Common Drug Review
Patient Group Input Submissions

Daclizumab beta (Zinbryta) for Multiple Sclerosis, relapsing

Patient group input submissions were received from the following patient groups. Those with permission to post are included in this document.
Multiple Sclerosis Society of Canada — permission granted to post.

CADTH received patient group input for this review on or before December 6, 2016.
CADTH posts all patient input submissions to the Common Drug Review received on or after February 1, 2014 for which permission has been given by the submitter. This includes patient input received from individual patients and caregivers as part of that pilot project.

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.

CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no personal information is included in the submission. The name of the submitting patient group and all conflict of interest information are included in the posted patient group submission; however, the name of the author, including the name of an individual patient or caregiver submitting the patient input, are not posted.

Multiple Sclerosis Society of Canada

Section 1 — General Information

Name of the drug CADTH is reviewing and indication(s) of interest		Daclizumab (Zinbryta*)
Name of the patient group		Multiple Sclerosis Society of Canada
Name of the primary contact for this submission:		[redacted]
Position or title with patient group		[redacted]
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Permission is granted to post this submission		Yes

1.1 Submitting Organization

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. The MS Society has become one of the largest funders of MS research in the world, and continues to lead the search for a cure.

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:

Between 2015 and 2016, the MS Society received educational grants from the following companies: Bayer, Biogen, 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 for this submission was obtained from publicly available information about the impact of MS and through an online survey posted from November 1, 2016 to November 14, 2016. The survey was offered in English and French and was shared with Canadians affected by MS through various channels (social media, e-newsletters, and email). This survey invited feedback from people living with MS who may or may not have had experience with daclizumab. Respondents with MS and their caregivers answered a series of questions about themselves, how MS impacts them, their experience with existing drug therapies, and their expectations of future therapies.

In this survey, 76% of respondents were women and the remainder were men. Most respondents had MS (95%), whereas the other small percentage self-identified as caregivers. Respondents' ages ranged from less than 20 years to 65 and older. Most respondents were between the ages of 35 to 54. The length of diagnosis varied from less than 2 years to more than 20 years, with the highest number of respondents being diagnosed between two to ten years. The type of MS reported by respondents had representation from the following MS categories: relapsing-remitting, secondary-progressive and primary-progressive. The highest number of respondents were living with relapsing-remitting MS (95%).

2.2 Impact of Condition on Patients

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) within the central nervous system. Damaged myelin causes an interruption or loss of the usual flow of nerve impulses along the axons resulting in a wide variety of symptoms, depending upon what part or parts of the central nervous system are affected. Approximately 85-90% of people are diagnosed with a relapsing-remitting course, wherein they experience 'attacks' caused by bouts of inflammation in the central nervous system, followed by full or near complete recovery. Within approximately 10 to 20 years, about half of these individuals are likely to develop 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-remitting 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. It has been diagnosed in children as young as two years old, and adults over 50. MS is more commonly diagnosed in women than men, and is prevalent in Northern countries. Canada has the highest rate of MS in the world.

Depending on the type and severity of the symptom, an individual's quality of life can be greatly impacted. Symptoms can have a negative impact on an individual living with MS as well as their family members and communities. 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.

"Being on a disease-modifying therapy from the beginning has given me some hope that I am doing the most to prevent progression and to keep me able to work at least part time and contribute to my family and my mental health. I feel even with 5 relapses in 9 years that's a positive response. With Canada having 1 in 291 persons affected by this disease we need to have as many options for disease-modifying therapies as possible."

2.3 Patients' Experiences With Current Therapy

There are eleven Health Canada approved drugs to treat relapsing forms of MS, collectively referred to as disease-modifying therapies, or DMTs. These medications have shown to be efficacious and safe in reducing annual relapse rates (ARR) between 30 and 70 per cent, depending on the agent being used. These drugs are also effective in slowing disability progression and reducing the number or new or enhanced lesions (as seen on MRI). Of the eleven therapies, three are considered second line or subsequent therapies and are recommended when an individual is intolerant or unresponsive to an initial DMT. Daclizumab will enter the Canadian market as the fourth subsequent therapy option for relapsing MS.

There is no standard MS disease-modifying therapy. Although several MS therapies have similar mechanisms of action, dosing and administration are not the same and therefore the options available to people are selected based on tolerance, known (expected) side-effects, lifestyle choices, disease course and cost. It is very common for one treatment to work well in one individual, and fail in another.

"It seems that different therapies work in different people so we need as many options as possible. We also each have a different tolerance for risk. Taking that risk should be our choice if we are well informed."

Side-effects of DMTs are generally well-managed with over-the-counter medications and lifestyle changes such as taking time to rest. Certain side-effects however can be more bothersome and unmanageable. In those cases, many people may choose to switch therapies. The option to try a different therapy is critical for people affected by MS to maintain their quality of life and control their MS as effectively as possible.

In addition to DMTs, symptom management medications, corticosteroid therapy and complementary and alternative therapies are also commonly used to treat MS. There are also many non-medicinal therapies and techniques used to manage MS, including physiotherapy, physical activity and other types of rehabilitation. At the time of this submission, there are no approved MS medications for progressive MS.

"There is always someone who can benefit from a different therapy and we should have as many as possible to choose from since the benefits of treatment vary so much from person to person. Drug therapies are the difference between life and death in my opinion. You want to have as normal a life as possible and that usually isn't possible without treatment."

"I think that, right now I wouldn't consider changing medications because I am doing well. However, at any time my body could change and I could potentially stop responding to my current regiment. For me it is all about choice. It may take a while to find something that works properly again."

2.4 Impact on Caregivers

Caregivers play an instrumental role in the overall care management plan of people living with MS. Depending on the type and severity of MS, a caregiver's role can 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. Regardless of the role caregivers play, most feel that providing care for a loved one living with multiple sclerosis impacts their day-to-day activities. With the advancement, and growing list of options, of MS treatments for relapsing forms of MS, the demand for a caregiver's role may decrease. Disability progression is being further delayed; relapses are decreasing, and symptoms are being managed more effectively. MS treatments allow those affected by MS to make family and social commitments more possible as well as remain in the work place. These factors greatly improve the quality of life for both the caregiver and their loved one with MS.

"I consider my father a dependent, he needs support for daily living and I am there for him daily. This makes working and caring for my children more challenging, emotionally, physically, and financially."

"I occasionally administer the drug which means I am needed near him at the time of dosage. Afterwards, he feels very ill and occasionally requires post-administration care. This requires me to shift plans and work schedules around, as well as provide transportation to his appointments."

Section 3 — Information about the Drug Being Reviewed

3.1 Information Gathering

Same as section 2.1.

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

Most respondents had no experience with daclizumab (97%) and only one respondent indicated the desire to switch to daclizumab once it is approved. Monoclonal antibodies, such as daclizumab, have been effective in managing aggressive forms of relapsing MS where other therapies have not had clinical benefit.

There are currently three subsequent therapies available for people who have had an inadequate response to other disease-modifying therapies. One of the subsequent therapies is an oral medication (sphingosine 1-phosphate receptor (S1PR) modulator) and the other two are monoclonal antibodies. Both currently available monoclonal antibodies require intravenous infusions to take place at specialized clinics and, all three subsequent therapies carry potentially serious adverse effects including a rare and potentially fatal brain infection, progressive multifocal leukoencephalopathy (PML).

Daclizumab will alleviate two significant gaps related to current subsequent therapies for MS. First, daclizumab is the only monoclonal antibody available as a subcutaneous injection, eliminating the need to travel to a specialized clinic for dose administration, which has been previously reported as a barrier to treatment with a monoclonal antibody. Second, unlike other subsequent therapies there was no increased risk of PML reported in clinical trials for daclizumab. Individuals who are considered high risk for PML will likely not be recommended for treatment with one of the current second line therapies as the risks may outweigh the benefits. Daclizumab may then be offered as a viable option versus no treatment at all. Compared with an initial therapy on the market (interferon beta-1a), daclizumab was

shown to reduce the annual relapse rate by 45% and significantly reduce disease activity as seen on MRI after three years of treatment.

Adverse effects reported for daclizumab include fatigue, headache, nausea, rash, musculoskeletal disorders, allergic reactions, infections, elevated liver enzymes, heart problems, and reduced platelet number. One death was reported in a daclizumab treated participant resulting from muscle abscess. In addition to elevated liver enzymes, there is also a potential for serious liver injury (liver failure and autoimmune hepatitis).

Section 4 — Additional Information

Common practice for individuals with aggressive relapsing multiple sclerosis with breakthrough disease activity, or those who were unable to tolerate first-line medications, is to initiate therapy with a second-line agent. There are nine first-line therapies for people to select based on dosing schedule, administration delivery, side-effect tolerance and lifestyle. Once the first line options are no longer effective or tolerated, these individuals should also be provided with a choice of dosing schedule, administration delivery, side-effect risk and lifestyle with a second line therapy. Adding daclizumab to the list of options will be welcomed as a second line treatment for MS as it will offer the efficacy of a monoclonal antibody without the increased risk of PML and the ease of injecting subcutaneously without the need to travel to a specialized clinic. With many treatment options now available, the vast majority of Canadians living with relapsing forms of MS are able to pick a treatment that is most suitable to their disease course and lifestyle, ultimately enabling them to continue working and maintain active roles within their families and communities. Providing options to people living with MS can also contribute to increased adherence, which benefits the person and health system.

"They should be either affordable, or have coverage so people with MS can take whichever therapy best meets their needs. If there wasn't special coverage for my medication, I wouldn't be able to afford it (cost more than my mortgage every month)."

"MS is a life changing disease for those that have it and their care givers. Any drug that could potentially help someone should be made available. Our health care system is going to be burdened by chronic illnesses like MS and anything we can do to slow the disease and increase quality of life should be available if the doctor feels it is right for the patient and cost effective."

"I truly believe that all persons with MS should have the right to (even for a specified period) to give ALL treatments a try."

"Every possible medication needs to be available if it can improve or maintain a quality of life."