telotristat (Xermelo™)

Policy # 00555
Original Effective Date: 05/17/2017
Current Effective Date: 06/10/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider telotristat (Xermelo™)‡ for the treatment of carcinoid syndrome diarrhea to be **eligible for coverage.****

Patient Selection Criteria
Coverage eligibility for telotristat (Xermelo) will be considered when the following criteria are met:

Initial (6 months)

- Patient has a diagnosis of carcinoid syndrome diarrhea; AND
- Patient is 18 years of age or older; AND
- Patient in inadequately controlled (e.g. has at least 4 bowel movements per day) with a long acting somatostatin analog after at least 3 months of therapy (e.g. octreotide product (Sandostatin LAR®‡) or lanreotide product (Somatuline Depot®‡); AND
  *(Note: The 3 month time frame and the bowel movement requirement, which are based on clinical study criteria, are additional Company requirements for coverage eligibility and will be denied as not medically necessary** if not met. The trial and failure of the long acting somatostatin analog will be denied as investigational* if not met)*
- Patient will continue to use telotristat (Xermelo) along with a somatostatin analog.

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Renewal (1 year)

- Patient will continue to use telotristat (Xermelo) along with a somatostatin analog; AND
- Patient has experienced a 30% reduction in bowel movement frequency while on telotristat Xermelo
  *(Note: This criterion is an additional Company requirement, based on clinical trials, for coverage eligibility and will be denied as not medically necessary** if not met.)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of telotristat (Xermelo) when the patient is NOT inadequately controlled (inadequate control is defined as greater than 4 bowel movements/day) on a long acting somatostatin analog after at least 3 months of therapy (time frame and bowel movement requirements only) to be **not medically necessary.****

Based on review of available data, the Company considers the use of telotristat (Xermelo) when the patient has NOT experienced a 30% reduction in bowel movement frequency while on telotristat (Xermelo) to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of telotristat (Xermelo) when the patient selection criteria are not met (EXCEPT those denoted as **not medically necessary****) to be **investigational.***

Background/Overview

Xermelo is a tryptophan hydroxylase inhibitor indicated for the treatment of carcinoid syndrome diarrhea in combination with somatostatin analog therapy in adults inadequately controlled by somatostatin analog therapy. The recommended dosage of Xermelo in adult patients is 250 mg three times daily. Xermelo is available in 250 mg tablets.

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Carcinoid Syndrome Diarrhea
Carcinoid tumors are the most common of the neuroendocrine tumors. Patients with carcinoid tumors may or may not have symptoms attributable to hormonal hypersecretion, specifically serotonin secretion. Normally, serotonin regulates gut motility. In those with neuroendocrine tumors, excess serotonin is produced, which leads to carcinoid syndrome. Symptoms of carcinoid syndrome include diarrhea, flushing, abdominal pain, and valvular hear disease. Patients who have metastatic neuroendocrine tumors should be treated with long acting somatostatin analogues (e.g. Sandostatin LAR or Somatuline Depot) for the chronic management of symptoms. Short acting octreotide can be added for rapid relief of breakthrough symptoms. Xermelo appears to be an add-on therapy for those that are uncontrolled with somatostatin analogues; however guidelines have not yet addressed the place in therapy of Xermelo.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Xermelo is a tryptophan hydroxylase inhibitor indicated for the treatment of carcinoid syndrome diarrhea in combination with somatostatin analog therapy in adults inadequately controlled by somatostatin analog therapy.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Xermelo was evaluated in a 12 week double-blind, placebo-controlled, randomized, multicenter trial in adult patients with well differentiated metastatic neuroendocrine tumors and carcinoid syndrome diarrhea who were having between 4 to 12 daily bowel movements despite the use of somatostatin analog therapy at a stable dose for at least 3 months. Patients were randomized to placebo or treatment with Xermelo 250 mg three times daily. The primary efficacy endpoint was the change from baseline in the number of daily bowel movements averaged over the 12 week treatment period. Those patients treated with Xermelo had an average decrease of 1.4 bowel movements per day over the 12 week period vs. a decrease in 0.6 bowel movements per day in the placebo group. The

treatment effect was observed as early as 1 to 3 weeks, and persisted for the remaining 9 weeks of the study. A treatment responder was defined as those with at least a 30% or greater reduction in bowl movement frequency for at least 50% of the double-blind period. In this study, 44% of Xermelo subjects and 20% of placebo subjects were considered treatment responders.

References

1. Xermelo [package insert]. Lexicon Pharmaceuticals, Inc, The Woodlands, Texas. Updated February 2017.
2. Xermelo Drug Evaluation. Express Scripts. Updated March 2017.

Policy History

Original Effective Date: 05/17/2017
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05/04/2017	Medical Policy Committee review
05/17/2017	Medical Policy Implementation Committee approval. New policy.
05/03/2018	Medical Policy Committee review
05/16/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/02/2019	Medical Policy Committee review
05/15/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/07/2020	Medical Policy Committee review
05/13/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/06/2021	Medical Policy Committee review
05/12/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/05/2022	Medical Policy Committee review
05/11/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/04/2023	Medical Policy Committee review

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05/10/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/02/2024 Medical Policy Committee review
05/08/2024 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 05/2025

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and

C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.