Medication Policy Manual

Policy No: dru518

Topic: Xermelo™, telotristat ethyl

Date of Origin: September 8, 2017

Committee Approval Date: September 8, 2017

Next Review Date: June 2018

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IMPORTANT REMINDER

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of Medication Policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Telotristat ethyl (Xermelo) is an oral tryptophan hydroxylase inhibitor indicated for the treatment of carcinoid syndrome diarrhea that is refractory to standard somatostatin analog (SSA) therapy. It works by blocking the intracellular production of serotonin and should be used in combination with a somatostatin analog, such as octreotide.

Policy/Criteria

I. Most contracts require prior authorization approval of telotristat ethyl (Xermelo) prior to coverage. Telotristat ethyl (Xermelo) may be considered medically necessary when criteria A, B, C, and D below are met.

A. A diagnosis of refractory carcinoid syndrome diarrhea is established by or in consultation with a specialist in oncology or gastroenterology.

AND

B. Treatment with octreotide (generic, Sandostatin LAR Depot) has been ineffective after at least 3 months of therapy.

AND

C. There is clinical documentation of significant diarrhea, defined as at least 4 bowel movements per day on average.

AND

D. Telotristat ethyl (Xermelo) will be used in combination with octreotide (generic, Sandostatin LAR Depot).

II. Administration, Quantity Limitations, and Authorization Period

A. OmedaRx considers telotristat ethyl (Xermelo) to be a self-administered medication.

B. When prior authorization is approved, telotristat ethyl (Xermelo) may be authorized in quantities of up to #84 250-mg tablets per 28 days.

C. **Initial authorization:** Authorization shall be reviewed at 3 months to confirm that current medical necessity criteria are met and that the medication is effective (e.g. reduction in bowel movement frequency and/or decrease in rescue SSA doses).

D. **Continued authorization:** After initial approval, authorization shall be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

III. Telotristat ethyl (Xermelo) is considered investigational when used for all other conditions, including but not limited to:

A. Diarrhea not associated with carcinoid syndrome

B. Other symptoms associated with carcinoid syndrome, including but not limited to flushing, abdominal pain, and heart disease

C. Treatment of neuroendocrine tumors (NETs)

Position Statement

Summary

- Telotristat ethyl (Xermelo) is an oral medication approved for the treatment of refractory carcinoid syndrome diarrhea when used in combination with a somatostatin analog (SSA).
- Carcinoid syndrome diarrhea results when metastatic neuroendocrine tumors (NETs) in the gut overproduce serotonin. Telotristat ethyl (Xermelo) works by blocking the intracellular production of serotonin.
- NETs and associated symptoms are typically treated with SSA therapy, such as octreotide. There is limited data on the treatment of refractory symptoms. Standard of care includes off-label SSA dose escalation, surgical debulking of the tumor(s), antidiarrheal agents, interferon alfa, and switching between different SSA therapies.
- Telotristat ethyl (Xermelo) has only been studied in patients with refractory carcinoid syndrome diarrhea (at least four daily bowel movements) despite being on stable doses of an SSA for at least 3 months.
- Patients should remain on SSA therapy while receiving telotristat ethyl (Xermelo). The safety and efficacy of telotristat ethyl (Xermelo) monotherapy for carcinoid syndrome diarrhea has not been established.
- Telotristat ethyl (Xermelo) is dosed at 250 mg orally three times daily with food. Higher doses were associated with increased adverse events without additional benefit.

Clinical Efficacy [1-3]

- One double-blinded, placebo-controlled randomized trial evaluated the efficacy of telotristat ethyl (Xermelo) add-on therapy compared to standard of care with a somatostatin analog (SSA) alone.
    * The primary outcome was the mean reduction in daily bowel movements (BM) from baseline averaged over 12 weeks. There was a statistically significant difference between telotristat ethyl (Xermelo) + SSA vs. SSA alone (-1.4 BM/day vs. -0.6 BM/day). However, the clinical significance of the results is uncertain given that there was only a 0.8 BM/day difference between both arms.
    * A reduction of ≥ 2 BMs/day was reported in 33% of patients receiving telotristat ethyl (Xermelo) + SSA compared to 4% of patients on SSA alone (statistical analysis not performed).
- There was not a statistically significant change in Quality of Life / Global Health Status between placebo and treatment arms. An improvement from baseline in the diarrhea subscore was observed in all groups at week 12.
- Telotristat ethyl (Xermelo) 500 mg three times daily did not show increased efficacy; however, it was associated with higher AE rates. As such, only the 250-mg dose was approved.

Investigational Uses

- Telotristat ethyl (Xermelo) has not been shown to improve other symptoms associated with carcinoid syndrome, including but not limited to flushing, abdominal pain, and heart disease.
- Telotristat ethyl (Xermelo) has not been studied for the treatment of non-carcinoid syndrome diarrhea nor has it been evaluated for the treatment of neuroendocrine tumors (NETs).

Safety [2,4]

- In general, AE rates were similar between the placebo and telotristat ethyl (Xermelo) treatment arms and appeared to be manageable overall.
- The most common AEs reported in clinical trials were GI-related (nausea, abdominal pain, and constipation), liver enzyme abnormalities, headache, and depression.
- It is unclear if the reported AEs were due to telotristat ethyl (Xermelo) treatment or the underlying disease state since patients with metastatic NETs typically develop tumors in the GI tract or liver.

Dosing [4]

- The recommended dose of telotristat ethyl (Xermelo) is 250 mg orally three times a day with food. Higher doses did not demonstrate additional efficacy and were associated with increased adverse events.
- Telotristat ethyl (Xermelo) should be used in combination with a somatostatin analog (SSA), such as octreotide.
- If treatment with short-acting octreotide is needed, it should be administered at least 30 minutes after telotristat ethyl (Xermelo) is given.

Cross References
Sandostatin® LAR Depot, octreotide long-acting release, dru489
Pituitary Disorder Therapies, dru488

Codes	**Number**	**Description**
ICD-10	E34.0	Carcinoid syndrome

References

1. Kulke, MH, Horsch, D, Caplin, ME, et al. Telotristat Ethyl, a Tryptophan Hydroxylase Inhibitor for the Treatment of Carcinoid Syndrome. *J Clin Oncol*. 2017;35:14-23. PMID: 27918724
2. Product dossier: Xermelo (telotristat ethyl) 250mg tablets. The Woodlands, TX; March 31, 2017. Lexicon Pharmaceuticals, Inc. 2017.
3. FDA CDER: Telotristat Medical Review 208794Orig1s000. [cited April 4, 2017]; Available from: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2017/208794Orig1s000MedR.pdf
4. Xermelo (telotristat ethyl) tablets. Woodlands, TX: Lexicon Pharmaceuticals, Inc.; Feb 2017

Revision History

Revision Date	Revision Summary
09/08/2017	New policy