PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 3/15/2018**
SECTION: DRUGS	**LAST REVIEW DATE: 8/19/2021**
	LAST CRITERIA REVISION DATE: 8/19/2021
	ARCHIVE DATE:

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

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

BLUE CROSS®, BLUE SHIELD® and the Cross and Shield Symbols are registered service marks of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield Plans. All other trademarks and service marks contained in this guideline are the property of their respective owners, which are not affiliated with BCBSAZ.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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

Criteria:

- **Criteria for initial therapy:** Syprine (trientine hydrochloride) and generic trientine hydrochloride is considered ***medically necessary*** and will be approved when **ALL** of 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. A confirmed diagnosis of Wilson's Disease (hepatolenticular degeneration)
  4. Individual has documented failure, contraindication per FDA label or intolerance 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 is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  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 not worsened while on therapy
     a. Worsening is defined as:
        i. Urinary copper excretion has increased over baseline
        ii. Elevated free and total serum copper levels
        iii. Increased liver enzymes
        iv. 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
     a. Significant adverse effect such as:
        i. Systemic lupus erythematosus
        ii. Myasthenia gravis
        iii. Severe dystonia
        iv. Severe muscular spasms

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

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 a Non-cancer Medications**

2. **Off-Label Use of a Cancer Medication for the Treatment of Cancer without a Specific Coverage Guideline**

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.

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

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 on August 2, 2021.

Trientine capsule product information, revised by Kadmon Pharmaceuticals, LLC. 12-2018. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on August 2, 2021.

Cupramine (penicillamine) capsule product information, revised by Bausch Health US LLC 10-2020. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on August 2, 2021.

Penicillamine capsule product information, revised by Par Pharmaceutical, Inc. 11-2018. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on August 2, 2021.

Depen (penicillamine) tablet product information, revised by Meda Pharmaceutical 01-2019. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on August 2, 2021.

Penicillamine tablet product information, revised by Par Pharmaceutical, Inc. 07-2018. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed on August 2, 2021.

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. Accessed on August 2, 2021.

Schilsky ML. Wilson disease: Treatment and prognosis. In: UpToDate, Runyon BS, Robson KM (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed on August 2, 2021.