CADTH

CADTH COMMON DRUG REVIEW

Patient Input

ozanimod (TBC)

(Celgene Inc.)

Indication: Multiple Sclerosis, relapsing - remitting

CADTH received patient input from:
MS Society of Canada

September 16, 2020

CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**Ozanimod for treatment of relapsing remitting multiple sclerosis**
Name of the Patient Group	**MS Society of Canada**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

The Multiple Sclerosis Society of Canada provides information, support and advocacy to people affected by MS, and funds research to find the cause and cure for the disease, bringing us closer to a world free of MS. Since 1948 the MS Society has contributed $200 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. The ozanimod for treatment of relapsing MS survey was posted August 4, 2020 and closed September 4, 2020. Due to the timing of multiple calls for patient feedback for two new drug submissions (ozanimod and ofatumumab), the survey sought feedback for both medications however provided separate tracks to obtain feedback for each medication separately. Based on the survey comments, respondents appear to be from Canada however country of origin was not a survey question.

In total we received 69 completed surveys; 61 English respondents and 8 French respondents. Of those who completed the survey, 52 were women and the rest were men. Over 90% of respondents identified as living with multiple sclerosis (63), and 4 responded as caregivers. The age ranges were relatively equally distributed with a slightly higher response rate from those aged 31-40 (23). The remaining age ranges reported were: 41-50 (18 respondents) and 51-60 (17 respondents).

The majority of respondents (49) identified as being diagnosed with relapsing-remitting MS, 3 with secondary progressive MS, 5 with primary progressive MS, 4 respondents did not know their type of MS, and 2 respondents had clinically isolated syndrome (possible MS).

3. Disease Experience

Multiple sclerosis is an unpredictable, often disabling disease of the central nervous system. MS occurs because of damage to myelin, the protective covering wrapped around nerve fibres (axons). Damaged myelin causes an interruption or loss of the usual flow of nerve impulses along the axons resulting in a wide variety of symptoms. Approximately 85-90% of people are diagnosed with a relapsing-remitting (RRMS) course, wherein they experience 'attacks' caused by bouts of inflammation in the CNS, followed by full or near complete recovery. Over time, about half of these individuals are likely to transition to secondary progressive MS, a form of the disease that steadily worsens over time and is marked by fewer or no attacks and advanced disability. Amongst those with RRMS, some will present with highly active disease, characterized by frequent relapses with incomplete recovery, and/or high radiological burden of disease, rapid accrual of disability after disease onset, with otherwise typical features of MS. Patients with highly active disease respond to higher efficacy DMTs (second-line) compared with low-moderate efficacy treatments. Higher-efficacy treatments have been shown in phase three trials to effectively reduce annual relapse rate (AAR), accumulation of disability and brain atrophy significantly more than low-moderate efficacy treatments. Early treatment with the most effective DMT that best meets the clinical presentation of the patient is imperative to manage the disease and protect brain health.

The remaining 10% of people are diagnosed with primary-progressive MS, characterized by a steady worsening of disease that is not preceded by a relapsing course. The most common symptoms of MS include fatigue, difficulty in walking, visual impairment, cognitive difficulties, depression, bladder problems, and pain. Other symptoms may include issues with balance, sexual dysfunction, spasticity, tremor, weakness and difficulty speaking and swallowing. MS can occur at any age, but is usually diagnosed between the ages of 15 to 40, peak years for education, career- and family-building.

Depending on the type and severity of the symptom, an individual's quality of life can be greatly impacted. The episodic nature of multiple sclerosis creates unique employment issues – many people are unable to maintain stable jobs or remain in the workplace due to relapses, symptoms, medication side-effects and disability progression. In addition to employment, MS can interfere with, or introduce a barrier to education, physical activity, family commitments, interpersonal relationships and social and recreational life.

Caregivers play an instrumental role in the overall care management plan of people living with MS, these roles range from providing emotional support and assistance with medication administration, to helping with activities of daily living such as personal care, feeding and transportation to and from appointments.

4. Experiences With Currently Available Treatments

Treating MS as early as possible following diagnosis with a disease modifying therapy (DMT) is associated with better long-term outcomes than delaying treatment. There are 15 DMTs in Canada approved for relapsing forms of MS however five of these medications are reserved as second-line therapies for patients who have not responded to, or are unable to tolerate first-line therapies for MS. Two-thirds of all respondents reported being treated with a DMT (67%). Depending on the DMT recommended by the prescribing neurologist, patients may currently choose from injected, oral or infused medications and dosing schedules ranging from daily to a two-week period per treatment year. There is an increasing trend towards the use of oral and infused medications as opposed to the injected DMTs, as reported through patient feedback surveys. With that said, the following DMTs were identified as the current treatment by survey respondents: Ocrevus (11), Tecfidera (7), Aubagio (7), Tysabri (5), Gilenya (4), Copaxone (4), Mavenclad (3), Avonex (2), and Rebif (2).

Treatment reimbursement criteria in Canadian provinces and territories requires that patients demonstrate clinical failure on at least one or more low-moderate efficacy treatment prior to initiating treatment with a high-efficacy agent at the time of diagnosis. Exceptions may be made for patients who present with and where a prescribing neurologist is able to justify induction therapy versus escalation (initiate a low-moderate efficacy treatment and monitor for response).

Based on previous CADTH patient feedback reports, the most commonly reported side-effects from DMTs are generally known and expected, and include injection site reactions, flushing, hair thinning, skin rash or hives, joint and/or musculoskeletal pain, gastrointestinal symptoms, increased risk of infections and flu-like symptoms. Due to the mechanism of action of most high efficacy agents, there is an increased risk of a more serious infections, including a rare brain infection, progressive multifocal leukoencephalopathy PML, a rare and potentially fatal side effect reported with treatment with a small number of DMTs (including Tysabri, Gilenya and Tecfidera).

There is a growing number of high-efficacy DMTs, with varied administrations, dosing schedules and decreased monitoring requirements, factors that are consistently identified as priorities for patients when selecting a DMT. Patients place high value in having a choice to select the administration, dosing schedule, side-effect profile and level of medication monitoring that best fits their lifestyle and personal preference. Without choice, adherence becomes an issue, resulting in decreased clinical benefits and health outcomes.

5. Improved Outcomes

Ozanimod is the only S1P receptor modulator that does not require first-dose monitoring. Patients treated with current S1P receptors, must take the first dose under medical supervision for up to six-hours, to monitor for potential adverse cardiac events (e.g. bradycardia). Instead, ozanimod offers patients a dose titration regimen, negating the requirement to take time away from work, school or other commitments. This fills a significant gap in MS treatment for patients who are recommended to be treated with a S1P receptor modulator as there is no requirement for first-dose monitoring, suggesting ozanimod has a favourable safety-profile. In addition, high efficacy medications have the potential to reduce the financial burden to health and social systems through fewer relapses requiring hospitalization, decreasing work absenteeism, and allowing people to remain active within their social networks.

6. Experience With Drug Under Review

The MS Society did not receive feedback from patients with current or previous experience with the drug ozanimod which is typical for our population when responding to our CADTH surveys. Over half, 60% (41) of all respondents had not heard about ozanimod as a new treatment for relapsing-remitting MS by their neurologist. Information related to mechanism of action, administration and dosing of ozanimod was provided in the introduction of the survey and we asked the following question about risks versus perceived benefits:

Given the following side-effects (most common to more serious), would you be willing to take ozanimod? Common: upper respiratory tract infections; low blood pressure when you stand up; back pain; elevated liver enzymes; painful and frequent urination (urinary tract infection); high blood pressure. More serious: Liver problems; Increased blood pressure; Breathing problems; Macular edema (swelling in the eye); Swelling and narrowing of blood vessels in your brain; Severe worsening of multiple sclerosis (MS) after stopping ozanimod; Allergic reactions.

Of those who answered this question, the majority (28) said they would not take the risk, 27 did not know if they were willing to trade the risks for perceived benefits, and 7 said they would be willing to take the risk.

7. Companion Diagnostic Test

More than two-thirds of the respondents (65%) reported the requirement of pre-treatment laboratory tests or post-treatment monitoring. Depending on the treatment, testing and monitoring may include (but is not limited to) CBC with lymphocyte counts, liver enzyme, thyroid function, screening for infections including Hepatitis B and C, HIV, TB, VZV as well as risk of PML (obtain JC virus antibody index) prior to treatment,

cardiac assessment, pregnancy test and immunization status. Half of the respondents indicated that they do not feel that pre-treatment tests or ongoing monitoring are challenging for them to fulfil. Those who did report challenges included time away from work, cost associated with pre-treatment vaccinations and delays in blood work results. While other similar therapies involve first-dose monitoring, taking time away from work, school or other commitments, ozanimod follows a drug titration regimen that allows the patient to remain at home for their first dose.

8. Biosimilar

N/A

Appendix: Patient Group Conflict of Interest Declaration

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

   No

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

   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.

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

Name: Jennifer McDonell
Position: Information Curator
Patient Group: Multiple Sclerosis Society of Canada
Date: September 11, 2020