

Clinical Policy: Telotristat Ethyl (Xermelo)

Reference Number: PA.CP.PHAR.337

Effective Date: 01/2018

Last Review Date: 04/2023

[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 PA Health & 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 clinically significant adverse effects are experienced or all are contraindicated;
3. Xermelo is prescribed in combination with an SSA unless clinically significant adverse effects are experienced or all are contraindicated ;
4. For Xermelo requests, member must use telotristat ethyl, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. 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 & 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 clinically significant adverse effects are experienced or all are contraindicated ;

5. For Xermelo requests, member must use telotristat ethyl, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. 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 PA Health & Wellness 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 <sup>®</sup> , Sandostatin <sup>®</sup> 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 <sup>®</sup> Depot (lanreotide)	Gastroenteropancreatic neuroendocrine tumors: 120 mg SC every 4 weeks	120 mg/4 weeks

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

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): history of hypersensitivity to telotristat
- Boxed warning(s): 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; September 2022. Available at: [www.xermelo.com](http://www.xermelo.com). Accessed January 24, 2023.
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 2.2022. Available at: [https://www.nccn.org/professionals/physician\\_gls/pdf/neuroendocrine.pdf](https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf). Accessed January 24, 2023.
4. Telotristat Ethyl. National Comprehensive Cancer Network Compendium. Available at: <https://www.nccn.org/>. Accessed January 24, 2023.
5. 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.	02/2018	
2Q 2019 annual review: references reviewed and updated.	04/2019	
2Q 2020 annual review: references reviewed and updated.	04/2020	
2Q 2021 annual review: no significant changes; references reviewed and updated.	04/2021	
2Q 2022 annual review: references reviewed and updated.	04/2022	

Reviews, Revisions, and Approvals	Date	Approval Date
2Q 2023 annual review: no significant changes; added redirection to generic telotristat for brand Xermelo requests; updated Appendix C to include contraindication per PI; references reviewed and updated.	04/2023	