

# INDIVIDUALIZE THIOLA EC® (tiopronin) DOSAGES TO HELP PREVENT STONE FORMATION

ThiolaEC  
(tiopronin)  
Delayed-Release Tablets 100mg/300mg



START

1

Start with the recommended dose of THIOLA EC.<sup>1\*</sup>



Pills shown are not actual size.

- **Adults:** May begin at 800 mg/day.
- **Children ≥20 kg:** May begin at 15 mg/kg/day and avoid dosages >50 mg/kg/day.



MONITOR

2

Measure urinary cystine 1 month after starting THIOLA EC, and every 3 months thereafter.<sup>1</sup>

- Conduct a 24-hour urine test to evaluate your patient's cystine levels.

Regularly monitor for early stone detection:

- Sand/gravel in urine<sup>2</sup>
- Imaging showing presence of stones<sup>3</sup>
- Kidney stone-related pain<sup>4</sup>



ADJUST

3

Reduction of urinary cystine is proportional to THIOLA EC dosage.<sup>1</sup>

- THIOLA EC should be dosed to effect to maintain urinary cystine concentration <250 mg/L.

| THIOLA EC Tablet <sup>†</sup> | Potential Urinary Cystine Reduction |
|-------------------------------|-------------------------------------|
| 300 mg                        | ~75 mg/day                          |
| 100 mg                        | ~25 mg/day                          |

Please see Dosing Guide on reverse side.

## Reminders<sup>1</sup>

- Advise patients to take THIOLA EC in combination with high fluid intake, alkali, and diet modification.
- Determine if your patient will be taking THIOLA EC with or without food. Taking THIOLA EC with food may decrease the levels of tiopronin in the blood by approximately 25%.
- Instruct your patients to take THIOLA EC in 3 divided doses, the same times each day.
- THIOLA EC tablets must be swallowed whole.
- Inform patients about the importance of compliance in order to help prevent stone formation.

\*Patients with a history of severe toxicity to d-penicillamine may start at a lower dose.

<sup>†</sup>The decrement in urinary cystine produced by tiopronin is generally proportional to the dose. A reduction in urinary cystine of 250–350 mg/day at tiopronin dosage of 1 g/day, and a decline of approximately 500 mg/day at a dosage of 2 g/day, may be expected.

## Indications and usage

THIOLA EC® (tiopronin) delayed-release tablets is 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 with severe homozygous cystinuria, who are not responsive to these measures alone.

## Important Safety Information

### Contraindications

THIOLA EC is contraindicated in patients with hypersensitivity to tiopronin or any other components of THIOLA EC.

### Warnings and precautions

- **Proteinuria:** Proteinuria, including nephrotic syndrome, and membranous nephropathy, has been reported with tiopronin use. Pediatric patients receiving >50 mg/kg of tiopronin per day may be at increased risk for proteinuria. Monitor patients for the development of proteinuria and discontinue therapy in patients who develop proteinuria.
- **Hypersensitivity Reactions:** Hypersensitivity reactions (drug fever, rash, fever, arthralgia and lymphadenopathy) have been reported.

### Adverse reactions

The most common adverse reactions (≥10%) are nausea, diarrhea or soft stools, oral ulcers, rash, fatigue, fever, arthralgia, proteinuria, and emesis.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

# THIOLA EC® (tiopronin) DOSING GUIDE

Guidelines to achieve expected cystine concentration based on AUA recommendations<sup>5</sup>

Dosing ranges based on a pH of 7.

| 24-hr cystine level per day (mg/day) | Urine output per day (L)* | Additional THIOLA EC dose per day (mg) | Expected cystine concentration (mg/L) |
|--------------------------------------|---------------------------|--|---------------------------------------|
| 500                                  | 2                         | 0                                      | 250                                   |
|                                      | 2.5                       | 0                                      | 200                                   |
|                                      | 3                         | 0                                      | 167                                   |
|                                      | 3.5                       | 0                                      | 143                                   |
|                                      | 4                         | 0                                      | 125                                   |
| 750                                  | 2                         | 1000                                   | 250                                   |
|                                      | 2.5                       | 500                                    | 250                                   |
|                                      | 3                         | 0                                      | 250                                   |
|                                      | 3.5                       | 0                                      | 214                                   |
|                                      | 4                         | 0                                      | 188                                   |
| 1000                                 | 2                         | 2000                                   | 250                                   |
|                                      | 2.5                       | 1500                                   | 250                                   |
|                                      | 3                         | 1000                                   | 250                                   |
|                                      | 3.5                       | 500                                    | 250                                   |
|                                      | 4                         | 0                                      | 250                                   |
| 1250                                 | 2                         | 3000                                   | 250                                   |
|                                      | 2.5                       | 2500                                   | 250                                   |
|                                      | 3                         | 2000                                   | 250                                   |
|                                      | 3.5                       | 1500                                   | 250                                   |
|                                      | 4                         | 1000                                   | 250                                   |
| 1500                                 | 2                         | 4000                                   | 250                                   |
|                                      | 2.5                       | 3500                                   | 250                                   |
|                                      | 3                         | 3000                                   | 250                                   |
|                                      | 3.5                       | 2500                                   | 250                                   |
|                                      | 4                         | 2000                                   | 250                                   |

\*Minimal urine output of 2.5 L/day is recommended.<sup>5</sup>

**Goal: Calculate dosing based on patient's cystine levels to achieve cystine concentration at 250 mg/L<sup>1</sup>**

**Example:**

- Cystine level = 725 mg/day
- pH level = 7
- Urine output per day = 2 L/day

**The dosing calculation is:**

24-hr cystine level/Urine output per day = Expected cystine concentration

**THIOLA EC dose: 900 mg/day**



Pills shown are not actual size.

Calculate your adult cystinuria patient's dosage at [THIOLAECDosingGuide.com](http://THIOLAECDosingGuide.com)

## Important Safety Information (cont.)

### Drug interactions

Avoid alcohol consumption 2 hours before and 3 hours after taking THIOLA EC as THIOLA EC is released faster in the presence of alcohol.

### Specific populations

- **Lactation:** Breastfeeding is not recommended during treatment with THIOLA EC.
- **Geriatric Use:** Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

You may report negative side effects to Retrophin® Medical Information at 1-877-659-5518, or to the FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.

**References:** 1. THIOLA EC [package insert]. San Antonio, TX: Mission Pharmacal Company. 2. Biyani et al. *EAU-EBU Update Series*. 2006;4(5):175-183. 3. Claes et al. *Pediatr Nephrol*. 2012;27(11):2031-2038. 4. What are cystine stones? The National Kidney Foundation website. <https://www.kidney.org/atoz/content/what-are-cystine-stones>. Published March 8, 2016. Accessed September 26, 2019. 5. Pearle et al. *J Urol*. 2014;192(2):316-324.



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