BlueCross BlueShield
Federal Employee Program

TIOPRONIN
Thiola (tiopronin) and Thiola EC (tiopronin delayed release tablets)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Cystinuria is an autosomal recessive disorder in which the kidney, due to a genetic defect in the cystine transporter, is unable to reabsorb cystine in the proximal tubule, resulting in urinary hyperexcretion of amino acids cystine, ornithine, lysine, and arginine. Of these, only cystine is relatively insoluble at normal urinary pH, leading to stone formation when cystine concentration rises above the solubility limit. The goal of treatment in cystinuria is to prevent recurrence of stones by decreasing urinary cystine concentrations to below the solubility limit (< 250 mg/L) or increasing the solubility of cystine. Tiopronin is a reducing agent that undergoes thiol-disulfide exchange with cystine to form tiopronin-cystine disulfide, which is more water soluble than cystine. As a result, the amount of sparingly soluble cystine in the urine is decreased and the formation of kidney stone is reduced (1-3).

Regulatory Status

FDA-approved indication: Tiopronin is a reducing and complexing thiol indicated, in combination with high fluid intake, alkali, and diet modification, for the prevention of cystine stone formation in adults and pediatric patients 20 kg and greater with severe homozygous cystinuria, who are not responsive to these measures alone (2-3).

Urinary cystine levels should be measured 1 month after initiation of treatment with tiopronin and every 3 months thereafter (2-3).
There is no well-established maximum dose for the approved indication according to the prescribing information (2-3).

The safety and effectiveness of tiopronin in pediatric patients have been established (2-3).

Summary

Tiopronin is a reducing agent that undergoes thiol-disulfide exchange with cystine to form tiopronin-cystine disulfide, which is more water soluble than cystine. As a result, the amount of sparingly soluble cystine in the urine is decreased and the formation of kidney stone is reduced. The safety and effectiveness of tiopronin in pediatric patients have been established (2-3).

BlueCross BlueShield
Federal Employee Program

TIOPRONIN
Thiola (tiopronin) and Thiola EC (tiopronin delayed release tablets)

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Tiopronin while maintaining optimal therapeutic outcomes.

References

1. Goldstein, Boss, and David S Goldfarb. “Early Recognition and Management of Rare Kidney Stone Disorders.” *Urologic Nursing*, U.S. National Library of Medicine, 2017, www.ncbi.nlm.nih.gov/pmc/articles/PMC5764757/. Accessed on April 20, 2023.
2. Thiola [package insert]. San Diego, CA. Mission Pharmacal Company. March 2021.
3. Thiola EC [package insert]. San Diego, CA. Mission Pharmacal Company. June 2019.