CADTH

CADTH COMMON DRUG REVIEW

Patient Input

ocrelizumab (Ocrevus)

Hoffman-La Roche Limited

Indication: Primary progressive multiple sclerosis

CADTH received patient input for this review from:

Multiple Sclerosis Society of Canada

November 16, 2017

Patient Group | Multiple Sclerosis Society of Canada

1. About Your Patient Group

The Multiple Sclerosis Society of Canada provides services to people with multiple sclerosis, their families and caregivers, and funds research to find the cause and cure for the disease. The mission of the MS Society is to be a leader in finding a cure for multiple sclerosis and enabling people affected by MS to enhance their quality of life. The mission is reflected in the organization's daily activities, which aim to support research into the cause, treatment and cure of MS, and provide programs and services that assist people with MS and their families. Since 1948 the MS Society has contributed over $140 million towards MS research. This investment has enabled the advancement of critical knowledge of MS, and the development of a pipeline of exceptional MS researchers.

2. Information Gathering

The MS Society of Canada launched an online survey posted to its national website www.mssociety.ca main page and Facebook page in both English and French. Some patient feedback provided in this report was collected in a previous MS Society of Canada online survey (launched May 24, 2017 and concluding July 7, 2017 on the same channels as described above) aimed to acquire qualitative data on quality of life and personal experiences with progressive MS. The Ocrevus for treatment of primary progressive MS survey was posted October 18, 2017 and closed November 8, 2017. In total we received 358 responses. Based on the survey comments, respondents appear to be from Canada however country of origin was not a survey question.

In total we received 358 completed surveys; 230 English respondents and 128 French respondents. Of those who completed the survey, 227 were women and 119 were men (some respondents skipped the question about gender). Over 90% of respondents identified as living with multiple sclerosis (314), and 44 responded as caregivers. The majority of respondents (208) were between the ages of 45-64; 68 respondents were between the ages of 35-44; 53 respondents were over 65 years of age and 20 respondents were between the ages of 25 and 34.

The majority of respondents (186) identified as being diagnosed with primary progressive multiple sclerosis, 55 with relapsing-remitting MS, 50 with secondary progressive MS, 19 respondents did not know their type of MS, and 4 respondents had a clinically isolated syndrome (possible MS). Most respondents had been living with primary progressive MS for between 5 and 10 years (72), the remainder between 11 and 20 years (41), between 2 and 4 years (32), less than 2 years (22) and 20 years or more (14). Respondents who identified a diagnosis other than primary progressive MS were not prompted to complete the full survey as the patient feedback request for Ocrevus indicated for relapsing multiple sclerosis had taken place in June 2017, however they were invited to provide feedback to the following statement: In June 2017 the MS Society submitted patient feedback based on survey results related to Ocrevus and relapsing MS. The purpose of this survey is to obtain patient feedback related to Ocrevus and primary progressive MS. If you are affected by MS, we invite you to share any feedback you may have about Ocrevus for the indication of primary progressive MS.

Feedback received in reaction to this statement was diverse and ranged from not knowing about Ocrevus to comparisons between Health Canada's regulatory process and the FDA's regulatory process.

3. Disease Experience

Primary progressive MS is characterized by a gradual but continuous worsening of the disease over time, without a (PPMS) preceding relapsing course. Approximately 15% of people diagnosed with MS are diagnosed with PPMS. PPMS differs from the more commonly diagnosed relapsing-remitting MS (RRMS) which makes up 85% of all MS diagnoses, in several key ways: it tends to be diagnosed after the age of 40, affects both genders equally, more lesions (damage) are located on the spinal cord and it is almost never diagnosed in childhood. People with progressive MS are more likely to need a wheelchair (more issues with mobility) and to have significant neurological disability. Symptoms include fatigue, cognitive impairment, weakness, spasticity, tremor, poor

coordination, bladder and bowel problems, sexual dysfunction, depression, pain, dizziness, visual issues and issues with speech and swallowing.

- *My quality of life is extremely affected. I am a slave to this disease. Very hard to look after myself because of the monster that has taken over our lives. So tired bored with life. Envious of the freedom my friends have.*
- *Quality of life gradually, often precipitately, disappears with increasing disability, as participation in the outside world becomes limited and social isolation ensues.*
- *I lost my job, ability to enjoy sports I love and outdoors, I lost my independence and dignity.*
- *I am unable to participate in many physical activities I used to. I am unable to work in the profession I love.*
- *I have gone from being very independent having mobility and able to get around to having no mobility and having to rely on family and caregivers 24/7.*

4. Experiences with Currently Available Treatments

Up until approximately twenty years ago there were no disease modifying treatments for multiple sclerosis, regardless of disease course or phenotype. There are now 14 Health Canada approved disease modifying therapies (DMT) on the market indicated for relapsing forms of MS. None of the DMTs have been approved for primary progressive MS and no drug to date, with the exception of Ocrevus, has shown therapeutic benefit in primary progressive MS. Approved therapies for relapsing MS largely focus on targeting inflammation in the CNS, and have demonstrated to be safe and effective in treating relapsing MS. Inflammation plays a smaller role in progressive MS, which is characterized primarily by neurodegeneration and reduced immune cell activity.

Although uncommon, some survey respondents indicated using one or more of the DMTs indicated for relapsing MS (49) and some were presently, or had previously been treated with an immunosuppressant (6) and 1 respondent had been treated with a medication used off-label (rituximab, the chimeric version of ocrelizumab). About 80% of people with primary progressive MS had no previous treatment with a DMT (250). The remainder (12) had been treated with a symptom management medication (not a DMT) indicated for walking improvement, fampridine. In rare cases of very rapidly progressive MS, typically occurring in patients under age 40, physicians may prescribe immunotherapy agents such as mitoxantrone or cyclophosphamide.

Of those who had used a DMT, only 15 felt the medication was beneficial while 26 stated the medication was not helpful, or they did not know if it was helpful. Not all respondents answered this question. A small number of respondents commented on experienced side effects (24) all of which typical, and known side effects of MS medications. Side effects were reported as being well-managed with, or without treatment (16), had diminished on their own (6) or were not well-managed (10) and included nausea, skin reactions, fatigue, headaches, infections, hair loss and shortness of breath. Treatments currently available to patients with primary progressive MS largely include symptom management medications, complementary and alternative therapies and many non-medicinal therapies and techniques, such as physiotherapy, physical activity and other types of rehabilitation.

- *This is a devastating disease. All therapies that show even a little promise need to be made available to patients.*
- *I suffer from primary progressive MS. It is unfair that there are no treatments available for people with progressive MS. When my doctor told me about Ocrevus and that it was an option for me, I was hopeful. Then Health Canada announces Ocrevus is for relapse remitting MS patients, only. All my hopes were dashed. My condition continues to slowly deteriorate. I ask that Health Canada allow me and people like me to access to Ocrevus. It is the only hope available to us.*
- *The perpetual loss of function that I have experienced since 2000 due to PPMS has had a devastating effect on my life. I have lost my job and my independence and most of all my identity. This would be the first disease modifying drug to help those suffering from PPMS. You have the power to give us hope where it has not existed before . Please help us by approving this drug.*

5. Improved Outcomes

Ocrevus will mark the first ever Health Canada approved DMT for primary progressive MS. In total 21 respondents stated that their health care provider suggested Ocrevus as treatment for their MS once approved by Health Canada. Other respondents (121) indicated their health care provider had not mentioned Ocrevus as a future treatment for their MS. When asked why their health care provider recommended Ocrevus as treatment for their MS once it is approved by Health Canada, responses included 'it is the only treatment available for primary progressive MS' (14) and that it would 'help slow the disease progression' (7). A number of respondents skipped this question.

- *I have been living with the effects of PPMS since 2000. Both legs and one arm are totally useless while the other arm is losing function. I do not have the strength to keep my body upright while sitting and my vision gets more blurry each year. I do not have the strength in my chest muscles to cough or blow my nose in order to expel anything. There has been no disease modifying drug available to me during all this time. If this drug has the potential to slow down or even stop the progression of this ugly insidious disease then all who suffer from it must be given the opportunity to have it.*

A list of common and serious adverse side-effects was provided to those without experience with Ocrevus and based on the adverse side-effects, they were asked if they would be willing to trade the risks with the perceived benefit of the drug. In total 175 individuals responded; 103 respondents said they would be willing to trade the risks for the perceived benefits, 24 said no they would not trade the risk and 15 were not sure. The main reasons provided for those not, or unsure of trading the risks for the perceived benefits of Ocrevus were the side effects and lack of long term safety data.

6. Experience with Drug Under Review

In total only 3 patients had experience with the drug, and it would have been received through a clinical trial and 178 respondents said they had no experience with Ocrevus. Of those being treated with Ocrevus, 1 respondent said they felt Ocrevus had helped their MS, 1 stated it had not helped and the third respondent did not know if it had helped. The patient who stated Ocrevus had helped provided the reason of 'easier drug administration'.

- *This drug has brought improvements to my quality of life I see hope finally.*

Experiences with side-effects of Ocrevus varied between the three patients; 1 patient indicated they experienced nausea, headaches, fatigue and pruritis, whereas the other 2 patients treated with Ocrevus stated they had no side-effects at all. Compared to previous treatments 1 patient stated Ocrevus was more effective in treating their MS, the remaining 2 patients treated with Ocrevus did not know if it was more effective. Two of the three patients listed challenges associated with treatment with Ocrevus, which included, getting to the infusion clinic (2) and high cost (1). Concerns related to treatment with Ocrevus were high cost (2), federal, provincial or territorial public coverage (2), common side-effects (1), serious adverse effects (1) and lack of long term safety data (1).

7. Companion Diagnostic Test

Hepatitis B Virus Screening, Vaccinations (administer all necessary immunizations according to immunization guidelines at least 6 weeks prior to initiation) and Infection Assessment (before every infusion) are required, this may include testing for the John Cunningham virus, which can cause progressive multifocal leukoencephalopathy (PML). We did not request information about companion diagnostic testing in the survey.

Appendix 1: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? **NO**

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? **NO**

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.
   As the marketing company for Ocrevus, Roche would have direct/indirect interest

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Bayer	X			
Biogen				X
EMD Serono				X
Novartis				X
Roche				X
Pfizer			X	
Genzyme – A Sanofi Company			X	
Allergan	X			
Teva Neuroscience		X		

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

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Position: Information Curator
Patient Group: MS Society of Canada
Date: November 9, 2017