



Common Drug Review *Patient Group Input Submissions*

rotigotine (Neupro) for treatment of the signs and symptoms of idiopathic Parkinson's disease. Neupro may be used both as early therapy, without concomitant levodopa, and as an adjunct to levodopa.

Patient group input submissions were received from the following patient groups. Those with permission to post are included in this document.

Parkinson Society Canada — permission granted to post.

CADTH received patient group input for this review on or before June 12, 2015.

The views expressed in each submission are those of the submitting organization or individual; not necessarily the views of CADTH or of other organizations.

While CADTH formats the patient input submissions for posting, it does not edit the content of the submissions.

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Parkinson Society Canada

Section 1 — General Information

Name of the drug CADTH is reviewing and indication(s) of interest	Neupro (Rotigotine) is a daily transdermal patch indicated for adults 18 years and older for the signs and symptoms of Parkinson's disease either alone or in combination with the drug levodopa and the signs and symptoms of moderate to severe Restless Legs Syndrome (RLS).
Name of the patient group	Parkinson Society Canada
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Permission is granted to post this submission	Yes

1.1 Submitting Organization

Parkinson Society Canada (PSC) is the national voice of Canadians living with Parkinson's, a neurodegenerative disease. Through regional partners and 240 chapters and support groups, we invest in research and provide education, support, and advocacy on behalf of almost 100,000 Canadians living with Parkinson's every day.

1.2 Conflict of Interest Declarations

Parkinson Society Canada adheres to the ethical fundraising practices of both the [Association of Fundraising Professionals](#) and [Imagine Canada](#) and is accredited under Imagine Canada's national standards program.

For the 2014/15 financial year, Parkinson Society Canada received financial contributions in the form of unrestricted education grants from AbbVie Corporation, Astra Zeneca Canada Inc, Baxter Corporation, Medtronic CryoCath, Medtronic Inc, Medtronic of Canada Ltd, Rx&D Canada's Research-Based Pharmaceutical Companies, Teva Canada Innovation GP, and UCB Canada Inc. Contributions from pharmaceutical companies accounted for less than one percent of the organization's gross revenue in 2014/15.

Parkinson Society Canada has no conflict of interest in respect of those playing a significant role in compiling this submission.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

To inform this section 2 of the submission, Parkinson Society Canada (PSC) cited the [Canadian Guidelines on Parkinson's Disease](#), and also used the results of a national survey conducted in April 2013 for people living with Parkinson's disease and their care partners. More than 600 individuals from coast to coast participated in the 2013 survey, which contained a variety of open-ended questions, scoring options (using a ten-point scale) and closed-ended questions. (Please see the Survey questions attached to this submission as Appendix A, a summary of English and French responses as Appendix B). 70% of survey respondents identified themselves as patients, and 30% identified themselves as caregivers.

2.2 Impact of Condition on Patients

Parkinson's disease (PD) is characterized by a constellation of clinical manifestations, which include slowness of movement, rigidity, tremor and postural instability. There is no cure. Parkinson's disease is a complex disorder that can be difficult to diagnose clinically, especially in the early stages.¹

Neuropsychiatric symptoms are prevalent even prior to the motor symptoms of PD and become more prominent and increasingly challenging to treat with disease progression. They contribute to increasing disability and a negative impact on quality of life. Symptoms include, but are not limited to, depression, dementia, psychosis, sleep disorders, autonomic dysfunction, urinary dysfunction, orthostatic hypotension, constipation and erectile dysfunction.²

Survey respondents' most commonly reported symptoms included loss of motor control/dexterity, muscle stiffness, nausea, tremors, fatigue, sleep disturbances, mood changes, reduced mobility, cognitive impairment, speech impairment, gait and balance problems and restless legs.

Parkinson's disease can affect many aspects of a person's daily life. People must carefully plan and make modifications to their day in order to conserve energy and reduce stress to overcome the difficulties associated with the disease. The most commonly reported impacts on daily life were an inability to maintain employment, reduced ability to perform household tasks and chores, reduced ability to participate in social activities and recreational events, and reduced ability to participate in family activities. Individual comments included:

"PD affects EVERY aspect of my life. From the moment I open my eyes in the morning to when I fall asleep at night, my mood, physical abilities and quality of life depend on how well my medications, stress level and exercise are working to help diminish the effects of Parkinson's."

"Cannot work. Physical weakness and balance issues. Memory and cognitive impairment. These symptoms restrict activities."

"They impact all areas of my life. I take pills every two hours and cannot be left alone because off periods, which strike quickly, and at any time leave me immobile."

¹ Canadian Journal of Neurological Sciences, [Canadian Guidelines on Parkinson's Disease](#), Suppl. 4 – S7, July 2012

² Ibid - Suppl. 4 – S16 – S21

"My symptoms are mostly motor/movement related. Specifically, I can barely move when I'm 'OFF'. It's a struggle every day to try to manage what I need to do as I need to try to do everything when I'm 'ON'. Also, I have not been able to work since a few years ago."

"All of the following impact management of my life to some extent (intermittently and at varying intervals and intensity) on any given day: fatigue, tremors, dyskinesia, voice and speech, restless legs (this later, especially at night), balance."

"It completely changed my daily life. I can no longer work, in business nor do much work around home. I need help with dressing, hygiene, and writing. I have trouble cutting meat and eating with a fork. My verbal responses are slow and my speech very soft and quiet, which has changed my social life. At night I cannot turn over in bed, have problems getting out of bed in the morning and need a walker to stay on my feet first thing in the morning and when I am tired."

Survey respondents reported the most important PD symptoms to control were tremors, cognitive issues, dyskinesia, impaired balance and mobility, muscle rigidity and sleep problems.

77% of survey respondents indicated that their quality of life has greatly decreased or decreased since being first diagnosed with Parkinson's disease. Comments included:

"I was diagnosed in my early '40's with two young sons, a job I loved, an active life, a happy confident nature and a bright future with my amazing husband. Parkinson's has taken away the job, the active life, the self-confidence and the bright future."

"It can be very difficult to accept, especially when you are on your own in the middle of the mall and you can't move your legs until your meds kick in."

"Constant suffering ... both physically & mentally ... especially during 'OFF' times."

"J'ai connu mon diagnostic à l'âge de 38 ans il y a 12 ans. J'ai arrêté de travailler il y a environ 4 ans [...]. De ces temps, j'ai beaucoup de difficulté avec les période "on off". Je ne peux pas prédire lorsque mes médicaments vont prendre effet ou pour combien de temps." ("It's been 12 years since I was diagnosed at 38. At this time, I have a lot of difficulty with on/off periods. I cannot predict when my medication will take effect or for how long.")

"For my husband who has Parkinson's he lives with exhaustion, mild to moderate dementia. He has lost his math and problem solving skills. His balance is bad when he comes down from his pills and now relies on a walker. He cannot sleep in his bed because of restlessness and difficulty getting in and out of it. For me it was exhaustion and is now worry and sadness to see my husband disappear piece by little piece."

"Life with Parkinson's probably started a good 10 years before the diagnosis at age 43. As the disease has progressed, I've had to alter some parts of my life, I changed the type of nursing I did, then moved into an allied health care field, until that too became too much. At first the medication gave a smooth response, with improved mobility and speed of movement. As time goes on the response has been getting more and more erratic and the window of opportunity when I can move freely and not awkwardly is getting smaller and smaller. All the things I would like to do can't be crammed into that half-hour 3 or 4 times a day. I am constantly prioritizing and adjusting expectations. Some things are difficult to plan, as I can't predict if the meds will be working well or not. Life is rich because we work very hard to make it so. But it's not easy. I've been anxiously awaiting a medication delivery method that would allow for a more consistent rate of absorption and a smoother beneficial effect."

2.3 Patients' Experiences With Current Therapy

Overview

There are a wide number of symptomatic treatments that are available for PD. These include medications, surgical procedures, physiotherapy, occupational therapy and other support services. All of these treatments can have a significant impact on improving an affected individual's quality of life and should be available. Despite the increase in non-pharmacological treatments, an individual with Parkinson's becomes more reliant on their medication to maintain their ability to function as the disease progresses. A balance between the side effects of the medication and the benefit often becomes more difficult with time. Medication schedules become more complex and the timing of when medications are given becomes crucial.

Once the diagnosis of PD is made, the next decision is the type of treatment. The decision about initiation of pharmacologic therapy in PD patients should be tailored to the individual with the goal of reducing motor symptoms, and improving quality of life without causing side effects. There is no one medication which is recommended for treatment initiation, and factors that influence this decision include: symptom severity, whether the symptoms affect the dominant hand, embarrassment, ability to continue working and/or participate in activities such as hobbies, cost, and patient preference.³

Medication is the primary way in which the symptoms of Parkinson's are treated. As the disease progresses, increased medication or adjustments to medications are needed because the beneficial response to the medication begins to "wear off."

Since many of the motor symptoms of Parkinson's are the result of a lack of dopamine in the brain, most drugs used to treat Parkinson's are aimed at temporarily replenishing or imitating dopamine. Dopamine agonists are a class of drugs that stimulate parts of the brain that are influenced by dopamine. Dopamine agonists are the second most potent class of medication for treating Parkinson's disease. They are useful as an initial treatment or used in combination with levodopa in advanced stages of the disease. **Neupro (Rotigotine) belongs to this class of drugs.**

Side effects of current therapy

Survey respondents stated the most common side effects to Parkinson's oral medications included nausea, vomiting, dizziness (drop in blood pressure), sleepiness and visual hallucinations.

In addition, a major issue with the use of all oral medications used in the treatment of Parkinson's is both the predictable and unpredictable "wearing-off times" referring to the waning effect of their medication, causing a pronounced return of symptoms. This "wearing-off" of medications can mean that a person who has been living with Parkinson's for a few years may need to take medication at specific intervals throughout a 24-hour period to sustain a therapeutic effect. Some, due to the severity of symptoms, set alarms during the night to take their medication so they do not wake up completely frozen and unable to function in the morning. Others rely on a caregiver to administer nighttime medication, disrupting sleep for both partners.

³ Ibid Suppl. 4 – S10

75% of survey respondents reported that, with current or previous treatments, they experienced “off” periods or “wearing off” periods. Of these respondents, 29% reported “off” periods of a duration of less than 1 hour, 57% reported a duration of 1-2 hours, and 14% reported a duration of periods of 2-5 hours.

Therapy Access Issues

It is imperative that people living with Parkinson’s disease, take medication at the right time, every time to avoid “wearing off” period mentioned previously. Individuals can take upwards of 50 pills throughout the day and night, depending on the severity and progression of the disease. In our survey, 42% of individuals reported that they found it difficult to adhere to their medication dosing schedule.

In addition to dosing issues, out of pocket expenses are problematic. **83% of respondents cited additional drug costs as having financial impact.**

2.4 Impact on Caregivers

As Parkinson’s disease changes over time, so does the caregiver role. 67% of respondents indicated that caring for a loved one with Parkinson’s disease has impacted their Quality of Life either very significantly or significantly.

Time spent on caregiving was reported as being directly related to the stage of Parkinson’s disease of the patient, with some caregivers reporting only a few hours a week of caregiving, and other caregivers, typically spouses or adult children reporting that with advanced Parkinson’s patients, caregiving was a 24/7 task.

“I am caregiver for my husband. The disease is a physical and mental decline. The brilliant caring man I fell in love with no longer exists. It is a struggle to go out. He cannot be trusted to be on his own. His sleep disorder has affected my health. For me each day I face physical, emotional and financial strain.”

“My husband has PD and we must be constantly aware of the time so that he takes his medications on time. Also lately I have to actually supervise to make sure he actually takes the drugs, so I must be with him at least every 3-4 hours, therefore can't go far from home on my own.”

“It has affected me greatly. I am his sole caregiver and work full time. Due to my spouse's advanced Parkinson's I have less time for myself. Need to get everything ready (pills, lunch, etc.) before I leave for work. Social activities have changed a lot. Can't enjoy a night out with friends/family without having to get home early unless I make arrangements to have a "baby sitter." Can't do overnight stays or weekend getaway. Sleep deprivation, financial stress, etc.”

Caregivers reported the most challenging symptom of Parkinson’s disease for them was their loved one’s mobility impairment, including dyskinesia, tremors, freezing, lack of energy and strength, and speech impairment. Additionally, caregivers noted that hallucinations, anxiety, and depression were extremely challenging.

“Watching my husband struggle with dignity trying to do things he once did without thought. Now even the most simple task becomes a mountain to climb, depending on medication-timing. Not being able to stop the "train" running down the track looking to take yet another life-event

away from him-wishing it were me and not him facing this disease. Wishing each and every day a cure will be found to help so very many people”

“Poor balance and danger of falling----danger of choking as there is difficulty swallowing--also inability to speak-----loss of vocal abilities.”

Caregivers frequently noted that certain Parkinson’s treatments cause hallucinations and mood changes, sleep disruption and sometimes obsessive compulsive behaviour. These adverse effects add to the physical challenges of Parkinson’s disease and have a tremendous impact on the caregiver, causing them much stress and fatigue. **Caregivers go to great lengths in ensuring medications are taken properly and on time. It’s not uncommon for caregivers to wake up during the middle of the night to help administer medications so the person with PD can sleep and prevent severe mobility challenges the next morning.**

Section 3 — Information about the Drug Being Reviewed

3.1 Information Gathering

To inform this section of the submission, Parkinson Society Canada, spoke with five Movement Disorder Specialists, neurologists with special training in movement disorders including Parkinson’s disease, about their clinical experience with Neupro. Parkinson Society Canada also conducted one-on-one interviews with ten Canadians using Neupro to treat their Parkinson’s symptoms.

3.2 What Are the Expectations for the New Drug or What Experiences Have Patients Had With the New Drug?

Neupro delivers a treatment similar to oral dopamine agonists by improving various PD motor symptoms such as tremor, slowness, rigidity, and dyskinesia. Neupro is a once-a-day transdermal patch which provides continuous medication for 24 hours. It is shown to improve sleep, reduce “off periods,” improve morning periods (reduced freezing, less rigidity so people can function when they get up), and other non-motor symptoms such as pain. This has an enormous impact on the quality of life for people living with Parkinson’s. It is additionally helpful to those with gastrointestinal and swallowing issues, which affect many people with PD, because the medication is delivered directly to the blood stream, rather than having to be swallowed/ingested. As a once-a-day patch, it also helps with compliance, leading to improved health outcomes. Oral dopamine agonists do not provide any of these advantages. To date, Neupro is the only Parkinson’s treatment that is both non-invasive and provides continuous flow of medication. The only other Parkinson’s therapy that provides continuous medication is Duodopa, which has shown great success, though it requires a gastrostomy and is intended only for those with advanced stages of Parkinson’s disease.

Negative effects of Neupro are similar to oral dopamine agonists and include: dizziness, nausea, impulse control issues, leg edema, daytime somnolence, and hallucinations. The only reported negative effect specific to Neupro is a slight skin irritation at the site of application, though most users of the treatment are willing to tolerate this. Impulse Control Disorders (ICDs) associated with dopamine agonists are a concern with all dopamine agonists. However, individuals and their caregivers are well-informed and are monitored for symptoms. ICDs can be corrected by lower dosages or removal from the dopamine agonists as the effects are not permanent. This treatment is not recommended for people with a history of hallucinations as dopamine agonists can exacerbate this issue.

Feedback directly from individuals taking Neupro and their caregivers:

“Neupro has decreased the occurrences and severity of my tremors, which has resulted in better mobility and greater ease in falling asleep. I have noticed less occurrences of freezing and although I still have some downtimes, they are not as severe or as long as they were before using Neupro.”

“The neurologist recommended Neupro as all other medication did nothing for my father. He was at the point where his tremors prevented him from talking, moving, and eating. Neupro was prescribed to him as his “last hope”. While I have seen some obsessive behaviour – my father would occasionally try to take apart his wheelchair and sunglasses for no reason, these effects are acceptable given that without Neupro, he wouldn’t be able to function. Without Neupro, my father would probably be dead right now.”

“Despite the annoyances caused by skin irritation, Neupro has improved my life noticeably. I don’t have to worry about waking up in the middle of night to take more of my medication. Related to sleep, I have noticed that I’m not waking up as often due to tremors and joint pains.”

“I no longer wake up from nightmares. My sleep has significantly improved and I no longer suffer from sharp pains in my legs and loud ringing in my ears. I also have no off periods whatsoever. I take the patch at around 10 in the morning and it lasts me the whole day and is easy to manage with other medications.”

“I noticed great improvement in my ability to multitask and rigidity does not seem to be an issue while taking it. It has also helped with sleep slightly - will not wake up due to sporadic pain & restlessness in my legs.”

“I would highly recommend Neupro to anyone with Parkinson’s. The patch has greatly improved my wife’s life – I could not imagine how my wife could live with Parkinson’s without it. It has really helped with her joint pain - her joints don’t hurt as much as they used to and while the patch causes skin irritation – she doesn’t consider it much of an issue - it’s just something you’re going to have to live with while using one.”

“I see overall improvements in my resting tremors and muscle stiffness. I sleep better at night. I’m not waking up in the middle of the night due to the wearing down of my medication. My off periods have improved greatly since going on Neupro but are not at the level I would like them to be - but a lot better than the medication I took prior. I have minor skin irritations but I’m willing to live with it. It has really improved my quality of life.”

Similar to oral dopamine agonists, Neupro has been shown to improve Parkinson’s motor symptoms. Due to the fact that Neupro provides continuous medication directly into the blood stream, it also offers additional advantages including greater steadiness throughout the day, reduced “off periods”, improved self-management, greater morning mobility and improved sleep, all of which have a huge positive impact on both the caregiver and individual living with Parkinson’s. While Neupro is not recommended for everyone, particularly those with a history of hallucinations, it is a good treatment option and one that is widely used and well received in Europe, parts of Asia, and in the United States. **It would be very beneficial if Canadians also had access to Neupro as a treatment option to improve their Parkinson’s symptoms and disease management.**