PHARMACY COVERAGE GUIDELINE

SYPRINE® (trientine hydrochloride) oral capsule
Trientine Hydrochloride oral capsule

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require precertification is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Criteria:

➢ **Criteria for initial therapy:** Syprine (trientine hydrochloride) is considered ***medically necessary*** and will be approved when **ALL** the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with a Gastroenterologist or Hepatologist.

2. Individual is 6 years of age or older.

3. Individual has a confirmed diagnosis of Wilson's Disease (hepatolenticular degeneration) due to excess copper.

4. Documented failure, contraindication per FDA label, intolerance, or not a candidate to penicillamine ***tablets***.

5. **Additional criteria for brand Syprine only:** Individual has documented failure, contraindication per FDA label, or intolerance to generic trientine.

6. There are no significant interacting drugs.

Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Syprine (trientine hydrochloride) and generic trientine hydrochloride are considered ***medically necessary*** and will be approved when **ALL** the following criteria are met **(samples are not considered for continuation of therapy**):

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with a Gastroenterologist or Hepatologist.

2. Individual's condition has responded while on therapy with response defined as **ALL** of the following:
    a. Urinary copper excretion has increased over baseline
    b. Elevated free and total serum copper levels
    c. Increased liver enzymes
    d. Worsening neurological status

3. Individual has been adherent with the medication.

4. Individual has not developed any significant adverse drug effects that may exclude continued use such as:
    a. Systemic lupus erythematosus
    b. Myasthenia gravis
    c. Severe dystonia
    d. Severe muscular spasms

5. There are no significant interacting drugs.

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-Cancer Medications**

2. **Off-Label Use of Cancer Medications**

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Description:

Syprine (trientine hydrochloride) and generic trientine hydrochloride indicated for the treatment of patients with Wilson's disease in those who are intolerant to penicillamine. Trientine is an oral chelating agent structurally dissimilar from penicillamine and other available chelating agents; it is an effective oral chelator of copper used to induce adequate cupriuresis.

Wilson's disease (hepatolenticular degeneration) is an autosomal inherited metabolic defect resulting in an inability to maintain a near-zero balance of copper. Excess copper accumulates because the liver lacks the mechanism to excrete free copper into the bile. Hepatocytes store excess copper but when their capacity is exceeded copper is released into the blood and is taken up into extrahepatic sites. This condition is treated with a low copper diet and the use of chelating agents that bind copper to facilitate its excretion from the body.

The pathologic effects seen in Wilson's disease are found in the brain, where degeneration is widespread; in the liver, where fatty infiltration, inflammation, and hepatocellular damage progress to cirrhosis; in the kidney, resulting in tubular and glomerular dysfunction; and in the eye, where characteristic corneal copper deposits are known as Kayser-Fleischer rings.

The majority of patients will die from liver disease (cirrhosis or acute liver failure), the rest die due to complications of progressive neurologic disease.

The diagnosis is suspected on the basis of family or individual history, physical examination, or a low serum concentration of ceruloplasmin. It is confirmed by the demonstration of Kayser-Fleischer rings or, in the asymptomatic patient, by the quantitative demonstration in a liver biopsy specimen of a concentration of copper in excess of 250 mcg/g dry weight.

There are two goals to treatment: (1) minimize dietary intake and absorption of copper; (2) promote excretion of copper deposited in tissues. The first objective is attained by a daily diet that contains no more than 1-2 milligrams of copper. The diet should exclude chocolate, nuts, shellfish, mushrooms, liver, molasses, broccoli, and cereals enriched with copper, and be composed to as great an extent as possible with foods with a low copper content. Distilled or demineralized water should be used if the patient's drinking water contains more than 0.1 mg of copper per liter.

For the second objective, a copper chelating agent is used. In symptomatic patients, this treatment usually produces marked neurologic improvement, a fading of Kayser-Fleischer rings, and a gradual amelioration of hepatic dysfunction and psychic disturbances. Noticeable improvement may not occur for one to three months.

There are two types of patients that require treatment for Wilson's disease: (1) the symptomatic, and (2) the asymptomatic, where the disease will develop in the future if the patient is not treated. Treatment of asymptomatic patients has been carried out for over ten years. Symptoms and signs of the disease appear to be prevented indefinitely if daily treatment can be continued.

Resources:

Syprine (trientine) capsule product information, revised by Bausch Health US LLC 09-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 14, 2022.

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Trientine capsule product information, revised by Actavis Pharma, Inc. 05-2017. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 14, 2022.

Cupramine (penicillamine) capsule product information, revised by Bausch Health US LLC 10-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 14, 2022.

Penicillamine capsule product information, revised by Actavis Pharma, Inc. 05-2018. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 14, 2022.

Depen (penicillamine) tablet product information, revised by Meda Pharmaceutical 01-2019. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 14, 2022.

Penicillamine tablet product information, revised by Par Pharmaceutical, Inc. 07-2018. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed July 14, 2022.

Schilsky ML. Wilson disease: Clinical manifestations, diagnosis, and natural history. In: UpToDate, Rand EB, Runyon BS, Aminoff MJ, Robson KM (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on May 04, 2022. Accessed July 14, 2022.

Schilsky ML. Wilson disease: Treatment and prognosis. In: UpToDate, Runyon BS, Robson KM (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Topic last updated on January 03, 2022. Accessed July 14, 2022.