Original Effective Date: 04/06/2024
Current Effective Date: 04/11/2025
Last P&T Approval/Version: 01/29/2025
Next Review Due By: 01/2026
Policy Number: C27292-A

Xphozah (tenapanor)

PRODUCTS AFFECTED

Xphozah (tenapanor)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Hyperphosphatemia

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. HYPERPHOSPHATEMIA:
   1. Documented diagnosis of chronic kidney disease (CKD) and member is on dialysis AND

2. Documentation member has phosphate level ≥ 5.5 mg/dL while adherent to treatment with a phosphate binder [DOCUMENTATION REQUIRED]
   AND
3. Documentation of trial/failure of or serious side effects to TWO preferred formulary/PDL phosphate binders (e.g., calcium acetate, sevelamer carbonate, etc.)
   AND
4. Prescriber attests or clinical reviewer has found that Xphozah (tenapanor) will be used as add-on therapy to phosphate binders (unless documented serious side effects)
   AND
5. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Xphozah (tenapanor) include: pediatric patients under 6 years of age, and patients with known or suspected mechanical gastrointestinal obstruction.]

CONTINUATION OF THERAPY:

A. HYPERPHOSPHATEMIA:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
   AND
3. Documentation of positive clinical response as demonstrated by reduction in serum phosphorous from pretreatment level or phosphate level < 5.5 mg/dL [DOCUMENTATION REQUIRED]
   AND
4. Prescriber attests or clinical reviewer has found that Xphozah (tenapanor) continues to be used as add-on therapy to phosphate binders (unless documented serious side effects)

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified nephrologist [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

18 years of age and older

QUANTITY:

30mg orally twice daily

PLACE OF ADMINISTRATION:

The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

Oral

DRUG CLASS:
CKD Agent-Sodium/Hydrogen Exchanger 3 (NHE3) Inhibitor

FDA-APPROVED USES:
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.

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Xphozah (tenapanor) is a first-in-class, phosphate absorption inhibitor that acts locally in the gut to inhibit the sodium hydrogen exchanger 3 (NHE3), thereby reducing phosphate absorption through the paracellular pathway, the primary pathway of phosphate absorption. It is indicated for the reduction of 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. Hyperphosphatemia occurs in essentially all patients with end-stage renal disease (ESRD) and has been associated with increased morbidity and mortality through observational studies, making it necessary for the majority of patients to be managed using dietary restrictions and phosphate binders.

Xphozah's ability to lower serum phosphorous in adults with CKD on dialysis was evaluated in 3 trials: TEN-02-201 [NCT02675998], TEN-02-301 [NCT03427125]), and TEN-02-202 [NCT03824587]). TEN-02-201 and TEN-02-301 were monotherapy trials and enrolled patients who, following a 3-week washout period, had an increase in serum phosphorus of at least 1.5 mg/dL (compared to pre-wash out value) and a serum phosphorus level of at least 6.0 mg/dL and not more than 10.0 mg/dL. Study TEN-02-201 included an 8-week randomized, double-blind period that evaluated three dosing regimens of Xphozah. This was followed by a 4-week placebo-controlled randomized-withdrawal phase, during which patients were rerandomized 1:1 to their current Xphozah treatment or to placebo. During the randomized withdrawal phase, the phosphorus concentration rose in the placebo group by 0.7 mg/dL (95% CI: (0.3, 1.2), p=0.003) relative to patients who remained on Xphozah. Study TEN-02-301 included a 26-week randomized, active-controlled open-label treatment period, followed by a 12-week, blinded placebo-controlled randomized withdrawal period. During the randomized withdrawal phase, the phosphorus concentration rose in the placebo group by 0.7 mg/dL (95% CI: (0.2, 1.1), p=0.002) relative to patients who remained on Xphozah.
Study TEN-02-202 was a randomized, parallel-group, double-blind, placebo-controlled study that evaluated the effect of Xphozah on the change in serum phosphorus when used as add-on therapy in patients on stable phosphate-binder therapy with serum phosphorus greater than or equal to 5.5 mg/dL. During the 4-week period, the serum phosphorus decreased by 0.7 mg/dL (95% CI: (0.3, 1.0), p=0.0004) in the add-on Xphozah group as compared to the add-on placebo group.
All three trials (which included more than 1000 patients) met their primary and key secondary endpoints, demonstrating that Xphozah significantly reduced elevated serum phosphorus in patients receiving maintenance hemodialysis.

The safety data for Xphozah is from 754 adults with CKD on dialysis taking Xphozah in the clinical trials. Among the 754 patients, 258 patients were exposed to tenapanor for at least 26 weeks and 75 were exposed to tenapanor for at least one year. Diarrhea, which occurred in 43-53% of patients, was the only adverse reaction reported in at least 5% of Xphozah-treated patients with CKD on dialysis across trials. Most diarrhea events in the Xphozah-treated patients were reported to be mild-to-moderate in severity and resolved over time, or with dose reduction. Diarrhea was typically reported soon after initiation but could occur at any time during treatment with Xphozah. Severe diarrhea was reported in 5% of Xphozah-treated patients in these trials.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Xphozah (tenapanor) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Xphozah (tenapanor) include: pediatric patients under 6 years of age, and patients with known or suspected mechanical gastrointestinal obstruction.

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Xphozah TABS 20MG
Xphozah TABS 30MG

REFERENCES

1. Xphozah (tenapanor) tablets for oral use [prescribing information]. Waltham, MA: Ardelyx, Inc.; October 2023.
2. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD). (2017). Kidney International Supplements, 7(1), 1–59. https://doi.org/10.1016/j.kisu.2017.04.001
3. Block, G. A., Rosenbaum, D. P., Yan, A., & Chertow, G. M. (2019). Efficacy and Safety of Tenapanor in Patients with Hyperphosphatemia Receiving Maintenance Hemodialysis: A Randomized Phase 3 Trial. Journal of the American Society of Nephrology, 30(4), 641–652. https://doi.org/10.1681/ASN.2018080832
4. Block, G. A., Bleyer, A. J., Silva, A. L., Weiner, D. E., Lynn, R. I., Yang, Y., … Chertow, G. M. (2021).

Safety and Efficacy of Tenapanor for Long-term Serum Phosphate Control in Maintenance Dialysis: A 52-Week Randomized Phase 3 Trial (PHREEDOM). Kidney360, 2(10), 1600–1610. https://doi.org/10.34067/kid.0002002021

5. Pergola, P. E., Rosenbaum, D. P., Yang, Y., & Chertow, G. M. (2021). A Randomized Trial of Tenapanor and Phosphate Binders as a Dual-Mechanism Treatment for Hyperphosphatemia in Patients on Maintenance Dialysis (AMPLIFY). Journal of the American Society of Nephrology: JASN, 32(6), 1465–1473. https://doi.org/10.1681/ASN.2020101398
6. Martin, K. J. (2021). How to evaluate phosphate control in patients on dialysis. Nephrology Dialysis Transplantation, 37, 1830–1832. https://doi.org/10.1093/ndt/gfab205

SUMMARY OF REVIEW/REVISIONS	DATE
ANNUAL REVIEW COMPLETED- No coverage criteria changes with this annual review.	Q1 2025
NEW CRITERIA CREATION	Q1 2024