Xphozah® (tenapanor) – New drug approval

- On October 17, 2023, Ardelyx announced the FDA approval of Xphozah (tenapanor), 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.

- Hyperphosphatemia affects the vast majority of the 550,000 patients in the U.S. with CKD on maintenance dialysis. The kidneys are responsible for eliminating excess phosphate and as kidney function declines, phosphate is not adequately eliminated from the body.

- Xphozah is a phosphate absorption inhibitor with a differentiated mechanism of action 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.

    — Tenapanor is also approved for irritable bowel syndrome with constipation, under the brand name Ibsrela®.

- The efficacy of Xphozah was established in 3 trials in adults with CKD on dialysis was evaluated in 3 trials: TEN-02-201, TEN-02-301, and TEN-02-202. Both monotherapy studies (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.

- 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. Among the 423 patients randomized to Xphozah, 255 patients completed the 26-week treatment period and were rerandomized to remain on Xphozah or receive placebo. 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-02-201 included an 8-week randomized, double-blind period that evaluated three dosing regimens of Xphozah. This period was followed by a 4-week placebo-controlled randomized-withdrawal phase, during which patients were rerandomized to their current Xphozah treatment or to placebo. Of the 219 patients included in the study, 164 patients completed the 8-week randomized treatment period and were rerandomized to receive Xphozah or 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-02-202 was a randomized, 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 or placebo 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.

- Xphozah is contraindicated in patients:

    — Under 6 years of age because of the risk of diarrhea and serious dehydration
    — With known or suspected mechanical gastrointestinal obstruction.

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- A warning and precaution for Xphozah is diarrhea.
- The most common adverse reaction with Xphozah use was diarrhea.
- The recommended dose of Xphozah is 30 mg orally twice daily before the morning and evening meals.
    - Serum phosphorus should be monitored, and the dosage should be adjusted as needed to manage gastrointestinal tolerability.
- Ardelyx plans to launch Xphozah in November 2023. Xphozah will be available as 10 mg, 20 mg, and 30 mg tablets.

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