About Neupro® (Rotigotine Transdermal System)

- **Neupro® (Rotigotine Transdermal System)—a dopamine agonist patch indicated for the treatment of the signs and symptoms of idiopathic Parkinson's disease (PD) and moderate-to-severe primary Restless Legs Syndrome (RLS)— provides continuous drug delivery for 24 hours**
- As of July 2012, Neupro® is available in six dosage strengths at U.S. retail pharmacies
- FDA approval was based on 7 pivotal trials that demonstrated Neupro®'s efficacy, safety, and tolerability in PD and RLS
- The precise mechanism of action of Neupro®as a treatment for these diseases is unknown, however:
    - In Parkinson's disease, the mechanism of action (MOA) of Neupro® is thought to be related to its ability to stimulate dopamine receptors within the caudate-putamen, the region of the brain that regulates movement
    - Similarly, in RLS, the MOA of Neupro® is thought to be related to its ability to stimulate dopamine receptors

Additional information about Neupro®, including a video on how to apply the patch and information about the Neupro® Patient Savings Program™, can be found at www.neupro.com.

For more information on the PD clinical trials, click here.

For more information on the RLS clinical trials, click here.

For more information on Neupro® pharmacy stocking, click here.

Neupro® PD Clinical Trials[1]

The effectiveness of Neupro® in the treatment of the signs and symptoms of idiopathic PD was established in 5 parallel-group, randomized, double-blind placebo-controlled trials conducted in the US and abroad. Depending on the trial design, patients underwent a weekly titration of Neupro® in 2 mg/24 hours increments to either the randomized dose or optimal dose.

- **In 3 trials, statistically significant improvements in the Unified Parkinson's Disease Rating Scale (UPDRS) Parts II and III combined score were observed in early-stage PD patients receiving Neupro® compared with patients receiving placebo†**
- **Two trials of Neupro® in patients with advanced-stage PD, who were also taking levodopa, examined change from baseline in "off" time periods when impaired motor function returns. Statistically significant reductions in off-times were observed in advanced-stage PD patients receiving Neupro® compared with those who received placebo**

In clinical trials, the most common adverse reactions (≥5% greater than placebo) for the highest recommended doses of Neupro® for treatment of PD were nausea, vomiting, somnolence,

application site reactions, dizziness, anorexia, hyperhidrosis, insomnia, peripheral edema and dyskinesia.

†The UPDRS is a multi-item rating scale intended to evaluate mentation, activities of daily living (ADL), motor performance, and complications of therapy. The 3 trials used a combined measure of ADL (Part II) and motor performance (Part III) of the UPDRS. UPDRS Part II contains 13 questions relating to ADL, such as speech, dressing, and cutting food with utensils, and Part III contains 27 questions related to the cardinal motor symptoms in PD patients—i.e., tremor, rigidity, bradykinesia, and postural instability.

Click here to receive more information about Neupro® from UCB, Inc.

Neupro® RLS Clinical Trials[1]

The efficacy of Neupro® in the treatment of RLS was primarily evaluated in 2 fixed-dose, randomized, double-blind, placebo-controlled trials with 6-month maintenance periods. Patients received Neupro® doses ranging up to 3 mg/24 hours, or placebo, once daily.

- **Statistically significant improvements in the International RLS Rating Scale (IRLS Scale) sum score and in the Clinical Global Impression-Severity (CGI-Item 1) assessment were observed in RLS patients receiving Neupro® compared with those receiving placebo‡**

The most common adverse reactions (≥5% greater than placebo) for the highest recommended dose of Neupro® for treatment of RLS were application site reactions, nausea, somnolence, and headache.

‡The IRLS Scale contains 10 items designed to assess the severity of sensory and motor symptoms, sleep disturbance, daytime somnolence, and impact on activities of daily living and mood associated with RLS. The CGI-1 is designed to assess severity of illness on a 7-point scale.

Click here to receive more information about Neupro® from UCB, Inc.

Neupro® Pharmacy Stocking Information

- Neupro® (Rotigotine Transdermal System) dosage strengths, quantities, and national drug code (NDC) numbers are as follows:

1 mg/24 hours	30 patches	NDC 50474-801-03
2 mg/24 hours	30 patches	NDC 50474-802-03
3 mg/24 hours	30 patches	NDC 50474-803-03
4 mg/24 hours	30 patches	NDC 50474-804-03
6 mg/24 hours	30 patches	NDC 50474-805-03
8 mg/24 hours	30 patches	NCD 50474-806-03

Please click here to review the full Prescribing Information for Neupro®.

Indication

Neupro® (Rotigotine Transdermal System) is indicated for the treatment of the signs and symptoms of idiopathic Parkinson's disease and moderate-to-severe primary Restless Legs Syndrome (RLS).

Important Safety Information for Neupro®

Neupro® contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people and is seen more frequently in people with asthma.

Patients treated with Neupro® have reported somnolence and falling asleep without warning signs during activities of daily living, including driving, which sometimes resulted in accidents. Some patients believed they were alert immediately prior to the event. Patients may not recognize or acknowledge increased drowsiness or sleepiness. Therefore, prescribers should directly question patients about these possible occurrences and continually reassess patients, as some events have been reported well after the start of treatment. Patients should be advised to exercise caution while driving, operating heavy machinery, or working at heights during treatment with Neupro®. If patients develop daytime sleepiness or episodes of falling asleep during activities of daily living, Neupro® should be discontinued.

There is an increased risk for hallucinations in patients with advanced-stage Parkinson's disease treated with Neupro®. Patients also may experience new or worsening mental status and behavioral changes, which may be severe, including psychotic-like behavior during Neupro® treatment or after starting or increasing the dose of Neupro®.

Neupro® may cause symptomatic postural/orthostatic hypotension, and Parkinson's disease patients appear to have an impaired capacity to respond to postural challenge. Both Parkinson's and RLS patients treated with dopamine agonists require careful monitoring for signs and symptoms of postural hypotension, especially during dose escalation, and should be informed of this risk. Neupro® may also cause syncope, elevated blood pressure, elevated heart rate, weight gain, and fluid retention. Neupro® should be used with caution in patients with severe cardiovascular disease.

Case reports suggest that patients can experience intense urges to gamble, increased sexual urges, intense urges to spend money, binge eating, and other intense urges, and the inability to control these urges while taking medications, including Neupro®, that increase central dopaminergic tone and that are generally used for the treatment of Parkinson's disease. Because patients may not recognize these behaviors as abnormal, prescribers should specifically ask patients and their caregivers about the development of new or increased urges while being treated with Neupro®. Dose reduction or discontinuation of Neupro® should be considered if such urges develop.

Neupro® may increase the dopaminergic side effects of levodopa and may cause and/or exacerbate pre-existing dyskinesia.

Neupro® can cause application site reactions, and some may be severe. In clinical trials, most reactions were mild or moderate in intensity and were limited to the patch area.

Patients with Parkinson's disease have a higher risk of developing melanoma than the general population. Patients should be monitored for melanomas frequently when using Neupro®.

Dopaminergic medicinal products, including Neupro®, may cause augmentation and rebound in RLS patients.

Neupro® should be removed before magnetic resonance imaging or cardioversion, because the aluminum backing layer in the patch could cause skin burns. Heat application has been shown to increase absorption several fold with other transdermal products. Therefore, patients should be advised to avoid exposing the application site to sources of direct heat, such as heating pads or electric blankets, heat lamps, saunas, hot tubs, heated water beds, and prolonged direct sunlight.

The most common adverse reactions (≥5% greater than placebo) for the highest recommended doses of Neupro® for treatment of Parkinson's disease are nausea, vomiting, somnolence, application site reactions, dizziness, anorexia, hyperhidrosis, insomnia, peripheral edema, and dyskinesia.

The most common adverse reactions (≥5% greater than placebo) for the highest recommended dose of Neupro® for treatment of Restless Legs Syndrome are application site reactions, nausea, somnolence, and headache.

Additional important safety information for Neupro® can be accessed here.

Reference

1. Neupro® (Rotigotine Transdermal System) Prescribing Information. Smyrna, GA: UCB, Inc.; 2012.