



## **FOR THE ATTENTION OF ACCREDITED MEDICAL WRITERS**

### **Clinical data presented at International Congress showed treatment with Neupro<sup>®</sup> (rotigotine) offers high rates of clinical remission and symptom freedom to patients with moderate to severe restless legs syndrome**

- *Data presented at the 13<sup>th</sup> International Congress of Parkinson's Disease and Movement Disorders, Paris, France*
- *Rotigotine showed high rates of symptom freedom and clinical remission in restless legs syndrome<sup>1</sup>*
- *Rotigotine improved overall quality of life in patients with idiopathic restless legs syndrome<sup>2</sup>*
- *Clinically relevant augmentation is not common over one-year treatment with rotigotine<sup>3</sup>*

**Paris, FRANCE – June 12, 2009 at 0700 CET** — Clinical data presented this week at the 13<sup>th</sup> International Congress of Parkinson's Disease and Movement Disorders in Paris, France, demonstrated that treatment with Neupro<sup>®</sup> (rotigotine transdermal patch) can lead to clinical remission<sup>‡</sup> and symptom freedom<sup>‡</sup> in patients with idiopathic restless legs syndrome (RLS).<sup>1</sup> Data also showed rotigotine improved patients' overall quality of life<sup>2</sup> with low levels of augmentation during the first year of treatment.<sup>3</sup>

Neupro<sup>®</sup> is approved in Europe for the symptomatic treatment of moderate to severe idiopathic restless legs syndrome in adults.\*<sup>4</sup>

**Rotigotine showed high rates of symptom freedom and clinical remission in RLS<sup>1</sup>**  
Analyses of pooled data from two 6-month, double-blind, placebo-controlled trials showed patients treated with rotigotine experienced higher rates of symptom freedom and clinical remission compared with placebo. A total of 843 patients were randomized to placebo or rotigotine (1-3 mg/24 h).

Patients were stratified by treatment group and severity of clinical symptoms using the International RLS Study Group rating scale (IRLS<sup>‡</sup>). Symptom freedom was defined as the proportion of patients with an IRLS score=0, and clinical remission was defined as the proportion of patients achieving an IRLS score of ≤10 at the trial endpoint.



At the end of six months, nearly a quarter (24.6%) of all rotigotine-treated patients were symptom free compared to one-tenth (10.8%) of patients receiving placebo. Further analysis of symptom freedom stratified for rotigotine-treated patients versus placebo-treated patients by the level of symptom severity showed an IRLS score of 0 was achieved by 28.5% versus 16.3% in moderate RLS, 24.8% versus 9.2% in severe RLS and 20.5% versus 10.0% in very severe RLS.

Almost half of all rotigotine-treated patients achieved clinical remission (49.7%) compared with just over a quarter (27.2%) of patients receiving placebo. Clinical remission for rotigotine-treated patients versus placebo-treated patients was achieved in 59.7% versus 48.8% in moderate RLS, 51.3% versus 25.0% with severe RLS and 36.4% versus 14.0% with very severe RLS.

### **Rotigotine improved overall quality of life in patients with idiopathic RLS<sup>2</sup>**

Results from a multicentre, randomised double-blind placebo-controlled trial showed that rotigotine in doses of 1 mg/24 h, 2 mg/24 h and 3 mg/24 h improved quality of life for patients with RLS over a six-month period.

Quality of life was assessed with the QoL-RLS<sup>±</sup> questionnaire, with sub-scale items including impact of RLS symptoms, sleep disorders, pain, coping behaviour and "all in all" QoL. 549 subjects were randomised to rotigotine (1 mg/24 h, 2 mg/24 h and 3 mg/24 h) and placebo.

The overall mean baseline IRLS score indicated, on average, severe RLS of the study population. At baseline QoL was moderately impaired with a QoL-RLS total score of  $32.2 \pm 11.8$ .

At the trial endpoint, QoL-RLS total score improved significantly in the pooled rotigotine groups compared with placebo ( $p < 0.001$ , Effect Size=0.58). Further analysis of each rotigotine group showed the mean change from baseline in total QoL-RLS score improved by -13.1 (1 mg/24 h), -15.7 (2 mg/24 h) and -17.5 (3 mg/24 h) compared with -7.3 with placebo.

Analyses of individual QoL-RLS sub-scale items showed markedly larger improvements than placebo with regard to the impact of RLS-specific symptoms (ES=0.56), sleep disorders (ES=0.49), coping behaviour (ES=0.46) and QoL "all in all" (ES=0.60). Pain and treatment side effects had an ES of 0.24.

### **Clinically relevant augmentation is not common over one-year treatment with rotigotine<sup>3</sup>**

Retrospective analysis of two (EU and US) one-year follow up trials showed that clinically relevant augmentation is not common during the first 12 months of treatment with rotigotine.



Augmentation was assessed using the Augmentation Severity Rating Scale (ASRS), IRLS, RLS-6, CGI and QoL-RLS. 620 patients exposed to rotigotine in dosages ranging from 0.5 to 3 mg/24 h were evaluated. Sixty patients (9.7%) met the Max Plank Institute (MPI) criteria for augmentation and the condition was clinically relevant for 18 patients (2.9%) for the one year of treatment.

No relationship between rotigotine dose and augmentation was detected.

#### ‡IRLS Scale

The International Restless Legs Syndrome Study Group Rating Scale (IRLS)<sup>5</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. The total IRLS score ranges from 0 (no symptoms) to 40 (very severe symptoms). A score of >20 indicates severe RLS.

#### ‡Clinical remission

Clinical remission is often described as the disappearance of the clinical characteristics of a disease. In the context of RLS, clinical remission is defined as an IRLS score of 10 or less at the end of maintenance.<sup>6</sup>

#### ‡Symptom freedom

Symptom freedom can be described as being clear of disease manifestations. In the context of RLS, symptom freedom is defined as an IRLS score of 0 at the end of maintenance.<sup>5</sup>

#### ‡ QoL-RLS

The restless legs syndrome quality of life (RLS-QoL) questionnaire consists of 12 items addressing the effects of the symptoms of restless legs syndrome on sleep, activities of daily living, mood, social interactions, and coping behaviours. Scores for each item range from 0 (not at all impaired) to 5 (extremely impaired).<sup>7</sup>

#### \*Notes to Editors

In June 2008 Neupro<sup>®</sup> supply in Europe was limited to patients already established on the drug after ongoing monitoring of marketed product revealed the appearance of crystals in some patches.

UCB has fully implemented a cold-chain storage and distribution system and all stocks of Neupro<sup>®</sup> have been replaced with product that is refrigerated from manufacturer to patient. On 29<sup>th</sup> May 2009 the European Medicines Agency recommended that the treatment restrictions for Neupro<sup>®</sup> in Europe be lifted. This recommendation is now passed to the European Commission for endorsement. Once this recommendation is endorsed by the European Commission, doctors in the European Union will then be able to prescribe Neupro<sup>®</sup> to patients in accordance with the approved product information.



### **About Neupro<sup>®</sup> in Europe<sup>4</sup>**

Neupro<sup>®</sup> is approved in Europe for the symptomatic treatment of moderate to severe idiopathic restless legs syndrome in adults, and for the treatment of the signs and symptoms of early-stage idiopathic Parkinson's disease, as monotherapy or in combination with levodopa 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> Important Safety Information<sup>4</sup>**

Adverse drug reactions reported in more than 10% of RLS patients treated with Neupro<sup>®</sup> (rotigotine transdermal patch) are nausea, application site reactions, fatigue and headache. Adverse drug reactions reported in more than 10% of Parkinson's patients treated with Neupro<sup>®</sup> are nausea, dizziness, somnolence and application site reactions. The incidence of some dopaminergic adverse events, such as hallucinations, dyskinesia, and peripheral oedema generally is higher when given in combination with L-dopa in Parkinson's patients. This should be considered when prescribing rotigotine.

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 or cardioversion. The backing layer of Neupro<sup>®</sup> contains aluminium. To avoid skin burns, Neupro<sup>®</sup> should be removed if the patient has to undergo MRI or cardioversion. Neupro<sup>®</sup> has been associated with somnolence including excessive daytime somnolence and sudden sleep onset episodes.

Neupro<sup>®</sup> has been associated with somnolence including excessive daytime somnolence and sudden sleep onset episodes. In isolated cases "sudden onset of sleep" occurred while driving and resulted in motor vehicle accidents. Patients treated with dopamine agonists including Neupro<sup>®</sup>, have been reported as exhibiting signs of pathological gambling, increased libido and hypersexuality, generally reversible upon reduction of the dose or treatment discontinuation.

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

If there is a skin rash or irritation from the transdermal system, direct sunlight on the area should be avoided until the skin heals. Exposure could lead to changes in the skin color. If a generalised skin reaction (e.g. allergic rash, including erythematous, macular, papular rash or pruritus) associated with the use of Neupro<sup>®</sup> is observed, Neupro<sup>®</sup> should be discontinued.

Cases of fibrotic complications: retroperitoneal fibrosis, pulmonary infiltrates, pleural effusion, pleural thickening, pericarditis and cardiac valvulopathy have been reported in some patients treated with ergot-derived dopaminergic agents. While these complications may resolve when treatment is discontinued, complete resolution does not always occur.



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.

#### **About Neupro<sup>®</sup> in the U.S.**

*UCB recalled Neupro<sup>®</sup> from the U.S. market in April 2008 after ongoing monitoring revealed that specific batches of Neupro<sup>®</sup> had deviated from their approved specification. UCB is working with the U.S. Food and Drug Administration (FDA) so that Neupro<sup>®</sup> can be available to patients with early-stage Parkinson's disease as soon as possible.*

#### **Further information**

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#### **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 10 000 people in over 40 countries, UCB achieved revenues of 3.6 billion Euro in 2008. 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.*

#### **References**

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<sup>2</sup> D. Garcia-Borreguero, C. Trenkwalder, R. Kohnen, L. Ferini-Strambi, E.Schollmayer, on behalf of the SP790 study group, effects of rotigotine transdermal system on quality of life in idiopathic restless legs syndrome, abstract presented at 2009 MDS 13th International Congress, Paris, France.

<sup>3</sup> H. Benes, D.Garcia-Borreguero, R. Allen, R. Kohnen, Augmentation in long-term therapy of the Restless Legs Syndrome with transdermal rotigotine – a retrospective systematic analysis of two large open-label 1-year trials abstract presented at 2009 MDS 13th International Congress, Paris, France.

<sup>4</sup> Neupro<sup>®</sup> Summary of Product Characteristics, April 2009.

<sup>5</sup> Decision Resources. "Restless Legs Syndrome." Cognos Study #3. November 2006.

<sup>6</sup> Trenkwalder C, Paulus W, Walters AS. The restless legs syndrome. *Lancet Neurol* 2005; 4: 465.

<sup>7</sup> Trenkwalder C, Beneš H, Poewe W et al. Successful use of low-dose rotigotine in RLS: a randomised, placebo-controlled, double-blind, large-scale trial with rotigotine transdermal patch. *Lancet Neurol* 2008; 7: 595-604.