Erratum to FDA Briefing Document

Joint Meeting of the Psychopharmacologic Drugs Advisory Committee (PDAC) and the Drug Safety and Risk Management (DSaRM) Advisory Committee

October 9, 2020

This erratum contains corrections to FDA's briefing information for the October 9, 2020, joint PDAC and DSaRM Advisory Committee Meeting. At this meeting, the committee will discuss the efficacy, safety, and benefit-risk profile of new drug application (NDA) 213378, olanzapine/samidorphan oral tablets, submitted by Alkermes, Inc., for the proposed indications of schizophrenia and bipolar I disorder.

1) **Page 8, first paragraph, first sentence:**

"In Study A303, using the Applicant's primary multiple imputation analysis, the mean change-from-baseline in weight between groups (ALKS 3831 – olanzapine) at week 24 was -2.38% (unadjusted 95% confidence interval (CI): -3.88%, -0.88%; p=0.002)."

Should be revised to read (change bolded and underlined)

"In Study A303, using the Applicant's primary multiple imputation analysis, the mean change-from-baseline in weight between groups (ALKS 3831 – olanzapine) at week 24 was -2.38% (unadjusted 95% confidence interval (CI): -3.88%, -0.88%; **adjusted p=0.003**)."

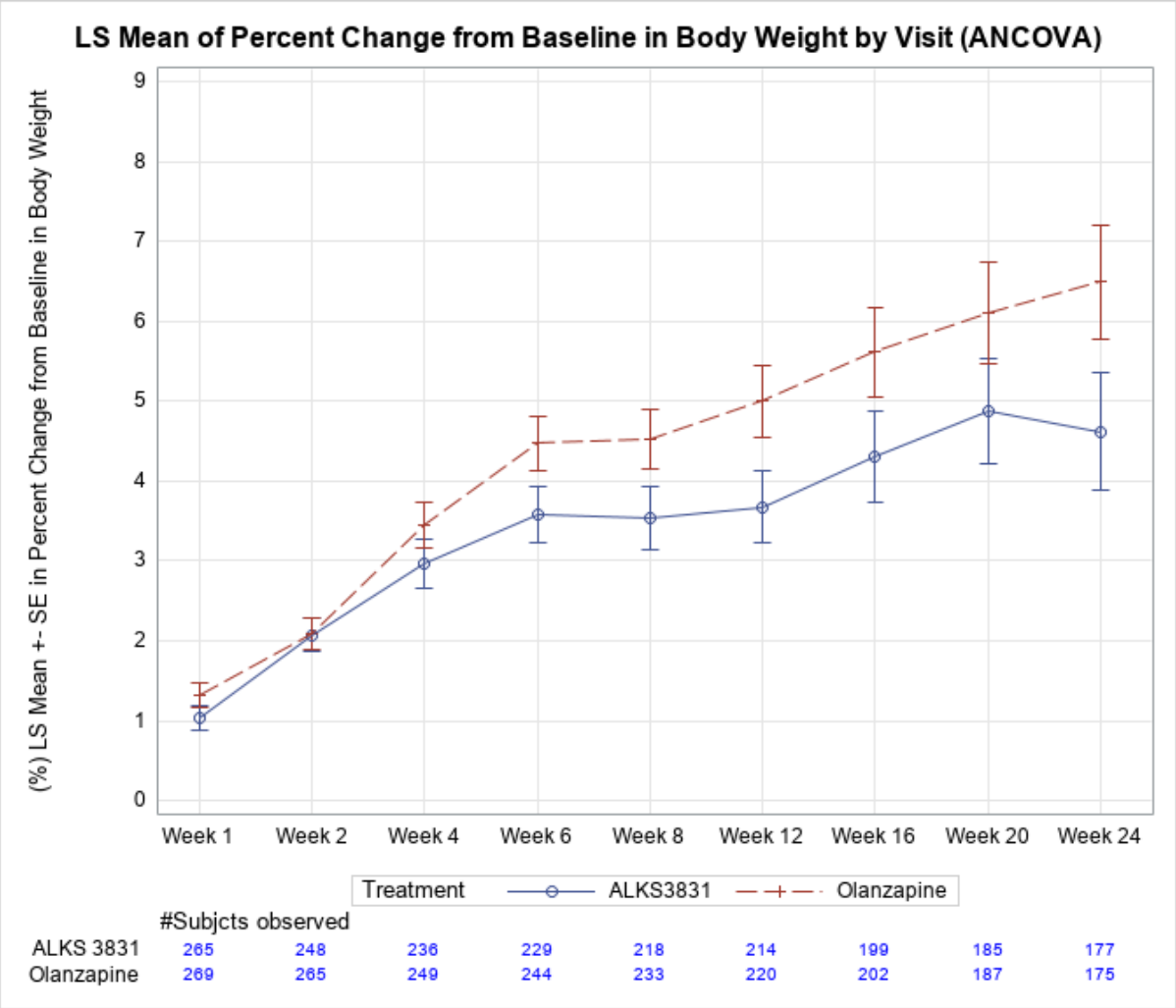
2) **Page 8, second paragraph, first sentence:**

"Drugs approved for weight loss in the treatment of obesity are found to be effective if mean weight loss is at least 5% greater than placebo or, on categorical analysis, at least two-times more subjects on drug lose at least 5% body weight as compared to those on placebo;…"

Should be revised to read (change bolded and underlined)

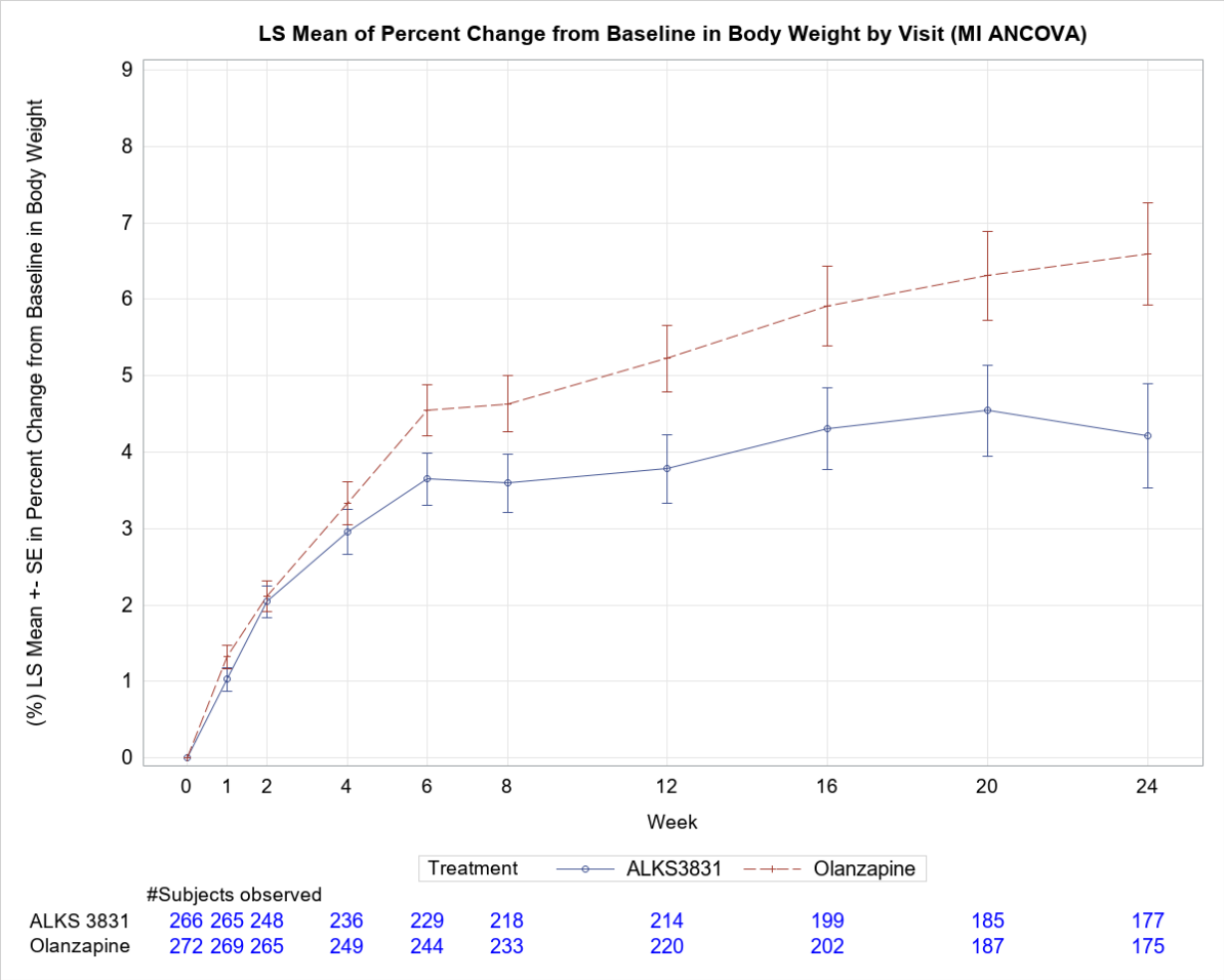
"Drugs approved for weight loss in the treatment of obesity are found to be effective if mean weight loss is at least 5% greater than placebo or, on categorical analysis, at least two-times more subjects on drug lose at least 5% body weight as compared to those on placebo **and must be at least 1 year in duration**;…"

3) Page 24, Figure 6 footnote



Source: FDA Statistical Reviewer.
Note: LS Mean is based on Primary Analysis Model ANCOVA at each visit, not that data from all visits were included in one model.
Abbreviations: ANCOVA = analysis of covariance, LS = least-squares, SE = standard error.

Should be revised to read (changed entire plot with updated footnote wording bolded and underlined)



Source: FDA Statistical Reviewer.
Abbreviations: **MI: Multiple Imputation;** ANCOVA: analysis of covariance; LS: least-squares; SE: standard error.
Note: **The MI ANCOVA model (Primary Analysis Model) was applied on Applicant's MI data (observed and imputed data) at each visit. LS Means are based on an individual ANCOVA model for each visit, not including data from all visits in one model.**

4) Page 47, last paragraph

"Additionally, in Study A308, a subject was hospitalized for an accidental oxycodone overdose leading to discontinuation of study drug: he reported ingesting four tablets of acetaminophen, but presentation and drug testing confirmed presence of oxycodone and absence of acetaminophen. Further narrative was not provided."

Should be revised to read (change struck through or bolded and underlined)

"Additionally, in Study A308, a subject was hospitalized for an accidental oxycodone overdose leading to discontinuation of study drug: **she** reported ingesting four tablets of acetaminophen,

but presentation and drug testing confirmed presence of oxycodone and absence of acetaminophen. **~~Further narrative was not provided.~~**