



June 1, 2018

Lundbeck and Otsuka's Rxulti® (brexpiprazole) receives positive opinion in EU from CHMP for the treatment of schizophrenia in adults

Press release

Valby, 1 June 2018

A final decision from the European Commission is expected within 67 days.

H. Lundbeck A/S (Lundbeck) and Otsuka Pharmaceutical Co., Ltd. (Otsuka) today announce that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has issued a positive opinion on Rxulti® (brexpiprazole) for the treatment of schizophrenia in adults.¹ A final decision from the European Commission is expected within 67 days.

Brexpiprazole is a once-daily second generation (atypical) oral antipsychotic; it provides a combination of partial agonist activity at serotonin 5-HT_{1A} and dopamine D₂ receptors, and antagonist activity at serotonin 5-HT_{2A} receptors.²

Brexpiprazole exhibits high affinity for these receptors as well as for noradrenaline alpha_{1B/2C} receptors.²

The submission to the EMA included efficacy and safety data of brexpiprazole in schizophrenia from six placebo-controlled clinical trials.³⁻⁸ The safety data were further included from a large cohort of patients evaluated in four long-term, open-label trials which included patients rolled over from the short-term trials as well as patients with no prior exposure to brexpiprazole.⁹

The Phase III efficacy trials comprise three short-term, phase III, fixed-dose trials,^{3,[4],[5]} one phase III, short-term, flexible-dose trial with quetiapine as active reference,⁶ and one phase III, long-term maintenance (relapse-prevention) trial.⁷ In the three fixed-dose, short-term trials (trials 1, 2 and 3, subjects were randomized to brexpiprazole 0.25 mg once daily, 1 mg once daily, 2 mg once daily, 4 mg once daily or placebo.^{3,4,5} Trial 4 assessed the efficacy, safety, and tolerability of brexpiprazole in a flexible dose range of 2 to 4 mg/day and 400 to 800 mg quetiapine XR for assay sensitivity.⁶ In the short-term trials, the primary efficacy endpoint was defined as the mean change from baseline to week 6 in Positive and Negative Syndrome Scale (PANSS) total scores.^{3,4,5}

In the long-term trial designed to assess the maintenance of effect of brexpiprazole by assessing the delay in time to impending relapse of schizophrenia, brexpiprazole demonstrated a significantly longer time to relapse compared with patients on placebo ($p < 0.0001$).⁷

Together, the trials demonstrated that brexpiprazole is an effective and well-tolerated treatment for schizophrenia^{3,4,5,7,8,9}

Brexpiprazole was discovered by Otsuka and is being co-developed by Otsuka and Lundbeck. Following the European Commission's final decision, Otsuka and Lundbeck will work with local pricing and reimbursement bodies in countries throughout Europe to help ensure that eligible patients are able to access this medicine.

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About Lundbeck

H. Lundbeck A/S (LUN.CO, LUN DC, HLUY) is a global pharmaceutical company specialized in psychiatric and neurological disorders. For more than 70 years, we have been at the forefront of research within neuroscience. Our key areas of focus are depression, schizophrenia, Parkinson's disease and Alzheimer's disease.

An estimated 700 million people worldwide are living with psychiatric and neurological disorders and far too many suffer due to inadequate treatment, discrimination, a reduced number of working days, early retirement and other unnecessary consequences. Every day, we strive for improved treatment and a better life for people living with psychiatric and neurological disorders — we call this Progress in Mind.

Read more at www.lundbeck.com/global/about-us/progress-in-mind.

Our approximately 5,000 employees in more than 50 countries are engaged in the entire value chain throughout research, development, production, marketing and sales. Our pipeline consists of several late-stage development programmes and our products are available in more than 100 countries. Our research centre is based in Denmark and our production facilities are located in Denmark, France and Italy. Lundbeck generated revenue of DKK 17.2 billion in 2017 (EUR 2.3 billion; USD 2.6 billion).

For additional information, we encourage you to visit our corporate site www.lundbeck.com and connect with us on Twitter at @Lundbeck.

About Otsuka

Otsuka Pharmaceutical Co., Ltd. is a global healthcare company with the corporate philosophy: "Otsuka-people creating new products for better health worldwide." Otsuka researches, develops, manufactures and markets innovative products, with a focus on pharmaceutical products to meet unmet medical needs and nutraceutical products for the maintenance of everyday health.

In pharmaceuticals, Otsuka is a leader in the challenging area of mental health and also has R&D programs on several under-addressed diseases including tuberculosis, a significant global public health issue. These commitments illustrate how Otsuka is a "big venture" company at heart, applying a youthful spirit of creativity in everything it does.

Otsuka established a presence in Europe in 1974 and today Otsuka Pharmaceutical Europe Ltd. employs approximately 600 people who channel their passion and energy into converting the latest science into much-needed medicines.

Otsuka Pharmaceutical Company is a subsidiary of Otsuka Holdings Co., Ltd. headquartered in Tokyo, Japan. The Otsuka group of companies employed 46,000 people worldwide and had consolidated sales of approximately EUR 9.8 billion in 2017.

All Otsuka stories start by taking the road less travelled. Learn more about Otsuka Pharmaceutical Company on its global website at <https://www.otsuka.co.jp/en>. Learn more about Otsuka in Europe at www.otsuka-europe.com or visit our Twitter page www.twitter.com/otsuka-europe.

¹ http://www.ema.europa.eu/docs/en_GB/document_library/Summary_of_opinion_-_Initial_authorisation/human/003841/WC500249801.pdf

² Maeda K, et al. *J Pharmacol Exp Ther*. 2014b; 350(3): 589—604.

³ Correll C, et al. *Am J Psychiatry*. 2015; 172:9: 870—880.

⁴ Kane J, et al. *Schizophrenia Research*. 2015; 164: 127—135.

⁵ Ishigooka J, et al. *Psychiatry and Clinical Neurosciences*. 2018; Available from: doi/pdf/10.1111/pcn.12682 [Accessed: May 2018].

⁶ Marder SR, et al. *Acta Neuropsychiatrica*, 2016; 29(5): 278—290.

⁷ Fleischhacker W, et al. *Int J Neuropsychopharmacol*. 2017 Jan; 20(1): 11—21; Available from: doi: 10.1093/ijnp/pyw076 [Accessed: May 2018].

⁸ Correll C, et al. *Schizophr. Res.* 2016 Jul; 174(1-3): 82—92. doi: 10.1016/j.schres.2016.04.012. Epub 2016 May 4. [Accessed: May 2018].

⁹ Kane J, et al. *Schizophr Res.* 2016 Jul; 174(1-3): 93—98. doi: 10.1016/j.schres.2016.04.013. Epub 2016 May 14. [Accessed: May 2018].

Attachment

- 1 [Lundbeck and Otsuka's Rxulti receives positive opinion in EU clean](#)