U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Neupro (Rotigotine) Transdermal System

Detailed View: Safety Labeling Changes Approved By FDA Center for Drug Evaluation and Research (CDER)

February 2015

Summary View (/Safety/MedWatch/SafetyInformation/ucm436827.htm)

WARNINGS AND PRECAUTIONS

Symptomatic Hypotension

- An increased risk for decreases in systolic and diastolic blood pressure were observed when supine, standing, and changing from supine to standing position in patients treated with NEUPRO. In patients taking the maximum recommended NEUPRO dose, orthostatic (change from supine to standing) decreases in systolic blood pressure (at least 20 mm Hg or greater) was 16% for NEUPRO and 14% for placebo in patients with early-stage Parkinson's disease, 32% for NEUPRO and 27% for placebo in patients with advanced-stage Parkinson's disease, and 13% for NEUPRO and 11% for placebo in patients with Restless Legs Syndrome.
- More severe decreases in systolic blood pressure (40 mm Hg or greater) and in diastolic blood pressure (20 mm Hg or greater) also occurred more frequently (NEUPRO incidence at least 2% greater than placebo) in patients with early- and advanced-stage Parkinson's disease…
- For the maximum recommended NEUPRO dose, the incidence of adverse reactions suggestive of hypotension/orthostatic hypotension was 29% for NEUPRO and 11% for placebo in early-stage Parkinson's disease, 27% for NEUPRO and 23% for placebo in advanced-stage Parkinson's disease, and 8% for NEUPRO and 7% for placebo in Restless Legs Syndrome.

Syncope

- … patients with severe cardiovascular disease should be asked about symptoms of syncope and pre-syncope.

Elevation of Blood Pressure and Heart Rate

- Some patients treated with NEUPRO exhibited increases in systolic blood pressure (greater than 180 mm Hg) and/or diastolic blood pressure (greater than 105 mm Hg) while supine or standing. In patients with advanced stage Parkinson's disease, this increased risk for systolic blood pressure greater than 180 mm Hg was 5% for NEUPRO and 3% for placebo and for diastolic blood pressure greater than 105 mm Hg was 4% for NEUPRO and 0% for placebo. In patients with Restless Legs Syndrome, this increased risk for diastolic blood pressure greater than 105 mm Hg was 8% for NEUPRO and 4% for placebo.
- Increases in systolic blood pressure (at least 20 mm Hg or more) and in diastolic blood pressure (at least 10 mm Hg or more) occurred more frequently (incidence at least 5% greater than placebo) in all patients (i.e., early and advanced-stage Parkinson's disease and Restless Legs Syndrome) taking the maximum recommended NEUPRO dose. These increases in systolic and diastolic blood pressure were observed when supine, standing…

Weight Gain and Fluid Retention

- In patients taking the maximum recommended NEUPRO dose, the incidence of peripheral edema was 3% for NEUPRO and 2% for placebo in early-stage Parkinson's disease and 9% for NEUPRO and 1% for placebo in advanced-stage Parkinson's disease. These treatment differences increased further with treatment at NEUPRO dosing above the maximum recommended doses. Monitor for weight gain and fluid retention when treating patients with concomitant illnesses such as congestive heart failure or renal insufficiency.

Dyskinesia

- For the maximum recommended NEUPRO dose, the incidence of dyskinesia was increased for NEUPRO (NEUPRO 14% vs. placebo 7%) in patients with advanced-stage Parkinson's disease, and this incidence increased with increasing dose. Patients treated with the maximum recommended dose of NEUPRO also had an increased risk (NEUPRO 3% vs. placebo 0%) for early discontinuation from the study because of dyskinesia.
- For the maximum recommended NEUPRO dose, the incidence of application site reactions was 32% for NEUPRO and 19% for placebo in patients with early-stage Parkinson's disease, 36% for NEUPRO and 13% for placebo in patients with advanced-stage Parkinson's disease, and 43% for NEUPRO and 4% for placebo in patients with Restless Legs Syndrome. ASRs exhibited a dose-dependent relationship for all doses for patients with early and…

ADVERSE REACTIONS

Laboratory Changes

- Patients with early-stage Parkinson's disease receiving NEUPRO had an increased risk for low hemoglobin below the normal reference range (NEUPRO 8% vs. placebo 2%) and for decreased hematocrit below the normal reference range (NEUPRO 8% vs. placebo 5%). Patients with advanced-stage Parkinson's disease receiving NEUPRO had an increased risk for a low hemoglobin below the normal reference range (NEUPRO
- 15% vs. placebo 11%) and for decreased hematocrit below the normal reference range (NEUPRO 17% vs. placebo 14%). Patients with RLS receiving NEUPRO had an increased risk for a decreased hemoglobin below the normal reference range (NEUPRO 15% vs. placebo 12%). There was also an increased risk for markedly decreased hemoglobin and hematocrit (NEUPRO 2% vs. placebo 0%) in patients with advanced-stage Parkinson's disease receiving NEUPRO and for markedly decreased hematocrit (NEUPRO 1% vs. placebo 0%) in patients with RLS receiving NEUPRO.
- Patients with early-stage Parkinson's disease receiving NEUPRO had an increased risk for elevated serum blood urea nitrogen (BUN) above the normal reference range (NEUPRO 11% vs. placebo 2%). There was also an increased risk for markedly elevated serum BUN (NEUPRO 3% vs. placebo 2%) in patients with advanced stage Parkinson's disease receiving NEUPRO.
- There was an increased risk for low serum glucose below the normal reference range in patients with early stage Parkinson's disease receiving NEUPRO (NEUPRO 15% vs. placebo 6%) and in patients with advanced stage Parkinson's disease (NEUPRO 10% vs. placebo 7%). There was also an increased risk for markedly decreased serum glucose (NEUPRO 1% vs. placebo 0%) in patients with advanced-stage Parkinson's disease receiving NEUPRO.
- Serum creatine phosphokinase (CPK) was elevated in Japanese patients taking NEUPRO for early- or advanced-stage Parkinson's disease in placebo-controlled, flexible-dose studies conducted in Japan. The frequency of CPK elevation observed in patients receiving NEUPRO for early-stage Parkinson's disease was 40% (35/88) in the NEUPRO group compared to 17% (15/89) in the placebo group. The frequency of CPK elevation observed in patients receiving NEUPRO for advanced-stage Parkinson's disease was 39% (99/253) in…

PATIENT INFORMATION

What are the possible side effects of NEUPRO?

- unusual urges: strong urges to spend money, binge eating

April 2012

Summary View (/Safety/MedWatch/SafetyInformation/ucm302285.htm)

WARNINGS AND PRECAUTIONS

Falling Asleep During Activities of Daily Living and Somnolence

- Patients with early and advanced Parkinson's disease and with Restless Legs Syndrome treated with Neupro have reported falling asleep while engaged in activities of daily living, including the operation of motor vehicles, which sometimes resulted in accidents...

Hallucinations/Psychotic-Like Behavior

- There was an increased risk for hallucinations in patients with advanced-stage Parkinson's disease treated with Neupro. For the highest recommended Neupro dose, the incidence of the treatment difference (Neupro % - Placebo %) for hallucinations was 4% for patients with advanced-stage Parkinson’s disease, and this difference increased with increasing dose…

Symptomatic Hypotension

- Dopaminergic agonists, in clinical studies and clinical experience, appear to impair the systemic regulation of blood pressure, resulting in postural/orthostatic hypotension, especially during dose escalation. Parkinson's disease patients, in addition, appear to have an impaired capacity to respond to a postural challenge.

Impulse Control/Compulsive Behavior

- Case reports suggest that patients can experience intense urges to gamble, increased sexual urges, intense urges to spend money, binge eating, and/or other intense urges, and the inability to control these urges while taking one or more of the medications, including Neupro, that increase central dopaminergic tone and that are generally used for the treatment of Parkinson’s disease…

Elevation of Blood Pressure And Heart Rate

- Mild-moderate increases in systolic blood pressure (> 20 mm Hg) and in diastolic blood pressure (> 10 mm Hg) occurred more frequently (Neupro % > 5 % greater than placebo %) in all patients (i.e., early and advanced-stage Parkinson's disease and Restless Legs Syndrome) with the highest recommended Neupro dose…
- In the placebo-controlled trials, there was an increased risk for hypertension as an adverse reaction with the highest recommended dose for advanced…

Augmentation and Rebound in RLS

- Augmentation is a worsening of RLS symptoms during treatment, leading to an increase in overall symptom severity or earlier time of symptom onset each day compared to before initiation of treatment. Dopaminergic medicinal products, including rotigotine, may result in augmentation.
- Rebound, an exacerbation of RLS symptoms, is considered to be an end of dose effect, related to the half-life of the therapeutic agent. Reports in the published literature indicate discontinuation or wearing off of dopaminergic medications can result in rebound.