Clinical Policy: Telotristat Ethyl (Xermelo)

Reference Number: PA.CP.PHAR.337
Effective Date: 01/18
Last Review Date: 04/19 Revision Log

Description
Telotristat ethyl (Xermelo™) is a tryptophan hydroxylase inhibitor.

FDA approved indication
Xermelo is indicated for the treatment of carcinoid syndrome diarrhea in combination with somatostatin analog (SSA) therapy in adults inadequately controlled by SSA therapy.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with PA Health and Wellness® that Xermelo is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Carcinoid Syndrome Diarrhea (must meet all)**:**

1. Diagnosis of carcinoid syndrome diarrhea;
2. Failure of a one month trial of an SSA (e.g., octreotide, lanreotide) at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
3. Xermelo is prescribed in combination with an SSA unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed 750 mg (3 tablets) per day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to PA.CP.PMN.53

II. Continued Therapy

A. Carcinoid Syndrome Diarrhea (must meet all)**:**

1. Currently receiving medication via PA Health and Wellness benefit or member has previously met initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy (*see Appendix D for examples*);
3. Member continues to have diarrhea;
4. Xermelo is prescribed in combination with an SSA unless contraindicated or clinically significant adverse effects are experienced;
5. If request is for a dose increase, new dose does not exceed 750 mg (3 tablets) per day.

Approval duration: 12 months

B. Other diagnoses/indications (1 or 2)**:**

1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.CP.PMN.53.

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
5-HIAA: 5-hydroxyindoleacetic acid
FDA: Food and Drug Administration
SSA: somatostatin analog

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Sandostatin®, Sandostatin® LAR Depot (octreotide)	Severe diarrhea or flushing associated with carcinoid syndrome: Sandostatin 100-600 mcg/day SC in 2-4 divided doses for 2 weeks, followed by Sandostatin LAR 20 mg IM every 4 weeks for 2 months; at 2 months, can reduce (10 mg) or increase (30 mg) dose as needed	Sandostatin: 600 mcg/day Sandostatin LAR: 30 mg/4 weeks
Somatuline® Depot (lanreotide)	Gastroenteropancreatic neuroendrocrine tumors: 120 mg SC every 4 weeks	120 mg/4 weeks

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: Management of Carcinoid Syndrome

- SSA therapy is the standard of care for carcinoid syndrome. While SSAs are highly effective, tachyphylaxis is a well-known occurrence. The duration of response to SSA therapy varies; some patients lose effectiveness within months of treatment initiation while others are able to retain control for years. Examples of inadequate response to SSA therapy include reduction of bowel movement by less than 3 or by less than 25%, or 4 or more bowel movements per day.
- Interferon alfa has historically been used to manage carcinoid syndrome as a second-line therapy in patients who are refractory to SSA therapy. It relieves symptoms such as

diarrhea and flushing in 40-50% of patients, but its use is largely limited by side effects such as fatigue, depression, myelosuppression, flu-like symptoms, weight loss, and alteration of thyroid function.

- In Xermelo's phase 3 trial TELESTAR, a reduction in bowel movement frequency was observed as early as 1-3 weeks of starting therapy and persisted for the remaining 9 weeks of the study. A 36-week open-label extension is currently ongoing to assess if response is sustained.
- Examples of positive response to therapy may include, but are not limited to:
  - Reduction in bowel movement frequency
  - Reduction in urinary 5-HIAA levels

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Carcinoid syndrome diarrhea	250 mg PO TID	750 mg/day

V. Product Availability

Tablet: 250 mg

VI. References

1. Xermelo Prescribing Information. The Woodlands, TX: Lexicon Pharmaceuticals, Inc; February 2017. Available at www.xermelo.com. Accessed January 7, 2019.
2. Kulke MH, Horsch D, Caplin ME, et al. Telotristat ethyl, a tryptophan hydroxylase inhibitor for the treatment of carcinoid syndrome. J Clin Oncol. 2016; 25(1): 14-23.
3. National Comprehensive Cancer Network. Neuroendocrine Tumors Version 4.2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf Accessed January 7, 2019.
4. Kunz PL, Reidy-Lagunes D, Anthony LB, et al. North American Neuroendocrine Tumor Society (NANETS) guidelines: consensus guidelines for the management and treatment of neuroendocrine tumors. Pancreas. 2013; 42: 557-577.

Reviews, Revisions, and Approvals	Date	Approval Date
2Q 2018 annual review: references reviewed and updated.	02.06.18	
2Q 2018 annual review: references reviewed and updated.	04.17.19	