

**Clinical Policy: Telotristat Ethyl (Xermelo)**

Reference Number: CP.PHAR.337

Effective Date: 06.01.17

Last Review Date: 05.19

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.*

It is the policy of health plans affiliated with Centene Corporation® 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 the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

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

1. Currently receiving medication via Centene benefit 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;

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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.

**Approval duration: Duration of request or 6 months (whichever is less); or**

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

**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 policies – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid 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 for all relevant lines of business and may require prior authorization.*

<b>Drug Name</b>	<b>Dosing Regimen</b>	<b>Dose Limit/ Maximum Dose</b>
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

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*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

**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](http://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](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.

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	03.17	06.17
2Q 2018 annual review: no significant changes; policies combined for Medicaid and Commercial lines of business; 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

**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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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**Note: For Medicaid members,** when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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