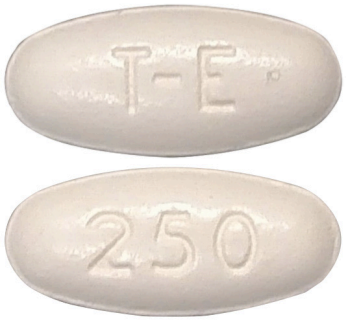
Xermelo

(telotristat ethyl)



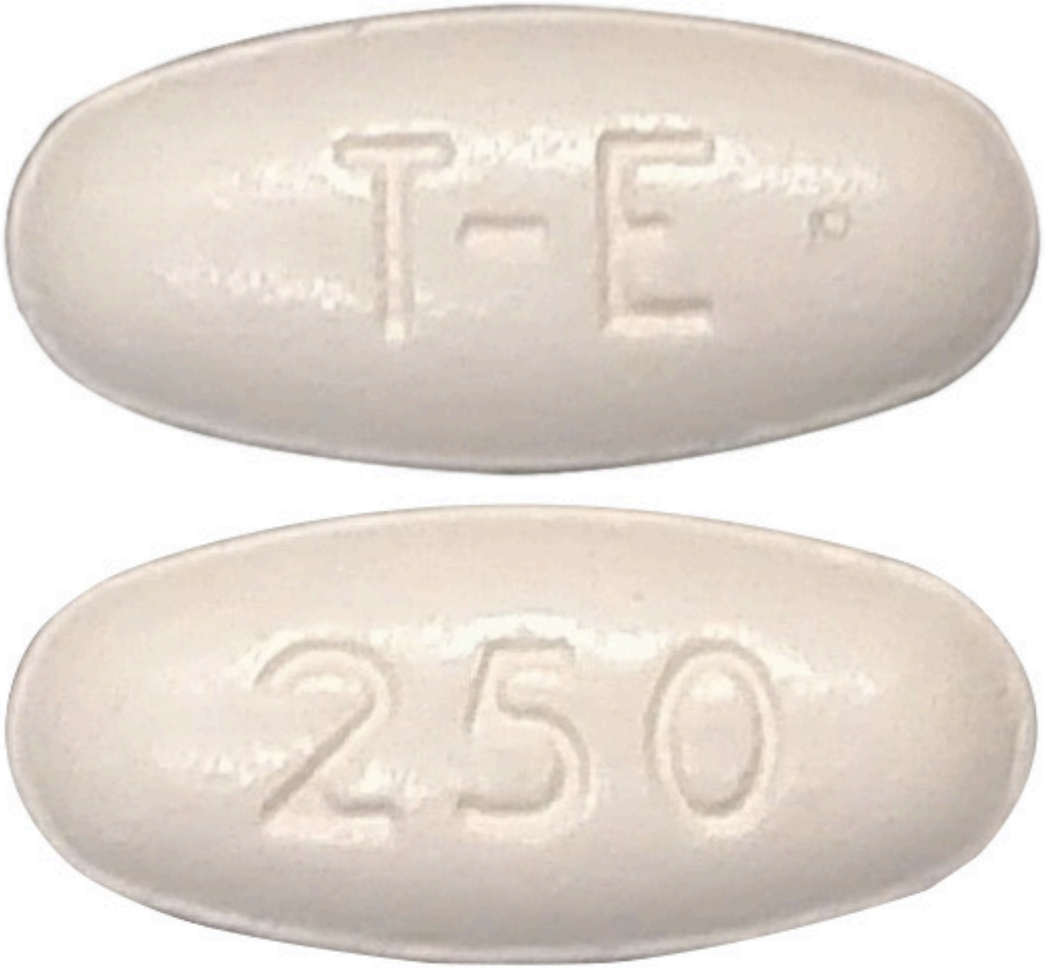
New Product
Slideshow

MPR

Introduction

- **Brand name:** Xermelo
- **Generic name:** Telotristat ethyl
- **Pharmacological class:** Tryptophan hydroxylase inhibitor
- **Strength and Formulation:** 250mg; tablets
- **Manufacturer:** Lexicon Pharmaceuticals
- **How supplied:** Monthly carton—4 x 7 daily dose packs
- **Legal Classification:** Rx

Xermelo



Indications

- In combination with somatostatin analog (SSA) therapy, to treat **carcinoid syndrome diarrhea** in adults inadequately controlled by SSA therapy

Dosage & Administration

- Take with food
- 250mg 3 times daily

Considerations for Special Populations

- **Pregnancy:** No human data with Xermelo use in pregnant women to inform a drug-associated risk
- **Nursing mothers:** Monitor infant for constipation
- **Pediatric:** Not established
- **Elderly:** No overall differences in safety or efficacy were observed
- **Renal impairment:** ESRD requiring dialysis: not studied

Warnings/Precautions

- Monitor for **constipation** and/or severe, persistent, or worsening **abdominal pain**; discontinue if develops

Adverse Reactions

- Nausea
- Headache
- Increased GGT
- Depression
- Flatulence
- Decreased appetite
- Peripheral edema
- Pyrexia

Interactions

- May antagonize **CYP3A4 substrates** (eg, midazolam); monitor and consider increasing dose of concomitant substrates if necessary
- Antagonized by **short-acting octreotide**; if concomitant use is necessary, give dose ≥30mins after Xermelo

Pharmacokinetics

- **Distribution:** >99% bound to human plasma proteins
- **Metabolism:** Hydrolysis via carboxylesterases; not a substrate for CYP enzymes
- **Elimination:** Fecal

Mechanism of Action

- Telotristat, the active metabolite of telotristat ethyl, is an inhibitor of tryptophan hydroxylase, which mediates the rate limiting step in serotonin biosynthesis
- Serotonin plays a role in mediating secretion, motility, inflammation, and sensation of the gastrointestinal tract, and is over-produced in patients with carcinoid syndrome
- Telotristat and telotristat ethyl **reduce the production of peripheral serotonin** and the frequency of carcinoid syndrome diarrhea

Clinical Trials

- A 12-week, double-blind, placebo-controlled, randomized, multicenter trial of Xermelo was conducted in adults with a well-differentiated metastatic neuroendocrine tumor and carcinoid syndrome diarrhea who were having 4-12 daily bowel movements despite the use of SSA therapy at a stable dose for at least 3 months

Clinical Trials

- Patients were randomized to placebo or Xermelo 250mg three times daily
- All patients were required to maintain their baseline SSA regimen and were allowed to use rescue medication (short-acting octreotide) and antidiarrheals for symptomatic relief
- 90 patients were evaluated for efficacy

Clinical Trials

- The **primary efficacy endpoint** was the change from baseline in the number of daily bowel movements averaged over the 12-week treatment period

- There was a mean change of **-1.4/day** in the Xermelo group vs. **-0.6/day** in the placebo group averaged over 12 weeks
  - Estimated treatment difference –0.8 (97.5% CI: –1.3, -0.3)

Clinical Trials

- A difference in average weekly reductions in bowel movement frequency between Xermelo and placebo was seen as early as 1–3 weeks, and persisted for the remaining 9 weeks of the study
- The average number of daily short-acting octreotide injections used for rescue therapy over the 12-week treatment period was **0.3** in the Xermelo group vs. **0.7** in the placebo group
- For more clinical trial data, see full labeling

New Product Monograph

- For more information view the product monograph available at:

  http://www.empr.com/xermelo/drug/34651/