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Otsuka and Lundbeck submit sNDA for FDA review of brexpiprazole and sertraline combination as potential treatment for PTSD

Otsuka Pharmaceutical Co., Ltd. (Otsuka) and H. Lundbeck A/S (Lundbeck) have submitted a supplemental New Drug Application (sNDA) for U.S. Food and Drug Administration (FDA) review of brexpiprazole as combination therapy with sertraline for the treatment of post-traumatic stress disorder (PTSD) in adults.

FDA validation of the submission dossier prior to FDA's decision whether to proceed with a full review is expected to take 60 or 74 days depending on whether FDA assigns priority or standard review.

The sNDA submission is based on previously disclosed results, including data from the two clinical phase 3 trials (#071 flexible dose trial, n=416[i]) and (#072 fixed-dose trial, n=553[ii]), and the clinical phase 2 trial (#061 flexible dose trial, n=321[iii]). All three trials investigated the treatment of PTSD in adults treated with brexpiprazole in combination with sertraline versus sertraline plus placebo.

The primary endpoint for all three trials was the change from Week 1 to Week 10 in the Clinician-Administered PTSD Scale (CAPS-5) total score for brexpiprazole and sertraline combination therapy versus sertraline plus placebo at Week 10 in patients diagnosed with PTSD according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5).

- Trial #071 and trial #061 demonstrated that the combination treatment of brexpiprazole and sertraline was superior to treatment with sertraline plus placebo.
- Although trial #072 did not demonstrate superiority of the combination treatment of brexpiprazole and sertraline compared to treatment with sertraline plus placebo, the change from baseline observed in the combination group (brexpiprazole and sertraline) was consistent with the reductions observed in Trials #071 and #061.
- Brexpiprazole in combination with sertraline was observed to be generally well-tolerated and the safety results of the three trials were consistent with the known safety profile of brexpiprazole.

Otsuka and Lundbeck intend to present detailed data from all three trials at the American Society of Clinical Psychopharmacology (ASCP), May 28 to 31, 2024, in Miami, Florida.

About Post-Traumatic Stress Disorder

Post-traumatic stress disorder is a psychiatric disorder that may occur in people who have experienced, or witnessed, a traumatic event, series of events or set of circumstances. An individual may experience this as emotionally or physically harmful or life-threatening and PTSD may affect mental, physical, social, and/or spiritual well-being.[i] Examples include natural disasters, serious accidents, terrorist acts, war/combat, rape/sexual assault, historical trauma, intimate partner violence and bullying.[iv]

PTSD can occur in people, of any ethnicity, nationality or culture, and at any age. It affects more than 13 million people in the U.S. and nearly 6 in 100 people will be diagnosed with PTSD in their lifetime.[v] Women are twice as likely as men to have PTSD.

Symptoms of PTSD are generally grouped into four types: intrusive memories, avoidance, negative changes in thinking and mood, and changes in physical and emotional reactions. Symptoms can vary over time or vary from person to person.[vi] Symptoms usually begin within three months of the traumatic incident, but they sometimes emerge later.[iv] To meet the criteria for PTSD, symptoms must last longer than 1 month, and they must be severe enough to interfere with aspects of daily life, such as relationships or work.[vii]

About brexpiprazole

Brexpiprazole was approved in the U.S. in 2015, as an adjunctive therapy to antidepressants in adults with MDD and as a treatment for schizophrenia in adults. Most recently, brexpiprazole was approved in the U.S. for the treatment of agitation associated with dementia due to Alzheimer's disease, in May 2023. Brexpiprazole was also approved by Health Canada for schizophrenia and adjunctive treatment of MDD in 2017 and 2019, respectively. It was approved by the Ministry of Health, Labour and Welfare in Japan and by the European Medicines Agency 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-HT_{1A} and dopamine D_2 receptors, antagonist activity at serotonin 5-HT_{2A} receptors, as well as antagonism of alpha 1B/2C receptors.

Citations

i. ClinicalTrials.gov Identifier: NCT04124614
ii. ClinicalTrials.gov Identifier: NCT04174170
iii. ClinicalTrials.gov Identifier: NCT03033069
iv. American Psychiatric Association. What is Posttraumatic Stress Disorder (PTSD). https://www.psychiatry.org/patients-families/ptsd/what-is-ptsd
v. U.S. Department of Veteran Affairs. PTSD: National Center for PTSD. https://www.ptsd.va.gov/understand/common/common_adults.asp
vi. Mayo Clinic. Post-traumatic stress disorder (PTSD). https://www.mayoclinic.org/diseases-conditions/posttraumatic-stress-disorder/symptoms-causes/syc-20355967
vii. National Institute of Mental Health. Post-Traumatic Stress Disorder. https://www.nimh.nih.gov/health/publications/post-traumatic-stress-disorder-ptsd