Clinical Policy: Telotristat Ethyl (Xermelo)

Reference Number: ERX.SPA.149
Effective Date: 09.01.17
Last Review Date: 05.20
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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

FDA Approved Indication(s)
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 (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 1 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. Dose does not exceed 750 mg (3 tablets) per day.

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
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. 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 (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents;

B. Other symptoms of carcinoid syndrome (e.g., flushing, abdominal pain, venous telangiectasia, bronchospasm, cardiac valvular lesions).

IV. 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 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: 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 pivotal 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

V. Dosage and Administration

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

VI. Product Availability

Tablet: 250 mg

VII. References

1. Xermelo Prescribing Information. The Woodlands, TX: Lexicon Pharmaceuticals, Inc; February 2017. Available at: www.xermelo.com. Accessed February 6, 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 February 6, 2020.
4. Teloristat Ethyl. National Comprehensive Cancer Network Compendium. Available at: https://www.nccn.org/. Accessed February 6, 2020.
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	P&T Approval Date
Policy created	03.17	08.17
2Q 2018 annual review: No significant changes. References reviewed and updated.	02.06.18	05.18
2Q 2019 annual review: no significant changes; references reviewed and updated.	01.07.19	05.19
2Q 2020 annual review: no significant changes; references reviewed and updated.	02.06.20	05.20

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.