Drug Therapy Guidelines

Xermelo™ (telotristat ethyl)

Medical Benefit

<table>
<thead>
<tr>
<th>Pharmacy- Formulary 1</th>
<th>x</th>
<th>Effective: 8/15/18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacy- Formulary 2</td>
<td>x</td>
<td>Next Review: 6/19</td>
</tr>
<tr>
<td>Pharmacy- Formulary 3/Exclusive</td>
<td>x</td>
<td>Date of Origin: 4/17</td>
</tr>
<tr>
<td>Pharmacy- Formulary 4/AON</td>
<td>x</td>
<td>Review Dates: 3/17, 6/17, 6/18</td>
</tr>
</tbody>
</table>

I. Medication Description

Telotristat, the active metabolite of telotristat ethyl, is an inhibitor of tryptophan hydroxylase, which mediates the rate limiting step in serotonin biosynthesis. The *in vitro* inhibitory potency of telotristat towards tryptophan hydroxylase is 29 times higher than that of telotristat ethyl. 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.

II. Position Statement

Coverage is determined through a prior authorization process with supporting clinical documentation for all requests.

III. Policy

Coverage of Xermelo is available when the following criteria have been met:

- Member is at least 18 years of age AND
- Medication is prescribed by an oncologist or gastroenterologist AND
- Member has carcinoid syndrome diarrhea that is uncontrolled (e.g. at least 4 bowel movements per day) despite stable maximum tolerated FDA-approved dosing with a somatostatin analog for at least 3 months AND
- Xermelo will be used in combination with a somatostatin analog

IV. Quantity Limitations

One monthly case (84 tablets) covered per each 28 days.

V. Coverage Duration

Initial coverage may be provided for up to 6 months and may be renewed.

VI. Coverage Renewal Criteria

Coverage can be renewed in up to 12 month intervals based upon the following:
- Stabilization of disease, including reduction in bowel movement frequency AND
- Absence of unacceptable toxicity from the drug (e.g. severe constipation, etc)

VII. Billing/Coding Information

Xermelo is dispensed in a monthly case for a total of 28 days of therapy
- Each monthly case contains four weekly boxes
- Each weekly box contains seven daily dose packs (day pack)
- Each child-resistant day pack contains three 250mg tablets

VIII. Summary of Policy Changes

- 4/28/17: new policy
- 6/21/17: no policy changes
- 8/15/18: updated coverage and renewal criteria: added a requirement for the medication to be prescribed by an oncologist or gastroenterologist, uncontrolled diarrhea clarified as 4 bowel movements or more, 3 months of somatostatin trial required before Xermelo initiation; initial coverage duration changed to 6 months

IX. References

11. Octreotide acetate injection [prescribing information]. Lake Zurich, IL: Fresenius Kabi, USA; May 2014.

The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

The preceding policy applies only to members for whom the above named pharmacy benefit medications are included on their covered formulary. Members with closed formulary benefits are subject to trying all appropriate formulary alternatives before a coverage exception for a non-formulary medication will be considered.

The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.