Harvard Pilgrim Health Care | TUFTS Health Plan

Pharmacy Medical Necessity Guidelines:
Zycubo (copper histidinate)

Effective: July 1, 2026

Guideline Type	☒ Prior Authorization ☒ Non-Formulary ☐ Step-Therapy ☐ Administrative

Applies to:

Commercial Products

☒ Harvard Pilgrim Health Care Commercial products; Fax: 617-673-0988

☒ Tufts Health Plan Commercial products; Fax: 617-673-0988

Public Plans Products

☒ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product); Fax: 617-673-0988

Note: While you may not be the provider responsible for obtaining prior authorization, as a condition of payment you will need to ensure that prior authorization has been obtained.

Overview

Food and Drug Administration – Approved Indications

Zycubo (copper histidinate) is a copper replacement therapy indicated for the treatment of Menkes disease in pediatric patients. It is not indicated for the treatment of Occipital Horn Syndrome (OHS).

Clinical Guideline Coverage Criteria

The plan may authorize coverage of Zycubo (copper histidinate) for Members when **ALL** of the following criteria are met:

1. Documented diagnosis of Menkes disease

AND

2. Documentation of **one (1)** of the following:
   a. Member has a molecular genetic test demonstrating a pathogenic or likely pathogenic variant in the *ATP7A* gene
   b. Member has plasma catecholamine analysis findings that are consistent with the diagnosis

   Note: Plasma dopamine/norepinephrine ratios (values > 0.2) or dihydroxyphenylacetic acid/dihydroxyphenylglycol ratios (values > 5) are diagnostic for Menkes disease
   c. According to the provider, the Member has findings suggestive of Menkes disease and genetic testing or plasma catecholamine analysis is in progress

AND

3. Patient is less than 17 years of age

AND

4. Medication is prescribed by or in consultation with a geneticist, neonatologist, neurologist, or a specialist who focuses on the treatment of Menkes disease

Limitations

1. Approval duration will be authorized for 12 months if the member has a molecular genetic test demonstrating a pathogenic or likely pathogenic variant in the *ATP7A* gene OR the Member has plasma catecholamine analysis findings that are consistent with the diagnosis.
2. Approval duration will be authorized for 6 weeks if the Member has findings suggestive of Menkes disease and genetic testing or plasma catecholamine analysis is in progress.
3. Zycubo will not be approved for the treatment of Occipital Horn Syndrome (OHS).

References

1. Menkes Disease. National organization for rare disorders NORD. Updated March 24, 2020. Available at: https://rarediseases.org/rare-diseases/menkes-disease/. Accessed on May 22, 2026.
2. Ramani PK, Parayil Sankaran B. Menkes Disease. [Updated 2023 Nov 14]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560917/
3. Zycubo subcutaneous injection [prescribing information]. Solana Beach, CA: Sentynl Therapeutics; January 2026.

Approval And Revision History

June 9, 2026: Reviewed by the Pharmacy & Therapeutics Committee.

Subsequent endorsement date(s) and changes made:

Background, Product and Disclaimer Information

Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. The plan makes coverage decisions on a case-by-case basis considering the individual member's health care needs. Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. The plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Pharmacy Medical Necessity Guideline and a self-insured Member’s benefit document, the provisions of the benefit document will govern.

Treating providers are solely responsible for the medical advice and treatment of members. The use of this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to member eligibility and benefits on the date of service, coordination of benefits, referral/authorization and utilization management guidelines when applicable, and adherence to plan policies and procedures and claims editing logic.