Pharmacy Policy Bulletin

Title: Telotristat ethyl (Xermelo®)

Policy #: Rx.01.201

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for **telotristat ethyl (Xermelo™)** as provided under the member's prescription drug benefit.

Description:

Carcinoid syndrome is a constellation of symptoms mediated by various hormones secreted by some carcinoid tumors. Two of the most common manifestations are flushing and diarrhea, which are associated with elevations in serum serotonin or its metabolite urinary 5-hydroxyindoleacetic acid (5-HIAA). More than 90 percent of patients with carcinoid syndrome have metastatic disease, typically involving the liver, with primary tumors in the distal small intestine or proximal colon (midgut).

Telotristat, the active metabolite of telotristat ethyl, is a tryptophan hydroxylase (TPH) inhibitor, which mediates the rate limiting step in serotonin biosynthesis. Serotonin plays a role in mediating secretion, motility, inflammation, and sensation of the gastrointestinal tract, and is over-produced in patients with carcinoid syndrome. Decreased production of peripheral serotonin by telotristat and telotristat ethyl through the inhibition of tryptophan hydroxylase results in a reduction of the frequency of carcinoid syndrome diarrhea.

Telotristat ethyl (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:

INITIAL CRITERIA: Telotristat (Xermelo®) is approved when ALL of the following are met:

A. Diagnosis of carcinoid syndrome diarrhea; AND
B. Diarrhea is inadequately controlled by a stable dose of somatostatin analog (SSA) therapy (e.g., octreotide [Sandostatin, Sandostatin LAR], lanreotide [Somatuline Depot]) for at least 3 months; AND
C. Used in combination with SSA therapy; AND
D. Prescribed by or in consultation with one of the following:
    1. Oncologist
    2. Endocrinologist
    3. Gastroenterologist

Initial authorization: 12 months

REAUTHORIZATION CRITERIA: Telotristat (Xermelo®) is reapproved when BOTH of the following are met:

A. Documentation of positive clinical response to Xermelo® therapy; AND

B. Xermelo® will continue to be used in combination with SSA therapy

Reauthorization: 2 years

Black Box Warning:

N/A

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company's products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Xermelo (telotristat ethyl) [package insert]. The Woodlands, TX. Lexicon Pharmaceuticals, Inc. October 2020. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=f11c21f8-f725-445e-b38e-1e4c5b05bcc6&type=display. Accessed March 31,2021.

Kulke MH, Hörsch D, Caplin ME, et al. Telotristat Ethyl, a Tryptophan Hydroxylase Inhibitor for the Treatment of Carcinoid Syndrome. J Clin Oncol 2017; 35(1): 14-23.

Strosber JR. Treatment of carcinoid syndrome. Uptodate. Last updated March 2020. Available at: https://www.uptodate.com/contents/treatment-of-the-carcinoid-syndrome?search=Treatment%20of%20carcinoid%20syndrome&source=search_result&selectedTitle=1~77&usage_type=default&display_rank=1. Accessed March 31,2021.

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Xermelo™	Telotristat ethyl

Cross References:

Off-Label Use Rx.01.33

Policy Version Number:	5.00
P&T Approval Date:	March 18,2021
Policy Effective Date:	July 01, 2021
Next Required Review Date:	March 18, 2022