



For the attention of Accredited Medical Writers Only

New data show low incidence of augmentation of Restless Legs Syndrome with 5-year Neupro® (rotigotine) treatment

- Rotigotine was associated with a low long-term 5-year incidence of augmentation, one of the main complications of dopaminergic treatment for RLS patients

Brussels (Belgium), 14 April 2011, 0700 CET – New 5-year data from the longest prospective open-label Restless Legs Syndrome (RLS) study to date, show that Neupro® (rotigotine) demonstrated continued symptomatic clinical benefit with a low risk of augmentation. Over the five year period, clinically significant augmentation occurred in 5.1% of patients receiving rotigotine at EU approved doses (1, 2 and 3 mg/24h) and in 13.2% of patients receiving one of the five evaluated doses of rotigotine (0.5[†], 1, 2 3 and 4.0[‡] mg/24h).^{1,4}

The study, presented at the 63rd Annual Meeting of the American Academy of Neurology (AAN) Hawaii, U.S., also reported that the frequency of newly diagnosed augmentation decreased over time, but that the new cases of augmentation were more likely to be clinically significant after the first year.¹

Augmentation is a recognised complication of dopaminergic treatment of RLS. Augmentation is characterized by an earlier onset of symptoms, an extension of symptoms to other body parts, an increased symptom intensity and/or shorter duration of relief from treatment. To date, no data were available on the long term use of the dopamine agonist therapeutic class for the treatment of moderate to severe RLS patients.

“In this, the longest prospective RLS study to date, rotigotine was associated with a low 5-year incidence of clinically significant augmentation, with the occurrence of new cases decreasing over time.” commented Dr Diego Garcia-Borreguero, lead investigator and Director of the Sleep Research Institute, Madrid, Spain. “These study findings support rotigotine as a long-term treatment option and improve our understanding of the clinical relevance of augmentation and its progressive course in studies greater than one year.”



This study was a 5-year, prospective, open-label follow up of a placebo-controlled Phase II trial with rotigotine. Patients were titrated to an optimal dose of rotigotine (0.5-4.0 [†] mg/24h) and periodically evaluated for safety and efficacy. Of the 295 patients in the study, 126 completed the 5-year follow-up.¹

Rotigotine showed an improvement in the International Restless Legs Syndrome Study Group Rating Scale (IRLS) score from 27.8±5.9 at baseline to 9.0±9.2 after 5 years. Computer screening identified 145 patients out of 295 (49.2%) with potential augmentation and this was confirmed in 69 patients (24.3%), according to the Max Planck Institute (MPI) diagnostic criteria for augmentation. An international panel confirmed that 39 patients (13.2%) had clinically significant augmentation. Of all patients with clinically significant augmentation, 61.5% were on the highest, unapproved dose of rotigotine (4 mg/24h [†]) and 61.5% experienced their first episode after one year. Frequency of newly diagnosed augmentation decreased over time, and new episodes were more frequently clinically significant.¹ Study discontinuation due to augmentation occurred in 12 cases (4.1%).

[†] *Neupro® (rotigotine) 0.5 mg/24h and 4mg/24h dose are not approved doses in the European Union for the symptomatic treatment of moderate to severe idiopathic Restless Legs Syndrome in adults.*

Notes to Editors

About Restless Legs Syndrome^{2,3}

Restless Legs Syndrome (RLS) is a neurological disorder characterized by unpleasant sensations in the legs and an uncontrollable urge to move when at rest in order to relieve these feelings. It affects between 3 and 10% of the population to some extent. Most people with RLS have difficulty falling asleep and staying asleep. Left untreated the condition causes exhaustion and daytime fatigue. Many people with RLS report that their job, personal relations and activities of daily living are strongly affected as a result of their exhaustion. They are often unable to concentrate, have impaired memory, or fail to accomplish daily tasks. Most than 80% of people with RLS also experience a more common condition known as periodic limb movement disorder (PLMD).

About Neupro® in Europe⁴

Neupro® is approved in the European Union for the symptomatic treatment of moderate to severe idiopathic restless legs syndrome in adults. Neupro® (rotigotine) is also approved in the European Union for the treatment of the signs and symptoms of early-stage idiopathic Parkinson's disease, as monotherapy (i.e. without levodopa) or in combination with levodopa, i.e. over the course of the disease, through to late stages when the effect of levodopa wears off or becomes inconsistent and fluctuations of the therapeutic effect occurs.



Neupro® in Europe Important Safety Information

Neupro® is contraindicated in case of hypersensitivity to the active substance or to any of its excipients, and in case of magnetic resonance imaging (MRI) or cardioversion. Neupro® should be removed if the patient has to undergo MRI or cardioversion.

It is recommended to monitor blood pressure, especially at the beginning of treatment, due to the general risk of orthostatic hypotension associated with dopaminergic therapy.

Neupro® has been associated with somnolence episodes of sudden sleep onset episodes. Patients treated with dopamine agonists including Neupro®, have been reported as exhibiting signs of pathological gambling, increased libido and hypersexuality.

Symptoms suggestive of neuroleptic malignant syndrome have been reported with abrupt withdrawal of dopaminergic therapy. Therefore it is recommended to taper treatment.

Neupro® contains sodium metabisulphite, a sulphite that may cause allergic-type reactions including anaphylactic symptoms and life threatening or less severe asthmatic episodes in certain susceptible people.

Hallucinations have been reported, and patients should be informed that hallucinations can occur.

Cases of cardiopulmonary fibrotic complications have been reported in some patients treated with ergot-derived dopaminergic agents. Neuroleptics given as antiemetic should not be given to patients taking dopamine agonists. Ophthalmologic monitoring is recommended at regular intervals or if vision abnormalities occur.

External heat, from any source should not be applied to the area of the patch. Exposure of a skin rash or irritation to direct sunlight could lead to changes in the skin color. If a generalized skin reaction (e.g. allergic rash) associated with the use of Neupro® is observed, Neupro® should be discontinued.

Caution is advised when treating patients with severe hepatic impairment or acute worsening of renal function, a dose reduction might be needed.

The incidence of some dopaminergic adverse events, such as hallucinations, dyskinesia, and peripheral oedema generally is higher when given in combination with L-dopa. This should be considered when prescribing Neupro®.

Neupro® should not be used during pregnancy. Breast-feeding should be discontinued.

Augmentation may occur in Restless Legs Syndrome patients. Augmentation refers to the earlier onset of symptoms in the evening (or early afternoon), increase in severity of symptoms, and spread of symptoms to involve other body parts.

Adverse drug reactions reported in more than 10% of Parkinson's patients treated with Neupro® are nausea, vomiting, application site reactions, somnolence, dizziness and headache.

Adverse drug reactions reported in more than 10% of RLS patients treated with Neupro® are nausea, application site reactions, asthenic conditions and headache.

All Neupro® supply should be stored in a refrigerator. There is no need for patients to transport Neupro® patches in special containers and they must not be stored in a freezer compartment.

Please refer to the European Summary of Product Characteristics for full prescribing information Neupro® European Summary of Product Characteristics (Approved February 2011)
<http://ec.europa.eu/health/documents/community-register/html/alfregister.htm>

About Neupro® in the U.S.



Neupro[®] (Rotigotine Transdermal System) is indicated in the U.S. for the treatment of the signs and symptoms of early-stage idiopathic Parkinson's disease.

In April 2008, UCB recalled Neupro[®] from the U.S. market after ongoing monitoring revealed that specific batches of Neupro[®] had deviated from their approved specification. Neupro[®] is currently not available in the U.S. UCB is working with the U.S. FDA so that Neupro[®] can be available to patients with early-stage Parkinson's disease as soon as possible.

References

- ¹ Garcia-Borreguero D, Benes H, Ferini-Strambi L, et al. Augmentation of restless legs syndrome (RLS) under rotigotine: Results from a 5-year prospective, multinational, open-label study. Presented at 63rd Annual Meeting of American Academy of Neurology, 9-16 April 2011, Hawaii, U.S.
- ² http://www.ninds.nih.gov/disorders/restless_legs/detail_restless_legs.htm (Accessed March 2011)
- ³ Trenkwalder C, Paulus W, Walters AS. The restless legs syndrome. *Lancet Neurol* 2005; 4: 465
- ⁴ Neupro[®] European Summary of Product Characteristics (Approved February 2011)
<http://ec.europa.eu/health/documents/community-register/html/alfregister.htm>

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About UCB

UCB, Brussels, Belgium (www.ucb.com) is a global biopharmaceutical company focused on the discovery and development of innovative medicines and solutions to transform the lives of people living with severe diseases of the immune system or of the central nervous system. With more than 8 500 people in about 40 countries, the company generated revenue of EUR 3.2 billion in 2010. UCB is listed on Euronext Brussels (symbol: UCB).

Forward looking statement

This press release contains forward-looking statements based on current plans, estimates and beliefs of management. Such statements are subject to risks and uncertainties that may cause actual results to be materially different from those that may be implied by such forward-looking statements contained in this press release. Important factors that could result in such differences include: changes in general economic, business and competitive conditions, effects of future judicial decisions, changes in regulation, exchange rate fluctuations and hiring and retention of its employees.