Xphozah (tenapanor) Prior Authorization with Quantity Limit Program Summary

This program applies to FlexRx Closed, FlexRx Open, FocusRx, GenRx Closed, GenRx Open, Health Insurance Marketplace, and KeyRx formularies.

This is a FlexRx Standard and GenRx Standard program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
07-01-2024	07-01-2024

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Xphozah® (tenapanor) tablet	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		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Hyperphosphatemia	Hyperphosphatemia in chronic kidney disease (CKD) patients is a potentially life altering condition that can lead to cardiovascular calcification, metabolic bone disease (renal osteodystrophy) and the development of secondary hyperparathyroidism (SHPT). In clinical practice, the management of hyperphosphatemia is focused on controlling factors that are responsible for the intake and removal of phosphate from the body. There are three main strategies for correcting hyperphosphatemia: dietary restriction of phosphate intake, removing phosphate with adequate dialysis, and reducing intestinal absorption using phosphate binders. Reducing dietary phosphate intake can be challenging, as it is usually incompatible with the recommended daily protein intake, and diet control alone is insufficient. Currently available dialysis techniques are usually ineffective in normalizing phosphate concentration. Using phosphate binders to assist in the management of hyperphosphatemia in patients undergoing dialysis is common, with more than 95% of patients being prescribed phosphate binders.(2) Tenapanor is a first-in-class, minimally absorbed, small-molecule sodium-hydrogen exchanger 3 (NHE3) inhibitor with a unique mechanism of action that effectively reduces phosphate levels. Inhibition of gastrointestinal NHE3 results in increased sodium and water excretion as well as reduced paracellular permeability to phosphate. This modest intracellular proton retention generated is proposed to modulate tight junction proteins (claudins) resulting in increased transepithelial electrical resistance (TEER) and reducing permeability specific to phosphate, thereby decreasing phosphate absorption through the paracellular pathway.(4)
Efficacy	The ability of tenapanor to lower serum phosphorus in adults with CKD on dialysis was evaluated in 3 trials: TEN-02-201 [NCT02675998], TEN-02-301 [NCT03427125]), and TEN-02-202 [NCT03824587]). Both monotherapy trials (TEN-02-201 and TEN-02-301) 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.(1) Study TEN-02-301 (PHREEDOM trial) was a 52-week phase 3 study. It included a 26-week randomized, active-controlled open-label treatment period, in which patients were randomized (3:1) to tenapanor 30 mg twice daily for 26 weeks (treatment period) or sevelamer carbonate (52-week safety period). Patients completing 26 weeks of treatment with tenapanor entered into a blinded placebo-controlled randomized withdrawal period and were rerandomized (1:1) to tenapanor or placebo for 12 weeks. These patients were eligible to enter the 14-week safety extension period. The primary efficacy end point was the difference in the change in serum phosphate from the end of the randomized treatment period to the end of the randomized withdrawal period, among participants who achieved a greater than or equal to 1.2 mg/dl decrease in serum phosphate during the randomized treatment period (efficacy analysis set). Efficacy was also evaluated in the intention-to-treat (ITT) analysis set. In the ITT analysis set, 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 tenapanor. In the efficacy analysis set, the difference in estimated mean change in serum phosphate level between tenapanor and placebo from the beginning to the end of the randomized withdrawal period was −1.4 mg/dl (*P*<0.0001). Loosened stools were the most frequently reported adverse event.(1,3) Study TEN-02-201 included an 8-week randomized, double-blind period that evaluated three dosing regimens of tenapanor (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 rerandomized 1:1 to their current tenapanor 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 tenapanor.(1) Study TEN-02-202 was a randomized, parallel-group, double-blind, placebo-controlled study that evaluated the effect of tenapanor 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 tenapanor group as compared to the add-on placebo group.(1)
Safety	Xphozah has the following contraindications:(1) • Pediactric patients under 6 years of age • Patients with known or suspected mechanical gastrointestinal obstruction

REFERENCES

Number	Reference
1	Xphozah prescribing information. Ardelyx, Inc . October 2023.
2	Shaman AM, Kowalski SR. Hyperphosphatemia Management in Patients with Chronic Kidney Disease. Saudi Pharm J. 2016;24(4):494-505. doi:10.1016/j.jsps.2015.01.009.
3	Block, Geoffrey A., Bleyer, Anthony J., et al. Efficacy and Safety of Tenapanor for Long-term Serum Phosphate Control in Maintenance Dialysis: A 52-week Randomized Phase 3 Trial (PHREEDOM). Kidney 360. 2021; 2(10):1600-1610. doi: 10.34067/KID.0002002021.
4	Kovesdy, Csaba P., Adebowale, Adebiyi, et al. Novel Treatments from Inhibition of the intestinal Sodium-Hydrogen Exchanger 3. International Journal of Nephrology and Renovascular Disease. 2021; 14: 411-420. doi: 10.2147/IJNRD.S334024.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Xphozah	tenapanor hcl tab	20 MG ; 30 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Xphozah	tenapanor hcl tab	20 MG	60	Tablets	30	DAYS			
Xphozah	tenapanor hcl tab	30 MG	60	Tablets	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Xphozah	tenapanor hcl tab	20 MG ; 30 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

CLIENT SUMMARY – QUANTITY LIMITS

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PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **PREREQUISITE GENERIC PHOSPHATE BINDER(S)** calcium carbonate calcium acetate calcium with magnesium sevelamer carbonate sevelamer HCl

Module	Clinical Criteria for Approval

PREREQUISITE PREFERRED BRAND PHOSPHATE BINDER(S)
Velphoro

Target Agent(s) will be approved when BOTH of the following are met:

1. ONE of the following:
   A. The requested agent is eligible for continuation of therapy AND ONE of the following:

Agents Eligible for Continuation of Therapy
All target agents are eligible for continuation of therapy

      1. The patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days **OR**
      2. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed **OR**
   B. BOTH of the following:
      1. ONE of the following:
         A. The patient has a diagnosis of chronic kidney disease (CKD) AND ALL of the following:
            1. The patient is on dialysis **AND**
            2. The patient has a phosphorus level of at least 5.5 mg/dL **AND**
            3. ONE of the following:
               A. ALL of the following:
                  1. The patient has tried and had an inadequate response to at least ONE generic phosphate binder **AND**
                  2. The patient has tried and had an inadequate response to at least ONE preferred phosphate binder **AND**
                  3. The patient will be using the requested agent in combination with phosphate binder therapy **OR**
               B. The patient is intolerant or has a hypersensitivity to at least ONE generic phosphate binder AND at least ONE preferred phosphate binder **OR**
               C. The patient has an FDA labeled contraindication to ALL generic phosphate binders AND ALL preferred phosphate binders **OR**
               D. The patient is currently being treated with the requested agent as indicated by ALL of the following:
                  1. A statement by the prescriber that the patient is currently taking the requested agent **AND**
                  2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND**
                  3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR**

Module	Clinical Criteria for Approval
	E. The prescriber has provided documentation that ALL generic phosphate binders and ALL preferred phosphate binders cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR** B. The patient has another FDA labeled indication for the requested agent and route of administration **AND** 2. If the patient has an FDA approved indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support for using the requested agent for the patient's age for the requested indication **AND** 2. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 6 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process [NOTE: Patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. ONE of the following: A. The patient is using the requested agent in combination with phosphate binder therapy **OR** B. The patient is intolerant or has a hypersensitivity to phosphate binder therapy **OR** C. The patient has an FDA labeled contraindication to ALL phosphate binders **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity Limit for the Target Agent(s) will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **OR** 3. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** C. There is support for therapy with a higher dose for the requested indication **Length of Approval**: Initial - up to 6 months; Renewal - up to 12 months