CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**onasemnogene abeparvovec** **Spinal muscular atrophy (SMA), pediatrics**
Name of the Patient Group	**Muscular Dystrophy Canada (MDC)**
Author of the Submission	**Homira Osman**
Name of the Primary Contact for This Submission	**Homira Osman**
Email	**homira.osman@muscle.ca**
Telephone Number	**1 800 567-2873 ext 9037**

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. www.muscle.ca

Muscular Dystrophy Canada (MDC) supports people affected by muscular dystrophies 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.

Since 1954, Muscular Dystrophy Canada has been the leading health charity for the neuromuscular community in Canada. MDC represents 30,896 Canadians impacted by neuromuscular disorders including 12,047 persons with neuromuscular disorders, and 18,849 family members/caregivers.

MDC’s mission is to enhance the lives of those impacted by neuromuscular disorders by continually working to provide ongoing support and resources while relentlessly searching for a cure through well-funded research.

Muscular Dystrophy Canada offers a range of programs and services that include: systems navigation, education and knowledge translation, access to financial supports for critical life-changing equipment and services to improve quality of life, peer-to-peer networking, emotional support, evidence-based information for new treatments, medical advances, and clinical trials and advocacy.

Spinal Muscular Atrophy (SMA) is one of the neuromuscular disorder types that falls under MDC’s umbrella. SMA affects the nerve cells that control voluntary muscle. These nerve cells are called motor neurons, and SMA causes them to atrophy (die off). 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 rare condition, occurring in approximately 1 out of every 6,000 live births. It is a autosomal recessive genetic disease. About 1 out of 40 people are genetic carriers of the disease (meaning that they carry the mutated gene but do not have SMA). SMA is caused by a missing or abnormal (mutated) gene known as survival motor neuron gene 1 (SMN1) motor neurons of the brainstem and spinal cord. 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.

The phenotype is influenced by the nearby gene SMN2: additional copies of SMN2, and the c.859G>C modification in exon 7 of SMN2, correlate with reduced severity of disease. Pediatric patients less than 2 years of age with SMA most commonly have two copies of SMN2. Such infants may appear normal at birth, but within 6 months typically develop severe flaccid paralysis; they do not achieve developmental milestones such as the ability to sit independently, and generally die of respiratory failure by age 2 years.

https://muscle.ca/wecallitnmd/spinal-muscular-atrophy/

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. As part of the System Navigation Program, the Neuromuscular Service Support Staff provide front-line support to thousands of Canadians affected by neuromuscular disorders. The program operates on collaboration and patient engagement principles. Neuromuscular Service Support Staff work directly with patients and family members to identify non-medical needs (e.g., housing, transportation, access to equipment) and provide them access to the right resources in a personalized customized manner. Neuromuscular Service Support Staff work in partnership with patients and their families to address barriers, network and make connections with others in the community, share education materials and resources, enhance life skills and self-coping strategies, embrace inclusion and ultimately provide supports to help positively improve the overall well-being and quality of life of the patient and their family members.

Patient and caregiver perspectives and experience in relation to living with SMA and their experiences with SMA treatment were solicited through interactive semi-structured telephone interviews. There are over 700 clients registered with MDC affected by Spinal Muscular Atrophy (SMA). Muscular Dystrophy Canada identified and contacted parents whose child (children) have Spinal Muscular Atrophy or adults living with SMA. 484 individuals impacted by SMA were interviewed from July 7th to July 21st 2017 and August 1st to 10th 2018. Using the same questions and

interview format, another 46 individuals affected by SMA were interviewed by Staff members from June 10th to June 17th 2020. The following submission reflects data from a total of 530 individuals impacted by SMA, but only quotes and statistics from the most recent 2020 interviews (n= 46) are included in this submission. Only 3 had been treated with onasemnogene abeparvovec. We sought the opinion on the value of having onasemnogene abeparvove approved for use in Canada. A qualitative descriptive approach, employing the technique of constant comparison, was used to produce a thematic analysis.

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 impacts 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?

In response to the question posed by MDC staff: *""Can you describe how SMA impacts your (or your child's) day-to-day life and quality of life? Are there any aspects of SMA that are more important to control than others?"* - the following 4 key themes were identified: negative impact on mental and emotional well-being; increased dependence and load on families; breathing, swallowing and mobility are mostly affected; loss of independence. The below quotes from individuals affected by SMA highlight that the impact of SMA is not purely physical, but that the condition impacts mental health, quality of life and the wellbeing of families.

Negative Impact on Mental and Emotional Well-Being

"I have a lot of able bodied friends making able bodied things more difficult for me to do. I get tired very easily, I have pain and don't sleep well due to my contractures. I am degrading...every two years I see a difference. It is ***depressing****. Mental state is something that I need to control more than anything. You have good days and bad days, but it is a constant grind. You see the light for the drugs, but you are not at the end of the tunnel, which is frustrating. Confusing about who to go to for what information."*

"Living with SMA is a nightmare. Breathing on a machine 24 hours a day and not being able while being fully aware and having a sharp mind is ***torturous*** *and makes you question life."*

"SMA is a 24/7 nuisance and sometimes worse than that depending on how the day is going. There isn't much of a life and there isn't anything that you can do. Incredible loss of independence."

"Our daughter is growing up very ***emotional*** *as she understands what she is not able to do."*

"Horrendous diagnosis, very fatal, ***scary, traumatic*** *to see your child like that."*

"SMA creates ***emotional stress*** *for child and family."*

"SMA robs a child of a normal life."

"SMA is ***taxing and exhausting*****.**"

"There is a lot ***more worry and stress*** *added to our regular day."*

"I try to have as good quality of a life as possible, but there is also the aspect of ***anxiety, depression and stress*** *which is directly related to living with SMA."*

*"SMA takes a **toll on our mental health**."*

*"SMA creates so much **fear**."*

*"It can **hurt to watch my body wither away before my eyes**, and to feel that this is the last time that I will do something."*

*"He has had accidents and surgeries that resulted in broken femurs and is due for spinal fusion which is **terrifying**."*

*"I **feel like I'm stuck** in hell, but I have to do the best for my son."*

*"Endless advocating is **exhausting and draining**."*

***"**She experiences **emotional outbursts**. She hates her body and wishes it could be like others. She wants to be able to walk up and down stairs and do what her friends can do so she is not left out."*

*"Not having access to treatment has left us feeling **depressed, abandoned and defeated**. My decline with SMA has led me down a **deep tunnel of sadness and despair**. I felt, and sometimes still do feel **worthless, incapable, and expendable**. I continually work on my mental health, trying to rewire my brain to see the good things I have and be grateful for it."*

*"Our son's **mental health has been compromised** by SMA."*

*"I feel his physical differences **impact his ability to make friends** and participate in varied social circles. His **self-esteem seems to be significantly impacted** because he lets his friends "walk all over him" because he's afraid they won't want to be his friends anymore if he speaks out. I feel this, in turn, affects his relationship with his younger brother in that he wants to take control in interactions with him because he knows his brother will never leave him. I feel that the social-emotional impact of SMA on younger kids is an important issue to address."*

*"It's **terrifying** to think about the future. Who would want to marry me?"*

*"It is **solemn** and fascinating to play the "What If?" game. What if I was born earlier? What if I could still walk? What if I had access to treatment? **What if…?**"*

*"I **worry** about dating and sex life."*

*"It's **frustrating** knowing that **my love life will take an unnecessary hit** due purely to my disability."*

Increased Dependence on Families/Caregiver Burnout

*"As parents our entire lives are **consumed around** our son's needs."*

*"He needs help with everything to eat, dress and bath. It is an **impact for the entire family**. We can't travel as easily as we wish. A few years ago our other son was assisting with our son's care, but now it is on us completely. He lost his ability to eat 2 years ago and loses his independence as time goes on."*

*"Our daughter requires breathing support and is **fully dependent on caregivers** for all transfers and activities of daily living. Breathing is the most problematic, unstable at night and there are a lot of unknowns about how it will progress."*

*"SMA **totally changed our lives**, Our son who is our first child, was not reaching any of his development milestones, for example when we practiced tummy time he would just lay there. It took about 4 months to get the SMA diagnosis for our son. After the diagnosis, I was in denial about it. The first time our sons great grandparents came to meet him we were in a restaurant, and our son had a cardiac arrest. The Fire fighters and paramedics were able to revive him, after that we were 7 months in the Children's Hospital , 4 months in the PICU and 3 months in the ward before we were able to go home. Our son has 24/7 BI-PAP, Oximeters, he is G-Tube fed and needs constant suctioning. He needs 24/7 care and because of that I haven't been able to work which puts a financial strain on our family. We do have home care come in during the night, which is great, but it does make it hard to have alone time with my partner."*

*"I think most parents, like us, are **making lots of sacrifices** for the chance to get the treatment and see improvements for their kids. We are doing whatever we can to see a difference in the positive direction for our child."*

*"There's a lot of things she can't do, like even just walking, so we are having to carry her. And she's only 3, but it can get **tiring for us**."*

*"It is very devastating for son and for family, a lot of **burden on the family** especially when there are other children. He cannot participate in anything. Most important is mobility it effects everyone. For some it is the lungs."*

*"It affects EVERYTHING about his life and ours. We haven't been able to travel because he is invasively intubated. SMA puts **limits on our ability to travel and socialize and our housing**. One parent has to be his caregiver, so we have gone down to a single income. Half of our income is just gone now."*

*"SMA effects everything. 100% of our lives. Everyday **it dictates how we operate as a family**, what our family experiences. It impacts our finances, emotions…everything."*

*"His care is **a lot of work**, so it takes up a lot of time to make sure we are doing everything we need to do to thrive."*

*"Our family **can't participate** in events. We feel **isolated**."*

*"**SMA impacts pretty much every aspect of our family life**. How we plan our day, working full-time, caregiver commitments and responsibilities, stress and concern for overall mental and physical health. We are fortunate he is a smart, strong-willed, resilient, independent young man, but SMA still gets in our way, in some form, everyday."*

*"I am single parent, let me tell you how tired I am. Constant appointments, work and just trying to keep her life as full as possible. **I don't have time to do anything for myself**."*

Breathing, Swallowing and Mobility Are Most Affected

*"His major issues are **swallowing and breathing."***

*"**Breathing was the most concerning issue**, **swallowing was difficult, and mobility.** Children are so bright, it's liked being trapped in your own body, would cry because he was not comfortable but couldn't readjust himself."*

*"Biggest issue for our daughter is **breathing and swallowing.** Has a new G-Tube and Bi-Pap machine."*

*"The **eating and swallowing aspect** are definitely things that are important for us to control. Our daughter is not trached, but we do have a feeding apparatus for the evenings when she is more tired."*

Loss of Independence

*"He always needs more help. **Someone always has to be with him** or near him in case he falls."*

*"It impacts my daily life in almost every aspect. I cannot get myself out of bed on my own (need to be lifted), there are many things I cannot lift or carry or grab due to their size/weight. I need help toileting/showering. I need help every time I want to leave my powerchair to be transferred somewhere. I am no longer able to drive, so I have to depend on others for rides and transportation. I **basically lack the freedom to be able to do anything on my own** 100% and must depend on others for many of my daily activities."*

*"The physical aspect of it is he is **not extremely independent**. He can't do a lot of things on his own, which limits our ability as a family to do normal things. From a social aspect it limits what we can participate in."*

"She can't do any activities of daily living on her own."

*"SMA is an all encompassing condition. It impacts life 24/7 and more so as the years go on. My son is 11 and has been diagnosed since age 3, he was able to crawl until age 4 and has used a power wheelchair since then. He needs help with every aspect of daily life: toileting, transfers, eating and meal prep, homework, repositioning and equipment management at night. **His independence is limited**, and he cannot do the things his friends are doing (like going outside to play) without an adult caregiver."*

*"The biggest impact of SMA is **loss of independence**."*

*"The foremost concern we have is our son remaining healthy and strong enough to continue being **independent** and happy."*

*"SMA impacts every aspect of his life and he is only 5. **He is dependent on us for anything and everything** including playing. Our family has worked really hard for our son to have a good a quality of life so that he doesn't think he has any restrictions in life."*

*"SMA impacts his everyday life from personal care and **relies on the entire family** for basic needs."*

*"My 6.5 year old **child has to do things for me like help me put my shoes on** and set my legs in a safe position when we want to go places together like the park or for a walk. He is a child and he has to help his mother in this way, it's not fair to him."*

"He **can't do a lot of things** that his peers can do at 14. Not being able to play on team sports."

*"SMA is restricting. I need help using a fork and I am by myself. I **had to stop going to school** in 2014 because it was too tiring. It is definitely the physical barriers that affect me."*

"SMA affects her independence and ability to do anything by herself."

"She's strong willed and wants to do things on her own and to control her body and legs. But she can't use her legs and wants more control over her body."

"I am dependent on people for small tasks like scratching my head."

*"It is frustrating (understatement) to be **dependent on people to do simple tasks**."*

*"It is **crushing to lose an ability and having to ask for help** for the first time. My parents raised me to know that there is nothing wrong with asking for help, nonetheless, it is embarrassing, especially if someone makes a comment like "can't you do that yourself?". In some ways it is worse when you can feel yourself losing an ability, every time doing a certain task and wondering if that would be the last time."*

"I cannot go over to friends' houses easily (nearly impossible) because most houses aren't accessible and I struggle to sit out of my chair for long periods of time."

*"Being tied to another human being almost 24/7 is frustrating. **Depending on another person for survival** is demoralizing."*

4. 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) approved onasemnogene abeparvove for the treatment of pediatric patients less than 2 years of age with spinal muscular atrophy with bi-allelic mutations in the survival motor neuron 1 (SMN1) gene. onasemnogene abeparvove has demonstrated clear efficacy across multiple phase clinical trials in infantile-onset SMA. Data from adequate and well-controlled trials provide substantial evidence of effectiveness for treatment of pediatric patients less than 2 years of age with SMA with bi-allelic mutations in the SMN1 gene. Efficacy was based on improvement in survival, and achievement of developmental motor milestones such as sitting without support.

In response to the question posed by MDC staff: *"How are you managing SMA with currently available treatments or therapies. For each therapy what are the benefits seen, and side effects experienced? Do you have any difficulties accessing these treatments?"* - the following 3 key themes emerged: difficulty accessing treatments; positive changes observed; cost and time lost is a significant barrier. The below quotes from individuals affected by SMA highlight that while there are more treatments available for SMA which has contributed to positive health outcomes, there remains significant barriers from a cost, loss of productivity and access perspective.

Difficulty Accessing Treatments

*"I have difficulty **accessing** these treatments. Drug studies are giving me hope because I feel like I am doing something! I wish there was more **available**."*
*"There are no treatments to **access** or receive because they are not approved or covered for me due to my spinal fusion."*

*"We could not **access** onasemnogene abeparvove in Canada. We had to move to the US to **access** this drug."*

*"My child was diagnosed six weeks ago. On a lottery to **access** onasemnogene abeparvove in Canada."*

*"I have not been able to secure **access** to any of the treatments (such as Spinraza) yet, as I am 32 and generally over the age cap that the government has put in place. I have tried physiotherapy, but it is also hard to find a good physiotherapist who can manage someone with SMA - as most of them are trained for athletic injuries and people who are generally able-bodied looking to recover from something. I do take Vitamins and Creatine, but I would say that the benefits seem minimal at best."*

*"I am not currently on any treatments. I talked with my doctor about Spinraza, but I am **not currently eligible**."*

*"A lot of work needed to be done to get Spinraza. **Jumping through unbelievable hoops to access treatment.** It has been extremely emotional on our family."*

*"Through no fault of my own and despite my best efforts, I have **zero access to any sort of SMA therapies or treatments**. Back in February all adult patients living in Alberta were declined special authorization for Spinraza. We are all in the dark on what is going on. It has been nearly a year since they said we would get **access** to treatment through this coverage, and yet here we are still without.*

Positive Changes & Side Effects Observed

*"Current treatment is Spinraza every 4 months. My child has had **some improvement**, can minimally breathe better for a couple of hours. Still can't hold head, move muscles, or swallow."*

*"On a clinical trial for an oral medication called Risdiplam. While it has **slowed down progression** of SMA, there has been weight gain."*

"Current treatment have not seen significant benefits, but no side effects."

*"My son is on Spinraza, he **hasn't declined** in function, and we haven't seen any side effects.*

*"Currently on Spinraza. **Definitely beneficial**."*

*"My daughter is on Spinraza – we have to be very careful when she first gets the injection, and told we will only see **major improvement in a year**, with physio, seeing little improvement with hand movement etc. not seeing any side effects. She feels some pain after the injection."*

*"My daughter has received 3 loading doses of Spinraza, first in hospital, 2 in-patient. Spinraza treatment appeared to be seamless and successful. She is now **able to move her hands** and head and crying louder, coughing, her **muscles are getting stronger**. Only one month has changed perspective and outlook. Already **improved quality life**. Downside is the spinal tap and fusion for the rest of her life."*

*"My son has been on Spinraza for two years. He is on dose number 11 or 12 and it has been **maintaining his strength** through a growth spurt. He had weight gain in the beginning, but it seems to have tapered. One spinal headache. Sometimes he can be grumpy with the drug."*

*"My son has received Spinraza since December 2017. That is the reason he **is alive today** - no doubt. He is trached. He does OT/PT daily to keep joint range of motion and prevent scoliosis. He uses sign language. He has a back brace. We are considering switching to Risdiplam."*

"My 4 year old is on Spinraza and my baby is on AVXS-101 – seeing improvements with both treatments."

"We are lucky to be in the clinical trial for Risdiplam and were told that we will be able to continue with the treatments after the trial is over. We have been very pleased as it is ***working really well****. The delivery systems is easier on my son – its only one dose orally every day with no side effects."*

"There has ***increase in strength*** *especially after the Spinraza treatment, and increase in strength and abilities but not as much as early on. Side-effects - no physical side-effects noticed but it is a long day at the hospital, blood work before and after - extra hospital visits. She must lay down for the rest of day as it treatment or the first night after the treatment is dozy and doesn't sleep well the first night."*

"Benefits are that he has ***gained motor function*** *from when my son started Spinraza. He is not losing any muscle and* ***is still alive*** *which is an enormous benefit to accessing treatment. It has* ***stopped the progression****. No side effects."*

"My daughter is on Sprinaza and has headaches for a couple of days, has ***gained neck strength****, has* ***seen some improvements****. When it gets close to the 3 month mark (when we are due for the next injection), we see more weakness until the next injection kicks in."*

"Spinraza has ***slowed down the progression****, building strength, starting to move,* ***still alive****. No side effects noted."*

"The boys are doing the Spinraza, need more time to see results."

"We noticed a ***difference in his movement and strength*** *after the first treatment of Spinraza and noticed changes after every dose.* ***Some changes are small and some are bigger but they are all in a positive direction.*** *He has had side effects associated with the delivery of Spinraza including spinal headache and nicked nerves."*

"Spinraza has benefits - have been amazing affecting all of her ability and mobility, being ***able to walk without the fear of falling and creating independence****. Can walk, dance, tries to run.... Sense of self is more confident. Before treatment, all she did was cry when she couldn't do things. Due to Spinraza, my daughter is willing to try more and is* ***much more happier****."*

"My son is currently on a maintenance schedule with Spinraza injections every 4 months. With Spinraza, he has been able to ***maintain the abilities*** *he currently has, and has not shown any regression or loss of abilities. Without Spinraza, he will most certainly regress and his abilities will be taken away from him, despite daily physiotherapy."*

"My son is on Spinraza and we have seen improvements in the last year. He is getting stronger – before treatment he couldn't move his finger and ***now he can move his finger****. He is more stable. It is a long day for a treatment, takes a whole day. It is an exhausting long day at clinic."*

"My son is on Spinraza and it has been beneficial and he ***has gained strength, fine motor skills and is able to do more on this own.*** *No side effects other than a head ache shortly after injection."*

"My son is on Spinraza and has been on it for 5 years. Benefits have been huge. At 7 months old he lost all of his movements, now he ***can sit up by himself and has learned how to swallow, breathe on his own and can control his own power chair.*** *The drawbacks have been that the trips for Spinraza have become traumatic regarding lumbar puncture. As he becomes older, the treatment is harder for him because is more scared."*

"My child is currently on Spinraza every four months but he has severe reactions. We are noticing he is ***getting strong and gaining weight and there is improved muscle tone.*** *It's easier for him to manage stairs and now able to ride his scooter and bike again before. He has had 6 doses, first 4 were really bad but it is working better now, pain medication and needle angle, each time the drug access got better. He developed severe headaches and then had very bad to vomiting and he was admitted so they could medicate the severe reaction."*

"My child can ***now sit up and play with things****. He has* ***achieved many milestones*** *and there have been no side effects."*

"Spinraza - approved by Canada's compassion care in 2017, she has done ***a lot better*** *can clear her throat, voice is louder and stronger. She is able use a tablet."*

"My daughter has stopped progressing through the treatment and ***gaining strength****. Side effects are related to the lumbar puncture such as severe back pain."*

"Our son is going in for his 4th Spinraza dose. We have recently starting to see ***gains in the amount of time he can remain on his feet without tiring out****. He is able to be out on his scooter with his friends for much longer than he could in the last couple of years. He has had limited side effects other than pain in his legs and a slight headache after his second dose."*

Our son (4 years old type 2) has received 9 doses of Sprinraza and we have seen ***tremendous improvement****. He was beginning to show signs of difficulty and unsteadiness in his independent sitting, lost his ability to crawl and could no longer get up into a seated position if he was laying down. These gross motor skills have improved he was able to sit up again after early dosing and is now slowly crawling and has great balance and core strength. His scores have increased dramatically and we are now able to change our thinking and planning for what might be. The sky is the limit! We have not seen any side effects and our private insurance covered the cost of treatment and had little difficulty accessing it."*

"I am a part of a drug trial for the drug Risdiplam. I can see ***positive changes****."*

"I am part of a drug trial, Risdiplam. This is a liquid oral drug that I take daily. I have definitely seen improvements. The primary one for me is that I have gained weight. I am the thinnest person that I know. I can see my rib cage, I'm so skinny. This is not due to a lack of food, or a lack of trying. For years I stayed the same weight while I just got longer. But, since taking the drug, I have gained nearly 10lbs in a year, which is absolutely incredible. I am definitely ***a healthier looking person*** *now. The thing with weight gain though, is that it means the muscles have that much more to hold up. The amazing thing about this drug though, is that I haven't gotten weaker even though I am gaining weight."*

Cost and Time Lost Is A Significant Barrier

"We are paying for benefits ***out of pocket*** *so he can receive the treatment. He also needs lab test completed before the lumber puncture."*

"Has to go to the hospital every 4 months for a spinal tap and injection, can be very risky. Has scoliosis that has no treatment and has to be managed by braces. We [both parents] have to take ***time off work*** *to accompany child. Spinraza costs 1 million dollars first year and after that $375,000 year. Not every insurance covers it, but has* ***to pay high premiums****, and it affects you as you can't change jobs, even if it is a good opportunity."*

*"My child has had onasemnogene abeparvove but had to move to US to access this drug which was costly. We are **still in debt and there were a lot of out of pocket expenses**. For Spinraza, it wasn't too bad as our family lives near Toronto but travel to hospital, parking and **time off** work adds up."*

*"My son is on compassionate dosing, and **funded access was difficult** but has gotten better over time."*

*"Physiotherapy is an **out of pocket** expense."*

*"Only approved for 6 sessions of physiotherapy covered by OHIP. Will be paying **out of pocket** for much needed physiotherapy."*

*"Taking a day off work is a bit of a struggle some times and we had to fight our insurance company to get paid **time off**."*

*"While there is no cost to accessing Spinraza, there is a **huge cost for missing work** to attend the treatments."*

"Physiotherapy 2-3 times a week is only possible via work benefits – which is really helpful."

*"My son is currently on Spinraza so every four months we **travel** to Toronto which **can be costly**."*

*"My daughter is currently on Spinraza. She has **no funding** for physiotherapy, paying out of pocket, needs night nursing."*

*"The **cost is just too astronomical**."*

"We need to go to London, ON which is a 3-4 hour drive. My child has anxiety over getting the injections. It is becoming increasingly difficult, needing time off work, expenses like meals and travel*."*

*"For us the constant appointments means **loss of pay (time off work).** If you look at my time sheet… throughout the year I have worked maybe 2 full pay periods. This is hugely problematic."*

*"My son has missed many days of school because of travel to get to appointments for Spinraza. We have missed many days of work. We do physiotherapy once a week, aquatic therapy once a week, ABM NeuroMovement lessons in series every 4 weeks, standing 3 times a week, clinic visits, doctors visits outside of clinic – all of these take **time, energy and money** (for therapy not covered by insurance)."*

*"In order to provide my daughter Spinraza, it requires 3 days, **travel, time off work**. We were able to access Spinraza privately for the first 2 years, now able to access through the government. The access was a **huge cost to the mental health, cost to the family** and it's been emotional. Spinraza is only offered in one hospital in BC and a lot of travel required to access and taking time off work."*

*"We currently do not have any difficulty accessing and receiving treatment, but if the Government of Alberta rescinds their agreement to fund these treatments, there would be **no way that we could pay for these treatments privately.**"*

*"It's **time, time off work, travel costs** – this is a huge barrier."*

*"The **cost** of Spinraza concerns our family if they have to pay."*

"I haven't been able to go back work. We have arranged a schedule to manage our children's appointments. This affects my husband and his work schedule."

*"Taking the **time off work** is difficult to get him to treatments but that will be easier once he is in the maintenance phase so we are only taking him every four months."*

*"With the near-constant rotation of caregivers it is difficult to maintain a routine and receive quality care, as it takes a bit to learn. A side effect is **time lost**. It often feels as though I have to choose between school and a social life, and maintaining my physical health."*

5. 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?

Improvements that patients and caregivers would like to see in a new treatment can be categorized as those that (1) improve independence and quality of life; (2) improve breathing, swallowing and motor functions; and (3) maintain skills and abilities/slow down rate of progression of disease.

Improved Independence and Quality of Life

*"The improvements of a treatment would be massive **if I were able to do things on my own**. I have wonderful care providers, but if I could call them less that would be great. I could transfer into cars and go on trips without a worry and could take my manual chair with me on trips. I could play more sports and get a regular bed instead of a hospital bed."*

*"Increased strength. If I had 20% stronger arms I would be 90% **less dependent** through the day."*

*"**Better quality of life** if able to do things by himself."*

*"A **better quality of life** for our son."*

*"More **independence**."*

*"To be able to transfer herself, or turn herself, would like **more mobility which means more independence.**"*

*"Anything that is going to give him better strength would be good. If he has **better motor strength**, he can do more for himself and **participate** more in life."*

*"A treatment is successful if my daughter wouldn't need as much help as she currently does and could have **more independence**."*

*"**Quality of life** should be considered when weighing treatments."*

*"For, a realistic goal would be to dress the upper half of me. Or maybe even be able to roll myself over at night. These would greatly **increase my independence** and **reduce my reliance on others**."*

*"The **improvement of quality of life** is very important to consider: not having to rely on so many people to help him in his every day activities."*

*"My dream is to be able to get a coat on and off myself without help. Having the strength to put on a coat would be massively **liberating for daily independence**. Having that strength also implies the strength to be able to do other tasks significantly easier. Tasks like pushing an elevator button, crosswalk button, opening lunch containers and pens, scratch my head, comb my hair, roll myself over at night."*

*"I want a treatment to give my daughter **as much independence** as possible."*

*"To have **regular independent friendships** and to talk openly with friends."*

*"To have **improved mental health** outcomes."*

*"Being able to go to bathroom **by herself.**"*

*"I would hope that treatment for my son would mean he would have less pain and more stamina to **keep up** with his peers and **enjoy the same activities** in more of the same way that they do."*

Improvements with Breathing, Swallowing and Mobility

*"Would like to see more improvement on **breathing, swallowing, and movement**."*

*"More **strength and mobility**."*

*"Reverse **motor** impairments."*

*"The **mobility gains**. It would be great if they can learn to walk on their own."*

*"I would love to see **more strength in his back and legs**. He has scoliosis, wouldn't it be amazing if his back muscles were strong enough to hold his back where it is. If his leg muscles were stronger."*

*"Increased **upper body function** would permanently change my life."*

*"If a treatment allowed him to **swallow and eat safely** on his own."*

*"We are hoping he will **gain back some strength** so that he could ride a bike with friends and climb and descend stairs **without falling**."*

*"**Reduce number of falls**."*

Maintenance of Skills and Abilities

*"If he was able to **keep his current abilities.** It would be great if he could eat by himself again. **It is little things**, but at the end of the end of the day it is a lot. If he could gain a little strength in his arms."*

*"Even something small like **energy** – preserving energy – that would be a benefit."*

*"Ideally a treatment would be able to reverse the damage of SMA. But it is important that some things are kept the same and not lost. **Stopping further progression** and loss of skill is still a win."*

In terms of trade-offs that patients, families, and caregivers consider when choosing therapy: unanimously all interviewees noted cost as a key consideration. Invasiveness (i.e., no need for lumbar puncture, no need for anesthesia), number and frequency of hospital visits (i.e., drug can be taken safely at home or a one-time visit), limited side effects and age (i.e., access to a drug regardless of age) were also noted as considerations when selecting between treatments.

6. 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? If applicable, please provide the sequencing of therapies that patients would have used prior to and after in relation to the new drug under review. Please also include a summary statement of the key values that are important to patients and caregivers with respect to the drug under review.

Only 3 had been treated with onasemnogene abeparvovec. 2 of the 3 received the drug in the United States. Only 1 received the drug in Canada via a "lottery" (Managed Access Programme (MAP)). All were under the age of 2 with infantile-onset SMA.

Benefits following onasemnogene abeparvovec were:

"My son is now feeding himself. He can roll, sit, starting to crawl. Also he can now move his legs and bear his own weight for 7 seconds. Every day we notice an improvement."

"Rapid results seen. Already noticed improved breathing and motor abilities."

Disadvantages following onasemnogene abeparvovec were:

"Had to be put on steroids and possibility of liver problems, but have had no issues to date."

"A bit moody and tired for 3 days after treatment."

"No side effects. Nothing bad to report at all. But haven't had it long enough to know about long-term side effects."

In terms of whether the drug was easier to use than previous treatment, all 3 families reported that it was easier than Spinraza given that it required only a one-time treatment vs. repeated treatments that tend to "wear off." They had also received Spinraza.

Although only a small number have received onasemnogene abeparvovec, others that were interviewed mentioned that they would "do anything" to get access for the treatment for their child and a few are currently on the MAP list and others are crowdfunding for access to the treatment in the United States.

The key value mentioned is an **expedited fair review process**, so that their child does not become *"too old"* for the drug and it doesn't *"become too late."*

7. Companion Diagnostic Test

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- Access to testing: for example, proximity to testing facility, availability of appointment.
- Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?
- Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?
- How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

40 out of the 43 (93%) reported that they did have genetic testing completed; this test confirmed their SMA diagnosis. The vast majority found it to be a fairly easy and straightforward process. Given the quick turn around time (reported to be 2 weeks on average) and the delays in development, the testing was necessary and did not cause significant anxiety. The test itself was done via blood draw and was simple. Below are quotes that further highlight the experiences of patients and caregivers with the testing:

"The process was easy for genetic testing."

"It was not complicated. Very easy, findings only took a couple of weeks."

"Genetic testing was done easily and seamlessly at 4 months old."

"It was quite easy and our whole family was tested."

"The process was easy."

"Testing was easy and confirmed SMA diagnosis."

"The genetic testing process was pretty easy, we were in Hospital for a week while we waited for test results, both my partner and I were also tested."

"As soon as she wasn't meeting milestones, they tested her right away."

"He received testing at his second birthday. It was very easy to access."

"First the doctor didn't know much about SMA, so it was difficult. I had to plea for the testing. I believe the diagnosis could have been done earlier and would have helped my son. There should be newborn screening and more knowledge needed in the medical community about SMA."

"Genetic testing was very easy to access. The team at the Hospital for Sick Children took care of everything, results took a month and they explained everything in a clear way. Following the diagnosis, it took a month to get approval for treatment and then another 4 months to get access to treatment."

"Very easy. They just took his blood and it came back saying he had SMA."
"There were no barriers to accessing genetic testing because he was already in respiratory failure and in the hospital. The only barriers were getting someone to take us seriously because it wasn't on the newborn screening so it wasn't caught, but I could see things were off, he had such low muscle tone. Once he was seen by the right person, the testing was not difficult to get."

"Delays in development led to being tested. The testing was pain free. The process was pretty efficient."

"I have received genetic testing, and it was a fairly easy process and mostly done through my former specialists office. I think I've had it done twice (at least), and it didn't seem like there were any barriers aside from the fact I had to physically get to the doctor's office to have it done."

"Our son has had his genetic testing but we had to travel to the USA to get it done as we found that we were having issues with Doctors wanting to prescribe the testing for him. The rest of my family has not undergone the testing completed as our son with SMA is adopted."

"Genetic testing was pretty straightforward, there were no barriers."

"We had testing done. We had to get it to get his current treatment. It took 1.5 weeks to get the results."

"We had to advocate to have the initial testing done. Initial access was terrible, was told I was an anxious parent. The actual process was pretty straightforward."

"The testing was very easy to do, went through The Hospital for Sick Children for the test and met with genetic counselor."

"No barriers to testing at all."

"It was easy to access the testing because our child was in hospital. The results were clear. But when the genetic testing results came about, Dad had a lot of problems with it more so from an acceptance perspective."

"Yes, we received genetic testing 18 months after the first major symptoms appeared. The genetic testing process was easy once it was recognized that it might be required, a simple blood draw. The barriers for us was a lack of knowledge about SMA as a possible diagnosis by our neurologist."

"We declined testing ourselves as we were not planning on having any other children. If there had been testing available when we found out we were pregnant, we would have done it. If it is a requirement for receiving AVXS-101, we would certainly have genetic testing done."

"We were lucky. Our doctor was familiar with SMA and knew who to refer to. The process was smooth. The barrier was needed to be referred to multiple people. When spoke to other families the barrier was most professionals didn't know about SMA and there was a delay in diagnosis and access to the Spinraza."

"It took 3 months to find the right physician to order the genetic testing."

"It was an easy blood test. It has hard on my son because he was 7 months and he was screaming.

"Pretty easy process. Yes, would do genetic testing again if another drug was available and if updated test results were needed."

"It took 4 years prior to the diagnosis of SMA. It was a process of elimination."

"They tested when she was 6 months old and went into emergency. The HCP assumed she had SMA and a week letter she had a cold and she was admitted into hospital. At first the hospital didn't do the genetic tests. Then the HCP did the tests as there were no improvements. Overall the testing was easy."

Yes, did receive two different tests: the first test provided a misdiagnosis, the second provided the accurate diagnosis. There were no issues with getting the test."

"We did and it was a pretty seamless process. We were quite fortunate that our referral turnaround time was short (within a week or two of initial neurology appointment) and we were easily tested. Extended family out of province who have tried to get tested have not been so fortunate and have found it to be challenging."

"I have had testing. I was an infant. Apparently my family struggled to find a doctor that would take my symptoms seriously."

"I was immediately tested as an infant as I am the second child with SMA (I have an older brother with it as well). Since it was already in the family, and a preexisting concern, it was a relatively smooth process, as far as I am aware."

8. Anything Else?

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

"We don't want other Canadians to have to go through what we have been through. We wish that this drug is available right away to all that need it. Please approve."

"The approval of this drug will be so important for early intervention."

"Any treatment that makes life longer and better is so appreciated."

"I am on borrowed time, don't take your time."

"AVXS-101 would be less expensive than Spinraza over the lifetime of a person with SMA and much more effective It would be nice to make it easily accessible, even for children over the age of 2."

"These breakthroughs are vital to the quality of life for the child as well as the whole family, also the timing is critical. It's a disease that is so close to a cure, it is imperative that more knowledge and effort is put in. It is horrific for families to have to go bankrupt to try to save their child's life. If this is added to newborn screening and children are treated pre-symptomatically, they will likely live normal lives."

"The main thing is how difficult this is, and how much of gift it would be to have one injection and to improve our child's quality of life. It would be very impactful for so many families in Canada."

"This drug is changing lives. If this came out when he was two I would have given it to him. Please don't let other Canadians miss out."

"This drug has the potential to actually deliver full copies of the gene he is missing, this could be a cure from what we have seen with this drug. The sooner they approve it, the sooner Type 1's can be addressed, and the more lives can be positively influenced. Families are going to make the decision to keep their children alive. To treat more children with this drug will lessen the cost on society for long-term treatment both medically and educationally in terms of teacher's aids in classrooms."

"If our family lived in Ontario, our daughter would have tested with newborn screening. Our daughter could have been diagnosed sooner and may have had access to the drugs sooner. But it is not available in BC."

"This disease impacts the whole family. Approving this drug would mean everything."

"I would just love the opportunity to be included in trials, or for them to open up the drug to anyone who's specialist believes they could benefit from it - regardless of age or SMA type."

"You can not take your time getting this approved. It needs to be approved as quick as possible. We need to get this treatment into newborn as soon as possible. It will not only save lives but can change lives for the better. It will also save health care systems millions of dollars in hospital stay, medical equipment and already available treatments."

"A one time administration sounds very appealing for people who do not live in current urban centers for where the current treatment is being administered."

"I think the key thing is to really speak to the people, my daughter is very bright, anything that would improve her quality of life, she has the same aspirations as anyone and how do you explain that you could have a normal life but because a drug is too expensive, you can't have it. I think that the cost of the hospital visits and stays counter balances the cost of the medication."

"I wish the CADTH committee would meet us families to be able to understand all the aspects as this impacts every aspect of every day. I live in fear every day that I am going to lose my child."

"TIME! The length of time it takes to get something approved in Canada, a person with SMA losses an ability or dies. The urgency that is felt by persons with SMA and their families is not felt by CADTH. Our process here in Canada needs to be improved."

"If children have access to this treatment early enough, who knows what the course of their life might be? If this treatment becomes available for older people who have SMA, we would absolutely consider it since it is a different method of treatment to Spinraza. Any treatment is a miracle, if the treatment halts the progression of the disease – miracle. If it helps a person get a little bit stronger to hold a cup and drink on their own – miracle. If it helps a baby who might have died from SMA early in life gain the ability to walk – miracle. Each person with SMA regardless of their age deserves access to these treatments."

"Having AVXS-101 available as a fully-funded treatment would make a very positive long-term impact on our entire family's life. Our son will require treatment in some form for his entire lifetime, and as his parents, we want him to be able to have a long, productive, independent life. Even at 14 years old, our son has dreams of going to university, having a challenging job and raising a family of his own – and we will stop at nothing to be able to make his aspirations come true."

"SMA is devastating condition that affects the whole family and any drug that can stop or reverse the condition will be beneficial. SMA affects the whole family, It is emotional and financial exhausting.. Any treatments available is beneficial."

"We don't have time..... we need more treatment options. Please don't take as long as you did with Spinraza. People don't have time. "

"If our daughter can go to school without a worry about receiving a cold or flu and to attend school on a regular basis to maintain and increase social interaction instead of being homeschooled throughout the year. The common cold can kill her. This will allow her to have more independence."

"I think it is very difficult for many children and families to make the frequency of the current treatment regimen work. It is scary, especially in this time of pandemic, to take your child to the hospital so frequently to get the Spinraza injections. If there was a way to decrease the frequency of injections, while maintaining the same benefits, that would be most beneficial for children and their families."

"Just because there is one approved treatment that patients are able to access does not mean that others can and should be ignored. Everyday things that people take for granted like being able to sit up, roll over, button a shirt, can be life altering and improving for patients with SMA."

"The ability to stop SMA from ever getting to the point that I'm at affects the whole family. My older, able-bodied siblings lost much of their childhood to my diagnosis. Suddenly the local physically challenged children stole all the attention and resources of the surrounding community. They needed to help babysit and lost the energy and involvement that my parents were previously able to give them."

"A disability in the family impacts everyone. Not just those who have it. It shapes the way a family operates, communicates, jokes, and even sees the world. Not having one does the same. And knowing what was evaded also has an impact. It is not one person's life that is affected, it is everyone's, for the good the bad, the peaks and the valleys, the celebrations and the mourning. While it is important to laugh and joke, it is equally important to be serious and respect the monster called SMA. It is a beast. It is a tough pill to swallow. If it is a beast that can be tamed, it should be."

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 we did not receive any help from outside of our organization.

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 we did not receive any help from outside of our organization.

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
Novartis				X ($60,000 in the last 2 years, including $50,000 for a SMA Summit (Medical and Scientific Conference sponsorship) and $10,000 as a gift towards a fundraising gala.

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: Homira Osman
Position: Director of Knowledge Translation & External Engagement
Patient Group: Muscular Dystrophy Canada
Date: July 15, 2020