Erratum to FDA Briefing Document

Cardiovascular and Renal Drugs Advisory Committee Meeting
November 16, 2022

This erratum contains corrections to FDA's briefing information for the November 16, 2022, Cardiovascular and Renal Drugs Advisory Committee Meeting. At this meeting, the committee will discuss new drug application 213931 for tenapanor tablets, submitted by Ardelyx, Inc., for the control of serum phosphorus in adults with chronic kidney disease on dialysis.

1) Correction of the last observation-carried forward (LOCF):

a) On page 13, second paragraph:

"The primary efficacy analysis was to be based on the EAS (i.e., an enriched population) using the last observation-carried-forward (LOCF) approach for handling missing data. The primary efficacy variable was the change in s-P from the end of the 8-week RT period to the end of the 4-week RW period or the endpoint visit for this period, which was defined as the last visit during the 4-week RW period."

Should be revised to read (change bolded and underlined)

"**The primary efficacy analysis was to be based on the EAS (i.e., an enriched population).** The primary efficacy variable was the change in s-P from the end of the 8-week RT period to the end of the 4-week RW period or the endpoint visit for this period, which was defined as the last visit during the 4-week RW period. **In other words, the last observed value in s-P during the 4-week RW period was to be used in the primary efficacy analysis. There was no imputation for missing data.**"

b) On page 15, second paragraph:

"The primary efficacy analysis was to be based on the EAS using the LOCF approach. The primary efficacy endpoint was the change in s-P from the end of the 26-week RT period to the endpoint visit of the 12-week RW period, where the endpoint visit was defined as the last visit with an s-P assessment during the 12-week RW period."

Should be revised to read (change bolded and underlined)

"**The primary efficacy analysis was to be based on the EAS**. The primary efficacy endpoint was the change in s-P from the end of the 26-week RT period to the endpoint visit of the 12-week RW period, where the endpoint visit was defined as the last visit with an s-P assessment during the 12-week RW period**. The primary analysis was based on the last observed value in s-P during the 12-week RW period. There was no imputation for missing data.**"

c) On page 17, first paragraph:

"Table 2 shows the results for the primary efficacy endpoint in the EAS. The LOCF approach was used as the primary efficacy analysis."

Should be revised to read

"Table 2 shows the results for the primary efficacy endpoint in the EAS."

d) On page 20, first paragraph:

"Relative to placebo, the LS mean difference in s-P level change from the period-level baseline to the end of the 12-week RW period was −1.4 mg/dL for the tenapanor group (p<0.0001) using the LOCF approach."

Should be revised to read

"Relative to placebo, the LS mean difference in s-P level change from the period-level baseline to the end of the 12-week RW period was −1.4 mg/dL for the tenapanor group (p<0.0001)."

2) On page 26, Table 8, titled "Percentage of Subjects With a ≥1.2 mg/dL Reduction in Serum Phosphorus at Week 26 or Serum Phosphorus Concentration <5.5 mg/dL at Week 26 Among Subjects With a ≥1.2 mg/dL Reduction in Serum Phosphorus in Early Weeks, Tenapanor Arm, Study TEN-02-301":

The cell located in row 3, column 5 of Table 8 should be revised to read "18 (12%)", not "16 (12%)."

See revised table below (change bolded and underlined)

Table 8. Percentage of Subjects With a ≥1.2 mg/dL Reduction in Serum Phosphorus at Week 26 or Serum Phosphorus Concentration <5.5 mg/dL at Week 26 Among Subjects With a ≥1.2 mg/dL Reduction in Serum Phosphorus in Early Weeks, Tenapanor Arm, Study TEN-02-301

	Subjects reached a s-P reduction ≥1.2 mg/dL at Week 1 or Week 2		Subjects reached a s-P reduction ≥1.2 mg/dL at Week 2 or Week 4		
	Yes (N=250)	No (N=157)	Yes (N=258)	No (N=149)	N=407*
Week 26 a s-P reduction ≥1.2 mg/dL	110 (44%)	24 (15%)	116 (45%)	**18** (12%)	134 (33%)
Week 26 s-P <5.5 mg/dL	68 (27%)	32 (20%)	72 (28%)	28 (19%)	100 (25%)

Source: FDA Statistical reviewer; Study TEN-02-301, adeffads.xpt, SAS.
Subjects with missing s-P at a particular week were treated as not reaching a s-P reduction ≥1.2 mg/dL or not reaching a target s-P level of 5.5 mg/dL (worst-case imputation approach).
* Intent-to-treat population for the RT period (subjects who met inclusion/exclusion criteria, received at least one dose of tenapanor, had at least one post baseline serum phosphate measurement, and did not have a serious GCP breach.
Abbreviation: s-P, serum phosphorus