# Copper Histidinate Becomes First, Only FDA-Approved Treatment for Menkes Disease

## Key Takeaways

- Copper histidinate is the first FDA-approved treatment for Menkes disease, improving copper absorption and utilization in affected children.
- Menkes disease is a genetic disorder causing severe neurodegenerative symptoms, primarily affecting boys, with high early childhood mortality.
- Clinical trials demonstrated significant survival benefits with early copper histidinate treatment, reducing mortality risk by up to 79%.
- Pharmacists are essential in monitoring treatment, managing adverse effects, and ensuring proper administration of copper histidinate.

*Subcutaneous copper histidinate injections deliver copper in a form that bypasses the genetic defect caused by Menkes disease.*

The FDA has approved copper histidinate injection (Zycubo [previously CUTX-101]; Sentynl Therapeutics), the first and only treatment for pediatric patients with Menkes disease, according to news releases from the FDA and Sentynl Therapeutics.[1,2]

**What is Menkes Disease?**

Menkes disease is a neurodegenerative, genetic condition that impacts how the body uses copper. The gene ATP7A is key in the development of Menkes disease; if ATP7A can't operate effectively, the body cannot correctly transport and absorb copper. The disease is characterized by a failure to gain weight and grow, intellectual disability, developmental delays, and seizures. It can severely damage a child's nervous system, leading to abnormalities in the bladder, bowel, bones, muscles, and vascular and nervous systems.[1,3]

Experts estimate that Menkes disease affects about 1 of every 100,000 to 250,000 live births across the world. Recent studies have shown that the disease affects boys more often than girls. Around 90% of children with the disease present with classical Menkes; these children begin to develop symptoms in infancy and often do not live past the age of 3 years.[1,3]

"With today's action, children with this devastating, degenerative disease will have an FDA-approved treatment option and the potential to live longer," Christine Nguyen, MD, deputy director of the Office of Rare Diseases, Pediatrics, Urologic and Reproductive Medicine in the FDA's Center for Drug Evaluation and Research, said in a news release from the FDA.[1]

## What is Copper Histidinate?

Copper histidinate is a copper replacement therapy administered in a subcutaneous injection. It allows for the delivery of copper in a form that bypasses the genetic defect in ATP7A that impairs intestinal absorption caused by Menkes disease, which allows the body to more effectively use the copper.[3]

FDA investigators conducted a pooled analysis of 2 open-label, single-arm clinical trials to determine the efficacy and safety of copper histidinate in pediatric patients who were treated for up to 3 years. They assessed overall survival (OS) by comparing treated patients with untreated patients from contemporaneous external control groups. The trial investigators categorized patients born after 1999 with severe loss-of-function ATP7A mutations from 2 trials into either an Early Treatment cohort (CuHis-ET; treatment initiated within 4 weeks of birth) or a Late Treatment cohort (CuHis-LT; treatment initiated after 4 weeks of birth).[1,4]

In patients treated with copper histidinate within the first 4 weeks of birth, there was a 79% reduction in risk of death when compared with untreated historical controls, with median OS being 177.1 and 16.1 months, respectively (hazard ratio [HR] = 0.208 [95% CI, 0.094–0.463]; P < .0001). A 75% reduction in the risk of death was observed in CuHis-LT subjects compared with historical controls, with median OS deemed 62.4 and 17.6 months, respectively (HR = 0.253 [95% CI, 0.119–0.537]; P < .0001).[4]

The FDA noted that nearly half of the early-treatment patients survived beyond 6 years, while some patients survived longer than 12 years, a significant improvement in mortality. Notably, there were no patients in the untreated control group who survived longer than 6 years. Patients who completed 3 years of early treatment with copper histidinate were able to attend school while remaining engaged and active.[1,4]

## How Can Pharmacists Counsel Patients and Caregivers?

Although treatment-emergent adverse effects (TEAEs) were reported in 61 subjects (92.4%), none were considered related to the study treatment. The most common TEAEs included pneumonia (30.3%), seizures (21.2%), dehydration (18.2%), failure to thrive (16.7%), and respiratory distress (15.2%). FDA officials recommend that patients receiving copper histidinate be closely monitored for potential copper toxicity, since the mineral can accumulate in the body.[1,4]

Pharmacists can play a key role in counseling parents and caregivers of children with Menkes disease who begin treatment with copper histidinate. Patients should be consistently monitored by pharmacists and other members of the care team to ensure that copper histidinate is being administered correctly and without adverse effects. If TEAEs are observed, a pharmacist can ensure referral to a specialty care team or hospital setting for prompt treatment. They can also recommend over-the-counter pain relief or prescribe treatments for more specific ailments related to Menkes disease.

“This milestone represents the culmination of decades of research into better understanding and ultimately finding an effective treatment for Menkes disease,” Stephen Kaler, MD, a clinical genetics and genomics specialist at the Columbia University Medical Center, said in a news release from Sentynl Therapeutics. “Increased awareness of Menkes disease and rapid testing upon suspicion are critical, as beginning copper histidinate therapy in affected neonates has been shown to reduce symptoms and prolong life.”[2]

**REFERENCES**


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