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Otsuka and Lundbeck announce FDA acceptance and priority review of sNDA for brexpiprazole for the treatment of agitation associated with Alzheimer's dementia

Otsuka Pharmaceutical Co., Ltd. (Otsuka) and H. Lundbeck A/S (Lundbeck) announce the U.S. Food and Drug Administration (FDA) has determined that the supplementary New Drug Application (sNDA) for brexpiprazole for the use in the treatment of agitation associated with Alzheimer's dementia (AAD) is sufficiently complete to permit a substantive review.

- The supplemental new drug application (sNDA) for brexpiprazole in the treatment of agitation associated with Alzheimer's dementia has been accepted and filed by the FDA under Priority review
- The FDA target date (PDUFA date) for completion of the review is May 10, 2023
- FDA is currently planning to hold a Psychopharmacologic Drugs Advisory Committee
- If approved, brexpiprazole would be the first pharmacological treatment indicated for agitation in patients with Alzheimer's dementia in the U.S.

The FDA has assigned the application priority review and a Prescription Drug User Fee Act (PDUFA) target action date of May 10, 2023. The FDA also indicated that they are currently planning to hold a Psychopharmacologic Drugs Advisory Committee meeting to discuss the application.

The sNDA submission includes data from two positive clinical phase III studies that investigated the treatment of brexpiprazole in patients with AAD. Study 331-12-283 demonstrated brexpiprazole 2 mg/day was statistically superior to placebo for the primary endpoint of mean change in Cohen-Mansfield Agitation Inventory (CMAI) Total Score from baseline to Week 12 ($p < 0.05$). In Study 331-14-213, treatment with brexpiprazole 2 and 3 mg/day showed statistically significant improvement compared with placebo for the primary efficacy endpoint, the mean change in CMAI Total Score from baseline to Week 12 ($p < 0.05$).

"Agitation associated with Alzheimer's dementia is complex and difficult to navigate for both patients and caregivers," said John Kraus, M.D., Ph.D., executive vice president and chief medical officer, Otsuka Pharmaceutical Development & Commercialization, Inc. "New treatments in this area are desperately needed. Our commitment to patients is unwavering as we work to provide them and their caregivers with an option to help lessen the symptoms

of agitation."

"This milestone is important in our efforts to bring patients with Alzheimer's dementia and their caregivers one step closer to having a potential treatment option that may address a major disabling neuropsychiatric symptom of the disease," said Johan Luthman, executive vice president, Lundbeck Research & Development.

About Agitation in Alzheimer's Dementia

Neuropsychiatric symptoms (NPS) of Alzheimer's dementia, such as agitation are associated with poor caregiver outcomes, including reduced quality of life and poorer health.[1-4]

Agitation is a common neuropsychiatric symptom of Alzheimer's dementia. It is reported in approximately 45 percent of patients with Alzheimer's dementia and has a large impact on quality of life for the patients, family members, and caregivers.[5-6] Agitation covers a large group of behaviors occurring in patients with Alzheimer's dementia, and it is an excessive/inappropriate manifestation of "normal" human emotions and behaviors. Such behaviors include pacing, gesturing, profanity, shouting, shoving, and hitting.[7]

Symptoms of agitation are also a consistent predictor of nursing home admission in patients with dementia.[8-10]

About Brexpiprazole

Brexpiprazole was approved in the U.S. on July 10, 2015, as an adjunctive therapy to antidepressants in adults with major depressive disorder and as a treatment for schizophrenia in adults. Brexpiprazole was also approved in 2017 in Health Canada and by the EMA in Europe in 2018 for the treatment of schizophrenia.

Brexpiprazole was discovered by Otsuka and is being co-developed by Otsuka and Lundbeck. The mechanism of action of brexpiprazole is unknown, however the efficacy of brexpiprazole may be mediated through a combination of partial agonist activity at serotonin 5-HT1A and dopamine D2 receptors and antagonism at noradrenaline alpha1B/2C receptors and at serotonin 5-HT2A receptors. In addition, brexpiprazole is an antagonist at noradrenaline alpha 1a, 1b, 1d and 2c receptors and partial agonist activity at serotonin 5-HT1A and dopamine D2 receptors all at pharmacologically relevant potencies.[11-12]

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