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Press release

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European CHMP issues a positive opinion for a label update of Abilify Maintena ® (aripiprazole for prolonged-release suspension for injection) to describe new clinical data for the treatment of acutely relapsed adults with schizophrenia

Labeling update (sections 5.1 and 4.4) provides description of controlled clinical study of Abilify Maintena for treating adult patients experiencing acute relapses of schizophrenia. Positive opinion was based on Abilify Maintena demonstrating efficacy, tolerability and safety in a 12-week study in acutely relapsed adults with schizophrenia

H. Lundbeck A/S (Lundbeck) and Otsuka Pharmaceutical Europe Ltd. (Otsuka) today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion for a type-II variation related to the update of the European summary of the product characteristics (SmPC) for Abilify Maintena.

The update of the SmPC includes new Abilify Maintena data related to its effect and safety on acutely relapsed adults with schizophrenia. The application was submitted to the European Medicines Agency (EMA) and the assessment started end November 2015.

Abilify Maintena is indicated for maintenance treatment of schizophrenia in adult patients stabilized with oral aripiprazole and the new data will support the physician in transitioning patients to the prolonged release formulation after symptom control has been achieved. Abilify Maintena should not be used to manage acutely agitated or severely psychotic states when immediate symptom control is warranted.

“These data — and the updated product labeling — establish the utility of Abilify Maintena in acutely relapsed adult patients and for the maintenance treatment of patients with schizophrenia”, said Anders Gersel Pedersen, Executive Vice President, Research & Development, Lundbeck.

“The addition of this data is another step towards confidently addressing the challenges associated with treating this population” said Marco Avila, Regional Vice-President Medical, Otsuka.

The opinion was based on results from a 12-week randomized, double-blind placebo-controlled study, which showed that treatment with Abilify Maintena (with concomitant oral aripiprazole for the first two weeks) significantly improved symptoms with an acceptable safety and tolerability profile in adult patients experiencing an acute relapse of schizophrenia.[1]

Clinical trial result

Efficacy of Abilify Maintena (aripiprazole) for the treatment of acutely relapsed adults with schizophrenia was demonstrated in a 12-week multicenter, randomized, double-blind, placebo-controlled trial. The primary measure used for assessing psychiatric signs and symptoms was the Positive and Negative Syndrome Scale (PANSS), a 30-item scale that measures positive and negative symptoms of schizophrenia and general psychopathology, using a rating scale of 1 (absent) to 7 (extreme). All patients entering the trial were inpatients who met DSM-IV-TR criteria for schizophrenia and experienced an acute psychotic episode as defined by both PANSS total score of 80 or higher, and a PANSS score greater than 4 on each of four specific psychotic symptoms (conceptual disorganization, hallucinatory behavior, suspiciousness/persecution, unusual thought content). Patients had a mean PANSS total score of 103 at study entry.[2]

A total of 339 patients received double-blind treatment with Abilify Maintena 400 mg (n=167) or placebo (n=172), with 64.3% (Abilify Maintena) and 49.4% (placebo) of patients completing 10 weeks of treatment. The primary efficacy outcome (change from baseline to 10-week endpoint in PANSS total score) demonstrated greater improvement with Abilify Maintena than with placebo (-26.8 vs. -11.7, respectively, p<0.0001); statistically significant improvements with Abilify Maintena were shown at all time points measured from week 1-12.[1] The key secondary efficacy outcome was change from baseline to 10-week endpoint in Clinical Global Impression Severity of Illness Scale (CGI-S) score and also showed statistically greater improvement with Abilify Maintena than with placebo (-1.4 vs. -0.6, respectively, p<0.0001). [1]

Safety of Abilify Maintena

The overall safety and tolerability profile of Abilify Maintena in this study was generally consistent with that observed in previous double-blind phase III studies. [2,3.] During 10 weeks of treatment, the most common reason for discontinuation was patient withdrawal of consent (19% vs. 9% for placebo) and lack of efficacy (7% vs. 29% for placebo.). Discontinuations due to adverse events occurred in 4% of patients receiving Abilify Maintena vs. 8% of patients receiving placebo. The symptoms which had at least twice the incidence of placebo were increased weight and akathisia. The incidence of weight gain of ≥ 7 % from baseline to last visit (Week 12) was 21.5% for Abilify Maintena compared with the placebo group 8.5%. Akathisia was the most frequently observed EPS symptom (Abilify Maintena 11.4% and placebo group 3.5%).

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About Abilify Maintena® (aripiprazole once-monthly)

Abilify Maintena is a once-monthly injection of a dopamine D2 partial agonist. It is available in the US for the treatment of schizophrenia and in a number of European countries for maintenance treatment of schizophrenia in adult patients stabilized with oral aripiprazole.[4 5] In Canada it is available for the treatment of schizophrenia in adult patients and in Australia for maintenance of clinical improvement in the treatment of schizophrenia.

Abilify Maintena, an atypical antipsychotic, is an intramuscular long acting injectable formulation of aripiprazole. It is a sterile lyophilized powder that, when reconstituted with sterile water for injection, forms an injectable suspension that can be administered monthly. After an initial injection of Abilify Maintena along with an overlapping 14-day dosing of oral antipsychotic treatment, subsequent injections of Abilify Maintena provide uninterrupted medication coverage for 30 days at a time. It provides a treatment option to address one of the most important considerations in the management of schizophrenia — reducing the risk of relapse, or the re-emergence of worsening of symptoms. Long acting injectable formulations of antipsychotic agents provide patients with concentrations of active drug that remain at a therapeutic range for an extended period of time. [2,3]

About schizophrenia

Schizophrenia is a disease characterized by a distortion in the process of thinking and of emotional responsiveness. It most commonly manifests as hallucinations, paranoid or bizarre delusions, or disorganized speech and thinking, and is accompanied by significant social or occupational dysfunction. Onset of symptoms typically occurs in young adulthood and the condition is chronic, often requiring life-long treatment to mitigate symptoms. It has been estimated that schizophrenia affects approximately 1,2% of the adult population in the EU, and approximately 24 million people worldwide.[6, 7] In the EU, there are approximately 5 million adults with schizophrenia, prevalent equally in both genders.[8,9] While there is no cure for the disease, symptoms and risk of relapse - the re-emergence or worsening of psychotic symptoms[10] - can be managed in most patients with appropriate antipsychotic treatment.

About the Otsuka and Lundbeck Global Alliance

Otsuka and Lundbeck established a global alliance in November 2011 to bring to bear their considerable experience and resources in the CNS area to introduce next-generation treatments for conditions such as schizophrenia, depression, Alzheimer's disease and alcohol dependency.

About Otsuka

Otsuka Pharmaceutical Co., Ltd. is a global healthcare company with the corporate philosophy: 'Otsuka-people creating new products for better health worldwide.'

At Otsuka the emphasis is on 'super people' who have a flair for the unconventional not 'super computers'. This has led us to become a leading firm in the challenging area of mental health. Beyond mental health, this thinking has resulted in the development of first-in-class products to treat kidney, cardiovascular and gastrointestinal disorders and blood-related cancers. Otsuka also has research programmes for several under-addressed diseases

including tuberculosis, a significant global public health issue. The Otsuka Group employs approximately 43,000 people globally.

Otsuka established a presence in Europe in 1979. Our 600 European employees focus their passion and energy into ensuring that patients have access to Otsuka's new products, including in 2015 the first-ever drug treatment in Europe for polycystic kidney disease. Otsuka also received approval in 2014 for the first new anti-tuberculosis drug in Europe in over 40 years.

Our stories all start by taking the road less travelled. Learn more here:
www.otsuka.co.jp/en/ (Global)
www.otsuka-europe.com (European)

About Lundbeck
H. Lundbeck A/S (LUN.CO, LUN DC, HLUYY) is a global pharmaceutical company specialized in brain diseases. 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 and Alzheimer's diseases.

An estimated 700 million people worldwide are living with brain disease 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 brain disease – we call this Progress in Mind.
Read more at www.lundbeck.com/global/about-us/progress-in-mind.

Our approximately 5,500 employees in 58 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. We have research centres in China and Denmark and production facilities in China, Denmark, France and Italy. Lundbeck generated core revenue of DKK 13.5 billion in 2014 (EUR 1.8 billion; USD 2.4 billion).

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

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