Errata to FDA Briefing Document

Joint Meeting of the Psychopharmacologic Drugs Advisory Committee (PDAC) and the Peripheral and Central Nervous System Drugs Advisory Committee (PCNSDAC)

April 14, 2023

This erratum contains corrections to FDA's briefing information for the April 14, 2023, joint PDAC and PCNSDAC Meeting. The committee will discuss supplemental new drug application (NDA) 205422/S-009, submitted by Otsuka Pharmaceutical Company, Ltd., and Lundbeck, Inc., for brexpiprazole for the proposed treatment of agitation associated with Alzheimer's dementia.

1) Page 2, Table of Contents, Section 4

"4 Summary of Benefit/Risk for the AC"

Revised text (deletions in strikethrough font and additions in bolded and underlined font):

"4 **Overview of Efficacy and Safety** ~~Summary of Benefit/Risk for the AC~~"

2) Page 2, Table of Contents, Appendix

6 Appendix, p. 41
6.1 CMAI Instrument, p. 41
6.2 CMAI Manual Criteria for Agitation Status, p. 43
6.3 Summarized List of Restricted and Prohibited Medications, p. 44
6.4 Abbreviated Schedule of Assessments for Studies 331-12-283 and 331-12-284, p. 45
6.5 Abbreviated Schedule of Assessments for Study 331-14-213, p. 46
6.6 Summary Case Narratives for Death Events, p. 47
6.7 Time Course Plots for Change in CMAI Total Score, p. 54

Revised text (deletions in strikethrough font and additions in bolded and underlined font):

6 Appendix, p. **39**~~41~~
6.1 CMAI Instrument, p. **39**~~41~~
6.2 **Summarized List of Restricted and Prohibited Medications** ~~CMAI Manual Criteria for Agitation Status,~~ p. **41**~~43~~
6.3 **Abbreviated Schedule of Assessments for Studies 331-12-283 and 331-12-284** ~~Summarized List of Restricted and Prohibited Medications~~, p. **42**43
6.4 Abbreviated Schedule of Assessments for **Study 331-14-213** ~~Studies 331-12-283 and 331-12-284~~, p. **43**~~45~~
6.5 **Baseline Disease Characteristics and Psychiatric History** Abbreviated Schedule of Assessments for Study 331-14-213, p. **44**~~46~~
6.6 Summary Case Narratives for Death Events, p. 47
6.7 Time Course Plots for Change in CMAI Total Score, p. **51**~~54~~

6.8 Time of Death Events Relative to Study Treatment Duration, p. 54
6.9 Review of FAERS and Medical Literature, p. 55
6.10 Summary of Safety Findings, p. 56

3) Page 11, Bullet 2

"September 27, 2017: Type C Meeting"

Revised text (deletions in strikethrough font and additions in bolded and underlined font):

"September **21**~~27~~, 2017: Type C Meeting"

4) Page 14, Figure 1, Source

"Applicant's 331-12-283 CSR Figure 3.1-1."

Revised text (deletions in strikethrough font and additions in bolded and underlined font):

"Applicant's 331-12-283 CSR Figure **9**~~3~~.1-1."

5) Page 15, Paragraph 3, third sentence

"The range of possible scores for Factor 1, 2, and 3 subscales were 12 to 24, 6 to 42, and 4 to 28, respectively."

Revised text (deletions in strikethrough font and additions in bolded and underlined font):

"The range of possible scores for Factor 1, 2, and 3 subscales were 12 to **84**~~24~~, 6 to 42, and 4 to 28, respectively."

6) Page 17 and 22, Disposition

"Efficacy sample consisted of all randomized subjects who received at least one dose of the double-blind study medication and had at least one post-baseline CMAI assessment."

Revised text (deletions in strikethrough font and additions in bolded and underlined font):

"Efficacy sample consisted of all randomized subjects who received at least one dose of the double-blind study medication, **a baseline CMAI assessment,** and had at least one post-baseline CMAI assessment."

7) Page 20, Subsection Title Header 4.1.2

"4.1.2 Note: MMRM method with model terms: treatment, trial site, visit, treatment by visit and baseline by visit interaction Study 331-12-284"

The footnote from the table was accidentally incorporated into the section heading. With revisions, text should include "Note…" as a footnote on Table 5, followed by new section 4.1.2 Study 331-12-284 (deletions in strikethrough font and additions in bolded and underlined font):

"**Note: MMRM method with model terms: treatment trial site visit treatment by visit and baseline by visit interaction**

4.1.2 ~~Note: MMRM method with model terms: treatment, trial site, visit, treatment by visit and baseline by visit interaction~~ Study 331-12-284"

8) Page 26, Figure 3, Source

"Applicant's 331-12-213 CSR Figure 3.1-1."

Revised text (deletions in strikethrough font and additions in bolded and underlined font):

"Applicant's 331-12-213 CSR Figure **9**~~3~~.1-1."

9) Page 30, Table 12, Source

"Study 331-14-213 Clinical Study Report, Table 11.4.1.1.1.-1, pg 83"

Revised text (deletions in strikethrough font and additions in bolded and underlined font):

"Study 331-14-213 Clinical Study Report, Table 11.4.1.**4**~~1~~.1.-1, pg 83"

10) Page 41 and 42, Appendix 6.3 Abbreviated Schedule of Assessments for Studies 331-12-283 and 331-12-284 and Appendix 6.4 Abbreviated Schedule of Assessments for Study 331-14-213, Tables

Medical and Psychiatric History Baseline (Day 0): check marked

Revised text:

Medical and Psychiatric History Baseline (Day 0): check mark removed

11) Page 42, Appendix 6.4 Abbreviated Schedule of Assessments for Study 331-14-213, Table

TSH, PT, aPTT, and INR (Wk 12/ET): check marked

Revised text:

Add footnote 1: "[1]**TSH, PT, aPTT, INR only collected at screening. Prolactin, HbA1c, and urine pregnancy assessments conducted at both screening and at Wk 12/ET visits."**

12) Page 44, Table, Care Setting n(%)

"Institutionalized BREX 0.5 to 2 mg = 73 (56.8%)"

Revised text (deletions in strikethrough font and additions in bolded and underlined font):

“Institutionalized BREX 0.5 to 2 mg = 73 (**55**~~56.8~~%)”

13) Page 55, Appendix 6.10, Paragraph 1, first sentence

“The most common AE (> 2% in the All BREX group and higher than placebo) included nasopharyngitis, urinary tract infection, dizziness, somnolence, and insomnia.”

Revised text (deletions in strikethrough font and additions in bolded and underlined font):

“The most common AE (> 2% in the All BREX group and higher than placebo) included nasopharyngitis, urinary tract infection,~~ dizziness~~, somnolence, and insomnia.”

14) Page 55, Table, Dizziness, Syncope, or Orthostatic Hypertension, related events for placebo

“9 (3.6%)”

Revised text (deletions in strikethrough font and additions in bolded and underlined font):

“**19 (4.9%)**~~9 (3.6%)~~”