EXPRESS SCRIPTS®

PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Xermelo™ (telotristat ethyl tablets – Lexicon Pharmaceuticals)

TAC APPROVAL DATE: 03/08/2017

LAY CRITERIA EFFECTIVE DATE: 04/04/2017

OVERVIEW

Xermelo is indicated for the treatment carcinoid syndrome diarrhea in combination with somatostatin analog (SSA) therapy in adults inadequately controlled by SSA therapy.[1] Telotristat, the active metabolite, inhibits tryptophan hydroxylase, 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 overproduced in patients with carcinoid syndrome. Xermelo specifically reduces the production of peripheral serotonin and decreases the frequency of carcinoid syndrome diarrhea.

GUIDELINES

According to the National Comprehensive Cancer Network (NCCN) guidelines for Neuroendocrine Tumors (version 1.2017), patients who have metastatic NETs and carcinoid syndrome should be treated with Sandostatin® LAR Depot (octreotide acetate for injectable suspension) or Somatuline® Depot (lanreotide injection) for the chronic management of symptoms (category 2A).[2] Short-acting octreotide can be added to the Depot formulation for rapid relief of symptoms or for breakthrough symptoms (category 2A). NCCN notes that the dose and frequency of SSA therapy may be increased for symptom control as needed. Although there are no other treatment options specifically indicated/recommended for carcinoid syndrome, NCCN lists Afinitor® (everolimus tablets) [category 2A], interferon alfa-2b (category 3), cytotoxic chemotherapy (category 3), and other hepatic-directed therapy (e.g., hepatic chemoembolization) [category 2A or 2B depending on therapy] for carcinoid tumor disease progression, primarily to reduce the tumor burden.

A Canadian consensus document on the diagnosis and management of gastrointestinal neuroendocrine tumors has the following recommendations[3]: for primary symptom control SSA therapy (depot formulations and short-acting octreotide) is recommended; for symptoms refractory to SSAs, Xermelo is recommended based on uniform consensus with high-level evidence. Interferon alfa (with careful attention to toxicity management) and SSA dose-escalation (Sandostatin LAR Depot up to 60 mg every 2 to 4 weeks or Somatuline Depot up to 180 mg every 3 weeks) are also listed as other options. For progressive disease on SSA therapy (not specific to carcinoid syndrome), single-agent Afinitor or in combination with SSA can be considered. Cytoreductive surgery and hepatic-directed therapies are recommended as loco-regional therapies in patients who remain symptomatic in spite of SSA therapy.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Xermelo. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Xermelo is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Carcinoid Syndrome Diarrhea.**
   - **A)** Initial Therapy. Approve for 3 years if the patient meets all of the following criteria (i, ii, and iii):
     - **i.** The patient has been on a long-acting somatostatin analog (SSA) therapy (e.g., Somatuline® Depot [lanreotide for injection], Sandostatin® LAR Depot [octreotide for injection]) for at least 3 consecutive months; AND
     - **ii.** While on a long-acting somatostatin analog therapy (prior to starting Xermelo), the patient continues to have at least four bowel movements per day; AND
     - **iii.** Xermelo will be used concomitantly with a long-acting somatostatin analog therapy.
   - **B)** Patient is Currently Receiving Xermelo. Approve for 3 years if the patient is continuing to take Xermelo concomitantly with a long-acting somatostatin analog therapy for carcinoid syndrome diarrhea.

   Xermelo is indicated for the treatment of carcinoid syndrome diarrhea in combination with SSA therapy in adults inadequately controlled by SSA therapy.[1] The inclusion criteria for the TELESTAR pivotal study required all patients randomized to Xermelo or placebo groups to have at least four bowel movements per day while on SSA therapy.[4] The study also required patients to be receiving a stable-dose of SSA therapy for at least 3 months prior to trial enrollment.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Xermelo has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions.

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Xermelo™ tablets [prescribing information]. The Woodlands, TX: Merck; February 2017.
2. The NCCN Neuroendocrine Tumors Clinical Practice Guidelines in Oncology (Version 1.2017). © 2017 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed March 2, 2017.
3. Singh S, Asa SL, Dey C, et al. Diagnosis and management of gastrointestinal neuroendocrine tumors: an evidence-based Canadian consensus. *Cancer Treat Rev.* 2016;47:32-45.
4. Kulke MH, Horsch D, Caplin ME, et al. Telotristat ethyl, a tryptophan hydroxylase inhibitor for the treatment of carcinoid syndrome. *J Clin Oncol.* 2017;35:14-23.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date	Lay Criteria Effective Date
New Policy	New criteria	03/08/2017	04/04/2017

TAC – Therapeutic Assessment Committee; * For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx.