

Patient Group Input to CADTH



Section 1 — General Information

Name of the drug CADTH is reviewing and indication(s) of interest	Therapeutic Review — Drug Therapies for Relapsing-Remitting Multiple Sclerosis
Name of patient group/Author of submission	Multiple Sclerosis Society of Canada
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1.1 Submitting Organization

The Multiple Sclerosis Society of Canada (MS Society) is the only national voluntary organization in Canada that supports both MS research and services for people with MS and their families. Its mission is to be a leader in finding a cure for multiple sclerosis and enabling people affected by MS to enhance their quality of life. That mission is reflected in the organization's two major programs, which provide hope for the future through the support of MS research into the cause, treatment, and cure of the disease, and hope for today through services that assist people with MS and their families. An estimated 13,500 volunteers carry out service programs, fundraising events, public awareness campaigns, and government relations activities. The MS Society has a membership of 20,500 and is governed by a National Board of Directors comprised of 14 volunteer members who are elected annually. The seven regional divisions and nearly 120 chapters are also governed by elected volunteer boards of directors.

1.2 Conflict of Interest Declarations

a) *We have the following declaration(s) of conflict of interest in respect of corporate members and joint working, sponsorship, or funding arrangements:*

In 2012, the MS Society received educational grants from the following companies: Bayer, Biogen Idec, EMD Serono, Novartis, Pfizer, Genzyme – A Sanofi Company, Allergan, and Teva Neuroscience. The contributions totalled less than two per cent of the MS Society's overall revenue and are subject to strict policies that prevent any control or influence by the donor on MS Society decision-making.

b) *We have the following declaration(s) of conflict of interest in respect of those playing a significant role in compiling this submission:*

Nothing to declare. This submission was developed and prepared solely by MS Society staff.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

Information in this section was obtained from publicly available information about the impact of MS, as well as from a specific MS Society survey conducted in February 2013, for the purpose of gathering data for patient input in the CADTH Therapeutic Review of MS disease-modifying therapies. This survey was conducted in both English and French, with the English version available from February 4 to March 1 and the French available from February 8 to March 1. Of note, one can assume that disease-modifying therapies is a top priority for people living with MS, as this was the largest response the MS Society has received to date for patient input specific to disease-modifying therapies following a call for feedback. In less than one month, 1,345 individuals had participated in the survey.

A link to this survey was posted on the MS Society website and sent via usual MS Society communications channels to members — predominantly those with MS, and their families. Respondents with MS answered a series of questions about themselves, how MS impacts them, their experience with existing drug therapies, and their expectations of future therapies. Caregivers answered a similar but shorter series of questions.

In this survey, 79.6% were women and the rest were men. Most respondents had MS (91.2%), whereas the rest identified themselves as caregivers (8.8%). Respondents reported ages ranging from less than 20 to more than 70, although the majority were between the ages of 41 to 60. Respondents were from all the provinces and territories. Ontario, Quebec, and Saskatchewan had the largest percentage of respondents at 26.2%, 19.5%, and 17.9%, respectively. Regarding length of diagnosis, this varied from less than 2 years to more than 20 years, with the highest percentage (28.9%) being diagnosed between 11 years of age to 20 years. The type of MS reported by respondents had representation in each of the following categories: possible MS (clinically isolated syndrome), relapsing-remitting, secondary-progressive, primary-progressive, and “do not know.” The highest percentage, however, was relapsing-remitting, with 70.1% of respondents reporting this type.

Limitations to the survey: It should be noted that this survey is not population based and cannot be interpreted as reflecting the views of all people with MS or caregivers in Canada. Instead, it provides the views of those who chose to answer the survey at a particular point in time.

2.2 Impact of Condition on Patients

MS is an unpredictable, often disabling disease of the central nervous system, the latter of which is composed of the brain and spinal cord. The disease attacks the myelin, a protective covering wrapped around the nerves of the central nervous system. When this happens, the usual flow of nerve impulses along nerve fibres (axons) is interrupted or distorted. The result may be a wide variety of MS symptoms, depending upon what part or parts of the central nervous system are affected. Common symptoms are difficulty in walking, fatigue, difficulty with coordination of arms or legs, loss of vision, numbness or tingling, memory or attention problems, and pain. These symptoms were validated in the survey, with respondents reporting all of these effects in varying degrees, and with fatigue reported the most (84.7%).

Respondents to the MS Society survey were asked which symptoms had major impacts on their lives. As aforementioned, people reported via the survey that there were multiple effects that impacted their lives, with the following mentioned most frequently as having major impacts: fatigue (76.6%), difficulty in walking (51.6%), memory or attention problems (39.1%), bladder problems (37.6%), numbness or

tingling (36.9%), and pain (35.8%). Additionally, in the comments, heat intolerance and sensitivity were reported.

In response to a question in the survey, 93.9% of respondents said MS had negatively affected their lives “somewhat” (48.4%) to “a lot” (45.5%). Only 6.5% said it had not affected their lives at all. Respondents did report being affected in their day-to-day lives in varying degrees, from “somewhat” to “a lot,” in all of the categories listed: work, sleep, attend school, socialize, mobility, live independently, drive a car, self-care, family relationships (partner or children) and recreational activities. Of note, 81% of respondents said their work lives had been affected from “somewhat” (25.6%) to “a lot (55.4%).” This is an important consideration, as employment affects many aspects of an individual’s life and, in particular, their and their family’s financial situation. Other aspects of day-to-day life that had been much affected were recreational activities (48.3%), sleep (34.1%), and mobility (33.4%). With socializing and recreational activities combined, respondents were affected 83.7% at least somewhat in these categories.

Some respondents commented about improvements in their MS condition since being treated for chronic cerebrospinal venous insufficiency (CCSVI), and others commented that these improvements were not always sustained. Some respondents commented that they only use alternative therapies (e.g., diet, exercise, vitamins, acupuncture) to manage their disease.

In the survey, respondents were offered the chance to comment about how MS had affected their lives. Here is a sampling of comments:

- *“I used to play sports like hockey, run, and hike. My life is changed dramatically because of MS.”*
- One respondent commented that they wanted to let people know that MS has affected *“Having children. The need to be off medication while attempting to get pregnant and while pregnant and breastfeeding. Or choosing to have children due to the medications and the disease itself.”*
- *“It has inhibited my ability to continue to pursue my passions (equestrian and playing music), which would otherwise help me cope with the condition.”*
- *“Even though many of my symptoms fluctuate between good days and bad days, it is a draining and never-ending challenge to live with MS and never, ever have one single moment without it. 24 hours a day, 7 days a week, 365 days a year, it is my silent shadow, and impacts every single aspect of what used to be a very happy, vital, and normal life.”*
- *“The unpredictable aspect is paramount since no 2 days are the same and no 2 hours are the same.”*

2.3 Patients’ Experiences With Current Therapy

Health Canada has approved seven therapies that reduce the frequency and severity of MS relapses. Some of the drugs also have some data to support that they may have an effect on slowing the accumulation of disability over time. They are: AVONEX (interferon beta-1a), BETASERON (interferon beta-1b); EXTAVIA (interferon beta-1b); COPAXONE (glatiramer acetate); GILENYA (fingolimod); Rebif (interferon beta-1a), and TYSABRI (natalizumab). In addition, there are a number of drugs that are used to help relieve MS symptoms such as spasticity, fatigue, and pain. The focus of this document will be on the disease-modifying therapies (DMTs).

None of these treatments are a cure, and none will prevent persistent symptoms, such as fatigue or numbness, although respondents indicated that they would like DMT’s to control both of these, as well as the effect — difficulty in walking. However, each of the DMTs has a proven record of effectiveness in reducing the frequency and severity of MS symptoms, as aforementioned, and several appear to slow the progression of disability. These both were stated by respondents as most important to be controlled

by a DMT; i.e., progression of disability (86.8%) and number and/or severity of relapses (69.9%). Unfortunately, no DMT has yet been approved to treat primary-progressive MS — the type of MS that shows steady progression at onset. The fact that there are no current therapies for progressive forms of MS was brought up numerous times by respondents in the survey as a concern and an area they would like focused on.

AVONEX, BETASERON, EXTAVIA, COPAXONE and Rebif have been shown in extensive clinical trials to reduce the relapse rate in MS by about one-third. The effect of TYSABRI and GILENYA on the relapse rate is higher, as is their serious side effects profile. The scientific literature relating to each of these drugs is well known and will not be repeated here. Instead, the focus of the rest of this section will be on those who responded to the MS Society survey. In the survey, more than half of the respondents were currently using a DMT (62.6%). The largest number of respondents in the survey were using COPAXONE (23.1%), with other usage, as follows: Rebif (16.5%); AVONEX (9.1%); TYSABRI (5.6%); BETASERON (5.3%); GILENYA (3%); and EXTAVIA (0.2%). Responding to the question about how the treatment was helping, 52.6% said it reduced the frequency and severity of relapses, 40.9% said it appeared to slow the progression of disability, 25.7% said it allowed them to have a better quality of life, and 25.1% said they generally felt better. A respondent commented that, "I presume it's doing all the above [in helping them]. I certainly would rather be taking my DMT, and not find out what may have happened if I didn't."

However, respondents did report side effects in varying degrees from "somewhat" to "a lot" in all of the categories listed: injection site reactions, fatigue, sore muscles and joints, headache, depression, chills, spasticity, fever, rapid heartbeat, and breathlessness. Complaints with injection site reactions ranked number one, followed by fatigue, sore muscles and joints, and headache. Other side effects not listed in the survey that respondents commented on include: lipoatrophy, thyroid problems, liver toxicity, poor sleep, nausea, low white blood cell count, and bruising on the skin. Most respondents (66.9%) said that side effects have not impacted their taking the therapy on a regular basis. Of those that said side effects did impact their taking the therapy, fatigue and injection site reactions were the most frequent reasons cited. There were many comments about uncertainty as to whether the side effects were from the drugs or were simply the symptoms of MS.

Respondents reported other factors that prevented them occasionally from taking their current MS DMT including: high cost of therapy/financial problems, do not like using a needle, cannot use a needle because of coordination problems, do not like the infusion process, and cannot travel to the infusion process site. The greatest factor was the cost of current and future therapies, followed by issues with a needle. Additional factors included anxiety associated with needles, rotation of sites, the bulk and bother with travel, and concerns with insurance coverage. There were also comments in the survey that indicated that the current DMT's did not work and respondents did not see any benefit in taking them. Other comments indicated a mistrust of drug companies, neurologists, and the MS Society, as respondents felt they were biased toward pushing these medications.

Following is a sampling of respondent comments:

- *"My whole way of life has been affected, as well as that of my children and husband! No matter what we would like to do, or like to go, it always comes down to "if mommy can." Having two young children and living with this disease has been difficult for us all! Emotionally, financially, and physically the disease has affected every aspect of my life, as well as my family!!!"*
- *"I believe I would be in a wheelchair without this medicine so I continue giving myself an injection once a day until a cure is found."*
- *"The therapy I have found for myself makes a big difference in my life."*

- *“I am not really sure there is any impact. My MS is generally stable, but I cannot say if that is due to DMT or to the nature of my MS.”*

2.4 Impact on Caregivers

The care and assistance that many people with MS receive from their spouses, other family members, and friends is a key factor in their ability to maintain their quality of life and independence in the community. Caregivers assist in many tasks — some that are medical and others that are non-medical — that enable the person with MS to have as normal a life as possible. In the MS Society survey, over half (52.6%) of caregivers reported they assisted in administering medications all or some of the time. When asked if providing assistance impacted their own daily routines, 41.1% reported that it did all the time and 32.1% reported that it did sometimes; 62% of caregivers responded that there are negative effects from the current DMT on the person they care for at least sometimes.

Following is a sampling of responses from caregivers related to assisting with therapy and the effects on the care recipient.

- A respondent commented on their family member’s condition after therapy: *“Extreme fatigue on the day of the injection. She also must take a day off work for her injection.”*
- *“My husband will get affected with severe flu-like symptoms, full body aches, and is generally incapacitated for 24 hours after the administration of his drugs. As a young family, his contribution to child care and help around the home is definitely affected by his drug therapy.”*
- *“The disease impacts my wife’s ability to work and perform other duties in the house. This in turn impacts my ability to work and, as a small business owner, this impacts my ability to earn income for the company.”*

Section 3 — Information About the Drug Being Reviewed

3.1 Information Gathering

Same as 2.1.

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

The vast majority of respondents to the MS Society survey had no experience with the new therapies (teriflunomide, dimethyl fumarate, or alemtuzumab). In commentary, many respondents said they looked forward to having a drug that did not involve injections because of the pain and injection-site reactions or infusion because of the inconvenience and concern about serious side effects. They noted that their quality of life would be improved considerably. When asked what they would like new DMT to do better than existing ones, their comments included: lower and/or limited side effects, be more affordable, be more convenient (e.g., no refrigeration), and improve everyday function. In one of the focus groups, they commented that they hoped it would be available as a first-line therapy, as it is an oral form and more tolerable than injections. Others noted that an oral drug would be beneficial in helping people take the medication as prescribed, as the anxiety about injections would no longer exist. Compliance is a concern related to any drug that must be injected. This can be a greater issue in a disease that can result in numbness and lack of coordination, which complicate self-injection.

Here is a sampling of comments about people's expectations of new and emerging therapies:

- *"It would be nice to have a therapy that was not injection-based. The cost is very high and it would be nice if that was lower and/or covered by the province."*
- *A respondent commented they would like a new DMT to "be taken orally and that there is a reasonable cost to the drugs."*
- *"I would be interested in trying new drugs if they have minimal side effects and were taken orally rather than injected."*
- *"I would like to see there be more access to DMTs. Certain provincial guidelines make it difficult to have certain medications covered unless a set treatment path is taken. Not every MS patient has the same reactions to DMTs, yet a patient can be "punished" for not wanting to try a class of meds that do not work for them."*

Since the results of emerging clinical trials are known, that information will not be repeated here. There were 45 individuals who reported that they had experience with the new therapies. Specific comments about the new therapies include:

- *"The BG-12 I am currently taking greatly impacted my life in a positive way. I would try anything that would better my life and think I have found it in the BG-12. I understand that it's not for everyone. What concerns me, would the drug be covered under insurance or the province?"*

The following comments were made in response to the questions regarding how the new drug manages the effects better. Note: Whichever emerging therapy the respondent had experience with was not indicated as part of the comment.

- *"I get very few, if any, relapses and when there are any they are quite mild."*
- *"A daily pill beats a daily needle any day!"*
- *"The new drug is very easy to use, as it is a pill. It is portable and requires no special equipment such as needles."*

Section 4 — Additional Information

People with MS must cope with a disease that is relentlessly unpredictable. Each day, they face the possibility that they may experience another symptom or another relapse. The current MS therapies have provided people with a way of reducing relapses and possibly slowing the progression of disability. The potential choice of more MS drugs that have greater efficacy and an easier mode of administration is exciting for many people with MS. Respondents in the survey commented on the importance of having options of several therapies to match an individual's disease and life situation. Choice is an important consideration, as one respondent stated: *"The disease is different for everyone so the drugs offered need be the same. Different ones for different individuals with MS."*