

CADTH COMMON DRUG REVIEW

Patient Input

CLADRIBINE (Mavenclad)

(EMD Serono, a Division of EMD Inc., Canada)

Indication: Multiple Sclerosis, relapsing

CADTH received patient input from:

Multiple Sclerosis Society of Canada

December 22, 2017

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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. The Mavenclad for treatment of relapsing-remitting MS survey was posted December 4, 2017 and closed December 18, 2017. Based on the survey comments, respondents appear to be from Canada however country of origin was not a survey question.

In total we received 190 completed surveys; 179 English respondents and 11 French respondents. Of those who completed the survey, 138 were women and the rest were men. Over 90% of respondents identified as living with MS (173), and 17 responded as caregivers. The age ranges were relatively equally distributed with a slightly higher response rate from those aged 25-44 (54). The remaining age ranges reported were: 45-54 (43 respondents), 25-34 (37 respondents) and 55-64 (33 respondents).

The majority of respondents (134) identified as being diagnosed with relapsing-remitting MS, 18 with secondary progressive MS, 9 with primary progressive MS, 8 respondents did not know their type of MS, and 5 respondents had a clinically isolated syndrome (possible MS). Most respondents had been living with MS for between 5 and 10 years (48), the remainder between 2 and 4 years (36), 11 and 20 years (35), less than 2 years (27) and 20 years or more (23).

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 course, wherein they experience 'attacks' caused by bouts of inflammation in the CNS, followed by full or near complete recovery. Within approximately 10 to 20 years, 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. 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.

The following quotes were submitted by caregivers of people living with MS.

Demanding nature of caring for a patient with a chronic illness is harder on the care giver than people realize, it is a 24/7 commitment.

Limits capacity for caregiver to enjoy their own life.

Families count on these medications. It is a matter of survival for many.

Cladribine should be approved as a first line treatment for MS. There is a huge unmet need for a highly effective drug to be indicated as a first line drug so treatment can be highly effective from the beginning.

4. Experiences With Currently Available Treatments

There are 15 disease modifying therapies (DMTs) approved for relapsing forms of multiple sclerosis. Of these, five (including Mavenclad) are reserved as second-line therapies for patients who have not responded to, or are unable to tolerate other available first-line treatments for MS. The majority of respondents were taking a DMT (102), and 68 were not. About half of all patients felt that their current DMT was effective in managing their disease (48), 31 did not know if their medication was effective, and 18 felt their medication was not effective at all. The following DMTs were listed, Copaxone (25), Tecfidera (22), Gilenya (14), Aubagio (10), Tysabri (6), Avonex (6) and Lemtrada (6). Other than one case of a rare brain infection call 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) all other patient reported side effects from treatment with current DMTs were common and expected (injection site reactions, flushing, hair thinning, skin rash or hives, joint and/or musculoskeletal pain, gastrointestinal symptoms and flu-like symptoms). Mechanism of action and administration differ between available DMTs; some of the more recent Health Canada approved treatments have reduced dosing schedules, which can improve adherence, provide additional freedom to travel, make long term plans and less time away from the workplace due to frequent medical appointments for drug administration (infusion) or side effects that can affect people post-administration (need for sick days). Administration of the drug (oral, injected, infusion as well as dosing schedule frequency) was reported as 'very important' by over 65% of all respondents (65), approximately 32% (31) said they didn't care about administration as long as the medication worked and only one person said administration wasn't important. Most respondents (92) reported that they took their medication as prescribed by their physician. Two respondents said they forget their medication from time to time.

5. Improved Outcomes

Mavenclad is the only second-line, short-course oral treatment indicated for MS that does not cause continuous immunosuppression. Immunosuppression is a known adverse side effect resulting from treatment with certain other MS therapies. Additionally, the mode of administration - oral is important for increasing independence for the individual, relying less on caregivers as well as reducing the need for additional time off work (and for caregivers) to travel to clinics for infusions. The following are patient quotes submitted as part of the survey. Given the number of MS medications now available on the market, patient choice continues to be strongly reinforced by people affected by MS.

It is important to patients to have a number of options to treat their disease, and have the help to acquire treatment, if a specific treatment is beneficial to treating the disease, it should be offered as an option to patients.

We need to be able to provide multiple different therapies to people with MS because people react differently to the same medication. Also because there is no "one size fits all" for MS we need to have different meds available.

More choices for people bring better outcomes. What doesn't work for one may work for another. When you've exhausted all other drugs a new one can bring hope where there is none. Cost should not have to be a determining factor in what therapy is chosen.

I think any drug is worth trying and everyone is affected differently. I am so happy to hear so many drugs are available to try out. It at least gives us an opportunity to better our lives from this disease.

At this point since there is no cure, all available medications should be available to those with MS.

Because each person responds differently to meds, and each MS patient is unique, I think it is important that different avenues of treatment are available.

Nothing else has helped me so far. I need something new to try.

I feel everyone has the right to have all options available to them for any chronic disease. It takes trial and error of medications to discover which one will improve ones quality of life.

6. Experience With Drug Under Review

The MS Society did not receive feedback from patients who have current or previous experience with the drug Mavenclad. Over 95% (94) of all respondents had not heard about Mavenclad as a new treatment for relapsing-remitting MS by their physician. We asked the following question about risks versus perceived benefits (using the Health Canada Mavenclad product monograph):

Based on clinical trial data, the most common side effects of Mavenclad include: nausea, headache, cold sores (oral herpes), rash, thinning or hair loss, fever, abdominal pain, toothache, flu and flu like symptoms, cold symptoms, bronchitis or other chest infections, symptoms of gastroenteritis (diarrhea, vomiting, abdominal pain), back pain, anxiety, vaginal infection. More serious side effects : reduction in the number of certain white blood cells, with symptoms such as infections, feeling unusually tired, fever, aches, pain and flu-like symptoms. Shingles, with symptoms such as localized 'band' of severe pain and blistering rash, typically on one side of the upper body or the face. Other symptoms may be headache, burning, tingling, numbness or itchiness of the skin in the affected area, feeling generally unwell or fever in the early stages of infection. Very rare serious side effects : tuberculosis, with symptoms such as cough that does not go away, fever or loss of weight.

Would you be willing to trade the risk of the adverse side effects of Mavenclad for the perceived benefits of the drug? Of those who answered this question, the majority (59) did not know if they were willing to trade the risks for perceived benefits, 43 said they would not take the risk and 36 said they would be willing to take the risk.

7. Companion Diagnostic Test

We did not gather information in this survey on pre-treatment laboratory tests or post-treatment monitoring.

8. Anything Else?

We recommend that this review take into consideration that one medication may not meet the needs of all patients living with a certain disease or condition. This is especially true for a disease like MS where no two patients have the same course of the disease and/or respond in the same way to the same medication showcasing the great variability in this disease.

MS impacts all Canadians - not only the affected individuals, but also their families. People living with MS are mothers, fathers, sisters, brothers, children, and friends. They are people who are impacted by this disease every day, every hour, and every minute. The needs of people with MS and their families should be at the centre of health and drug policy decisions. Therefore, their perspectives and experiences should be a top priority in this review.

Appendix: Patient Group Conflict of Interest Declaration

- Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.
No.
- 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.
- 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
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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 Date: December 18, 2017