POLICY NUMBER UM ONC_1303	SUBJECT Xermelo™ (telotristat ethyl)		DEPT/PROGRAM UM Dept	PAGE 1 OF 2
DATES COMMITTEE REVIEWED 03/08/17, 11/08/17, 10/10/18, 10/09/19, 12/11/19	APPROVAL DATE December 11, 2019	EFFECTIVE DATE December 11, 2019	COMMITTEE APPROVAL DATES (latest version listed last) 03/08/17, 11/08/17, 10/10/18, 10/09/19, 12/11/19	
PRIMARY BUSINESS OWNER: UM APPROVED BY: Dr. Andrew Hertler		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
URAC STANDARDS HUM 1		NCQA STANDARDS UM 2	ADDITIONAL AREAS OF IMPACT	
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS All	

I. PURPOSE

To define and describe the accepted indications for Xermelo (telotristat ethyl) usage in the treatment of cancer.

II. DEFINITIONS

Xermelo (telotristat ethyl): Telotristat ethyl and the active metabolite, telotristat, are tryptophan hydroxylase inhibitors; although, the in vitro inhibitory activity of the telotristat metabolite is 29 times higher than that of telotristat ethyl. Production of peripheral serotonin, which affects the gastrointestinal tract and is over-produced in patients with carcinoid syndrome, is reduced via inhibition of tryptophan hydroxylase.

Xermelo (telotristat ethyl) is a first-in-class new molecular entity and is FDA approved for the treatment of carcinoid syndrome diarrhea in combination with somatostatin analog (SSA) therapy in adults inadequately controlled by SSA therapy.

Xermelo (telotristat ethyl) is available in 250 mg tablets.

III. POLICY

New Century Health is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century Health may be deemed as not approvable and therefore not reimbursable. Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

Inclusion Criteria: Xermelo (telotristat ethyl) may be considered medically necessary when any of the following selection criteria are met:

1. **Neuroendocrine Tumors**
    a. The member has metastatic neuroendocrine tumors and Xermelo (telotristat ethyl) is being used in **ALL** the following:
        i. In combination with somatostatin analog (SSA) i.e. octreotide or lanreotide
        ii. The member has intractable diarrhea associated with carcinoid syndrome
        iii. The member is currently receiving at the minimum dose of Octreotide LAR 30 mg every 4 weeks or Lanreotide Depot 120 mg every 4 weeks
        iv. Has poor control or response which is defined as a baseline stool frequency of ≥ 4 bowel movements a day.

Exclusion Criteria: Xermelo (telotristat ethyl) is not considered medically necessary when any of the following selection criteria are met:

1. Xermelo (telotristat ethyl) is being used in member with any of the following
    a. History of short bowel syndrome
    b. Chemotherapy induced diarrhea
    c. Non-diarrhea carcinoid syndrome: symptoms such as flushing, valvular heart disease and abdominal pain
    d. Severe constipation
2. Dosing exceeds single dose limit of Xermelo (telotristat ethyl) 250 mg
3. Treatment exceeds the maximum limit of 90 (250 mg) tablets/month
4. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable

IV. PROCEDURE

Requests for Xermelo (telotristat ethyl) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. **Dosage and Administration:** 250 mg orally three times daily with food. If taking with short-acting octreotide, administer telotristat ethyl at least 30 minutes before short-acting octreotide. Increasing the dose of telotristat ethyl to 500 mg three times daily increased the incidence of adverse reactions without increasing benefit and is not recommended.
2. **Dosage Adjustments:** dosage adjustments are not required for renal or hepatic impairment
3. **Monitoring**
    a. Improvement in symptoms of carcinoid syndrome diarrhea may indicate efficacy.
    b. Constipation
    c. Severe persistent or worsening abdominal pain
    d. CYP3A4 Substrates (e.g., midazolam): Efficacy of concomitant drugs may be decreased; monitor for suboptimal efficacy and consider increasing the dose of the concomitant drug.

V. APPROVAL AUTHORITY

1. Review – UM Department
2. Final Approval – UM Committee

VI. ATTACHMENTS

None

VII. REFERENCES

1. Xermelo PI prescribing information. Lexicon Pharmaceuticals, Inc. Woodlands, TX 2017.
2. Clinical Pharmacology Elsevier Gold Standard. 2018.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2018.
4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2018.
5. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2018.