

DRUG POLICY

Zycubo® (copper histidinate)

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the policy is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. The indications below including FDA-approved indications and compendial uses are considered covered benefits provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Zycubo is indicated for the treatment of Menkes disease in pediatric patients.

Limitations of Use

Zycubo is not indicated for the treatment of Occipital Horn Syndrome (OHS).

POLICY

Required Documentation

Submission of the following information is necessary to initiate the prior authorization review:

1. Initial requests:
 - a. Chart notes or medical records confirming diagnosis of Menkes disease confirmed by lab test, genetic test, or signs and symptoms
2. Continuation requests:
 - a. Chart notes or medical records confirming diagnosis of Menkes disease confirmed by lab test or genetic test (if applicable)
 - b. Chart notes or medical records confirming positive clinical response from baseline

Prescriber Specialties

The requested medication must be prescribed by or in consultation with one of the following:

1. Neurologist
2. Geneticist
3. Specialist in the treatment of Menkes disease

Exclusions

Coverage will not be provided for members who are diagnosed with Occipital Horn Syndrome (OHS).

Criteria for Initial Approval

Menkes disease

1. Authorization of 6 months may be granted for the treatment of Menkes disease (MD) in members ≤17 years of age when all of the following criteria are met:
 - A. Diagnosis of Menkes disease through one of the following:
 - i. Biochemical (plasma catecholamine analysis, elevated DOPAC:DHPG and dopamine:norepinephrine ratios) or genetic confirmation of ATP7A mutation consistent with a severe MD phenotype. Biochemical or genetic testing to be confirmed on continuation approval.
 - ii. Documentation of clinical signs and symptoms (including but not limited to characteristic Menkes kinky hair, skin abnormalities, progressive neurologic impairment, growth and developmental delays, and multisystem complications affecting the brain, bones, and connective tissues) that are strongly consistent with Menkes disease when biochemical or genetic results are pending, and delay would result in harm.

Continuation of Therapy

Menkes disease

1. Authorization of 12 months may be granted for continued treatment in all members (including new members) when all of the following criteria are met:
 - A. Member has previously received treatment with Zycubo or compounded copper histidinate prior to FDA approval
 - B. Member is experiencing positive clinical response and there is no evidence of unacceptable toxicity
 - C. If diagnosis was not previously confirmed upon initial approval, documentation of genetic or biochemical testing confirming diagnosis of Menkes disease
 - D. Documentation of continued benefit-to-risk for use beyond 3 years total treatment duration

Other

Zycubo (copper histidinate) is considered **not medically necessary** for members who do not meet the criteria set forth above.

Dosing and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Quantity Limits Apply

Medication	Standard Limit	FDA Recommended Dosing
Zycubo (copper histidinate) 2.9 mg/ 0.5 mL vial*	60 vials per 30 days	Less than 1 year of age: 1.45 mg subcutaneously twice daily 1 to 17 years of age: 1.45 mg administered subcutaneously once daily

*Each vial contains 2.9mg of copper histidinate per 1mL, once reconstituted. The unused portion must be discarded after each single use.

REFERENCES

- Zycubo [package insert]. Solana Beach, CA: Sentynt Therapeutics, Inc.; January 2026.
- Ramani PK, Sankaran BP. Menkes Disease. StatPearls.2026 November 14. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK560917/>.
- Kaler SG, et al. Neonatal diagnosis and treatment of Menkes disease. N Engl J Med. 2008; 358(6):605-14.

POLICY HISTORY

Policy #: 05.06.30

Original Effective Date: May 21, 2026

Reviewed: August 2026

Revised: August 2026

Current Effective Date: October 3, 2026