Xermelo™ (telotristat) Prior Authorization with Quantity Limit Criteria Program Summary

This prior authorization applies to Commercial, NetResults A series, NetResults F series and Health Insurance Marketplace formularies.

OBJECTIVE
The intent of the Xermelo (telotristat) prior authorization (PA) program is to appropriately select patients for therapy according to the Food and Drug Administration (FDA) approved product labeling and/or clinical practice guidelines and/or clinical studies. This program will require the patient has a diagnosis of carcinoid syndrome diarrhea and has tried and failed to respond to somatostatin analog therapy for at least 3 months. The program will also require the patient will use telotristat in combination with a somatostatin analog. The initial length of approval will be 6 months. Subsequent approvals will be for 12 months when the patient has demonstrated clinical improvement from treatment with telotristat. The program will require the prescribed dose of telotristat is within FDA labeling.

TARGET DRUG(S)
Xermelo™ (telotristat)

QUANTITY LIMIT

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

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Initial Evaluation
Xermelo™ (telotristat) will be approved when ALL of the following are met:

1. The patient has ONE of the following diagnoses:
   A. Carcinoid syndrome diarrhea
   OR
   B. Another FDA approved indication
   AND
2. If the diagnosis is carcinoid syndrome diarrhea, BOTH of the following:
   A. The patient has tried and failed therapy with a somatostatin analog for at least 3 months
   AND
   B. The patient will use the requested agent in combination with a somatostatin analog (e.g. Sandostatin (octreotide), Sandostatin LAR (octreotide), Somatuline depot)
   AND
3. The patient does not have an FDA labeled contraindication to therapy with the requested agent
   AND
4. ONE of the following:
   A. The prescribed dosage is within the program limit (FDA approved labeled dosage) **OR**

B. The quantity (dose) requested is within FDA approved labeling and the prescribed dose cannot be achieved using a lesser quantity of a higher strength that does not exceed the program quantity limit

Length of Approval: 6 months

Renewal Evaluation
Xermelo™ (telotristat) will be approved when ALL of the following are met:

1. The patient has been previously approved for therapy with the requested agent through Prime Therapeutics PA process
   AND
2. The patient has had clinical improvement (e.g. reduction in average number of daily bowel movements) from treatment with the requested agent
   AND
3. The patient will use the requested agent in combination with a somatostatin analog (e.g. Sandostatin (octreotide), Sandostatin LAR (octreotide), Somatuline depot)
   AND
4. The patient does not have an FDA labeled contraindication to therapy with the requested agent
   AND
5. ONE of the following:
   A. The prescribed dosage is within the program limit (FDA approved labeled dosage) **OR**
   B. The quantity (dose) requested is within FDA approved labeling and the prescribed dose cannot be achieved using a lesser quantity of a higher strength that does not exceed the program quantity limit

Length of Approval: 12 months

Agent	Contraindication(s)
Xermelo (telotristat)	None

This pharmacy policy is not an authorization, certification, explanation of benefits or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All pharmacy policies are based on (i) information in FDA approved package inserts (and black box warning, alerts, or other information disseminated by the FDA as applicable); (ii) research of current medical and pharmacy literature; and/or (iii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

The purpose of Blue Cross and Blue Shield of Alabama's pharmacy policies are to provide a guide to coverage. Pharmacy policies are not intended to dictate to physicians how to practice medicine. Physicians should exercise their medical judgment in providing the care they feel is most appropriate for their patients.

Neither this policy, nor the successful adjudication of a pharmacy claim, is guarantee of payment.

FDA APPROVED INDICATIONS AND DOSAGE[1]

Agent	Indication	Dose
Xermelo™ (telotristat)	Treatment of carcinoid syndrome diarrhea in combination with somatostatin analog (SSA) therapy in adults with inadequately controlled by SSA therapy.	250 mg three times daily

Clinical Rationale

Carcinoid syndrome diarrhea[2,3]
Carcinoid syndrome is a group of symptoms caused by various hormones that are secreted by carcinoid tumors. These are neuroendocrine tumors that develop in areas such as the gastrointestinal tract and lungs. The two most common symptoms of carcinoid syndrome are flushing and diarrhea (carcinoid syndrome diarrhea). Other symptoms include broncho-constriction and palpitations. The severity of the carcinoid syndrome depends on the number and size of tumors as well as extent of metastases.

Safety[1]
The most common adverse reactions (≥5%) associated with telotristat are nausea, headache, increased gamma-glutamyl transferase (GGT), depression, flatulence, decreased appetite, peripheral edema, and pyrexia. Telotristat is also associated with abdominal pain and constipation. It is recommended to discontinue telotristat if severe constipation develops.

Efficacy[1]
The efficacy of telotristat was demonstrated in a 12 weeks 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 SSA regimen.

The primary outcome was change from baseline in the number of daily bowel movements averaged over the 12-week treatment period.

Change from Baseline in Bowel Movements/Day Averaged Over 12 weeks[1]

	Parameter	Xermelo 250 mg three times daily	Placebo
Bowel Movements/Day At Baseline[a]	Number of Patients	45	45
	Baseline Mean (SD)	6.1 (2.1)	5.2 (1.4)
	Median (Min, Max)	5.5 (3.5, 13.0)	5.1 (3.5, 9.0)
Change From Baseline In Bowel Movements/Day Averaged Over 12 Weeks	Change Averaged over 12 Weeks: Mean (SD)	-1.4 (1.4)	-0.6 (0.8)
	Median (Min, Max)	-1.3 (-6.1, 1.6)	-0.6 (-2.7,0.8)
	Estimate of Treatment Difference (97.5% CL)[b]	-0.8[c] (-1.3, -0.3)	---

CL=confidence limit; SD=standard deviation.
[a] Baseline Bowel Movements/Day was assessed over the 3-4 week screening/run-in period.
[b] Statistical tests used a blocked 2-sample Wilcoxon Rank Sum statistic (van Elteren test) stratified by the u5-HIAA stratification at randomization. CLs were based on the Hodges-Lehmann estimator of the median paired difference.
[c] $p<0.001$

REFERENCES

1. Xermelo prescribing information. Lexicon. February 2017.
2. Strosberg, JR. Treatment of the carcinoid syndrome. UpToDate, Waltham, MA. March 2017.
3. 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.