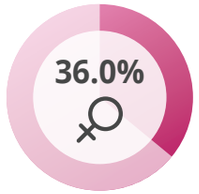
PHREEDOM (Phase 3) | A 52-week, randomized, placebo-controlled, open-label, phase 3 trial of tenapanor for hyperphosphatemia

Baseline Characteristics During the RTP

564 patients with hyperphosphatemia receiving maintenance dialysis



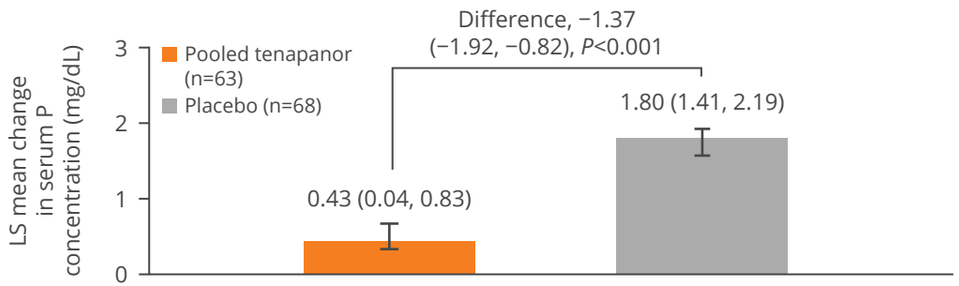
Average age **58 years**

Average time since first dialysis: **56 months**

Patients receiving **hemodialysis and peritoneal dialysis** were included

Primary Endpoint

Difference in the change in serum P between tenapanor and placebo from the beginning to end of the RWP in the EAS[a]



Safety and Tolerability

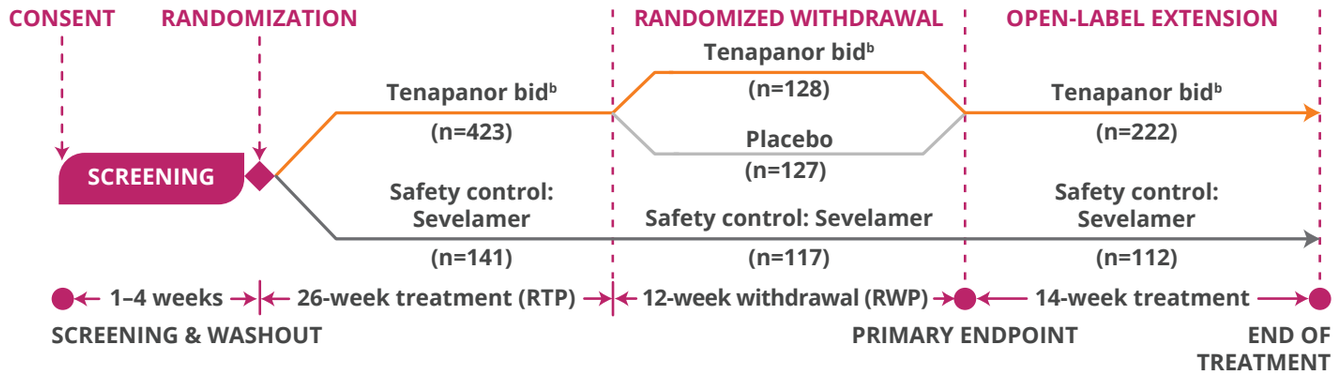
Patients reporting diarrhea during the RTP (tenapanor and sevelamer carbonate):

222/419 (53%) **10/137 (7%)**

Serious adverse events during the RTP (tenapanor and sevelamer carbonate):

73/419 (17%) **32/137 (23%)**

Trial Design



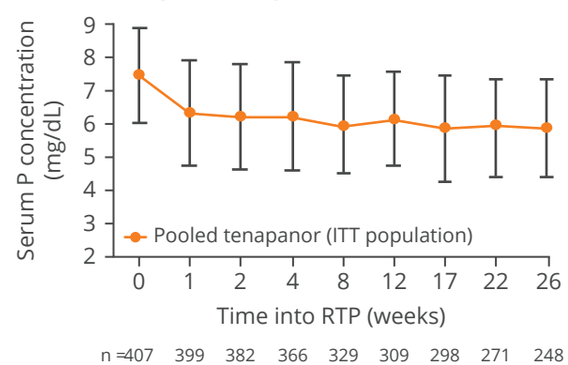
Secondary and Exploratory Endpoints

Secondary Endpoint: Difference in the Change in Serum P Between Tenapanor and Placebo From the Beginning to End of the RWP by Dose Group

Comparison	LS mean difference	P value[c]
TEN 30 mg bid vs placebo	−0.78	0.0015
TEN 20 mg bid vs placebo	−0.53	0.1047
TEN 10 mg bid vs placebo	−0.32	NE
TEN 30 mg bid vs placebo	−1.69	<0.0001*
TEN 20 mg bid vs placebo	−0.96	0.0138*
TEN 10 mg bid vs placebo	−1.02	NE

Analysis Population: ☐ ITT ☐ EAS

Descriptive Analysis: Serum P Over the RTP



In the ITT ANALYSIS SET[a], mean serum P decreased from **7.4** mg/dL at period-specific baseline to **5.9** mg/dL at week 26, with a mean (SD) decrease of **1.4 (1.8)** mg/dL

Hierarchical statistical testing failed with regard to the difference in the change from baseline in serum P in the ITT population when the 20-mg bid dose of tenapanor was compared with placebo, which prevented the testing of significance for key secondary endpoints that were lower in the testing hierarchy. The endpoints are displayed in the table in the order of the testing hierarchy.
*Unadjusted P value.

Study Limitations

- Participants who discontinued tenapanor during the RTP were not included in subsequent study periods; thus, the RWP and safety extension periods may have been enriched for individuals who were better able to tolerate tenapanor
- Results from the RTP should be interpreted with caution as this part of the trial was open label with no placebo control

The LS mean and P values were from an ANCOVA model with treatment and geographic region as factors and period-specific baseline value as a covariate.
[a]The ITT analysis set included all participants who met the enrollment criteria, received ≥1 dose of tenapanor and/or placebo, and had ≥1 post-treatment serum P measurement for that study period. Participants assigned to the sevelamer (safety control) group were not included in the ITT analysis set for any study period.The efficacy analysis set was a subset of the ITT analysis set of the RWP who also received ≥1 dose tenapanor during the RTP, completed the RTP, and achieved a reduction of ≥1.2 mg/dL in serum P from baseline to the end of the RTP. [b]The starting dose for patients randomized to receive tenapanor was 30 mg bid; participants were allowed to titrate between 10 mg bid and 30 mg bid in 10 mg increments during the RTP and safety extension period. [c]Only dose groups with ≥15 participants were included in statistical comparisons with placebo.

ANCOVA, analysis of covariance; bid, twice a day; EAS, efficacy analysis set; ISI, important safety information; ITT, intent-to-treat; LS, least squares; NE, not evaluated; P, phosphate; RTP, randomized treatment period; RWP, randomized withdrawal period.
NCT03427125. Block GA et al. *Kidney 360*. 2021;2:1600-10.

Please see ISI on the reverse side of this card.
MED-US--2500560 12/2025

INDICATION

XPHOZAH (tenapanor) is 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.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

XPHOZAH is contraindicated in patients under 6 years of age.

XPHOZAH is contraindicated in patients with known or suspected mechanical gastrointestinal obstruction.

WARNINGS AND PRECAUTIONS

Diarrhea

Patients may experience severe diarrhea. Treatment with XPHOZAH should be discontinued in patients who develop severe diarrhea.

MOST COMMON ADVERSE REACTIONS

Diarrhea, which occurred in 43% to 53% of patients, was the only adverse reaction reported in at least 5% of XPHOZAH-treated patients with CKD on dialysis across trials. The majority of 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.

For the full prescribing information, click here.

CKD, chronic kidney disease.

XPHOZAH (tenapanor hydrochloride). Prescribing information. Ardelyx, Inc; 2025.
Available at: ardelyx.com/XPHOZAH-Prescribing-Information

MED-US--2500560 12/2025