CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**Spinraza/** Nusinersen
Name of the Patient Group	**Muscular Dystrophy Canada**
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1. About Your Patient Group

If you have not yet registered with CADTH, describe the purpose of your organization. Include a link to your website.

Muscular Dystrophy Canada (MDC) supports people affected by muscular dystrophy and related muscle diseases. Together, these rare conditions are referred to as "**neuromuscular disorders."**

Neuromuscular disorders are a group of diseases that weaken the body's muscles. The causes, symptoms, age of onset, severity and progression vary depending on the exact diagnosis and the individual.

Muscular Dystrophy Canada is a national, non-profit organization of dedicated volunteers and staff who continually work to provide support and resources to clients like you who are impacted by 1 of over 150 neuromuscular disorders. Through well-funded research, we are on a mission striving to find a cure as soon as possible.

Muscular Dystrophy Canada has close to 60 years of experience in helping to improve the lives of those affected by neuromuscular disorders.

Muscular Dystrophy Canada reaches over 10,000 people living with a neuromuscular disorder. Muscular Dystrophy offers a basket of services that include system navigation, education, financial assistance, accessing coping and emotional support and advocacy.

Spinal Muscular Atrophy (SMA) is one of the neuromuscular disorder types that falls under MDC's umbrella. Spinal Muscular Atrophy (SMA) is a group of inherited genetic muscle-wasting disorders. SMA affects the nerve cells that control voluntary muscles. These nerve cells are called motor neurons, and SMA causes them to die off. Without motor neurons, the brain cannot deliver signals to the muscles. When unable to fully use them, the muscles of a person with SMA will waste away.

People with SMA are generally grouped into one of four types (I, II, III, IV) based on their highest level of motor function or ability.

- **Type I (severe)** – also known as infantile-onset or Werdnig-Hoffman disease
- **Type II (intermediate)**
- **Type III (mild)** – also known as Kugelberg-Welander disease
- **Type IV** – also known as adult SMA

SMA is caused by a missing or abnormal (mutated) gene known as survival motor neuron gene 1 (SMN1). In a healthy person, this gene produces a protein in the body called survival motor neuron (SMN) protein. In a person with mutated genes, this protein is absent or significantly decreased, and causes severe problems for motor neurons. Motor neurons are nerve cells in the spinal cord, which send out nerve fibers to muscles throughout the body. Since SMN, protein is critical to the survival and health of motor neurons, nerve cells may shrink and eventually die without this protein, resulting in muscle weakness.

www.muscle.ca

2. Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include **when** the data were gathered; if data were gathered **in Canada** or elsewhere; demographics of the respondents; and **how many** patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

Muscular Dystrophy Canada has Neuromuscular Service Support Staff in all provinces across Canada. The Neuromuscular Service Support Staff provide front line support to thousands of Canadians affected by neuromuscular disorders. Support includes, navigating systems and

accessing resources, providing information and education so that people affected by neuromuscular disorders can make informed decision as well connecting people for peer support. The Staff conducted interviews over the time from July 7th to July 21st. by telephone and in person. There are over 700 clients registered with MDC affected by Spinal Muscular Atrophy (SMA). Over 350 caregivers and 123 patients were interviewed.

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient's perspective. Describe how the disease affects patients' and caregivers' day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

Spinal Muscular Atrophy affects people in different ways. Most types of SMA can affect either males or females. The onset depends on the type of SMA involved. SMA Type 1 is the most common genetic cause of infant mortality. With SMA Type 2 motor milestones are delayed, respiratory issues are present and may have a shortly life expectancy. With SMA Type 3 often experiences muscle weakness that is progressive in nature. With SMA Type 4 is adult onset and muscle weakness will vary. Dealing with a fatal and or progressive disease is devastating. Patients most often need to rely on caregivers (mainly parents) for all daily living activities that include feeding, bathing, transferring, dressing, etc. Caregivers and patients face many barriers that affect a patient's quality of life that include lack of resources both in the medical and community sectors, , dealing with a progressive muscle disease also has such a significant impact on physical and psychological well being, social isolation and over all quality of life.

Here are the most prevalent responses:

- ✓ Ongoing loss of independence
- ✓ Fear of the unknown
- ✓ Ongoing deterioration and progressive loss
- ✓ Watching my child decline
- ✓ Caregiver burnout

Here is responses form the interviews that were conducted by MDC:

"We had no clue what spinal muscular atrophy was. We never heard of it and no one in our family has ever had it. It was as we were stopped head on, right in our tracks. We were told, however, that he has the mild form of the disease. It is still hard to categorize the word "mild" when the phrase "He will lose the ability to walk" accompanies that word. ***We are now so devastated to see him not walking just under 3 months****"*

"The hardest part is watching yourself get weaker and weaker and needed more and more help with things you use to be able to do"

"Life of parent is consumed with appointments and therapies and constantly monitoring child. Not able to work and need to have additional family support to help in these situations"

"As my child ages it gets difficult for bathing, toileting, Physio, exercise, a lot of pressure on me as a caregiver"

"Nothing in life is easy, everything has to be thought out meticulously and planned. I love to do activities like any other families but with that comes a lot of planning and additional expense, often it is easier to turn down invitations to go places or travel in fear of what is going to be a struggle."

"I have got progressively weaker, I have lost my independence and unable to breath or swallow independently"

"Affects everything, physical health, emotional, mental, along with parents because of transfers, lifting, live with worry every day and extra time takes to navigate normal things. Affects ability to make friends and siblings emotionally. Literally all encompassing and drives every decision in family."

"From a caregiver perspective, takes time, very expensive, physically hard on body (from moving), tough job. Disheartening to watch decline, have a certain level of independence and gradually losing it over time. Knowing there is treatments coming give hope".

"Went from walking to standing to power chair in 5 years, progresses very quickly and change life. Make it difficult to move away from home and go to school/ find work. Financially and emotionally."

"Physical, mental and emotional part. From a caregiver perspective difficult watching progression of disease, loosing strength that have. The hardest part the lack of control. The unknown of the diagnosis"

"Every part of my life is affected by this disease, raising my children, marriage, physical and emotional well-being."

"Muscle weakness has constantly been progressing since infancy. As a child and teenager, I was able to brush my teeth, wash my hair, shave, etc., independently. I used a manual wheelchair indoors and a motorized wheelchair outdoors until late teens, where I eventually transitioned uniquely to the motorized wheelchair because I was no longer able to propel myself in the manual wheelchair. As an adult, I can no longer perform my own daily hygienic activities, such

as brush my teeth, wash my hair, or shave without the assistance of personal care attendants. It is more difficult to swallow as well as move my arms, hands and fingers. I now rely more on personal care attendants to help with positioning in my wheelchair during the days and in bed during the night, which means I need more hours of personal care attendants each day compared to the past. It is difficult for family members because I require constant assistance and some of my personal care can be complex and physically difficult"

"My son is 12 years old and has SMA type 3. He is currently walking for short distances, and is gradually losing his mobility. He will soon spend most of his time in a motorized wheelchair. For us the aspect that is most important to control is the loss of mobility, which includes walking, and being able to write during class as his hands are quickly tired."

Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

The United States (US) Food and Drug Administration (FDA) have approved Spinraza for use in all patients with SMA. Spinraza has demonstrated clear efficacy in SMA type I, II and III. Data from the infantile SMA has been published. Moreover, larger clinical trials involving infants ('ENDEAR' study) and older children with type II and III ('CHERISH' study) have been closed when interim analysis demonstrated Spinraza to be effective. These children (including some Canadian children) are continuing to receive open-label treatment of Spinraza through "SHINE" open-label extension study.

In July 2017, Health Canada approved SPINRAZA for the treatment of 5q SMA. Because of the the robust efficacy and safety profile demonstrated in the clinical trials it is believed that SPINRAZA will have a meaningful impact on individuals living with this devastating disease.

The Health Canada approval of SPINRAZA was based on positive results from multiple clinical studies in more than 170 patients.

Here are some responses from MDC's interviews:

"*Travel costs is a barrier and so is taking time off work for parents to take children to therapies or clinic visits"*

"*Our friends have access in BC, but we don't have access in Manitoba"*

"*My daughter's joints have stopped contracting . her tendons have relaxed, and her joints are moveable"*

*"Streng*th *seems to be improving during the trial"*

"The cost is stressful"

"There was no other treatments been given to him before, because there is none for him. (type one). With the new medication, all of his caregivers, and both me and my husband all feel he had improving"

"He is getting stronger. We have hope"

"I know that the costs are extremely expensive but quality of life should not be measured in dollars. Giving people potential to improve quality of life would makes a huge impact, cost should not be the issue quality of life can not be measured by financial numbers."

"Today at age 4, after having been very lucky to take part in the phase 3 trials for Nusinersen, our son has not regressed at all. He is continuing to gain strength after every injection. He can now bare weight on his legs again with his braces, he can maintain a 4-point position and is slowly starting to shift his own weight to crawl, we never worry about him falling when sitting, he has gain much core strength (can bend over to pick up his toys and pick himself back up from his wheelchair), he has not had the need for a power chair at this point and only uses a manual wheelchair. He has great dexterity and head control and recovers for colds and illnesses much quicker. He has had no hospitalizations due to pulmonary infections since starting the medication. We are hopeful that by continuing his treatments, he will one day be able to do his own transfers and maybe even walk with a walker or crutches like so many of the other kids that have the same type as our son have been doing since starting the drug."

Here are the most prevalent responses from clients when asked about difficulties in accessing Spinraza

- ✓ Affordability – this was the greatest concern.
- ✓ Access due to not having SMA type 1
- ✓ Difficult to travel due to complex care needs
- ✓ Difficulty navigating the process
- ✓ Access due to living in rural areas

Here are most prevalent responses from clients when asked about side effects:

- Constipation
- Headache

4. Improved Outcomes

CADTH is interested in patients' views on what outcomes we should consider when evaluating new therapies. What improvements would patients and caregivers like to see in a new treatment that is not achieved in currently available treatments? How might daily life and quality of life for patients, caregivers, and families be different if the new treatment provided those desired improvements? What trade-offs do patients, families, and caregivers consider when choosing therapy?

There is evidence that this medication offers definite benefit to children with all forms of SMA. In particular, children, who are showing rapid disease progression may benefit the most from treatment. Clients expressed without Spinraza, patients are at an extremely high risk of completely losing the ability to walk independently and even bear weight on their legs. Furthermore, are at a of high risk of developing progressive weakness in upper extremities. It was felt that Spinraza could prevent the permanent and irreversible loss of motor neurons that is resulting in muscle atrophy and weakness. Without Spinraza, individuals are at a high risk of losing the ability to perform basic self-care tasks such as feeding themselves, bathing or changing his clothes. Without treatment individuals will be placed at heightened risk for needing permanent, invasive, respiratory supports that could include night-time BiPAP or even tracheostomy and mechanical ventilation.

Here are the most prevalent responses from our interview process:

- Regain some range of motion
- Slow the process of degeneration & maintain muscle strength
- Be less dependent on others
- More freedom & better quality of life
- Decrease in respiratory health issues

5. Experience With Drug Under Review

CADTH will carefully review the relevant scientific literature and clinical studies. We would like to hear from patients about their individual experiences with the new drug. This can help reviewers better understand how the drug under review meets the needs and preferences of patients, caregivers, and families.

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug

easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways?

Spinraza was accessible via clinical trials. No other treatment has been available. Clients have shared they are on other medications that include Salbutamol, VPA, creatine, celecoxib.

It is believed that Spinraza will have positive outcomes for all forms of SMA.

Here are some responses from our interview process:

"Through SAP (special access program) doctor worked to get it for him. Experiences movement of fingers and legs more, louder (lung function has improved) oxygen levels more stable. No direct disadvantages, did get sick on first treatment (head ache, dizzy)"

"2 years ago, called centres for trials and put on waitlist, clinical trial. Increase in strength, increase in cough strength, and confidence. Disadvantages, anxiety form lumbar puncture, anxiety from sedation and pinched nerve, spinal headache (all manageable). Gives hope for the future"

"Respiratory has improved and she is sitting up better than before the trial"

"I don't have access to Spinraza because I don't have SMA type 1. Please can I have access?"

Throughout the interview process, no disadvantages were expressed about the medication. Challenges expressed involved access, traveling with a person who has complex care needs, navigating complex process and costs associated with travel.

6. Anything Else?

Is there anything else specifically related to this drug review that CADTH reviewers or the expert committee should know?

SMA is a devastating disease. Through our interview process, it was apparent that affordability and access to Spinraza was the greatest concern. Spinraza has demonstrated remarkable positive outcomes that will make a significant impact on the lives of people affected by SMA. The ability to hold a utensil to eat independently to eliminating the need for invasive procedures like relying on a ventilator to breathe is life changing. Spinraza can allow the opportunity for patients to live fuller and better quality of lives. Spinraza will assist in decreasing caregiver burnout and alleviate some of the pressures families deal with every minute of the day. Often clients affected by SMA require total care for all daily living activities. It was expressed that medical and community resources are lacking in all provinces, leaving the burden to families to be the main caregivers while managing other responsibilities.

The affordability of Spinraza is also a great concern. Families affected by SMA expressed overwhelmingly there concern about their current financial situation. Living with SMA is expensive. Travel visits to clinics, the need for assistive devices that are often not covered by government funding and or insurance, modifications to homes and vehicles, the need for ongoing expenses due to the progressive nature of this disease. Often, one family member needs to leave employment to provide care to their child.

The other concern was related to the challenges of accessing Spinraza in their respective provinces. Many were concerned with the process of accessing the medication. Many expressed a concern with navigating a very complicated health care system and provinces often have very different processes in approving a medication and access, which cause barriers and delays. Another, concern with regards to access, relates to patients having access to Spinraza who are affected with other forms of SMA. Clients expressed that there is medical opinion that Spinraza can have good outcomes for other forms of SMA and the desire to have this medication accessible to other SMA patients.

Appendix: 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? 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
Biogen		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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Patient Group: Muscular Dystrophy Canada
Date: July 21, 2017