



Therapeutic Class ReviewSM

Neurology – Rotigotine Transdermal System (Neupro[®])

December 2007

New Product for Review:

Rotigotine transdermal system (Neupro[®])
[UCB/Schwarz Pharma]

Dossier Provided by Manufacturer:

Dossier Evaluation: 2

- 1 - Dossier missing significant clinical trial(s).
- 2 - Mfg. provided all relevant trials; Missing pharmacoeconomic model.
- 3 - Mfg. provided all relevant trials and information.

Available Therapeutic Alternatives:

Preferred/Formulary	Non-Prefer/Non-Formulary
<i>MAO B Inhibitors</i>	
selegiline (Eldepryl [®]) – generic	rasagiline (Azilect [®]) [Teva Neuroscience]
<i>Dopamine Agonists</i>	
pramipexole (Mirapex [®]) [Boehringer-Ingelheim]	rotigotine (Neupro [®]) [UCB Pharma]
ropinirole (Requip [®]) [GlaxoSmithKline]	
bromocriptine (Parlodel [®]) – generic	
<i>COMT Inhibitors</i>	
entacapone (Comtan [®]) [Novartis]	tolcapone (Tasmar [®]) [Valeant]

Executive Summary

- Parkinson’s disease (PD) a neurodegenerative disorder.
 - Classic symptoms include:
 - Bradykinesia
 - Rigidity
 - Rest tremor
 - Incidence ~ 13/100,000
 - Prevalence ~ 300/100,000
 - Prevalence of PD is rising slowly with aging population.
- Rotigotine (Neupro) is indicated for the treatment of early-stage idiopathic Parkinson’s disease.
 - Rotigotine transdermal system (Neupro) is a topical patch that provides a continuous 24-hour supply of rotigotine.
 - Rotigotine is a non-ergolinic dopamine agonist active at the D1, D2, and D3 dopamine receptors.
 - There are ongoing studies in restless legs syndrome (RLS) and advanced Parkinson’s disease.

- Rotigotine (Neupro) has been available in Europe for several years and is indicated there for advanced PD and RLS, as well as early PD.
 - Two large phase-III US trials examining the use of rotigotine (Neupro) in patients with RLS were recently presented at the AAN conference.
 - The manufacturer has been unable to provide this data despite repeated requests.
 - It is likely that rotigotine (Neupro) will be used off-label for RLS and advanced PD.

Evidence

- There is no useful evidence that rotigotine (Neupro):
 - Provides superior safety or efficacy than other formulary dopamine agonists for the treatment of early PD.
 - Results in improved compliance or persistence than other formulary dopamine agonists for the treatment of early PD.
 - Is effective for indications other than early PD.
- Considerations in Subpopulations:
 - **Pediatrics** - The safety and effectiveness of rotigotine (Neupro) in the pediatric population have not been studied.
 - **Geriatrics**: Plasma concentrations of rotigotine in patients 65 to 80 years of age were similar to those in younger patients, approximately 40 to 64 years of age. Although not studied, exposures in older subjects (>80 years) may be higher due to skin changes with aging.
 - **Gender**: Female and male subjects and patients had similar plasma concentrations (body weight normalized).
 - **Race, ethnicity**: The pharmacokinetic profile was similar in Caucasians, Blacks, and Japanese. No dose adjustment is necessary based on ethnicity.

Product Value

Rotigotine (Neupro) provides another treatment option for patients with early PD. The once-daily transdermal dosage form may provide additional convenience for PD patients with dysphagia or other swallowing difficulties, though this has not been specifically studied. Rotigotine (Neupro) appears to provide similar efficacy to other formulary dopamine agonists when used for the treatment of early PD.

Conclusion

Rotigotine (Neupro) is non-preferred/non-formulary because:

- It provides no proven benefit over current preferred/formulary alternatives.
- There appears to be an increased potential for adverse events related to application site reactions and other skin reactions.

Products¹²

Drug Products	FDA approval ^a	Patent Expiration(s) ^d	FDA approved indications	Usual Dose/Route	Cost ^b	Potential Off-label Uses ^c
MAO B Inhibitors						
selegiline (generic)	06/1989	N/A	- Parkinson's disease; Adjunct	5mg bid PO	\$120	- Alzheimer's disease – Dementia - Attention deficit hyperactivity disorder - Dementia – HIV infection - Depression - Narcolepsy - Parkinson's disease, initial treatment - Periodic limb movement disorder - Schizophrenia; Adjunct
rasagiline (Azilect)	05/2006	2016	- Parkinson's disease - Parkinson's disease; Adjunct	1mg qd PO	\$269	- None noted
Dopamine Agonists						
pramipexole (Mirapex [®])	07/1997	2011	- Parkinson's disease - Parkinson's disease; Adjunct - Restless legs syndrome	1mg tid	\$232	- Depression - Panic disorder - Schizophrenia
ropinirole (Requip [®])	09/1997	May 2008	- Parkinson's disease - Parkinson's disease; Adjunct - Restless legs syndrome	2mg tid	\$231	- None noted
bromocriptine (generic)	06/1978	N/A	- Parkinson's disease - Parkinson's disease; Adjunct - Acromegaly - Hyperprolactinemia-Associated Dysfunctions	10 mg tid	\$200	- Numerous
rotigotine (Neupro [®])	05/2007	2019	- Early Parkinson's disease	4 mg to 6 mg applied daily.	\$289	- None noted
COMT Inhibitors						
tolcapone (Tasmar [®])	01/1998	2012	- Parkinson's disease; Adjunct	100mg tid	\$362	- Depression
entacapone (Comtan [®])	10/1999	2009	- Parkinson's disease; Adjunct	200mg with each dose of levodopa (3 to 8 times daily)	\$250 - \$668	- Restless legs syndrome

^a Date applies to approval date for the original brand name medication where there are now generics available.

^b Cost estimate based on AWP (average wholesale price) listed in First Data Bank as of November 2007 for 1 month of therapy.

^c As listed in © 1974 - 2007 Thomson MICROMEDEX database or as referenced.

^d Based on patents listed in Orange Book as of November 2007

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