Pharmacy Policy Bulletin: J-0721 Xermelo (telotristat ethyl) – Commercial and Healthcare Reform	
Number: J-0721	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0721-010	**Original Date:** 05/10/2017
Effective Date: 02/14/2025	**Review Date:** 01/29/2025

Drugs Product(s):	• Xermelo (telotristat ethyl)
FDA-Approved Indication(s):	• Treatment of carcinoid syndrome diarrhea in combination with a somatostatin analog (SSA) therapy in adults inadequately controlled by SSA therapy.

Background:	• Carcinoid syndrome (CS) diarrhea is caused by an overproduction of serotonin, leading to increased gastrointestinal (GI) motility. Xermelo inhibits tryptophan hydroxylase, thus inhibiting serotonin biosynthesis leading to a decrease in the frequency of bowel movements (BMs) and control of CS symptoms. • Neuroendocrine tumors (NETs) arise from enterochromaffin cells found in neuroendocrine tissues, with most occurring in the GI tract. Small-bowel NETs are frequently associated with CS. The most common symptoms of CS are cutaneous flushing, diarrhea, wheezing from bronchospasm, valvular heart disease due to thickening and restricted mobility of predominantly right-sided heart valves, and hyperkeratosis and pigmentation. Carcinoid syndrome diarrhea occurs in 80% of CS patients and poses a substantial symptomatic and economic burden. Treatment options range from surgical debulking to liver-directed therapies to treatment with somatostatin analogs, nonspecific anti-diarrheal agents, and a tryptophan hydroxylase inhibitor. • The first-generation SSAs, octreotide and lanreotide, are indicated and widely used for the management of NETs. The National Comprehensive Cancer Network (NCCN) guidelines recommend octreotide LAR or lanreotide as first-line treatment options for CS and Xermelo as an additional therapy option in patients with poorly controlled CS with SSA monotherapy. Symptomatic benefit can sometimes be delayed for several weeks after initiation of the drug. • Prescribing Considerations: ○ Xermelo is not indicated for monotherapy. ○ Xermelo should be discontinued if constipation or severe abdominal pain develops.

Approval Criteria

I. Initial Authorization
When a benefit, coverage of Xermelo may be approved when all of the following criteria are met **(A. through D.)**:
- **A.** The member is 18 years of age or older.
- **B.** The member has a diagnosis of carcinoid syndrome (ICD-10: E34.0) diarrhea.
- **C.** The member will be using Xermelo in combination with a somatostatin analog.
- **D.** The member was inadequately controlled on a somatostatin analog alone.

II. Reauthorization
When a benefit, reauthorization of Xermelo may be approved when all of the following criteria are met **(A. and B.)**:
- **A.** The member has experienced a reduction in average number of daily bowel movements.
- **B.** The member will continue to use Xermelo in combination with a somatostatin analog.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drugs addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

Initial Authorization -

- Commercial and HCR Plans: If approved, up to a 3 month authorization may be granted.
- For Delaware Commercial fully-insured and ACA members, a 12 month authorization must be granted pursuant to 18 Del. C. §§3376(a) and 3586(a) and market conduct examination docket #5467 (Exam Authority #53287-22-701).

Reauthorization -

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Xermelo [package insert]. The Woodlands, TX. Lexicon Pharmaceuticals, Inc.; September 2022.
2. 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.
3. Naraev BG, Halland M, Halperin DM, et al. Management of Diarrhea in Patients with Carcinoid Syndrome. *Pancreas*. 2019;48(8):961-972.

4. NCCN Guidelines. Neuroendocrine and Adrenal Tumors v.2.2024. National Comprehensive Cancer Network. Available at: https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Accessed December 10, 2024.