Clinical Policy: Tegaserod (Zelnorm)

Reference Number: ERX.NPA.122
Effective Date: 09.01.19
Last Review Date: 11.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Tegaserod (Zelnorm™) is a serotonin-4 (5-HT_4) receptor agonist.

FDA Approved Indication(s)
Zelnorm is indicated for the treatment of adult women less than 65 years of age with irritable bowel syndrome with constipation (IBS-C).

Limitation(s) of use: The safety and effectiveness of Zelnorm in men with IBS-C have not been established.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Zelnorm is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Irritable Bowel Syndrome with Constipation (must meet all)**:**

1. Diagnosis of IBS-C;
2. Age ≥ 18 years and < 65 years;
3. Failure of one bulk forming laxative (e.g., psyllium [Metamucil®], methylcellulose [Citrucel®], calcium polycarbophil [FiberCon®]), unless clinically significant adverse effects are experienced) or all are contraindicated;
4. Failure of generic lubiprostone, Linzess®, or Trulance® (whichever is preferred), unless clinically significant adverse effects are experienced or all are contraindicated;
   **Prior authorization may be required for Linzess, lubiprostone, and Trulance*
5. At the time of request, member does not have any of the following contraindications: a history of myocardial infarction, stroke, transient ischemic attack, or angina;
6. Dose does not exceed 12 mg (2 tablets) per day.

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Irritable Bowel Syndrome with Constipation (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. At the time of request, member does not have any of the following contraindications: a history of myocardial infarction, stroke, transient ischemic attack, or angina;

4. If request is for a dose increase, new dose does not exceed 12 mg (2 tablets) per day.
Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
IBS-C: irritable bowel syndrome with constipation
MACE: major adverse cardiovascular events

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
psyllium (Metamucil®)	1 rounded teaspoonful, tablespoonful, or premeasured packet in 240 mL of fluid PO, 1 to 3 times per day (2.4 g of soluble dietary fiber per dose)	7.2 g (as soluble dietary fiber)/day
calcium polycarbophil (FiberCon®)	2 tablets (1,250 mg calcium polycarbophil) PO 1 to 4 times daily	8 tablets/day (5,000 mg/day)
methylcellulose (Citrucel®)	Caplet: 2 caplets PO up to 6 times daily Powder: 1 heaping tablespoonful in at least 240 ml of water PO, given 1 to 3 times per day as needed	Caplet: 12 caplets/day Powder: 3 tablespoons/day
lubiprostone (Amitiza®)	8 mcg PO BID	16 mcg/day
Linzess® (linaclotide)	290 mcg PO QD	290 mcg/day
Trulance® (plecanatide)	3 mg PO QD	3 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s):
  - Major adverse cardiovascular events (MACE): history of myocardial infarction, stroke, transient ischemic attack, or angina
  - History of ischemic colitis or other forms of intestinal ischemia
  - Severe renal impairment (eGFR < 15 mL/min/1.73 m^2) or end-stage renal disease
  - History of bowel obstruction, symptomatic gallbladder disease, suspected sphincter of Oddi dysfunction, or abdominal adhesions
  - Moderate or severe hepatic impairment (Child-Pugh B or C)
  - Hypersensitivity to tegaserod
- Boxed warning(s): none reported

Appendix D: General Information

- On June 30, 2022, Alfasigma USA, Inc. announced the withdrawal of the NDA for Zelnorm (tegaserod) effective June 30th. Alfasigma USA, Inc will no longer make the product available in the US marketplace.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
IBS-C	6 mg PO BID at least 30 minutes before meals. Discontinue in patients who have not had adequate control of symptoms after 4 to 6 weeks of treatment.	12 mg/day

VI. Product Availability

Tablet: 6 mg

VII. References

1. Zelnorm Prescribing Information. Covington, LA: Alfasigma USA Inc; July 2019. Available at: www.myzelnorm.com. Accessed August 18, 2022.
2. NDA/BLA Multi-Disciplinary Review and Evaluation for Zelnorm (tegaserod). Silver Spring, MD. Food & Drug Administration (FDA): March 22, 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/021200Orig1s015MultidisciplineR.pdf., Accessed August 18, 2022
3. FDA Briefing Document for Zelnorm (tegaserod maleate) for treatment of Irritable Bowel Syndrome with Constipation (IBS-C). Louisville, KY: Sloan Pharma, US WorldMeds: October 2018. Available at: https://www.fda.gov/media/119013/download. Accessed August 18, 2022.
4. Lacy BE, Pimentel M, Brenner DM, et al. ACG Clinical Guidance: Management of Irritable Bowel Syndrome. Am J Gastroenterol. 2021; 2021; 116 (1): 17-44.
5. Guidance for Industry: Irritable Bowel Syndrome- Clinical Evaluation of Drugs for Treatment: FDA; 2012 [08-10-2017]. Available from: https://www.fda.gov/downloads/Drugs/Guidances/UCM205269.pdf.
6. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: https://www.clinicalkey.com/pharmacology. Accessed August 18, 2022.
7. Ford AC, Moayyedi P, Chey WD, et al. American College of Gastroenterology Monograph on Management of Irritable Bowel Syndrome. Am J Gastroenterol. 2018 June; 113 (Suppl 2):1-18.
8. Zelnorm (tegaserod) notice of withdrawal from market. Press release. Published June 30, 2022. Available at: https://www.myzelnorm.com/assets/pdfs/Press%20Release%20on%20Notice%20of%20Withdrawal.pdf. Accessed August 18, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	05.14.19	08.19
3Q 2020 annual review: no significant changes; references reviewed and updated	05.08.20	08.20
3Q 2021 annual review: no significant changes; modified Amitiza to reference generic lubiprostone; references reviewed and updated.	04.12.21	08.21
3Q 2022 annual review: no significant changes; references reviewed and updated.	03.22.22	08.22
4Q 2022 annual review: no significant changes; references reviewed and updated.	08.18.22	11.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.