PDL NEW DRUG REVIEW

Proprietary Name: Neupro®
Common Name: rotigotine transdermal system
PDL Category: Anti-Parkinson Agents

Comparable Products	Preferred Drug List Status
Pramipexole	Preferred
Ropinirole	Preferred

Summary

Indications and Usage: Treatment of the signs and symptoms of idiopathic Parkinson's disease. It is also indicated for the treatment of moderate-to-severe primary restless legs syndrome (RLS). This is a pregnancy category C medication. The safety and efficacy of use in children under the age of 18 have not been established.

Dosage Forms: Transdermal systems: 1mg, 2mg, 3mg, 4mg, 6mg, and 8mg per 24 hours.

Recommended Dosage: One patch is to be applied once daily to clean, dry, intact, healthy skin on the front of the abdomen, thigh, hip, flank, shoulder, or upper arm. It should be applied about the same time every day. For early-stage Parkinson's disease, the dose should be started at 2mg/24hrs, and then based upon individual response increase by 2mg/24hrs weekly to the highest recommended dose of 6mg/24hrs. For advanced Parkinson's disease, the dose should be started at 4mg/24hrs up to a maximum recommended dose of 8mg/24hrs. With RLS, the dose should be started at 1mg/24hrs. Based upon individual response, the dose may be increased by 1mg/24hrs per week to the highest recommended dose of 3mg/24hrs. Dosage adjustment is not required in those with renal impairment, or in those with mild or moderate hepatic impairment; however, there is a lack of data for use in those with severe hepatic impairment.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions = reported % incidence for drug minus reported % incidence for placebo in a trial with those with early-stage Parkinson's disease on a 4mg/24hr dose.* The most common adverse events reported with Neupro® include tinnitus (2%), nausea* (25%), vomiting* (13%), anorexia (2%), dyspepsia (2%), application site reactions (2%), fatigue (15%), upper respiratory tract infections (5%), WBC positive in urine (1%), dizziness (3%), somnolence *(11%), lethargy (2%), insomnia (4%), abnormal dreams* (5%), depression (3%), hiccups* (2%), erythema* (3%), and hyperhidrosis (0%). Those events with an * beside it were labeled as such because the % given was dose-related.

In those being treated with Neupro®, there have been reports of subjects falling asleep during activities of daily living, including the operation of motor vehicles which resulted in some accidents. While there were some reports of somnolence, many did not have warning signs such as excessive drowsiness. Therefore, it is recommended that subjects be advised and educated regarding the possibility of somnolence with Neupro® use and to use caution while driving and to avoid other potentially dangerous activities.

There was an increased risk of hallucinations in those with advanced-stage Parkinson's disease treated with Neupro®. In trials, 3% discontinued treatment due to the severity of this effect. In post-marketing reports, there have been reports of hallucinations, as well as new or worsening mental status and behavioral changes. It is recommended that those with major psychotic disorder not ordinarily be treated with Neupro®.

Contraindications: Hypersensitivity to rotigotine or any component of the transdermal system.

Manufacturer: UCB, Inc

Analysis: Rotigotine, the active ingredient of Neupro®, is a non-ergoline dopamine agonist that lasts for 24 hours. It's exact mechanism of action when used in those with Parkinson's disease or RLS is not known; however, it is thought to be related to its ability to stimulate dopamine receptors.

There were 5 registration studies comparing Neupro® with placebo in those with idiopathic Parkinson's disease, two in those with advanced-stage and three in those with early-stage Parkinson's disease. The primary outcome for the early-stage studies was the change from baseline in the Unified Parkinson's Disease Rating Scale (UPDRS). The change from baseline in time spent 'off' (hours) based on daily diaries was the primary outcome for the advanced-stage studies. Results suggest that differences between Neupro® and placebo were statistically significant.

There were 2 registration studies comparing Neupro® with placebo in those with RLS (N=1309). The co-primary efficacy endpoints included the International RLS Rating Scale (IRLS Scale) and the Clinical Global Impression-Improvement (CGI-I) assessment. Again, differences between Neupro® and placebo were statistically significantly.

As no comparator trials were found, there is no evidence at this time to suggest that Neupro® is more efficacious or safer than the currently available, more cost effective medications. Therefore, it is recommended that Neupro® remain non-preferred and be available to the few who are unable to tolerate any preferred medications.

PDL Placement:

- ☐ **Preferred**
- ☒ **Non-Preferred**
- ☐ **Preferred with Conditions**

References

[1] Neupro [package insert]. Smyrna, GA: UCB, Inc; 2012.