BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 3/15/18
LAST REVIEW DATE: 3/15/18
LAST CRITERIA REVISION DATE:
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.

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.**

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 clinical manifestations of Wilson disease are predominantly hepatic, neurologic, and psychiatric, with many patients having a mixture of symptoms. Copper accumulation in the liver leads to the development of cirrhosis, patients with neurologic Wilson disease, neurologic disease progresses such that the patient may become severely dystonic, akinetic, and mute. The majority of patients will die from liver disease (cirrhosis or acute liver failure), the rest die due to complications of progressive neurologic disease.

Syprine (trientine hydrochloride)
Trientine hydrochloride

Medication class:
- Chelating Agents

FDA-approved indication(s):
- Treatment of patients with Wilson's disease (excess copper) who are intolerant of penicillamine.

Limitations of use:
- Not recommended in cystinuria or rheumatoid arthritis.
- Not indicated for biliary cirrhosis.

Recommended Dose:
- Adults: initial dose 750 to 1,250 mg/day in divided doses 2, 3, or 4 times/day
  - Dose adjustment: increase dose if clinical response is not adequate or the concentration of free serum copper is persistently above 20 mcg/dL
  - Determine optimal long-term maintenance dosage at 6- to 12- month intervals
- Pediatric: initial dose 500 to 750 mg/day in divided doses 2 to 4 times daily
  - Dose adjustment: increase dose if clinical response is not adequate or the concentration of free serum copper is persistently above 20 mcg/dL
  - Determine optimal long-term maintenance dosage at 6- to 12- month intervals
- Elderly: Use with caution; initiate at the low end of the dosing range

SYPRINE® (trientine hydrochloride) oral capsule
Trientine hydrochloride oral capsule (cont.)

Maximum dosage
- Adults: 2,000 mg/day
- Pediatric patients 12 years and younger: 1,500 mg/day

Available Dosage Forms:
- Capsule, 250 mg

Warnings and Precautions:
- *Copper deficiency*: Induced by treatment; may lead to hepatic iron overload and/or sideroblastic anemia; reassess dose
- *Anemia*: May cause iron-deficiency anemia; monitor closely, especially women
- *Neurologic worsening*: May occur with treatment initiation; less common than with penicillamine
- *Hypersensitivity*: Not reported with use; however, industrial workers exposed to trientine for prolonged periods have reported asthma, bronchitis, and dermatitis

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 Hematologist, Hepatologist, or Oncologist
  2. Individual is 6 years of age or older
  3. A confirmed diagnosis of Wilson's Disease (i.e., hepatolenticular degeneration)
  4. For brand Syprine: Individual has failure, contraindication or intolerance to generic trientine
  5. Individual has failure, contraindication or intolerance to Depen (penicillamine)
  6. There are **NO** contraindications.
     - Contraindications include:
       - Hypersensitivity to trientine hydrochloride or any component of the formulation

  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 in consultation with a Hematologist, Hepatologist, or Oncologist
  2. Individual's condition has not worsened while on therapy

- Worsening is defined as:
  - Urinary copper excretion has increased over baseline
  - Elevated free and total serum copper levels
  - Increased liver enzymes
  - Worsening neurological status

3. Individual has been adherent with the medication

4. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
   - Contraindications as listed in the criteria for initial therapy section

5. There are no significant interacting drugs

Renewal duration: 12 months

Resources:

Syprine. Package Insert. Revised by manufacturer 12/2016. Accessed 2/22/18.

UpToDate: Wilson's disease: Clinical manifestations, diagnosis, and natural history. Current through Feb 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/wilson-disease-clinical-manifestations-diagnosis-and-natural-history?search=wilson's%20disease&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1#H69501155

UpToDate: Wilson's disease: Treatment and prognosis. Current through Feb 2018. https://www-uptodate-com.mwu.idm.oclc.org/contents/wilson-disease-treatment-and-prognosis?search=wilson's%20disease&source=search_result&selectedTitle=3~150&usage_type=default&display_rank=3

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:		Dosage Form:
Directions for Use:	Quantity:	Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.