidelines: Wilson's disease. *J Hepatol*. 2012;56(3):671-85.