Pharmacy Policy Bulletin: J-1340 Xphozah (tenapanor) – Commercial and Healthcare Reform	
Number: J-1340	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Oral = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1340-002	**Original Date:** 12/06/2023
Effective Date: 12/20/2024	**Review Date:** 12/04/2024

Drugs Product(s):	• Xphozah (tenapanor)
FDA-Approved Indication(s):	• 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

Background:	• Xphozah is a locally acting inhibitor that targets the sodium/hydrogen exchanger 3 (NHE3). Inhibition of NHE3 results in reduced sodium absorption and decreased phosphate absorption by reducing phosphate permeability through the paracellular pathway. • Hyperphosphatemia is a secondary disorder of CKD that causes vascular calcifications and bone-mineral disorders. The kidneys are responsible for eliminating excess phosphate and as kidney function declines, phosphate is not adequately eliminated from the body. Symptoms of high phosphorus include muscle cramps, bone and joint pain, weak bones, itchy skin, and rash. Approximately 11-15% of Americans have CKD, and it is estimated that more than 60% of patients on hemodialysis (HD) in the United States (U.S.) have serum phosphorus levels above the recommended goal of 5.5 mg/dL. Patients with hyperphosphatemia in CKD have higher rates of mortality. It is thought that the direct stimulus to vascular calcification caused by hyperphosphatemia may be a cause of cardiovascular (CV) events contributing to the excess mortality of CKD. • Several phosphate binders are currently approved by the FDA and have the ability to lower phosphorus absorption from the gastrointestinal (GI) tract to variable levels. Each choice has advantages and disadvantages that should be taken into consideration when deciding which treatment option would be optimal for each patient. • Calcium-based binders include calcium acetate and calcium carbonate, which are some of the most commonly used binders due to being inexpensive and available as over-the-counter formulations. Calcium-based binders can contribute to hypercalcemia, which is a risk factor for CV calcification and

	mortality. Variability in gastric pH may also affect disintegration or dissolution, and thus phosphate-binding efficacy. • Iron-based binders include Auryxia (ferric citrate) and Velphoro (sucroferric oxyhydroxide). These agents can improve anemia but can also result in iron overload and toxicity. Velphoro is a newer agent with minimal systemic absorption and no evidence of iron accumulation. • Resin binders include Renvela (sevelamer carbonate) and Renagel (sevelamer hydrochloride). These binders have no systemic absorption and can lower cholesterol, which can lead to beneficial effects on vascular calcification. Renagel carries the risk of metabolic acidosis, a problem that has been overcome with development of the carbonate formulation. Some studies have shown that all-cause mortality and risk of hypercalcemia were lower in dialysis patients receiving sevelamer when compared with calcium-based binders. • Fosrenol (lanthanum carbonate) is a phosphate binder that is non-calcium-based and has a high affinity for phosphate. Fosrenol works over a wide range of pH, however it can produce adverse GI effects and has uncertain long-term effects on the liver and nervous tissues due to its systemic absorption. • The 2017 Kidney Disease: Improving Global Outcomes (KDIGO) recommendations on management of high phosphorus and maintenance of normal calcium levels in patients with CKD recommends for patients in CKD stages 3-5: ○ Management decisions should take into account combined effects of phosphate, calcium, and parathyroid levels. ○ Consider restricting the dose of calcium-based phosphate binders in adults receiving phosphate-lowering treatment. ○ Avoiding long-term use of aluminum containing phosphate binders. ○ Consider limiting dietary phosphate intake in treatment of hyperphosphatemia alone or in combination with other treatments. ○ Phosphate binders are equivalently effective in lowering phosphate. The choice of phosphate binder should be based on patient specific factors such as, but not limited to renal function, serum calcium levels, adverse effects, and patient adherence. • Prescribing Considerations: ○ Xphozah is contraindicated in pediatric patients under 6 years of age and in patients with known or suspected mechanical GI obstruction. ○ The safety and efficacy of Xphozah in pediatric patients has not been established.

Approval Criteria

I. Approval Criteria

When a benefit, coverage of Xphozah may be approved when all of the following criteria are met **(A., B., and C.)**:

A. The member is 18 years of age or older.

B. The member has a diagnosis of CKD and is on dialysis (ICD-10: Z99.2).

C. The member meets one (1) of the following criteria **(1. or 2.)**:

1. The member is using Xphozah as an add-on therapy and has had an inadequate response to all of the following plan-preferred phosphate binders **(a. and b.):**

a. Calcium acetate

b. Sevelamer carbonate tablet

2. The member has experienced intolerance or contraindication to all of the following plan-preferred phosphate binders **(a. and b.)**:

a. Calcium acetate

b. Sevelamer carbonate tablet

II. Reauthorization

When a benefit, reauthorization of Xphozah may be approved when the following criterion is met **(A.)**:

A. The prescriber attests that the member has experienced positive clinical response to therapy.

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

1. Xphozah [package insert]. Waltham, MA: Ardelyx, Inc.; October 2023.
2. Hruska KA, Mathew S, Lund R, et al. Hyperphosphatemia of chronic kidney disease. Kidney Int. 2008;74(2):148-57.
3. Qunibi WY. Consequences of hyperphosphatemia in patients with end-stage renal disease (ESRD). Kidney Int Suppl. 2004;(90):S8-S12.
4. Rastogi A, Bhatt N, Rossetti S, Beto J. Management of Hyperphosphatemia in End-Stage Renal Disease: A New Paradigm. J Ren Nutr. 2021 Jan;31(1):21-34.
5. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Update Work Group. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). Kidney Int Suppl (2011). 2017;7(1):1-59.
6. Ketteler M, Block GA, Evenepoel P, et al. Executive summary of the 2017 KDIGO Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD) Guideline Update: what's changed and why it matters. Kidney Int. 2017;92(1):26-36
7. Ruospo M, Palmer SC, Natale P, et al. Phosphate binders for preventing and treating chronic kidney disease-mineral and bone disorder (CKD-MBD). Cochrane Database Syst Rev. 2018;8:Cd006023.
8. Vervloet MG, van Ballegooijen AJ. Prevention and treatment of hyperphosphatemia in chronic kidney disease. Kidney Int. 2018;93(5):1060-1072.