



**For the attention of Accredited Medical Writers Only**

## **New data showed sustained 5-year benefit of Neupro<sup>®</sup> (rotigotine) on symptoms of Restless Legs Syndrome**

- Latest safety and efficacy results for rotigotine in the treatment of moderate to severe restless legs syndrome presented at major North American neurology congress

**Brussels (Belgium), 13 April 2010, 1430 CET - press release** – New data presented at the 62<sup>nd</sup> American Academy of Neurology annual meeting in Toronto, Canada, showed that patients with moderate to severe Restless Legs Syndrome (RLS) using rotigotine achieved sustained improvements in symptoms over 5 years of treatment<sup>1</sup>.

“Many people with RLS will have spent months or years trying to get a diagnosis and find a treatment that can help them. So these 5-year results provide additional evidence that once they start using rotigotine people with RLS may experience long term relief from their symptoms, and a significant proportion may become symptom free,” said Diego Garcia-Borreguero, MD, Director Sleep Research Institute, Madrid, Spain.

This study of rotigotine in patients with moderate to severe RLS was the longest ever open label prospective follow-up of a placebo-controlled phase II trial in RLS. The final 5-year results confirm the safety and efficacy of rotigotine seen at previous interim analyses<sup>2,3</sup>, with over a third of patients followed up remaining symptom free after five years of treatment.

Of the 295 patients with moderate to severe RLS who entered the study, 126 (43%) completed the 5-year follow up. The mean dose of rotigotine was 2.43mg/24 hours after initial titration and 3.09mg/24 hours at the end of the study. Fifty nine per cent of patients were classified as remitters (IRLS<sub>≤</sub> 10), and 39% as symptom-free (IRLS=0).

The study looked at improvement in symptoms based on the International Restless Legs Syndrome Study Group Rating Scale (IRLS)<sup>4\*</sup>. The total IRLS score ranges from 0 (no symptoms) to 40 (very severe symptoms). A score of >20 indicates severe RLS. The



mean IRLS\* score was 27.8 at baseline, improving by 18.7 points to 9.0 at the end of the study. Sustained improvements were also seen in quality of life and other RLS rating scales.

Most adverse events (AEs) were mild to moderate in intensity, the most common AEs being application site reactions (58%), nasopharyngitis (19%), back pain (14%), nausea (12%) and fatigue (11%). Thirty per cent of patients discontinued the study due to an AE.

A comparison of 1, 2 and 5-year efficacy data (with 220, 191 and 126 patients respectively) showed that improvements in RLS symptoms remained stable throughout the follow-up period. Improvements in IRLS scores were 17.4 points at 1 year<sup>2</sup>, 17.2 points at 2 years<sup>3</sup>, and 18.7 points at 5 years<sup>1</sup>.

*\* The International Restless Legs Syndrome Study Group Rating Scale (IRLS)<sup>4</sup> is a ten-item scale developed and validated by The International Restless Legs Syndrome Study Group and considered to be the best scale for evaluating the severity and frequency of RLS symptoms and the degree to which they affect sleep and daily life. It is administered by clinicians and includes questions related to the severity of sensory and motor symptoms, sleep disturbance, daytime somnolence and impact of RLS on activities of daily living and mood.*

#### **For further information**

*On-site at meeting*

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#### **Notes to Editors**

##### **About Restless Legs Syndrome<sup>5,6</sup>**

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. Some researchers estimate that RLS affects as many as 12 million Americans. However, others estimate a much higher occurrence because RLS is thought to be under-diagnosed and in some cases mis-diagnosed. 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<sup>®</sup> in Europe<sup>7</sup>**

Neupro<sup>®</sup> (rotigotine) is 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<sup>®</sup> is also approved in the European Union for the symptomatic treatment of moderate to severe idiopathic restless legs syndrome in adults.

**Neupro<sup>®</sup> in Europe Important Safety Information**

Neupro<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> has been associated with somnolence episodes of sudden sleep onset episodes. Patients treated with dopamine agonists including Neupro<sup>®</sup>, 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<sup>®</sup> 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<sup>®</sup> is observed, Neupro<sup>®</sup> 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<sup>®</sup>.

Neupro<sup>®</sup> 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<sup>®</sup> are nausea, vomiting, application site reactions, somnolence, dizziness and headache.

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

All Neupro<sup>®</sup> supply should be stored in a refrigerator. There is no need for patients to transport Neupro<sup>®</sup> 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 (Approved 15<sup>th</sup> March 2010): <http://www.emea.europa.eu/humandocs/PDFs/EPAR/neupro/emea-combined-h626en.pdf>



## 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.

## Important Safety Information – U.S.

Some patients treated with Neupro® reported falling asleep while engaged in activities of daily living, including operation of motor vehicles, which sometimes resulted in accidents. Some patients perceived no warning signs, such as excessive drowsiness. Hallucinations were reported in 2.0% of patients treated with Neupro® compared to 0.7% of patients on placebo. Neupro® contains metabisulfite. Neupro® should be used with caution in patients, especially those at risk for cardiovascular disease, because of the potential for symptomatic hypotension, syncope, elevated heart rate, elevated blood pressure, fluid retention, and/or weight gain. All Parkinson's disease patients are at a higher risk for melanoma and should be monitored regularly. The most commonly reported side effects in clinical trials were nausea, application site reactions, somnolence, dizziness, headache, vomiting, and insomnia. Some subjects who received Neupro® experienced a decline in blood hemoglobin levels (about 2% relative to subjects who received placebo). It is not known whether this change is readily reversible with discontinuation of Neupro®.

## Neupro® is not approved or available in Canada for the treatment of idiopathic Parkinson's disease or for the treatment of Restless Legs Syndrome.

Neupro® is a registered trademark of the UCB Group of companies.

## References

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6. Trenkwalder C, Paulus W, Walters AS. The restless legs syndrome. *Lancet Neurol* 2005; 4: 465.
7. Neupro® European Summary of Product Characteristics (Approved March 15<sup>th</sup> 2010) <http://www.emea.europa.eu/humandocs/PDFs/EPAR/neupro/emea-combined-h626en.pdf>

**About UCB**

*UCB, Brussels, Belgium ([www.ucb.com](http://www.ucb.com)) is a biopharmaceutical company dedicated to the research, development and commercialization of innovative medicines with a focus on the fields of central nervous system and immunology disorders. Employing more than 9 000 people in over 40 countries, UCB produced revenue of EUR 3.1 billion in 2009. 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.*