RXADVANCE
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Clinical Policy Title:	telotristat ethyl
Policy Number:	RxA.305
Drug(s) Applied:	Xermelo®
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of business

Background

Telotristat ethyl (Xermelo®) is a tryptophan hydroxylase inhibitor. Telotristat is indicated for the treatment of carcinoid syndrome diarrhea in combination with somatostatin analog (SSA) therapy in adults inadequately controlled by SSA therapy.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Telotristat ethyl (Xermelo®)	Carcinoid syndrome diarrhea	250 mg PO TID	750 mg/day

Dosage Forms

- Tablet: 250 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

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
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
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
Commercial: 12 months
Medicaid: 12 months

III. Appendices

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
- Contraindication(s):
  - None reported
- Boxed warning(s):
  - None reported

APPENDIX D: General Information
- 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:
  o Reduction in bowel movement frequency
  o Reduction in urinary 5-HIAA levels

References

1. Xermelo Prescribing Information. The Woodlands, TX: Lexicon Pharmaceuticals, Inc; February 2017. Available at: www.xermelo.com. Accessed June 30, 2020.
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 1.2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf Accessed June 30, 2020.
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.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Clinical Policy Title was updated 2. Drug(s) Applied was updated 3. Line of Business Policy Applies to was updated 4. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 5. Commercial approval duration and Medicaid approval duration updated. 6. References were updated	06/30/2020	09/14/2020