Clinical Policy: Tegaserod (Zelnorm)

Reference Number: CP.PMN.206
Effective Date: 05.14.19
Last Review Date: 11.23
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.

It is the policy of health plans affiliated with Centene Corporation® 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, unless contraindicated or clinically significant adverse effects are experienced;
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 (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial and CP.PMN.53 for Medicaid, or evidence of coverage document.

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 for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
psyllium (Metamucil®) [OTC]	1 rounded teaspoonful, tablespoonful, or premeasured packet in 240 mL of fluid PO, QD to TID (2.4 g of soluble dietary fiber per dose)	7.2 g (as soluble dietary fiber) per day
calcium polycarbophil (FiberCon®) [OTC]	2 tablets (1,250 mg calcium polycarbophil) PO 1 to 4 times daily	8 tablets/day (5,000 mg/day)
methylcellulose (Citrucel®) [OTC]	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

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)
  - Hypersensitivy to tegaserod
- Boxed warning(s): none reported

Appendix D: General Information
- On June 30, 2022, Alfasigma USA, Inc. announces the withdrawal of the NDA for Zelnorm (tegaserod) effective June 30th. Alfasigma USA, Inc will no longer make the product available in the US market place. The decision to remove Zelnorm from the market is strictly a business decision and was not based on product efficacy, safety, or an imposed recall.

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. Alfasigma USA, Inc: Covington, LA; July 2019. Available at: www.myzelnorm.com. Accessed July 06, 2023.
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. Assessed July 11, 2023.
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 July 11, 2023.
4. Lacy BE, Pimentel M, Brenner DM, et al. ACG Clinical Guideline: Management of Irritable Bowel Syndrome. Am J Gastroenterol. 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: http://www.clinicalpharmacology-ip.com/. Accessed July 11, 2023.
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 July 11, 2023.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	05.14.19	08.19
Removed HIM line of business per SDC.	12.03.19	
3Q 2020 annual review: no significant changes; references reviewed and updated	05.08.20	08.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2021 annual review: modified Amitiza redirection to reference generic lubiprostone; removed Trulance and Linzess as redirect options per June SDC; references reviewed and updated.	04.12.21	08.21
2Q 2022 annual review: no significant changes; references reviewed and updated.	01.27.22	05.22
4Q 2022 annual review: no significant changes; references reviewed and updated. Template changes applied to other diagnoses/indications and continued therapy section.	08.18.22	11.22
4Q 2023 annual review: no significant changes; references reviewed and updated.	07.06.23	11.23

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

©2019 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene® and Centene Corporation® are registered trademarks exclusively owned by Centene Corporation.