Clinical Policy: Tenapanor (Ibsrela, Xphozah)

Reference Number: CP.PMN.224
Effective Date: 03.01.20
Last Review Date: 02.24
Line of Business: Commercial, Medicaid

Revision Log

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

Description

Tenapanor (Ibsrela®, Xphozah®) is a sodium/hydrogen exchanger 3 (NHE3) inhibitor.

FDA Approved Indication(s)

Ibsrela is indicated for treatment of irritable bowel syndrome with constipation (IBS-C) in adults.

Xphozah is indicated to reduce serum phosphorus in adults with chronic kidney disease (CKD) on dialysis as add-on therapy in patients who have an inadequate response to phosphate binders or who are intolerant of any dose of phosphate binder therapy.

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 Ibsrela and Xphozah are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Request is for Ibsrela;
2. Diagnosis of IBS-C;
3. Age ≥ 18 years;
4. 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;
5. Failure of generic lubiprostone, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 100 mg (2 tablets) per day.

Approval duration: 12 months

B. Hyperphosphatemia (must meet all)**:**

1. Request is for Xphozah;
2. Diagnosis of hyperphosphatemia associated with CKD;
3. Member is on dialysis;
4. Prescribed by or in consultation with a nephrologist;
5. Age ≥ 18 years;

6. Member meets one of the following (a, b, c, or d):
   a. Failure (e.g., serum phosphorus > 5.5 mg/dL) of a 4-week trial of calcium acetate at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   b. Hypercalcemia as evidenced by recent (within the previous 30 days) corrected total serum calcium level > 10.2 mg/dL;
   c. Plasma parathyroid hormone (PTH) levels < 150 pg/mL on 2 consecutive measurements in the past 180 days;
   d. History of severe vascular and/or soft-tissue calcifications;
7. Failure (e.g., serum phosphorus > 5.5 mg/dL) of a 4-week trial of a non-calcium phosphate binder (e.g., lanthanum carbonate, sevelamer carbonate, *see Appendix B*) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;
   **Prior authorization may be required for non-calcium phosphate binders*
8. Xphozah is prescribed as add-on therapy to phosphate binder therapy;
9. Dose does not exceed (a and b):
   a. 60 mg per day;
   b. 2 tablets per day.

Approval duration: 12 months

C. 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. Request is for Ibsrela;
2. 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);*
3. Member is responding positively to therapy;
4. If request is for a dose increase, new dose does not exceed 100 mg (2 tablets) per day.

Approval duration: 12 months

B. Hyperphosphatemia (must meet all)**:**
1. Request is for Xphozah;
2. 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);*
3. Member is responding positively to therapy (e.g., reduction in serum phosphorus from pretreatment level; maintenance of serum phosphorus level ≤ 5.5 mg/dL);
4. Xphozah is prescribed as add-on therapy to phosphate binder therapy;
5. If request is for a dose increase, new dose does not exceed (a and b):
   a. 60 mg per day;
   b. 2 tablets per day.

Approval duration: 12 months

C. 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 documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
IBS-C: irritable bowel syndrome with constipation
NHE3: sodium/hydrogen exchanger 3
CKD: chronic kidney disease

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®)	**IBS-C** 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®)	**IBS-C** 1,000 mg 1 to 4 times per day or as needed	6,000 mg/day
methylcellulose (Citrucel®)	**IBS-C** Caplet: 2 caplets (total 1 g methylcellulose) PO with at least 240 mL (8 oz) of liquid, up to 6 times per day as needed Powder: 1 heaping tablespoonful (2 g methylcellulose per 19 g powder) in at least 240 mL (8 oz) of water PO, given 1 to 3 times per day as needed	Caplet: 12 caplets/day Powder: 6 grams/day
lubiprostone (Amitiza®)	**IBS-C** 8 mcg PO BID	16 mcg/day
calcium acetate	**Hyperphosphatemia** 2 capsules PO TID with meals; titrate to phosphorus < 6 mg/dL and calcium < 9.5 mg/dL	1,500 mg/day total elemental calcium
lanthanum (Fosrenol®)	**Hyperphosphatemia** 1,500 mg PO daily in divided doses; titrate by 750 mg/day every 2 to 3 weeks based on serum phosphorus level	4,500 mg/day
sevelamer carbonate (Renvela®)	**Hyperphosphatemia** *Starting dose for adult dialysis patients based on serum phosphorus level* If serum phosphorus is: > 5.5 to < 7.5 mg/dL: 0.8 g PO TID w/ meals ≥ 7.5 mg/dL: 1.6 g PO TID w/ meals *Starting dose for pediatric patients (6 years and older) based on body surface area (BSA)* ≥ 0.75 to < 1.2: 0.8 g PO TID w/ meals ≥ 1.2: 1.6 g PO TID w/ meals	14 g/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Starting dose for patients switching from calcium acetate to Renvela based on calcium acetate 667 mg/capsule dosing schedule • Calcium acetate 1 capsule PO TID: Renvela 0.8 g PO TID w/ meals • Calcium acetate 2 capsules/tablets PO TID: Renvela 1.6 g PO TID w/ meals • Calcium acetate 3 capsules/tablets PO TID: Renvela 2.4 g PO TID w/ meals	
ferric citrate (Auryxia®)	**Hyperphosphatemia** 2 tablets PO TID with meals; titrate by 1 to 2 tablets/day at 1-week or longer intervals based on serum phosphorus level	12 tablets/day
sevelamer hydrochloride (Renagel®)	**Hyperphosphatemia** *Starting dose based on serum phosphorus level* • > 5.5 to < 7.5 mg/dL: Renagel 800 mg - 1 tablet PO TID; 400 mg - 2 tablets PO TID w/meals • ≥ 7.5 to < 9 mg/dL: Renagel 800 mg - 2 tablets PO TID; 400 mg - 3 tablets PO TID w/meals • ≥ 9 mg/dL: Renagel 800 mg - 2 tablets PO TID; 400 mg - 4 tablets PO TID w/meals *Starting dose for patients switching from calcium acetate to Renagel based on calcium acetate 667 mg/tablet dosing schedule* • Calcium acetate 1 tablet PO TID: Renagel 800 mg - 1 tablet PO TID; 400 mg - 2 tabs PO TID • Calcium acetate 2 tablets PO TID: Renagel 800 mg - 2 tablets PO TID; 400 mg - 3 tabs PO TID • Calcium acetate 3 tablets PO TID: Renagel 800 mg - 3 tablets PO TID; 400 mg - 5 tablets PO TID	13 g/day
sucroferric oxyhydroxide (Velphoro®)	**Hyperphosphatemia** 500 mg PO TID with meals	3,000 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): patients < 6 years of age due to the risk of serious dehydration; patients with known or suspected mechanical gastrointestinal obstruction
- Boxed warning(s) - *Ibsrela only*: contraindicated in patients < 6 years of age; avoid use of Ibsrela in patients 6 years to < 12 years of age; the safety and effectiveness of Ibsrela have not been established in patients < 18 years of age

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Ibsrela	IBS-C	50 mg PO BID	100 mg/day
Xphozah	Hyper-phosphatemia	30 mg PO BID before morning and evening meals	60 mg/day

VI. Product Availability

Drug Name	Availability
Ibsrela	Tablet: 50 mg
Xphozah	Tablets: 10 mg, 20 mg, 30 mg

VII. References

1. Ibsrela Prescribing Information. Fremont, CA: Ardelyx, Inc.; April 2022. Available at: https://ardelyx.com/wp-content/uploads/2021/11/IBSRELA-Prescribing-Information-1.pdf. Accessed October 12, 2023.
2. Xphozah Prescribing Information. Waltham, MA: Ardelyx, Inc.; October 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/213931s000lbl.pdf. Accessed October 26, 2023.
3. Chang L, Sultan S, Lembo A, et al. American Gastroenterological Association clinical practice guideline on the pharmacological management of irritable bowel syndrome with constipation. Gastroenterology. 2022; 163:118-136.
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8. Kidney Disease: Improving Global Outcomes (KDIGO) CKD–MBD Work Group. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease–mineral and bone disorder (CKD–MBD). *Kidney Inter.* 2017; 92(1):26-36.
9. Lin C, Chey WD, Imdad A, et al. American Gastroenterological Association-American College of Gastroenterology clinical practice guideline: Pharmacological management of chronic idiopathic constipation. Gastroenterology 2023;164:1086-1106.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	11.05.19	02.20
1Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	10.16.20	02.21
1Q 2022 annual review: added redirection to generic lubiprostone per SDC; references reviewed and updated	11.16.21	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.06.22	
1Q 2023 annual review: no significant changes; references reviewed and updated.	10.26.22	02.23
Per August SDC, removed HIM line of business. RT4: added Xphozah to policy.	10.26.23	12.23
1Q 2024 annual review: no significant changes; references reviewed and updated.	10.12.23	02.24

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.