Xermelo (telotristat) Prior Authorization with Quantity Limit Program Summary

Your health benefit plan may not cover certain prescription drug products or drug categories included in this document. Please consult your benefit plan materials for details about your particular benefit.

This document may include drugs that are not included on your plan's formulary. For drug coverage status, please consult your plan's formulary.

FDA APPROVED INDICATIONS AND DOSAGE[1]

Agent(s)	Indication(s)	Dosage
Xermelo® (telotristat ethyl) Tablet	Treatment of carcinoid syndrome diarrhea in combination with somatostatin analog (SSA) therapy in adults inadequately controlled by SSA therapy	250 mg three times daily

CLINICAL RATIONALE

Neuroendocrine Tumors

Neuroendocrine tumors (NETs) are thought to arise from cells throughout the diffuse endocrine system. They comprise a broad family of tumors, the most common of which are in the gastrointestinal (GI) tract, lungs and bronchi, thymus, and pancreas. A carcinoid tumor is a type of NET that arises in the GI tract, lungs, or thymus. Sites of origin within the GI tract include the stomach, small intestine, appendix, and rectum.[3] NETs arising in the small intestine or appendix are more commonly associated with carcinoid syndrome, related to the secretion of serotonin, histamine, or tachykinins into the systemic circulation causing episodic flushing and diarrhea.[2,3]

Patients who have metastatic NETs and carcinoid syndrome should be treated with the long-acting somatostatin analogs (SSA) octreotide LAR or lanreotide.[2,3,5] Nearly 80% of NETs express somatostatin receptors, which octreotide and lanreotide bind to on the tumor cells. Both agents are usually well-tolerated and significantly improve diarrhea and flushing.[2] Short-acting octreotide can be added to octreotide LAR for rapid relief of symptoms and/or breakthrough symptoms.[3] If carcinoid syndrome is poorly controlled, telotristat (Xermelo) may be considered for persistent symptoms (e.g., refractory diarrhea) in combination with long-acting SSA.[2-4] For refractory diarrhea (i.e. suboptimal control), telotristat is considered a more appropriate choice than an increase in SSA dose or addition of short-acting octreotide to baseline SSA regimen.[5] Symptomatic benefit can sometimes be delayed for several weeks after initiation of the drug.[3]

Appropriate diagnosis and treatment of NETs often involves collaboration between specialists in multiple disciplines, using specific biochemical, radiologic, and surgical methods. Specialists include pathologists, endocrinologists, radiologists, and oncologists.[3]

Efficacy

Telotristat, the active metabolite of telotristat ethyl, is an inhibitor of 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 over-produced in patients with carcinoid syndrome. Through inhibition of tryptophan

hydroxylase, telotristat and telotristat ethyl reduce the production of peripheral serotonin, and the frequency of carcinoid syndrome diarrhea.[1-4]

The efficacy of telotristat was demonstrated in a 12-week double-blind, place-controlled, randomized, multicenter trial. The trial enrolled patients (n =135) with metastatic neuroendocrine tumor carcinoid syndrome diarrhea. The patients were required to have between 4 to 12 daily bowel movements despite the use of somatostatin analog (SSA) therapy at a stable dose for at least 3 months. Patients were randomized to receive either telotristat 250 mg daily or placebo and were required to stay on their baseline long-acting SSA regimen. Patients were allowed to use rescue medication (i.e., short-acting octreotide).[1-4]

The primary outcome was change from baseline in the number of daily bowel movements averaged over the 12-week treatment period. In the 12-week study, a difference in average weekly reductions in bowel movement frequency between Xermelo and placebo was observed as early as 1 to 3 weeks and persisted for the remaining 9 weeks of the study. The median number of bowel movements in the Xermelo group was 5.5 daily at baseline and 4.2 daily after treatment. The baseline number of bowel movements in the placebo group was 5.1 daily at baseline and 4.5 daily after 9 weeks.[1,2]

Safety[1]
Xermelo has no contraindications.

REFERENCES

1. Xermelo prescribing information. Lexicon Pharmaceuticals, Inc. February 2017.
2. Strosberg JR, et al. Treatment of the Carcinoid Syndrome. UpToDate. Last updated March 2020. Literature review current through February 2021. Accessed March 2021.
3. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Neuroendocrine and Adrenal Tumors (Version 2.2020 – July 2020). Accessed March 2021.
4. Larouche V, Akirov A, Alshehri S, Ezzat S. Management of Small Bowel Neuroendocrine Tumors. *Cancers*. 2019 Sep;11(9):1395.
5. Strosberg JR, Halfdanarson TR, Bellizzi AM, et al. The North American Neuroendocrine Society (NANETS) Consensus Guidelines for Surveillance and Medical Management of Midgut Neuroendocrine Tumors. *Pancreas*. 2017 Jul;46(6):707-714.

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TARGET AGENT(S)
Xermelo® (telotristat)

Brand (generic)	GPI	Multisource Code	Quantity Limit (per day or as listed)
Xermelo (telotristat)			
250 mg tablets	52570075100330	M, N, O, or Y	3 tablets

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Initial Evaluation
Target Agent(s) will be approved when ALL of the following are met:

1. ONE of the following:
   A. The patient has a diagnosis of carcinoid syndrome diarrhea and BOTH of the following:
      i. The patient has tried and had an inadequate response with a long-acting somatostatin analog (e.g., Sandostatin LAR [octreotide], Somatuline Depot [lanreotide]) for at least 3 months
      AND
      ii. The requested agent will be used in combination with a long-acting somatostatin analog (e.g., Sandostatin LAR [octreotide], Somatuline Depot [lanreotide])
   OR
   B. The patient has another FDA approved indication for the requested agent
   AND
2. ONE of the following:
   A. The patient's age is within FDA labeling for the requested indication for the requested agent
   OR
   B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication
   AND
3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., oncologist, endocrinologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis
   AND
4. The patient does NOT have any FDA labeled contraindications to the requested agent
   AND
5. ONE of the following:
   A. The requested quantity (dose) does NOT exceed the program quantity limit
   OR
   B. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
      AND
      ii. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication
      AND
      iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit

Length of Approval: 6 months

Renewal Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process
   AND
2. ONE of the following:
   A. For a diagnosis of carcinoid syndrome diarrhea, BOTH of the following:
      i. The patient has had clinical benefit with the requested agent (e.g., reduction in average number of daily bowel movements)
         AND
      ii. The requested agent will be used in combination with a long-acting somatostatin analog (e.g. Sandostatin LAR [octreotide], Somatuline Depot [lanreotide])

   OR

   B. For another FDA approved indication, the patient has had clinical benefit with the requested agent

   AND
3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., oncologist, endocrinologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis
   AND
4. The patient does NOT have any FDA labeled contraindications to the requested agent
   AND
5. ONE of the following:
   A. The requested quantity (dose) does NOT exceed the program quantity limit
      OR
   B. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit
         AND
      ii. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication
         AND
      iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit

Length of Approval: 12 months