CADTH

CADTH COMMON DRUG REVIEW

Patient Input

Nusinersen (Spinraza)

Biogen Canada Inc.

Indication: Indicated for the treatment of 5q Spinal Muscular Atrophy.

CADTH received patient input from:

Canadian Organization for Rare Disorders and Cure SMA Canada

Muscular Distrophy Canada

August 14, 2018

CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**Spinraza (nusinersin) for Spinal Muscular Atrophy (Resubmit)**
Name of the Patient Group	**Canadian Organization for Rare Disorders and Cure SMA 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 Canadian Organization for Rare Disorders is registered charity that provides a strong common voice to advocate for health policy and a healthcare system that works for those with rare disorders. CORD provides education and resources to patient groups to enable them to better meet their members' needs.

Cure SMA Canada is the national registered charity; supporting families and individuals affected by Spinal Muscular Atrophy from the point of diagnoses, through the life course and even after loss of life. Cure SMA Canada also funds critical Canadian research projects with the aim of affecting accessible treatments for SMA. Cure SMA Canada provides advocacy, information and resources to families, communities and health professionals.

2. Information Gathering

This submission should be read in conjunction with the original Patient Input dated 19 July 2017. The broader community input remains the same. In this input, we have chosen to focus on those Canadian patients of all types who have been using Spinraza, as support to the resubmission. Cure SMA Canada (CSC) identified and contacted parents whose child (children) were receiving Spinraza. Of the 14 families identified, 11 were contacted and individually interviewed by a researcher from the Canadian Organization for Rare Disorders (CORD) using a semi-structured interview format that included a few rating scales and multiple-choice questions. All interviews were conducted during August 2018 by the same interviewer. The interviews were taped but analysis was conducted on detailed notes rather than recordings, which were used to assure accuracy. A deductive analytic approach was used to code interview data according to pre-defined themes with the opportunity for emerging themes to be included.

The 11 interviewees represent the spectrum of SMA patients who currently and potentially benefit from use of Spinraza. Specifically there were three identified as Type 1, one ventilated and two not ventilated, ranging in age from 3 to 18 years old. There were four classified as Type 2 (though one is close to Type 1) ranging in ages from 5 to 10 years old. Three were identified as Type 3 and range from1.5 to 17 years old. Finally one patient with confirmed SMA was started on Spinraza from birth and now at age of 1 year old had developed no symptoms.

3. Disease Experience and

4. Experiences With Currently Available Treatments

It is a testament to the lack of effective treatments for SMA that most have had accessed almost no drugs or few other interventions. Most of the patients with Types 1 and 2 use some form of mechanical ventilation (BiPap), all started prior to Spinraza. None of the Type 3 required respiratory assistance. One Type 2 patient had experienced removal of tonsils and adenoids to improve breathing. One Type 2 and one Type 3 patient had been treated (short term) with Salbutamol (albuterol) to open up airways and manage tremors.

All of the Type 1 patients had a G-tube for feeding though this was not necessarily their only source of nutrition. Parents of some patients with Type 2 SMA reported need for modified foods to aid swallowing and avoid choking but none had of the Types 2 or 3 in this cohort reported use of G-tube feeding.

5. Improved Outcomes

6. Experience With Drug Under Review

Start and Duration: The age at which patients in this cohort begin Spinraza ranged from birth to 17 years old. Two of the Type 1 patients started at age of 10 months or less and one at age 17. Three of the Type 2 patients started between 6 and 8 years of age and one at age two. Type 3 patients varied with one at age 1 year, one at 9 years old, and one at 17 years old. At the time of the interview, the duration of their access to Spinraza ranged from 7 months to 3 years, with about half having access for less than one year and the rest from one to three years. While the experience is not very long term, all respondents observed significant improvements that were consistent with the research findings and demonstrated real improvements in functioning, quality of life, and family impact. The progression in outcomes also suggests that short-term benefits are indicative of continued improvement in capability and not just slowing or halting loss of function.

Funding: The funding for these patients are representative of access pathways for all those on treatment, with six gaining access through clinical trials that are either current or completed with extended compassionate access. Three patients have access through their workplace private insurance plan, with funding from Biogen patient support program to cover some or all of the additional costs not covered. Two of the patients are personally funded by the family (through contributions from a GoFundMe campaign).

Impact

The discussion of the impact of Spinraza treatment on patients is structured around key common themes, with differences among those with Types 1, 2, and 3 specified when evidenced. It is noteworthy that patients across all Types 1, 2, and 3 at all ages experienced improvements in functioning which translated into improved participation in activities of daily living, improved school performance, and better quality of life, all of which translate into improved family, social, and work life. There are also noted societal benefits in terms of less use of healthcare resources, improved ability of parents to engage in work and contributions to community well being.

Physical Abilities: All patients (based on parent reports) experienced varied but noticeable and mostly significant improvements in core physical abilities, namely, sitting, rolling over, standing, using a walker, and walking. In terms of the Type 1 children, these were often abilities that the children had either lost or had never exhibited prior to start of Spinraza. *"She is now able to sit in a chair without choking." "She can sit in a wheelchair for six hours at a time,"* which means she can do so much more and go places with us. The parent of another Type 1 child who had experienced significant loss of function ("unable to hold his head up on his own" or "move head from side to side," "losing the ability to move his hands") reported

that after nearly three years on Spinraza treatment, *"…he now can sit independently for two minutes at a time, can sit in power chair for 3 hours at a time, can talk, holds his own head up, can lift his legs."* "*He never lifted his head as a baby, never sat in my lap."* Now starting Spinraza at age 17, *"the neuron pathways are … more damaged"* so *"improvement is not stellar"* but "*he is sitting up in a chair."*

The impact on mobility for the Type 2 patients was, in some cases, very pronounced. According to the parent of a five-year-old Type 2 who *"could never do 4-point crawl but could only do 'commando crawl', had stopped moving her legs and had stopped rolling"* after treatment on Spinraza for the past three years, *"she is walking with a walker and some supports."* Another parent said, "*she can ride manual wheelchair around house; doesn't need a chest strap; can sit on the toilet without needing a support."*

A third parent described the progress from the state where she "*never crawled, never walked, never supported own weight; now, able to stand in her stander for up to three hours a day."*

Finally, the mother of a fourth Type 2 six-year-old child who has been on treatment for about 10 months reported, *"Since treatment she has gained the ability to fully undress and dress herself ('which is amazing'); she can get from her bed into her wheelchair on her own and doesn't need help with small tasks such as removing marker lids; she is playing the piano again (she lost the ability to play with both hands just before sixth birthday); and she can get off the toilet on her own."*

With respect to the Type 3 patients, most notable was the increased independence. *"Now he is able to get up on his own from the ground independently and can now walk upstairs (slowly)." "She was close to losing her ability to walk, which was a huge load on me [especially] having to do two [children with SMA] it just made it so hard to get out of the house. But since treatment she is doing so well, she still falls but is able to walk around and not get tired or be carried."*

A third patient (Type 3, age 17) had spinal fusion at 13 … then lost ability to walk; now can balance [standing]and can lift arms above head; is doing weightlifting and biking."

Breathing, Eating, And Talking: Parents spoke about the significant impact of Spinraza treatment on ability to breathe, eat, and talk.

For parents of the Type 1 children, the ability to be off the ventilator even for periods of time has significant impact. *"She is no longer ventilated 24 hours and can breathe on her own for half an hour at time, so we can do daily activities like get dressed or transfer." "She is no longer choking."* And for the 18-year old, the mother noted his *"voice projection, so he no longer needs a microphone to speak."*

The mother of a Type 2 child noted two milestones, *"A few weeks ago she called for me in her sleep; she had rolled over in her bed and got herself tangled up in her blanket. She hadn't rolled over since she was 8 months old, and the strength of her voice … was significant."* Another noted that were no longer "breathing or swallowing issues."

Use of Hands: Another area of significant impact raised by parents was the child's ability to "use his/her hands." Said the mom of a Type 1 child who had lost the ability to use her hands, *"she can hold a marker and now won't stop colouring; she is also learning sign language."*

For the (Type 1) 18-year-old, the priority for [patient] was to *"maintain function in three fingers; he enjoys using his computer and has better stamina and control with his fingers so will be on the computer for a few hours a day without becoming tired. This is important since he is starting college in the fall."*

There were similar comments from parents of Type 2 and Type 3 patients. *"She is not as tired in the afternoons/early evening, more ability to eat meals; stays up at night to watch a movie after dinner." "I am getting stronger, just slowly."*

Illness and Recovery: Parents reported significant improvements in illness and recovery, which also translate into less hospitalization use of healthcare resources. The mom of one Type 1 patient said, *"She went from three to four illnesses a year lasting three to four weeks to now just one lasting two to three days."* For a Type 2 patient, "*This is the first winter he was not hospitalized; from two to three respiratory visits a year versus none this year."* Similarly, *"If she gets a virus it passes in a few days; no pneumonia or hospitalization due to respiratory illness." "He has not had any pneumonia since the treatment (was previously a common concern)."*

Activities: Importantly, improvement in functioning translates into improved participation in a variety of activities. The parent of a Type 1 child who had been unable to breathe on her own or to sit independent, reported, *"She drives a manual wheelchair around and can go swimming."* For the parent of a Type 2 child, a significant event was the fact that *"we were able to send [her] to sleep away camp alone this past summer; last year, we went to family camp because she needed assistance."* Another Type 2 child is doing swimming and therapeutic riding for the first time and another parent reported, *"she is able to swim four times a week for physical therapy." "She has noticeable improvement in core strength and is able to play the piano."*

Finally, the parent of a Type 3 17-year-old noted, *"if you are in university/school and your goal is to keep your fingers strong so that you can continue attending school then that is just as important as a 12-year-old needing to continue to walk."*

Family impact: Parents discussed the impact of Spinraza treatment on the whole family. One mom of a Type 1 child said, *"The nine-year-old sibling had been diagnosed with severe anxiety and depression due to lack of attention and care due to high demand of [patient's] care; during times of hospitalities he was moved between family members, affected schooling. With less hospitalization, there has been a 360-change in [brother] … significantly happier, helps in his sister's care."* Said another Type 1 parent, *"As a result of SMA treatment and personal improvement they are able to do more family activities together."*

Several Type 2 parents commented on ability of the family to do things. *"Travelling is a lot easier because not as concerned about [patient] in terms of illness and eating. Also, I began working 3 days a week (previously 2) because I am confidant and more comfortable leaving [her] at school." "Before we would never go anywhere in the winter; if she got a simple cold we would be worried that we would, have to go into the children's hospital." "The improvements in stamina around self-care; brushing her own teeth and hair, repositioning herself in her chair; the impact on our family alone, you wouldn't believe how it changes our productivity."*

Said one Type 3 parent, *"He has a 17-month-old sibling that he plays with; lives on a farm and … activities include horseback riding and swimming; important to maintain function so these activities can be continued; we're very family oriented and we do everything together."* Another Type 3 parent spoke of the impact on daily family life. *"She can get from her bed into her wheelchair on her own …and start getting ready … without assistance. I cannot emphasize enough what a huge impact this has on the family."*

S**ocial and Health System Impact:** One parent of a Type 1 child noted that even *"small functional improvement (example that patient can cough on her own) can eliminate health care spending in the long run; since receiving therapy, hospital visit duration and number of visits has declined significantly; (example, one-night stay versus multiple weeks/months); now receiving care at outpatient clinic rather than the hospital ICU."*

Said another, "Typically, he would get three to four illnesses a year during cold and flu season and since Spinraza he has only had one a year. And duration of illness is being reduced from three to four weeks to two to three days; this is a significant reduction of annual cost on the health system.

Finally, one parent said, *"I think what has made the biggest difference in [his] life is that he is not missing school. In terms of academics he isn't trying to catch up weeks of learning. He is back in the game very quickly and the severity of the illness has just been greatly reduced."*

Ratings and Scalar Responses: The following summarizes the responses of parents to the rating and multiple choice questions.

- 10/10 or 100% or all participants 'agree to strongly agree' that Spinraza has improved the quality of life of the individual/SMA patient
- 10/10 or 100% or all participants 'agree to strongly agree' that Spinraza has improved the quality of life of the family
- 10/10 or 100% of participants believe that all patients with SMA (all types) should have immediate access to Spinraza
- Among those who provided an answer to the rating question, there was a slight-to-moderate improvement when considering quality of life and function of their child (SMA patient) compared to a child that does not have SMA.

7. Companion Diagnostic Test

We are not aware of any specific companion diagnostic tests to determine response to the therapy.

8. Anything Else?

Participants acknowledged that their personal ranking/indication of improvement is often higher and more significant than improvements indicated in clinical testing because the testing fails to take into consideration improvements in areas of importance to the patients, including stamina, strength of voice, and fatigue.

This is an important context for the question: Do you agree that in individual cases where the clinical team has agreed that Spinraza treatment was not working [no measurable benefit or negative outcomes outweigh the benefit of treatment] that it would then be acceptable to stop the Spinraza treatment?

Parent answers:

- *This is a tricky one to answer because [others] may not be seeing progress but [the child] may not be declining either; I feel like the physio test and the nerve test are all good examples but they do not [tell everything].*
- *The last time [son] received his [drug trial] in July, he didn't do very well because he was agitated, frustrated, had just had a blood test so the results didn't show how he was actually doing. It was not an accurate representation of real world situation and ability.*
- *It needs to be taken into consideration that these are kids and they aren't going to do exactly what you want, so the testing is not going to be perfect or accurate. I know it's not perfect for my son anyway.*

In conclusion, parents and patient organizations support the value of "outcomes-based" access but it is important that outcomes are defined with the patients and parents as well as the clinical experts and that assessments take into consideration the context and circumstances as well as feedback from parents and patients themselves.

Appendix (A): 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 outside help was provided. CORD and Cure SMA Canada collaborated to perform the background research, conduct the interviews, prepare the survey, analyze the data, and prepare the submission.

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.

See above.

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.

Name: Durhane Wong-Rieger
Position: President & CEO
Patient Group: Canadian Organization for Rare Disorders
Date: 20 August 2018

Appendix (B): 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.

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

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See above.

6. 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			
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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.

Name: Susi Vander Wyk
Position: Executive Director
Patient Group: Cure SMA Canada
Date: August 20, 2018

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**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	[redacted]

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 is registered with CADTH.

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 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 over 60 years of experience in helping to improve the lives of those affected by neuromuscular disorders.

Muscular Dystrophy Canada represents over 10,000 people living with a neuromuscular disorder. Muscular Dystrophy offers a basket of services that include system navigation,

education, financial assistance, making connections and influencing positive changes at local, provincial and federal levels.

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.

SMA can be devastating for individuals living with the disorder and their family members. Often, resulting in a lower quality of life and tremendous stress on caregivers who are for the most part family members. MDC represents over 1000 people affected by SMA including individuals living with SMA and their family members.

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 Specialists offering direct support to thousands of clients across Canada. Support includes, navigating systems including access to

treatment and clinical trials, providing information and education so that people affected by neuromuscular disorders can make informed decisions, as well as, connecting people for peer support. The Neuromuscular Service Specialists conducted client interviews from July 23, 2018 to August 14th by telephone and in person. There are over 700 clients registered with MDC affected by Spinal Muscular Atrophy (SMA). To assist in building this submission, 265 caregivers and 125 people living with SMA were interviewed. **It is important to note that all clients living with different types of SMA were interviewed. It was evident that during the interview process that clients living with SMA regardless of the type, had extremely positive outcomes when being treated by Spinraza.**

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 shorter life expectancy. People living with SMA type 3 often experiences muscle weakness that is progressive in nature. People living with SMA Type 4 has an 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 from our client interviews related to their "disease experience":

- ✓ **Ongoing loss of independence with loss of mobility** – often people experience progression of muscle weakness resulting in reliance of mobility device i.e. wheelchair, assistance of some or all of their personal daily living activities i.e. dressing, bathing, eating, toileting, transferring from one location to another and even breathing. Often people affected by SMA will require a minimum of 20 hours of personal care a week up to 24 hours of personal care a day, depending on the progression of their SMA. Often, as parents age and community supports are not available in the community, people living with SMA may have no other choice but to reside in a long term care facility. Our clients have expressed that this is not an ideal situation and often result in isolation and mental health issues i.e. depression and anxiety. In addition, long term care facilities are not able to accommodate complex care situations due to lack of resources. Living with SMA is expensive. Mobility and assistive devices are expensive. Often not covered

by government and or private insurance. As the disease progresses and as people age, they will require a number of devices to assist in achieving some independence, overall well being and addressing health and safety concerns for their caregivers (often family).

- ✓ **Dealing with ongoing deterioration and progressive loss** – our clients (both people who have SMA and their family) have informed us that dealing with ongoing deterioration is devastating. Often, supports cannot keep up with the progressive nature of the disease leading to physical and psychological challenges. Clients were extremely vocal with regards to even slowing down the progression would be extremely beneficial. There would be more to time to prepare and plan for future care needs. This would alleviate some of the pressures experienced by people living with SMA and family members.
- ✓ **Caregiver burnout** – often parents have the responsibility of providing personal care for their children living with SMA. Community supports cannot meet the complex care needs of people living with SMA. As parents age, their child's needs become more complex and require more care. Often this includes all daily living activities. Including 24 hour support i.e. assistance during the night with turning, respiratory supports etc. In addition, during the interview process, many parents were forced to leave employment so that mom or dad could be a full time caregiver. Clients expressed significant concerns re: additional stressors that can contribute to burnout including financial hardship.

<u>Here is responses form the interviews that were conducted by MDC:</u>

"*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 if 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 in just under 3 months***"

"The hardest part is watching yourself get weaker and weaker and needing 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 becomes 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 gotten progressively weaker, I have lost my independence and am 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 the extra time it takes to navigate normal things. Affects ability to make friends and siblings emotionally. Literally all encompassing and drives every decision in the 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 gives hope".

"Went from walking to standing to power chair in 5 years, progresses very quickly and changes life. Makes 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 I 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."

"My daughter, 2 years old and has SMA type 2. Our daughter has below normal strength and stamina, particularly regarding mobility. She's precarious when she walks and falls quite frequently and can't go very long distances, she requires help with anything that requires bending knees, the squatting motion or any thigh strength. Getting up and down stairs, picking things up from the ground, carrying playthings, moving onto the toilet, and dressing herself is particularly taxing for her. When tired, her needs increase and one parent needs to be with her almost at all times, as she gets frustrated with her lack of function."

"My son is affected by SMA type 2" and it affects most aspects of our life. He requires daily care giving from getting dressed and eating to toileting and bathing. I'm a single mother and he's in my care the majority of the time, so these responsibilities are placed on me. I've had to give up my full time job as the demands of caring for him are great. I now work part time as an accessible school bus driver which allows me the flexibility I need. Especially when he is ill or going to specialist appointments."

"My son is affected by SMA type 3. SMA impacts every aspect of daily living as much for the person affected than to the parents/caregiver. Whether it be a need in a physical task such as transfers, picking up/holding items, eating, toileting or assuring exercising/stretching time, making sure they spend time in a standing position or that their posture is protected and well adjusted to prevent quick progression of scoliosis and hip dysplasia, there is always something to assist with or worry about. This is without mentioning controlling the common colds to avoid potential life threating lung infections, cough assist machines to help normal lung function and Bi-PAP machines at nighttime to promote a good night sleep and a healthy oxygen and CO2 flow. Daily activities are limited by the person's lack of mobility and venues accessibility. Every outing is calculated and planned. The emotional and physical strain of daily life and the unknowns that come with the disease's progression causes immense stress and impacts the whole family."

"How can one answer a question like this. Simply it has changed everything. SMA is all encompassing. Travel, plans , times with friends, dates, the day and how it is structured all predicated on the disease. The house you wish to live in, the van you choose and even the way you raise your other children are in large part due to the considerations of SMA."

"My adult son has SMA Type 2. We have literally waited a lifetime for such a treatment. I would like to touch on a few points, which I'm sure you've already heard, but I would like to emphasize once again. Quality of life is different for everyone. Improved quality of life for my son could mean lifting a glass to his mouth, rolling over in bed or toileting himself unaided. Improved quality of life could mean taking a deeper breath or holding his girlfriend in his arms. Even if Spinraza will maintain and extend his existing quality of life, we would be thrilled. No one else can judge what quality of life is for another, but I do know that comparing cost effectiveness to what decision makers believe is quality of life, is wrong. We cannot fully predict how each SMA patient will respond to Spinraza, just as we cannot fully predict how a

cancer patient will respond to Chemo treatments. If SMA patients are never given this chance, we will never witness the positive life changing improvements in our loved one's abilities."

"My daughter is affected by SMA type3 and 2 years old. SMA patients have particularly sensitive immune systems and the muscle deterioration accelerates if they get sick, including catching common colds/flus from others. We have to be extra mindful to keep our daughter very healthy and away from situations where there could be these types of germs. Since our daughter is in daycare for a portion of the week to allow us to continue working, heightened communication from care provider and other parents in her day care centre about illnesses are extremely important so that we can keep her home if there is a bug going around. This means that one of us will need to forego work to stay home with our daughter."

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"*

"When/if new treatments become available, it would be fantastic if the levels of government could work faster in order for patients to receive them. The fact that spinraza is so extremely expensive makes accessing it impossible for most families. As the only drug available for SMA, it should have been approved and covered just like it has been in many other countries. It's extremely frustrating for all families when there is a therapy and hope, but they can't access it."

"Once again, I will stress that Spinraza is the only treatment available to date, therefore, it meets all criteria the population is looking for. The ultimate trade-off all types of SMA are looking for when choosing a treatment is a stop in progression. In second is the gains in strength and the gains in abilities."

"Strength seems to be improving during the trial" (son affected by SMA Type 3)

"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 been improving"

"He is getting stronger. We have hope" (son affected by SMA Type 2)

"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 affected by SMA Type 2, 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."

"More than just the physical, scheduling and planning challenges though, having SMA at such a young age affects our daughter's (2 years old) sense of self and confidence level. Our daughter is aware that she is not as physically strong as other kids. When she is alone with us, she is so happy to play and try new equipment. However when on a playground or in public venues

where there are others around, she gets very timid and shies away from equipment where other kids are playing. Our daughter has learned from the countless times that she's been knocked over by someone just passing or gently bumping her and chooses to avoid contact with others. However, the day after our daughter received her first dose of Spinraza, her daycare teacher texted both of us excitedly! She shared that our daughter seemed to be more confident when playing and was also attempting to climb all of the different slides and steps that they have in the backyard! Our daughter is intelligent, mindful, kind and incredibly curious. If given the chance and the appropriate support especially during these formative years, Our daughter will be able to become a full contributing member of society. She is empathetic, kind and determined. We truly believe that if given the right tools, she will make the world a better place."

"*Before receiving our daughter's diagnosis, affected by SMA type 2, 2 years of age., I had planned to complete a Master's program in order complete a to switch careers and potentially build my own business. After the diagnosis, however, I am forced to retain my current employment since the Spinraza access is contingent upon through the private insurance provided by my current employer. My husband is under-employed and works part-time in order to manage our daughter's care including diet, physiotherapy, stretching, equipment, and building specific muscle strength though swimming, walking, climbing, etc our daughter's SMA diagnosis and limited access to Spinraza impacts our career choices and work schedules."*

"This drug should be broadly funded by the government without restrictions as it has been in many other countries. It's the only drug for SMA and clearly has positive results from personal experience. All families should be able to access this treatment for their children. Surely the long term cost on the health care system without the drug is greater in the long run." (male affected by type 2 SMA 35 years old)

"What would your panel like to know: This drug is the hope for hundreds and thousands of families. We cannot sit and debate whether someone should or should not get this drug." (mother of son affected by SMA type 3)

"My adult son has SMA Type 2. We have literally waited a lifetime for such a treatment. I would like to touch on a few points, which I'm sure you've already heard, but I would like to emphasize once again. Quality of life is different for everyone. Improved quality of life for my son could mean lifting a glass to his mouth, rolling over in bed or toileting himself unaided. Improved quality of life could mean taking a deeper breath or holding his girlfriend in his arms. Even if Spinraza will maintain and extend his existing quality of life, we would be thrilled. No one else can judge what quality of life is for another, but I do know that comparing cost effectiveness to what decision makers believe is quality of life, is wrong. We cannot fully predict how each SMA patient will respond to Spinraza, just as we cannot fully predict how a

cancer patient will respond to Chemo treatments. If SMA patients are never given this chance, we will never witness the positive life changing improvements in our loved one's abilities.

We do not understand not wanting to treat the disease, but we will treat the complications brought on by the disorder, repeatedly if necessary. Why is Canada struggling to come to this decision, when so many other countries see the value of treating the disorder firstly.

We understand your financial obligations to taxpayers, but you also have a responsibility to Canadian citizens to provide lifesaving treatments. We have been led to believe that negotiations between the provinces and Biogen, for broad access, are nearing completion, negotiations that include Spinraza for ALL SMA PATIENTS.

We cannot see how you can recommend anything but total access for all. Please do not let more families say good bye to their loved ones with this devastating disorder."

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

- ✓ **Affordability** - this was the greatest concern. Fears and anxiety that Canada does not have a framework in place for reimbursement purposes for orphan medications. The medication is expensive. This including barriers related to provincial jurisdiction with making decisions re: reimbursement. For the most part, private insurance will not cover Spinraza. There were some incidents where private carriers covered Spinraza but it was the minority. Clients expressed concerns with regards to inequity and felt that Canada doesn't "care" because they have a rare disease. They felt abandoned. While they are hopeful that CADTH will recommend broader access for all SMA types, how will clients afford the medication?
- ✓ **Access due to current reimbursement criteria** - Throughout MDC's interview process, it was clear that Spinraza had significant positive impact for individuals who were affected by other types of SMA. All clients who were interviewed and have access to Spinraza, have experienced an improvement in their muscle strength. The outcomes were significant in nature including increased mobility that greatly enhanced independence and inclusion (being able to participate in their communities, school, play etc., over all better well being, decreased unnecessary preventable complications i.e. respiratory complications due to productive cough, decrease in medical visits, decrease in caregiver burnout due to a decrease in the need for the same level of support with daily living activities) Clients expressed their feelings of frustration and anxiety related to knowing that there is a treatment available but out of their reach.

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

It is extremely important to note that no side affects mentioned during the interviews. It was clear that during the interview process, not one side affect was mentioned.

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?

Here are the most prevalent responses from our clients:

SMA is a progressive, rare genetic disease with a high unmet need.
There is no other treatment – we need to address this unmet need. There is a treatment available. The SMA community needs access to this proven treatment.

All patients regardless of type or age should get access to treatment if they need it.
People living with SMA have different experiences. It is not fair to decide that one type of SMA is more deserving than another. There is evidence that this medication offers benefit to other types of SMA other than type 1. In particular, individuals who are showing rapid disease progression may benefit the most from treatment. Clients expressed without Spinraza, people living with SMA are at an extremely high risk of completely losing the ability to walk independently and even bear weight on their legs. Furthermore, people living with SMA are at a 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 dressing. 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.

Urgency of treatment does not depend on age or Type of patient but on the ability to gain motor milestone function.
We need to make informed decisions based on motor milestone function, not the type of SMA or age of individual – this isn't fair.

Criteria for treatment depends on the treating physician and his or her assessment of the need for treatment.
My doctor needs to work with me or my (child's) treatment plan – our health care systems promises to provide care with a patient centred approach. Living with SMA varies from one person to another – my experience and needs are unique.

A Type 2/3 patient could be as urgent as a Type 1 patient.
During our interviews, it was clear that no one type of SMA was more urgent than another. Clients living with other types of SMA experienced devastating symptoms i.e. respiratory challenges – requiring ventilation, loss of mobility in legs, arms, hands etc.

The importance of maintaining motor milestone function in adults so as to keep them independent, working going to school and continue to improve their quality of life.
As individuals living with SMA age, Spinraza can play a significant role in decreasing muscle weakness resulting in the ability to have more independence in daily living activities. This includes going to school, participating fully in the community, attaining vocational activities, forming relationships – all important factors in living a fuller quality of life. Clients also expressed that even the ability to eat independently, scratch and or shift in assistive device can have a significant impact on independence and alleviating caregiver burnout. Often people take this for granted – however, living with a progressive muscle disease you quickly learn that any movement is extremely valuable and important.

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 manufacturer (Biogen 360 program). A small majority of clients have their private insurance cover Spinraza – **most do not.** No other treatment has been available.

<u>Here are some responses from our interview process:</u>

"*Through SAP (special access program) doctor worked to get it for him (son affected with SMA type 2, 12 years of age) . Experiences movement of fingers and legs more, louder (lung function has improved) oxygen levels more stable."*

"*2 years ago, called centres for trials and put on waitlist, clinical trial. Increase in strength, increase in cough strength, and confidence." (son affected by SMA type 2, 16 years old)*

"*Respiratory has improved and she is sitting up better than before the trial" (daughter affected by SMA Type 2 ,18 years of age)*

"Our son who has type 2 SMA, age 4 has been a part of the clinical trial for Spinraza for 3 years. His condition had very drastically progressed in a short amount of time and he had lost most of his abilities (crawling, standing, cruising, and even sitting independently without falling over). Shortly after his enrollment in the trial, we started to notice better stamina, better sleep, less tremors, less nighttime sweating which means better breathing, less illnesses (ex. Pneumonia, hospital stays), better and stronger coughs, the ability to stay on all fours in a crawling position once again, the ability to stand once more and to sit without falling, the ability to manoeuvre a manual chair with ease without getting tired (he still does not use a power chair), the ability to pick things off the floor and pick himself back up, the capability to go from a lying to a sitting position alone. The list goes on and 3 years later, the small but steady gains are still noticeable. Some kids his age and his type are learning to walk with walkers and/or crutches and are seeing huge improvements. All types are seeing a halt in the progression and to know that the condition is not getting any worse, is the ultimate goal and a miracle in itself. I will stress that this has been observed throughout the different types and age groups affected by SMA. No adverse affects have been noted. For our son, the procedures have been quite quick and easy and he has not complained of any side affects"

"In January 2018 upon receiving our daughter's (2 years of age) diagnosis, SMA type 3, we worked tirelessly to build our case for private insurance coverage for the only treatment available, Spinraza. Knowing that no other SMA affected families in British Columbia had been successful in gaining approval for private coverage, paired with the bleak approval rate across the country, we knew that this was the most important application we had ever put together. We needed to give our daughter her best chance at a full life.

For 3 weeks, we coordinated with dozens of companies, community based organizations and health professionals. Our final application included:

- *Signed letters of support from all of the CEOs of my employer's portfolio*
- *Letters of support from community advocacy groups related to our daughter's condition (For example, Muscular Dystrophy Canada)*
- *Letter of support from our daughter's physiotherapist and a report sharing her mobility testing score and what she could stand to gain from receiving treatment.*
- *Letters of support from our daughter's neurologist, including what she could stand to gain, previous findings from the use of the drug, costs that would incur if she did not receive treatment, etc*
- *The latest CHERISH study published about Spinraza and effectiveness*
- *A personal appeal from our family*

All of these went in to one 75 page long submission package. Concurrently, we ran a (very positive!) social media campaign which engaged several thousand individuals showing their support for our daughter and our family in order to apply gentle pressure our insurance company.

Although we were and are so thankful to get a positive judgement back from Great West Life in order to cover the drug on a year by year basis, the costs were not insignificant. Both my husband and I have taken significant time away from work in order to organize our daughter's application as well as manage her trips to BC Children's Hospital in Vancouver during the loading dose period and her other medical appointments including physiotherapy, orthopedic specialists, and many rounds of bloodwork.

Additionally, upon approval, there were significant delays in actually receiving her first dose of Spinraza due to hospital administration not having a standing procedure for the drug treatment yet. With deteriorative conditions like SMA, each day equals more muscle loss, so the wait was excruciating. We received coverage on March 22, her first injection was on May 16th, and she has now completed the 4 loading doses with the first maintenance dose scheduled for November. Our hope for the future is that a seamless procedure will be built and families will have quick access to this life-preserving, life-saving drug."

"*Beginning day one after treatment, we noted significant increases in our daughter's stamina, strength, quality of sleep, and confidence in independent movement. Examples include:*
Prior to treatment, our daughter originally needed help to lift her knee and move each foot when climbing our local playground's climbing wall. 1 month after treatment she climbed the same wall on her own, with no assistance. Two weeks following that, our daughter climbed the same wall triumphantly, 7 times in a row!
Again prior to treatment, our daughter would walk about a fourth of a block before falling over and/or getting frustrated by her instability. She'd also get quite tired and ask to be picked up quite a bit. Now that the loading doses are complete, our daughter frequently walks 2+ blocks fully unassisted and without falling. Her quality of life and confidence levels are soaring!
Our daughter regularly goes to physiotherapy to help build on the success we are seeing with treatments, and when she is not in official therapy, we are both working with her to build strength through play. We have seen incredible improvements in her walking, climbing and stamina but we've also seen new skills developing that were not even present before. In particular, our daughter has been beginning to learn how to bend her knees properly in order to go up and down steps on her own. She still needs quite a bit of reminding for proper form, but the fact that she keeps attempting to do it and we see progress if so wonderful. Hopefully one day with continued treatment and practice, she'll be able to walk up and down stairs safely on her own! ***Because of Spinraza, is our daughter is stronger****. She is more confident, more able to participate in everyday life, exploring her environment and learning to control her body.*

Spinraza has given our family hope for our daughter's future, where previously there was only fear, grief and acceptance of an inevitable decline in function and quality of life. With continued medical treatment and physiotherapy, she has a chance to live not only a normal life but an extraordinary one." (affected by SMA type 2, 2 years of age)

My son who is affected by SMA Type 2 is currently receiving spinraza through the special access program with Biogen. He's received 6 doses so far and is showing signs of improvement. He can control his head much better. He can roll from side to side which is something he hasn't been able to do since he was 4. He can raise his arms off his tray about 2 inches. Overall, his energy has increased as well as his appetite. The only negative really is the drive to London. It's over 3 hours away and we have to stay overnight."

"*My daughter's (affected by SMA Type 2) joints have stopped contracting . Her tendons have relaxed, and her joints are moveable."*

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.

Name:Stacey Lintern
Position: COO
Patient Group: Muscular Dystrophy Canada
Date: August 14, 2018.