



For the attention of accredited medical writers only

Patients with Parkinson's disease treated with Neupro[®] (rotigotine) showed low rates of dyskinesias with long term treatment

- Data presented at the 7th International Congress on Mental Dysfunction and Other Non-Motor Features in Parkinson's Disease and Related Disorders

Brussels (Belgium), 10th December 2010, 0800 CET – Data presented at this week's 7th International Congress on Mental Dysfunction and other Non-Motor Features in Parkinson's Disease and Related Disorders (MDPD) showed low dyskinesia[†] rates with Neupro[®] (rotigotine) treatment for up to six years in patients with Parkinson's disease and a generally good tolerability profile of rotigotine regardless of age.^{1,2}

Rotigotine showed low dyskinesia rates with long term treatment

Patients in two 6-month, placebo-controlled trials of rotigotine transdermal system in early-stage Parkinson's disease were offered enrolment in long-term open-label extension studies (median follow-up: 1918/1543 days [5.3/4.2 years]) (NCT00594165, NCT00599196). Open-label rotigotine was titrated to optimal dose (up to 16 mg/24 h)^{††} and concomitant L-dopa was allowed after one month of maintenance. The incidence of dyskinesias in patients treated with Neupro[®] for up to 6 years was low, and mostly occurred with concomitant L-dopa.²

"After treatment of up to six years with rotigotine, only 5% of patients reported dyskinesias when they were taking rotigotine alone, and dyskinesias were generally described as "not disabling" or "mildly disabling". Of all the patients in the study who reported dyskinesia, only 15% reported that they were affected for more than 25% of the waking day," commented Dr Nir Giladi, Presenting Author, Chairman of the Department of Neurology and director of the Movement Disorders Unit at Tel-Aviv Sourasky Medical Centre, Sackler School of Medicines, Tel-Aviv University, Tel-Aviv, Israel.

Of 596 patients who entered the open-label extension studies no patient discontinued due to dyskinesia. Of study participants, 123 (21%) reported dyskinesia, 31 (5%) prior to/without L-dopa and 92 (15%) after starting concomitant L-dopa.



Of patients who reported dyskinesias during the study, 84% reported no dyskinesia or dyskinesia with a duration of $\leq 25\%$ of the waking day at end of maintenance. In addition at end of maintenance, 94 (16%) patients reported "not disabling" dyskinesia (70 after L-dopa), 20 (3%) "mildly disabling" (17 after L-dopa), 5 (0.8%) "moderately disabling" (4 after L-dopa), and 4 (0.7%) "severely disabling" (1 after L-dopa).

Rotigotine was generally well tolerated

Results of two early-PD trials and two advanced-PD trials also presented at the Congress showed that rotigotine was generally well tolerated, regardless of age, with no age-related differences in incidence ($>5\%$) in the majority of adverse events (AEs).¹

Data from the two early-PD trials (n=396) and the two advanced-PD trials (n=434) were pooled separately, and the incidence and severity of adverse events (AEs), and discontinuations due to AEs, were characterized by age (65- and 75-year cut-offs).

No age-related differences in incidence ($>5\%$) of the majority of AEs were observed for early- or advanced-PD pools. Nausea and headache were more common in younger patients with early-PD, whereas falls, somnolence and dizziness were more often observed in older patients.

Using the 65-year cut-off, nausea occurred in 37.6% of younger patients with early PD, compared to 29.9% of older patients, and headache in 15.3% and 9.0% respectively. In advanced-PD, 5.6% of younger patients had falls, compared to 11% of older patients.

Using the 75-year cut-off, the largest ($\geq 10\%$) differences by age were recorded for nausea (35.5% younger patients/20.0% older patients), falls (4.6%/13.3%), somnolence (26.0%/33.3%), and dizziness (15.0%/26.7%) in early-PD, and nausea (23.1%/11.4%) and falls (7.7%/12.9%) in advanced-PD. In both early- and advanced-PD patients, the incidences of severe-intensity AEs and serious AEs were low. Discontinuations due to AEs were low ($<10\%$) in all pools.

[†] *Dyskinesia is the term used to describe unintended, involuntary and uncontrollable movements and includes twitches, jerking, twisting or simple restlessness. Dyskinesia affects each person differently both in its timing, frequency and severity and the most common areas of the body to be affected are the limbs and trunk.*⁴

^{††} *The maximum recommended dose of Neupro[®] in patients with early stage Parkinson's disease is 8 mg/24h. The maximum recommended dose in patients with advanced stage Parkinson's disease is 16 mg/24h.*



For further information

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About Neupro® in the EU/EEA³

Neupro® (rotigotine) is approved in the EU/EEA 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 EU/EEA for the symptomatic treatment of moderate to severe idiopathic restless legs syndrome in adults.

Neupro® in the EU/EEA 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 (Approved 18th August 2010): http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000626/WC500026397.pdf

About Neupro[®] in the U.S.

In May 2007 Neupro[®] (rotigotine transdermal system) was approved by the U.S. Food and Drug Administration (FDA) 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.

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. 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[®] may potentiate the dopaminergic side effects of L-dopa and may cause and/or exacerbate pre-existing dyskinesia. Dyskinesia was reported at a similar rate in patients treated with Neupro[®] (0.5%) or placebo (0.3%).

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

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

References

1. Ghys L, LeWitt P, Grieger F, Bauer L, Boroogjerdi B, Oertel W. Treatment of patients with early and advanced Parkinson's disease (PD) with transdermal rotigotine: age relationship to safety and tolerability. Presented at 7th International Congress on Mental Dysfunctions & Other Non-Motor Features in Parkinson's Disease & Related Disorders (MDPD), Barcelona, Spain, December 9-12, 2010
2. Giladi N, Jankovic J, Watts RL, Surmann E, Boroogjerdi B, on behalf of the SP702 and SP716 study groups. Effects of long-term treatment with rotigotine transdermal patch on dyskinesias in early-stage Parkinson's disease (PD): results from two open-label extension trials. Presented at 7th International Congress on Mental Dysfunctions & Other Non-Motor Features in Parkinson's Disease & Related Disorders (MDPD), Barcelona, Spain, December 9-12, 2010
3. Neupro[®] European Summary of Product Characteristics http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000626/WC500026397.pdf
4. <http://www.rewritetomorrow.eu.com/pdsymptoms/dyskinesia/> [accessed December 6th 2010]



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 8 000 people in about 40 countries, the company generated 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.