tegaserod (Zelnorm®)

EOCCO POLICY

Policy Tpe: PA/SP Pharmacy Coverage Policy: UMP087

Description

Tegaserod (Zelnorm) is an orally administered serodonin-4 (5-HT4) receptor agonist.

Length of Authorization

- Initial: Three months
- Renewal: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit	DDID
tegaserod (Zelnorm)	6 mg tablets	Irritable bowel syndrome with constipation	60 tablets/30 days	077781

Initial Evaluation

I. Tegaserod (Zelnorm) may be considered medically necessary when the following criteria below are met:
   A. The condition being treated is a covered line according to the Oregon Health Plan List of Prioritized Services; **AND**
   B. The member is 18 years of age or older AND is less than 65 years of age; **AND**
   C. The medication is prescribed by, or in consultation with, a gastroenterologist; **AND**
   D. A diagnosis of **irritable bowel syndrome with constipation (IBS-C)** when the following are met:
      1. The member does not have current or historical cardiovascular disease; **AND**
      2. The member is female; **AND**
      3. The member has had an inadequate response to the ALL of the following:
         i. Dietary modifications (e.g., removal of offending foods, increased fiber intake) AND increased physical activity; **AND**
         ii. At least one osmotic laxative (e.g., polyethylene glycol); **AND**
         iii. lubiprostone (Amitiza); **AND**
         iv. One of the following: linaclotide (Linzess) OR plecanatide (Trulance); **OR**
            a. The member is contraindicated to all of these therapies

II. Tegaserod (Zelnorm) is considered <u>not medically necessary</u> when criteria above are not met and/or when used for:
   A. Irritable bowel syndrome with constipation in males

III. Tegaserod (Zelnorm) is considered investigational when used for all other conditions, including but not limited to:
   A. Idiopathic chronic constipation
   B. Opioid or other drug induced constipation
   C. Gastroesophageal reflux disease (GERD)

Renewal Evaluation

I. The condition being treated is a covered line according to the Oregon Health Plan List of Prioritized Services; **AND**
II. The member is 18 years of age or older AND the member is less than 65 years of age; **AND**
III. The medication is prescribed by, or in consultation with, a gastroenterologist; **AND**
   A. **A diagnosis of irritable bowel syndrome with constipation (IBS-C)**; **AND**
      1. The member does not have a history of, or established, cardiovascular disease; **AND**
      2. The member has experienced a response to treatment (e.g., increase in rate of bowel movements)

Supporting Evidence

I. Tegaserod (Zelnorm), a serotonin-4 (5-HT4) receptor agonist. It is FDA-approved and indicated for the treatment of irritable bowel syndrome with constipation (IBS-C) in women < 65 years. It was originally approved in 2002, for short-term treatment of women with IBS-C; however, it was withdrawn from the market in 2007 due to an unfavorable cardiovascular (CV) suicidal ideation and behavior (SI/B) safety profile.
II. Efficacy to support reintroduction of tegaserod (Zelnorm) was based on evidence established at the time of original approval. No new evidence on efficacy was added. Tegaserod (Zelnorm) was evaluated in three multicenter, double-blind, placebo-controlled, 12-week trials of 2,470 women that had at least a three-month history of IBS-C. Response rate (RR) was the primary outcome, and was based on subjective response on a five parameter scale measured each week indicating: completely relieved, considerably relieved, somewhat relieved, unchanged, or worse. Responders within a month were classified as those with complete relief or considerable relief for at least two of the four weeks, or somewhat relieved for all of the four weeks. Tegaserod (Zelnorm) had superior response rates compared to placebo ranging from 6 to 28%. Secondary outcomes of pain, discomfort and bloating were evaluated on six-to-seven point intensity scale. Positive response, defined as at least a 1-point reduction, was measured to be 1-10% superior for tegaserod (Zelnorm) for abdominal pain or discomfort and 4-11% for bloating. The baseline

bowel movement rate averaged 3.8 per week, and increased to 6 per week for tegaserod (Zelnorm) and 5.5 for placebo.

III. Tegaserod (Zelnorm) is contraindicated in those with established CV history, renal impairment, hepatic impairment, bowel obstruction, gallbladder disease, suspected sphincter of Oddi dysfunction, or abdominal adhesions. In regards to CV disease, the product label specifically indicates: myocardial infarction, stroke, transient ischemic attach, angina. Warnings and precautions include CV ischemic events, major adverse CV events (MACE), ischemic colitis, volume depletion with diarrhea, and SI/B. Common adverse effects (≥ 2%) include headache, abdominal pain, nausea, diarrhea, flatulence, dyspepsia, and dizziness. Approval of tegaserod (Zelnorm) reintroduction was supported by a complete safety review by the FDA and FDA-assembled Gastrointestinal Drugs Advisory Committee (GIDAC). Retrospective analyses of pooled data from 18,645 patients in 29 placebo-controlled trials in various disease states of at least four weeks duration were included. The imbalance in CV events was measured to be 0.1% for tegaserod (Zelnorm) versus 0.01% in placebo. There was one death, attributed to suicide, during the trial. The member has a history of mild depression. The rate of SI/B is measured to be 0.07% for tegaserod (Zelnorm) vs. 0.02% for placebo.

IV. First-line treatment options include dietary modifications, increased fiber intake and physical activity. Adjunctive pharmacotherapy includes over-the-counter osmotic laxatives. When lifestyle modifications and osmotic laxatives fail to produce sufficient relief of constipation, further pharmacologic therapy with lubiprostone (Amitiza), linaclotide (Linzess), or plecanatide (Trulance), may be warranted. Due to the limited efficacy and concerning safety profile, tegaserod (Zelnorm) shall be reserved for those that have exhausted other treatment options.

Investigational or Not Medically Necessary Uses

I. Irritable bowel syndrome with constipation (IBS-C) in males
   A. Two randomized, placebo-controlled, double-blind trials of 288 men did not show differences in efficacy of tegaserod (Zelnorm) versus placebo. This information is stated in the product labeling.

II. Clinical trials are underway, but have not yet been completed to provide insight to safety and efficacy of tegaserod (Zelnorm) in the following settings:
   A. Idiopathic chronic constipation
   B. Opioid or other drug induced constipation
   C. Gastroesophageal reflux disease (GERD)

References

1. Zelnorm [Prescribing Information]. Sloan Pharma/WorldMeds LLC. Louisville, KY. 2019.
2. Black CJ, Burr NE, Ford AC. Relative Efficacy of Tegaserod in a Systematic Review and Network Meta-analysis of Licensed Therapies for Irritable Bowel Syndrome with Constipation. Clin Gastroenterol Hepatol. 2019.

3. Vakil N, Laine L, Talley NJ, et al. Tegaserod treatment for dysmotility-like functional dyspepsia: results of two randomized, controlled trials. Am J Gastroenterol. 2008;103(8):1906-19.
4. Weinberg D.S., Smalley W. Heidelbaugh J.J., et al. American Gastroenterological Association institute guidelines on the pharmacological management of irritable bowel syndrome. Gastroenterology. 2014;144: 1146-1148.
5. Chandar AK. Diagnosis and treatment of irritable bowel syndrome with predominant constipation in the primary-care setting: focus on linaclotide. Int J Gen Med. 2017;10:385-393.
6. Clinicaltrials.gov

Policy Implementation/Update:

Date Created	August 2019
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Last Reviewed	

Action and Summary of Changes	Date