Xphozah® (tenapanor)

Policy # 00872
Original Effective Date: 04/08/2024
Current Effective Date: 04/08/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider Xphozah®‡ (tenapanor) to be **eligible for coverage**** when the patient selection criteria are met.

Patient Selection Criteria

Coverage eligibility will be considered for Xphozah (tenapanor) when the following criteria are met:

- Patient is greater than or equal to 18 years of age; AND
- Patient has chronic kidney disease (CKD) and is receiving dialysis; AND
- Patient has evidence of progressively or persistently elevated serum phosphate >5.5 mg/dL; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient has tried and failed at least 2 of the following generic alternatives unless there is clinical evidence or patient history that suggests the use of the following generic alternatives will be ineffective or cause an adverse reaction to the patient: sevelamer carbonate, calcium acetate, lanthanum carbonate, sevelamer hydrochloride.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of Xphozah (tenapanor) when the patient does not have evidence of progressively or persistently elevated serum phosphate >5.5 mg/dL to be **not medically necessary.****

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When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of Xphozah (tenapanor) when patient selection criteria are not met (except those denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Xphozah is a sodium hydrogen exchanger 3 (NHE3) inhibitor indicated to reduce serum phosphorus in adults with chronic kidney disease (CKD) on dialysis. It is only approved to be used 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. The active ingredient in Xphozah, tenapanor, is also available as brand name Ibsrela®‡ which is indicated for the treatment of irritable bowel syndrome with constipation (IBS-C). For phosphorus reduction, Xphozah should be dosed as 30 mg orally twice daily before the morning and evening meals. It has a warning for diarrhea and should be discontinued in patients who develop severe diarrhea.

Hyperphosphatemia, defined as elevated levels of phosphate in the blood, is a common condition among people with CKD on maintenance dialysis. It is associated with calcification, fractures, cardiovascular mortality, and all-cause mortality. Reduction of serum phosphate is often a part of a comprehensive cardiovascular risk-reduction strategy. Generally, normal serum phosphate levels range from 2.5 to 4.5 mg/dL in adults. Current strategies for managing hyperphosphatemia include increasing hemodialysis session length or frequency, dietary phosphate restrictions, phosphate binder therapy, and controlling hyperparathyroidism. Phosphate binder therapy is associated with poor GI tolerability, frequent dosing, and high pill burden, which can lead to suboptimal adherence. Phosphate binders are categorized as calcium-containing and non-calcium containing. Calcium containing binders include calcium carbonate and calcium acetate. Non calcium-containing binders include sevelamer, lanthanum, ferric citrate, and sucroferric oxyhydroxide. There is currently no consensus about whether any particular type of phosphate binder should be used in patients with CKD.

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FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Xphozah was approved in October 2023 to reduce serum phosphorus in adults with chronic kidney disease (CKD) on dialysis as add-on therapy in patients who have inadequate response to phosphate binders or who are intolerant of any dose of phosphate binder therapy.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The ability of Xphozah to lower serum phosphorus in adults with CKD on dialysis was evaluated in 3 trials: TEN-02-201, TEN-02-301, and TEN-02-202. TEN-02-301 and TEN-02-202 were monotherapy trials that 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-02-301 included a 26-week randomized, active-controlled open-label treatment period, followed by a 12-week, blinded placebo controlled randomized withdrawal period. A total of 564 patients were randomized into the 26-week treatment period (423 to Xphozah and 141 to the control arm). Among the 423 patients randomized to Xphozah, 255 patients completed the 26-week treatment period and were rerandomized 1:1 to remain on Xphozah (n=128) or receive placebo (n=127). During the randomized withdrawal phase, the phosphorus concentration rose in the placebo group by 0.7 mg/dL (95% CI: [0.1, 1.1], p=0.002) relative to patients who remained on Xphozah.

Study TEN-02-201 included an 8-week randomized, double-blind period that evaluated three dosing regimens of Xphozah (3 mg twice daily, 10 mg twice daily, or a titration regimen). This period was followed by a 4-week placebo-controlled randomized-withdrawal phase, during which patients were randomized 1:1 to their current Xphozah treatment or to placebo. Of the 219 patients included in the trial, 164 patients completed the 8-week randomized treatment period and were rerandomized 1:1 to receive Xphozah (n=82) or placebo (n=82). 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-02-202 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. A total of 236 patients were randomized to receive Xphozah (n=117) or placebo (n=119) for 4 weeks. 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.

References

1. Xphozah [package insert]. Ardelyx, Inc. Waltham, MA. Updated October 2023
2. Xphozah Drug Evaluation. Express Scripts. Updated October 2023.

Policy History

Original Effective Date: 04/08/2024
Current Effective Date: 04/08/2024
03/07/2024 Medical Policy Committee review
03/13/2024 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 03/2025

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

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B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.