Xermelo (telotristat) Prior Authorization with Quantity Limit Program Summary

This program applies to FlexRx Closed, FlexRx Open, FocusRx, GenRx Closed, GenRx Open, Health Insurance Marketplace, and KeyRx formularies.

This is a FlexRx Standard and GenRx Standard program.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
9/1/2023	7/1/2018

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Xermelo® (telotristat ethyl) Tablet	Treatment of carcinoid syndrome diarrhea in combination with somatostatin analog (SSA) therapy in adults inadequately controlled by SSA therapy		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

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.(2,3,4) 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.(1,2,3,4) 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).(1,2,3,4) 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	Xermelo has no contraindications.(1)

REFERENCES

Number	Reference
1	Xermelo prescribing information. TerSera Therapeutics. September 2022.
2	Strosberg JR, et al. Treatment of the Carcinoid Syndrome. UpToDate. Last updated February 2022. Literature review current through January 2023.
3	National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology: Neuroendocrine and Adrenal Tumors (Version 2.2022 – December 2022).
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.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Xermelo	telotristat ethyl tab	250 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Xermelo	Telotristat Etiprate Tab 250 MG (Telotristat Ethyl Equiv)	250 MG	90	Tablets	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Xermelo	telotristat ethyl tab	250 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Xermelo	Telotristat Etiprate Tab 250 MG (Telotristat Ethyl Equiv)	250 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical 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: 1. 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** 2. 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. If the patient has an FDA approved indication, ONE of the following:

Module	Clinical Criteria for Approval
	A. The patient's age is within FDA labeling for the requested indication for the requested agent for the requested indication **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 **Length of Approval:** 6 months NOTE: If Quantity Limit applies, please refer to Quantity Limit criteria **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: 1. The patient has had clinical benefit with the requested agent (e.g., reduction in average number of daily bowel movements) **AND** 2. 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 **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit criteria

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity Limits for the Target Agent(s) will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. 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:** Initial 6 months; Renewal 12 months

