Original Effective Date: 07/2019
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Last P&T Approval/Version: 01/31/2024
Next Review Due By: 01/2025
Policy Number: C16325-A

Xermelo (telotristat ethyl)

PRODUCTS AFFECTED

Xermelo (telotristat ethyl)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Carcinoid syndrome diarrhea

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. CARCINOID SYNDROME DIARRHEA:
1. Documentation member has a carcinoid/neuroendocrine tumor and has a diagnosis of carcinoid syndrome

AND

2. Prescriber attests pancreatic exocrine deficiency and bile acid diarrhea have been ruled out
   AND
3. Documentation that member has had a 2-week trial and failure or an inadequate response to antidiarrheals (e.g., loperamide)
   NOTE: Nonspecific antidiarrheals (i.e., loperamide, diphenoxylate/atropine, tincture of opium) can be beneficial for management of refractory diarrhea, regardless of the cause (NE-J 1 of 2)
   AND
4. Documentation member has been receiving therapy with the FDA-approved maximum (or highest tolerated) dose of a somatostatin analog therapy (SSA) (i.e., octreotide solution/depot or lanreotide depot) for at least 3 months
   AND
5. Prescriber attests that member will continue to receive SSA therapy in combination with Xermelo
   AND
6. Documentation that member's baseline bowel movements per day are ≥4

CONTINUATION OF THERAPY:

A. CARCINOID SYNDROME DIARRHEA:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
   AND
3. Documentation of positive clinical response as demonstrated by a decrease in bowel movements and/or improvements in the condition's signs and symptoms

DURATION OF APPROVAL:

Initial authorization: 12 weeks, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with an oncologist or gastroenterologist [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

18 years or age and older

QUANTITY:

250mg three times daily

PLACE OF ADMINISTRATION:

The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Oral

DRUG CLASS:

Tryptophan hydroxylase inhibitor

FDA-APPROVED USES:
Indicated for the treatment of carcinoid syndrome diarrhea in combination with somatostatin analog (SSA) therapy in adults inadequately controlled by SSA therapy

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Xermelo (telotristat ethyl) is an FDA-approved treatment for carcinoid syndrome diarrhea, used in combination with somatostatin analog (SSA) therapy for adults who are inadequately controlled by SSA therapy. Telotristat, the active metabolite of telotristat ethyl, is a tryptophan hydroxylase inhibitor. This enzyme is responsible for the rate limiting step of serotonin biosynthesis. The in-vitro inhibitory potency of telotristat towards tryptophan hydroxylase is 29 times greater than that of telotristat ethyl. Serotonin plays a role in mediating secretion, motility, inflammation, and sensation of the gastrointestinal tract, and is over-produced in patients with carcinoid syndrome. By inhibiting tryptophan hydroxylase, telotristat and telotristat ethyl will reduce the production of peripheral serotonin and the frequency of carcinoid syndrome diarrhea.

Studies to support the effectiveness of Xermelo were performed in patients with a well-differentiated metastatic neuroendocrine tumor and carcinoid syndrome diarrhea who were having between 4 to 12 daily bowel movements despite the use of SSA therapy at a stable dose for at least 3 months.
The primary outcome measurement, the change in number of daily bowel movements averaged over the 12-week treatment period, was significantly lower in patients receiving Xermelo compared to placebo, based on an analysis of a 12-week double blind, placebo-controlled, randomized, multicenter trial.
“Carcinoid syndrome” is a term identifying the symptoms mediated by some carcinoid tumors. About80% of patients with carcinoid syndrome will likely present with flushing and diarrhea. Diarrhea occurs so often in this population, causing for an often misdiagnosis of irritable bowel syndrome.
Patients will typically experience episodic diarrhea occurring after meals. Historically, medical treatment of Carcinoid diarrhea has included Octreotide, Sandostatin LAR, and Somatuline Depot. Xermelo may reduce the number of daily bowel movements in patients who are concomitantly using somatostatin analog therapy at a stable dose compared to that of placebo treatments. However, other symptoms of carcinoid syndrome including flushing did not show any improvements with Xermelo. Quality of life is improved with the reduction in episodes of bowel movements and may be feasible with effective treatment. Counseling for the member is an important part of the overall strategy in managing diarrhea episodes associated with carcinoid syndrome.
Xermelo is supplied as an oral tablet; each tablet contains 250 mg of telotristat. The suggested dosing is 1 tablet by mouth three times daily with food. If the short-acting octreotide is used in combination with Xermelo, administer the short-acting octreotide at least 30 minutes following Xermelo administration.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Xermelo (telotristat ethyl) are considered experimental/investigational and therefore, will follow Molina’s Off-Label policy. Contraindications to Xermelo (telotristat ethyl) include: history of hypersensitivity to telotristat.

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
N/A	

AVAILABLE DOSAGE FORMS:
Xermelo TABS 250MG

REFERENCES

1. Xermelo (telotristat ethyl) [prescribing information]. The Woodlands, TX: Lexicon Pharmaceuticals Inc; September 2022.
2. Maroun. J, Kocha W, Kvols L, et al. Guidelines for the diagnosis and management of carcinoid tumors. Part 1: The gastrointestinal tract. A statement from a Canadian National Carcinoid Expert Group. Current Oncology. 2006 Apr; 13(2):67-76.
3. National Comprehensive Cancer Network. 2023. Neuroendocrine and Adrenal Tumors (Version 2.2022). [online] Available at: < neuroendocrine.pdf (nccn.org) > [Accessed 3 January 2023].
4. National Comprehensive Cancer Network. 2023. Neuroendocrine and Adrenal Tumors (Version 1.2023). [online] Available at: < neuroendocrine.pdf (nccn.org) > [Accessed 28 December 2023].

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information References	Q1 2024
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Prescriber Requirements Age Restrictions Contraindications/Exclusions/Discontinuation Available Dosage Forms References	Q1 2023
Q2 2022 Established tracking in new format	Historical changes on file