



For the attention of Accredited Medical Writers Only

RECOVER analyses highlighted need to address motor, sleep and other non-motor symptoms of Parkinson's disease

- Post hoc analyses of RECOVER study suggested only small correlations between severity of early morning motor symptoms and nocturnal sleep disturbances and between early morning motor and non-motor symptoms in PD patients^{1,2}

Brussels (Belgium), 13 April 2011, 1930 CET – New rotigotine data shown in four poster presentations at the 63rd Annual Meeting of the American Academy of Neurology (AAN) in Hawaii, U.S., highlighted the importance in Parkinson's disease (PD) of addressing both motor- and non-motor symptoms, such as sleep. The data also demonstrated the long-term efficacy and tolerability of rotigotine and showed that plasma rotigotine levels remained stable following patch removal and application of a new patch in advanced Parkinson's disease.^{1,2,3,4}

Treating motor and non-motor symptoms of PD

Post-hoc analyses of the Randomized Evaluation of the 24-hour Coverage: Efficacy of Rotigotine (RECOVER) study showed only small correlations between changes in early morning motor and non-motor symptoms and between severity of nocturnal sleep disturbances and early morning motor symptoms in patients with Parkinson's disease.^{1,2}

"The low correlation between motor and non-motor symptoms, specifically early morning motor function and night-time sleep disturbances, has an important bearing on clinical practice. The analyses suggest that we cannot assume that by treating motor symptoms we will also improve non-motor symptoms. We need to be sure to ask patients about all their Parkinson's symptoms and address their specific needs, if we are to improve functionality and well-being," commented Dr Todd Swick of the University of Texas, U.S.

The RECOVER study was a double-blind, placebo-controlled trial (n=287) that reported significant benefits with rotigotine for both early morning motor function (Unified Parkinson's Disease Rating Scale; UPDRS Part III) and nocturnal sleep disturbances (Parkinson's Disease Sleep Scale; PDSS-2), compared with placebo (p=0.0002 and p<0.0001, respectively).⁵



The new post hoc analyses have shown:

- Small correlations (Pearson correlation coefficients) between severity of early morning motor symptoms, as measured by UPDRS III, and non-motor symptoms, as measured by PDNMS scores at baseline ($r=0.35$, $p<0.0001$), and end of maintenance (EoM) treatment ($r=0.38$, $p<0.0001$), and small correlations between change from baseline to EoM between UPDRS III and PDNMS scores ($r=0.32$, $p<0.0001$)²
- Small correlations between severity of early morning motor symptoms, as measured by UPDRS III, and nocturnal sleep disturbances, as measured by PDSS-2 total scores; Pearson correlation coefficients for UPDRS III and PDSS-2 total scores were 0.26 ($p<0.0001$) at baseline, 0.30 ($p<0.0001$) at EoM, and 0.36 ($p<0.0001$) for change from baseline to EoM.¹

Rotigotine provided long-term efficacy and tolerability

Results from an open-label extension of a 6 month, Phase III, randomized, double-blind, placebo- and ropinirole-controlled trial (mean total duration 45 ± 23 months) showed that rotigotine was generally well tolerated and that UPDRS motor and daily activity scores (UPDRS II+III) remained improved, compared to baseline, for over 4 years of treatment. This open label study enrolled 380 patients.³

Rotigotine plasma levels remained stable following transdermal patch removal and new patch application

Mean trough plasma concentrations of rotigotine generally remained stable throughout a 4-month investigation of the effects of daily patch replacement on rotigotine plasma concentrations in 56 patients with advanced Parkinson's disease, taking part in a large multinational trial.⁴

About Neupro[®] in Europe⁶

Neupro[®] (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[®] is also approved in the European Union for the symptomatic treatment of moderate to severe idiopathic restless legs syndrome in adults.

Neupro[®] in Europe Important Safety Information⁶

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 (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.



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[®]. Please go to http://www.neupro.com/documents/Neupro_PI_071207.pdf for US Full Prescribing Information.

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

References

1. Swick R, Surmann E, Boroogerdi B, Moran K, Ghys L, Trenkwalder C. Association between early morning motor symptoms and nocturnal sleep disturbance in patients with Parkinson's disease (PD) - a post hoc analysis of the Randomized Evaluation of the 24-hour Coverage: Efficacy of Rotigotine (RECOVER) study. Presented at the 63rd Annual Meeting of the American Academy of Neurology, 9 – 16 April, 2011, Hawaii, U.S..
2. Chaudhuri KR, Surmann E, Boroogerdi B, Moran K, Ghys L, Friedman J. Association between motor and nonmotor symptoms in patients with Parkinson's disease (PD): a post hoc analysis of the Randomized Evaluation of the 24-hour Coverage: Efficacy of Rotigotine (RECOVER) study. Presented at the 63rd Annual Meeting of the American Academy of Neurology, 9-16 April, 2011, Hawaii, U.S.
3. Boroogerdi B, Surmann E, Giladi N, on behalf of the SP716 study group. The safety and efficacy of transdermal rotigotine over a 6-year period in patients with early-stage idiopathic Parkinson's disease. Presented at the 63rd Annual Meeting of the American Academy of Neurology, 9-16 April, 2011, Hawaii, U.S.
4. Whitesides J, Cawello W, Woltering F, Boroogerdi B, Poewe W. Stable plasma levels of rotigotine following transdermal patch removal and new patch application during long-term treatment of patients with advanced Parkinson's disease. Presented at the 63rd Annual Meeting of the American Academy of Neurology, 9-16 April, 2011, Hawaii, U.S.
5. Trenkwalder C, Kies B, Rudzinska M, Fine J, Nikl J, Honczarenko K, Dioszeghy P, Hill D, Anderson T, Myllyla V, Kassubek J, Steiger M, Zucconi M, Tolosa E, Poewe W, Surmann E, Whitesides J, Boroogerdi B, Chaudhuri KR, and the RECOVER study group. Rotigotine Effects on Early Morning Motor Function and Sleep in Parkinson's Disease: A Double-Blind, Randomized, Placebo-Controlled Study (RECOVER). *Movement Disorders*, 2011;26(1):90-99.
6. Neupro[®] European Summary of Product Characteristics (Approved February 2011) <http://ec.europa.eu/health/documents/community-register/html/alfregister.htm>



For further information

Nancy Nackaerts, External Communications, UCB
T +32.473.864.414, nancy.nackaerts@ucb.com

Eimear O'Brien, Associate Director, Global CNS Communications UCB
T +32.2.559.9271, eimear.obrien@ucb.com

Onsite at Congress

Andrea Levin, Senior Manager, Communications & PR, U.S.
T +770.970.8352, andrea.levin@ucb.com

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.