Medical Policy

BlueCross BlueShield of Kansas
An independent licensee of the Blue Cross Blue Shield Association

Title: Xermelo (telotristat)

- **Prime Therapeutics will review Prior Authorization requests**
  Prior Authorization Form:
  https://www.bcbsks.com/CustomerService/Forms/pdf/PriorAuth-6503KS-XERM.pdf

  Link to Drug List (Formulary):
  https://www.bcbsks.com/drugs/

Professional
Original Effective Date: December 1, 2017
Revision Date(s): December 1, 2017; April 1, 2018; October 1, 2018
Current Effective Date: October 1, 2018

Institutional
Original Effective Date: December 1, 2017
Revision Date(s): December 1, 2017; April 1, 2018; October 1, 2018
Current Effective Date: October 1, 2018

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

DESCRIPTION

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 had an inadequate response 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 Agent(s)

- **Xermelo™** (telotristat)

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 inadequately controlled by SSA therapy.	250 mg three times daily

POLICY

Prior Authorization and Quantity Limit Criteria for Approval

Initial Evaluation

Xermelo™ (telotristat) 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 somatostatin analog for at least 3 months
      AND
      ii. The patient will use the requested agent in combination with a somatotatin analog (e.g. Sandostatin (octeriotide), Sandostatin LAR (octeriotide), Somatuline depot)
   OR
   B. The patient has another FDA approved indication.
   AND
2. The patient does not have an FDA labeled contraindication to therapy with the requested agent
   AND
3. ONE of the following:
   A. The prescribed quantity (dose) is less than or equal to the program limit
   OR

B. The requested quantity (dose) is greater than the program limit and BOTH of the following:
   i. The requested quantity (dose) is less than or equal to the FDA labeled dose
   AND
   ii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the 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 (octeriotide), Sandostatin LAR (octeriotide), 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 quantity (dose) is less than or equal to the program limit
   OR
   B. The requested quantity (dose) is greater than the program limit and BOTH of the following:
      i. The requested quantity (dose) is less than or equal to the FDA labeled dose
      AND
      ii. The requested quantity (dose)cannot be achieved with a lower quantity of a higher strength that does not exceed the limit

Length of Approval: 12 months

Agent	Contraindications
Xermelo (telotristat)	None

Brand (generic)	Quantity Per Day Limit
Xermelo (telotristat) tablets	
250 mg tablets	3 tablets

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.

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] $p<0.001$

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.

REVISIONS

12-01-2017	Policy added to the bcbsks.com web site.
04-01-2018	In Policy section: ▪ Initial Evaluation (IE) and Renewal Evaluation (RE) ▪ In Item IE 4 A RE 5 A removed "dosage is within" and "(FDA approved labeled dosage)" and added "quantity (dose) is less than or equal to" to read "The prescribed quantity (dose) is less than or equal to the program limit" ▪ In Item IE 4 B removed "within FDA approved labeling" and "prescribed" and added "greater than the program limit" and "BOTH of" to read "The requested quantity (dose) is greater than the program limit and BOTH of the following:" ▪ In Item RE 5 B removed "is within FDA approved labeling and the prescribed" and added "is greater than the program limit and BOTH of the following:" to read " The requested quantity (dose) is greater than the program limit and BOTH of the following:" ▪ Added Item IE 4 B i and RE 5 B i "The requested quantity (dose) is less than or equal to the FDA labeled dose" In Item IE 4 B ii and RE 5 B ii removed "program quantity" and added "requested quantity to read "The requested quantity (dose)cannot be achieved with a lower quantity of a higher strength that does not exceed the limit"
10-01-2018	Description section updated
	In Policy section: Summary of revisions: • Reformatted indications but no change to intent or requirements - Moved all requirements for carcinoid syndrome under one item • Update language for prerequisites to “tried and had an inadequate response to” <u>Initial Evaluation</u> ▪ In Item 1 A revised wording to "The patient has a diagnosis of Carcinoid syndrome diarrhea and BOTH of the following:" (there is no policy intent change with this revision) ▪ In Item 1 A i removed "failed therapy" and added "had an inadequate response" to read "The patient has tried and had an inadequate response with a somatostatin analog for at least 3 months" ▪ The above revisions do not have any change on the intent of the policy.
	Rationale section updated
	References updated

REFERENCES

1. Xermelo prescribing information. Lexicon. February 2017.
2. Strosberg, JR. Treatment of the carcinoid syndrome. UpToDate, Waltham, MA. February 2018.
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.