CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**Risdiplam** **Spinal muscular atrophy (SMA)**
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 and voice of 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 critical 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.

Funded by Canadians from coast to coast, our investment in the research community is advancing the development of important new treatments. Our programs and services play a critical role in informing and supporting members of the neuromuscular community by funding equipment to improve daily life; hosting family and caregiver retreats; providing emotional and educational support; and with providing access to vital resources and support systems. Our advocacy efforts focus on enhancing public policy at all levels of government to bring about positive change. We are currently working to bring new treatments and trials to

Canada. Advances in medicine have resulted in individuals with neuromuscular disorders living longer but not necessarily living better. As their disorder progresses and changes, so do their needs and financial strains.

Our desire is to provide support through all stages of disease progression by providing the tools, resources and support individuals need to live a full and rich life.

Spinal Muscular Atrophy (SMA) is one of the neuromuscular disorders 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 over time. Depending on the type of SMA, an individual's physical strength and their ability to walk, eat or breathe can be significantly diminished or lost.

https://muscle.ca/wecallitnmd/spinal-muscular-atrophy/
https://muscle.ca/wp-content/uploads/2020/05/Webinar-Report_MDC_NMD4C_v7.pdf

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 virtual 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. 530 individuals impacted by SMA were interviewed for the patient drug submissions for nusinersen (Spinraza) and AVXS-101 (Zolgensma). Using the same questions and interview format, another 90 individuals affected by SMA were interviewed by Staff members from November 10th to December 4th, 2020. The following submission reflects data from a total of 620 individuals impacted by SMA, **but only quotes and statistics from the most recent autumn 2020 interviews (n= 92) are included in this submission**. Only 4 had been treated with Risdiplam. We sought the opinion on the value of having Risdiplam approved for use in Canada. A qualitative descriptive approach, employing the technique of constant comparison, was used to produce a thematic analysis. We have included patients' quotes to ensure their voices are captured in this report and to provide context for quantitative elements. A report capturing all patient comments is also available for review.

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 5 key themes were identified (in order of frequently reported): **1-enormous impact on activities of daily living (walking feeding, dressing and grooming, toileting, bathing, transferring) and instrumental activities of daily living (e.g., managing finances, managing transportation, shopping and meal preparation, housecleaning, managing communication, managing medications); 2- breathing, swallowing and mobility are mostly affected; 3- significant dependence on informal and formal caregiving supports; 4- loss of independence and control; 5- pain, age-related fatigue and mental health; 6-fear of falling**. 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.

Significant Impact on Activities of Daily Living (ADLs) and Instrumental Activities of Daily Living (IADLs)

*"Spinal Muscular Atrophy Type II **greatly impacts both my day-to-day life and my quality of life**. Daily, I rely heavily on the assistance of PSW's to meet all of my physical needs from getting dressed, toileting, transferring to my power chair, shifting several times to get comfortable, washing my face, fixing my hair, getting breakfast … the list goes on and on. **Basically, I require help to do all things physical, even putting my arms around my son to give him a hug**."*

*"Spinal Muscular Atrophy **affects every part of my life** – from most basic activities to the most complex."*

*"**Accommodations are necessary for almost every aspect of daily life** but, just when you've got them in place, some new 'issue' arises."*
*"For me **day-to-day life is something of a struggle** and I count myself lucky in that my SMA is relatively mild (I walked until age 10). Still, I require assistance for nearly every physical action."*

*"I **require help every day for basic elements of daily living**."*

*"I struggle to think of way it doesn't impact my life. It's something **I deal with from the time I wake up to going to bed**."*

*"My **daily life is significantly compromised**. I can't dress myself, I need food cut up but can eat, need help toileting and showering."*

*"SMA **impacts all physical aspects of daily life**."*

*"SMA impacts how my daughter goes about many parts of her day. My daughter **needs help getting dressed and bathing**."*

*"In regards to how the disease impact my day-to-day and quality of life – it **affects every single part** of it."*

*"I require assistance with **all aspects of daily personal care**. Dress, bathing, food preparation, cleaning, laundry, etc."*

*"I need assistance for daily living, I'm confined to a wheelchair, and **need help with absolutely everything**; showering, eating, everything."*

*"My son's day to day is very limited, he **needs help with all is personal care**, getting dressed, going to bed and getting up in the morning."*

*"**Impacts me in every way** can't sleep well, dressing, work, social life."*

*"It limits my son's **ability to participate in some basic everyday activities**."*

"I am losing ability all the time, can't hold my coffee cup now, impacts me with my work."

*"SMA **impacts every aspect of my daily life**, personal grooming, work, social activities."*

*"SMA has a devastating impact on our day to day life, my daughter has SMA Type 1. **We could not exaggerate day to day challenges of SMA**."*

*"It **impacts all aspects of your daily life**. I don't walk at all anymore over the last 10 years, and struggled to walk for many years before that. It makes every aspect of my life and my day more difficult."*

*"Spinal Muscular Atrophy **affects every aspect of my life**, as I require help with anything physical including personal hygiene, eating, transportation, and many other day-to-day activities."*

*"**It is difficult, or perhaps impossible, to point to an aspect of my life that is untouched by this disease**. Feeding, transfers, personal care, and transportation are all severely different than those without this disease. My daily life is also greatly changed as I require help with most simple tasks (drinking, completing school-work, showering, toileting, dressing, etc.). The activities that I can engage in, and places I can visit, are strictly limited by the accessibility of buildings/areas (for example: the height of my wheelchair limits my ability to sit at tables of regular height, I can only sit at tables that are bar height)."*

*"I have never really known on adult life where I could walk or transfer myself or brush my hair, but **not being able to use a pen or type an email or feed myself** are the aspects of my disease that worry me the most."*

*"He **requires assistance with all daily activities of living** and needs his airway monitored 24/7."*

"I have SMA type 2, I would love to be able to write again, to use a mouse and keyboard, to lift certain things, as of know I can still manage to feed myself but that is becoming more difficult."

Significant Dependence on Informal and Formal Caregiver Supports and Negative Impact on the Entire Family

*"I am confined to a wheelchair and **rely on the assistance of others to complete any aspect of personal care**."*

*"I need assistance with everything in my life from personal grooming, eating, working, personal care. **Starting the day I need someone to give me assistance**. Employer has to provide technology support. I can't even access an elevator at work without support or help."*

*"I require **24/7 care from family, friends, and caregivers**."*

*"I need **direct assistance throughout the day such as with eating, getting dressed, moving or repositioning for comfort, help with operating medical equipment**, and other such tasks. I also need **'indirect' assistance**, such as: cooking, cleaning, laundry, grocery shopping, etc."*

*"My operation of my computer becomes more difficult as the disease progresses, and **the burden of caregiving also increases**."*

*"Because of the COVID-19 pandemic, I am not able to have my regular home care services in my home. This has **required my husband to do my care**. I need assistance with many things in the home and often feel like my quality of life suffers because of how little I can do."*

*"I require **24/7 assistance with everything from my day to day needs**, such as feeding, dressing, bathing, going to the bathroom, etc."*

*"Right now with COVID -19 we are having to be even more careful as a family. We have had to do **all of my son's caregiving responsibilities**, as we are not allowing people in to our home at this time. We have **lost friends** over how careful we have to be as they don't understand how much planning has to be done for us."*

*"I require assistance with cooking, dressing, going to the washroom, opening doors (if no door opener within reach), showering and drying off. Almost **every aspect of my life requires assistance from others**."*

*"I **rely on everyone to assist me on day to day life**."*

*"I require **24-hour attendant care** for all activities of daily living."*

*"It is tough for me as well as **my day revolves around my 22-year-old son**, we have to plan ahead for everything."*

*"**Taking care of a toddler with SMA is very difficult**. On top of life and work, it requires a lot of medical appointments."*

*"I **rely on personal support workers**."*

*"I **rely on my kids a lot**, taking away all my independence."*

*"I use attendant services, who have become more like family to me. I am **reliant on staff for everything**, I can't even scratch my own nose."*

*"I **require 24hr care** because I can't do anything for myself. The reason for that is SMA, up until 12 I could feed myself, and up until about 21 I could do smaller things like change the channel with a remote."*

""As a caregiver – there is not a single aspect that is not touched by my son's diagnosis, from daily living needs, the type of home we can live in, the support we need, the vehicles we drive, the need for PSWs in our home, all of his care from personal care to meals, homework support, social activities."

*"SMA **affects everything our family does** from, running normal day to day errands, family vacations, where we go dinner, everything."*

*"I **need someone to help me with everything**."*

*"**Relying on others for personal care is complex because it is always dealing with different people**."*

*"It is a big stress on her because she can't go to the bathroom until someone can help. Her head falls and she needs someone to move it. **Always relying on someone**."*

*"I have to have homecare, I am wheelchair-bound all day, there is lifts and lots of equipment. I used to be able to stand and pivot BUT **I can no longer do that without help**."*

*"I **need 24/7 care** so I can't live on my own unless it's in a facility which I never want. So **I live with my parents who are pushing 60 and when I don't have my personal care attendants, they struggle to take care of me**."*

*"I almost got a divorce because the muscle loss just keeps getting worse and **I'm able to do less and less which puts more responsibility on my husband and kids**."*

*"I **require a personal support worker to help with day-to-day living** and personal care including dressing, bathing, personal hygiene, meal preparation, household tasks etc. in recent months I have noticed a decline in my final making it difficult to eat, type and hold objects. I have switched to using voice activated software on both personal phone and my place of work. These declines are the most challenging as they are beginning to prevent me from living a relatively independent life and **I rely more heavily on others to ensure that basic needs are met**."*

*"My disease has caused me to be **reliant on others for the most mundane things**, up to the most complicated."*

*"There is essentially nothing I can do independently and **I constantly require supervision and assistance from health care workers or family. Putting undue burden on them**."*

*"I've been having a hard time finding home-care workers because no one wants to work in the pandemic. I am so weak so there are a lot of things that I can't do to take care of myself. **My muscle weakness is important for me to control because otherwise I can't be independent, especially when I don't have caregivers**."*

*"I **always need someone** with me, I can never be alone even when I want to be."*

Breathing, Swallowing and Mobility Are Most Affected

*"SMA affects our son's day-to-day **mobility** (i.e. ability to walk long distances, ability to do stairs, etc.). He also has **hand tremors**, which are impacting his fine motor skills. **Mobility is important** for his quality of life as we associate this with him being able to remain independent in the long term."*

*"I have **extremely limited mobility**, particularly in the use of my arms and legs, but increasingly there are declines in other functions."*

*"To stop the **muscle loss** would be my most important goal. It's had such an impact on my life, with raising my kids, running a household and even my marriage."*

*"My **weakness in my arms** doesn't allow me to do things I could do a year ago or 6 months ago. It is getting critical now because I have run out of tricks to be able to do. I need help or to stop doing them entirely."*

*"SMA affects my whole body, most notably **gross motor functions, such as walking, lifting, and reaching.** It also affects **fine motor functions, such as swallowing, respiratory function, finger dexterity, and neck control.** The condition caused scoliosis of my spine at an early age, and I received spinal rod fusion at the age of 7. I cannot bend or twist my back well as a result of the surgery and have to be handled very carefully in situations of transfer."*

*“In terms of aspects of the illness that are more important to control, I would focus on general strength in the lungs, throat, and arms. The most difficult problems to overcome as I have gotten older are my **breathing** and loss of my arms.”*

*“Her **hand movements are quite minimal**. Even to brush her hair and put on a Halloween costume, she can't do that.”*

*“My **lung capacity is most affected** and important to me.”*

*“I frequently have pneumonia and have been hospitalized many times, for me the **loss of the use of my hands and arms have been an enormous loss for me**.”*

*“The biggest risks I have experienced are **respiratory illnesses, like pneumonia**, since SMA also affects **respiratory function**, due to its effects on physical strength. Controlling respiratory function is therefore one of the most important aspects of my condition.”*

*“I am getting **weak muscles in the arms and difficulties swallowing**. I also find it difficult to project my voice, some days are better than others. On occasion I get some real bad muscle spasms in my legs which are incredibly painful. The most important aspect for me is muscle strength.”*

“*As far as priorities of care it is extremely important that I eat slowly and carefully so that I don’t **aspirate food and develop pneumonia**.”*

*“As the disease progresses, there are many other health conditions arising as a result of aging and being in a wheelchair. I also have difficulties with **chewing and swallowing** which also make proper nutrition and social activities a challenge.”*

*“Maintaining **limited function in hands** and **breathing** are important to control/maintain a bit of strength in my core and neck would be nice. I only am able to physically control an expensive micro joystick on my wheelchair.”*

*“**Breathing** is more important than other aspects.”*

*“SMA affects **swallowing, breathing and respiratory function** the most.”*

*“We worry about **muscle strength, muscle loss and falls** a lot.”*

*“I am **very concerned about my lungs**, that is most important. Also my **hand and arm strength** to keep being able to brush my teeth and participate in basic activities.”*

*“**Fine motor skills** have been lost over time, however I’ve never really had main gross motor function.”*

*“One of the major things that I have is **respiratory issues, sleep apnea**, so I have a bi-pap for that, and because my lungs are too weak to cough on my own so I have a cough assist machine.”*

*“My main goal would be to improve my **respiratory issues** so that things like COVID are not a life of death for me.”*

“*While I am of course concerned about **lung** and **heart** function, as these are muscles too, it is the use of my **hands** and my **voice** that in part my livelihood my physical well-being and my mental state.”*

*“For my daughter - her **mobility, feeding and breathing** are all hard for her. Many nights when we check on her she is soaking in sweat due to her working so hard at just breathing. We have to make sure her food is a safe texture for her to eat so it doesn’t become a choking hazard.”*

*"Before I could walk a bit, but now I am in a wheelchair and bed all the time, and I have a hard time to **use my hands**."*

*"I would say that it is important to not let my son's muscles atrophy more than they have, because that results in him requiring more support. Before Spinraza, he had to use a plastic fork because the metal forks were too heavy for him. If he loses the ability to use a fork, then next is the **chewing, and swallowing** – it's very scary to think about."*

*"**I can't breathe**, I'm stuck in a chair, **I can't eat, I can only use my thumbs**. I am **not able to swallow** at all - which is extremely I need to breathe and swallow and mobility in general annoying. Body temperature - it doesn't matter if it's a hot sunny day or the dead of winter, I am always cold. Because being in a wheel chair, I have **brittle bones** - my bone break easily - osteopenia. I am ventilator dependent and require regular suctioning."*

*"SMA has quite literally stripped me of 90% of my physical abilities. It affected my **respiratory so bad** that I spent a majority of my childhood in and out of the hospital which means I saw many things that no child should."*

*"The most impactful symptom of SMA for myself and many others is our **decreased lung function**, which can cause so many health scares. Over time my **ability to eat safely and speak clearly** has decreased, so I believe that this aspect of SMA is the most important to control and treat."*

*"The most pressing aspect of the disease is a **progressive loss of function in the lungs and throat**. Many people with this disease progress to a point of requiring a full-time ventilator or trach, and losing their ability to swallow. As I get older I've noticed a significant decrease in my ability to swallow, leading to higher chances of choking, coughing, and possible lung infection. Additionally I have needed to start using a BiPap at night, as my breathing has become irregular and shallow."*

"SMA has caused secondary diagnoses of scoliosis, kyphosis, and GERD."

*"The most important aspects of SMA to control would be for my son's core muscles, especially his intercostal muscles to become strong enough so that he could **breathe independently**. If these muscles became that strong, it would also be likely that his esophageal muscles would also be strong enough for him to have a proper swallow and his GERD would be reduced. This would be huge because he could have G-tube feeds rather than J-tube feeds and reduce the amount of time he was tied to a feeding pump each day."*

*"If my son had proper tongue movement and **swallow** he would be able to eat by mouth and we would be able to speak. Socially, these would be monumental achievements that would allow him to interact with other people and have more shared experiences. From a medical perspective having a **proper swallow** and effectively managing secretions would mean that he would be at reduced risk for aspiration pneumonia and would pair with stronger breathing abilities to mean that he could be de-cannulated (no longer require a tracheostomy). Not having a tracheostomy would again help with his ability to communicate verbally as air would be passing his vocal chords and open up water based activities which would be extremely therapeutic for his muscles."*

Loss of Independence and Control

*"I have enough muscle strength to **maintain independence** but there is a constant risk that this ability will be lost as I grow older."*

*"As my SMA progressed over the years, so did my **dependence**."*

*"Spinal muscular atrophy (type 2) **greatly limits my independence**."*

*"I **need to maintain as much independence** as I can."*

*"The few capabilities I retain (like being able to eat unassisted) are helped by various 'cheats'. If I could halt my SMA's progression at its current stage it would be gigantic relief. I treasure what **little independence** I have left and would hate to lose even a piece of that going forward…a fate that is unavoidable without medical intervention."*

*"SMA affects life in just about every way. I need help to do almost everything that I need to do. Ironically, I still have some mobility that gives me **some independence**."*

*"I am currently completely unable to walk, stand, or bear any weight on my legs. I have had to use a powered wheelchair for the vast majority of my life. My condition is degenerative, which results in a chronic course of worsening and **loss of independence**."*

*"I **lack independence**. I lack of ability to do things on my own time."*

*"Being able to still work and contribute to society is critical. **Being independent** is critical."*

*"I am still able to operate a computer mouse, which allows me the only true **independence** I have."*

*"I have to have a wheelchair vehicle in order to get anywhere and then not only that, but I worry about how accessible the place is going to be once I get there – which is **out of my control**. What is accessible to one person is not access to the max. Especially if you are in a wheelchair full-time."*

*"Having to face my body weakening and **not have control**. There is a constant fight to keep my body moving and keep what I have."*

*"**There isn't a single thing in my everyday life that I can do by myself**. The most important type of treatment would be to slow or possibly stop the progression entirely."*

*"I would like to maintain, or increase, my hand and arm strength in order to be able to do more **activities independently**."*

*"Being able to **maintain my independence** is very important to me."*

*"She can't do anything herself she needs assistance for everything, everyday and every minute. **Affects her independence and safety**, everything."*

*"She is **dependent** on me for absolutely everything."*

*"She has **no control of her life** and she would like privacy."*

*"Due to COVID, I go nowhere and it has affected my sense of **control** on life."*

*"I live on my own, so I don't get to see family and friends due to COVID and I am having to rely on my assistants, but it would be nice to not have that and have more **control of my life**."*

*"I really want to **maintain my independence** as much as possible."*

"If I could have **control** *over one aspect it would be my ability to walk or do things myself, so I can be **independent**."*

*"I use an electric wheelchair to get around for **independence** and activities. It changes everything that I can do for myself."*

*"My own schedule is often to work around my caregivers' schedules so that really **limits me** in terms of anything social."*

*"My mobility is a big deal in that **I have no independence**. I do lots on my own and hope to keep it that way as long as I can and would prefer to stay in my own apartment and not a retirement home."*

"*It is difficult to plan for the future when the future is very unknown. All of this never leaves my mind and while I live a very full and intellectually active life, there is always in the back of my mind the **concern about the loss of my independence and my "expiration date".** These are aspects that are fundamental to my identity, to how I present myself and the world, and frankly my livelihood."*

"I used to drive and I can't drive anymore."

Age-Related Fatigue and Mental Health

*"With loss of function, he said at age 11 '**This is no life, a life not worth living**.'"*

*"Being able to **maintain my positive mental health** is very important to me."*

*"Things that your average individual typically doesn't think about, takes significant planning in order to find success. **As frustrating as the physical limitations are, it's the impact to the mental health that is far more difficult to cope with**. Struggling with the notion that **you're not quite good enough for those in your life** because you can't act on the thoughts you have. To be able to do things for those you care about. Personally, that is where I find the significant struggle."*

*"**I live with pain**. I over compensate by using other muscles, I live with constant pain in my neck and shoulders."*

*"I **need to take more breaks/rest**."*

*"As a person **ageing with SMA, fatigue** impacts your day. A 8 - 10 hour day feels like 18 hours.."*

*"As I **get older I get fatigued quickly** and my energy levels drop."*

*"Lately it's been a **challenging to keep my energy** - in order to fulfill my commitments important to me."*

*"**As I get older my energy is not the same**."*

*"**Physically exhausting, more and more as I age**. It is getting harder and I am more tired."*

*"It would be nice to not be so **fatigued** with my fine motor movements."*

*"I have **chronic pain** from the SMA2 so, some days it hurts to move."*

*"While I live on my own and worked for the federal public service, these limitations and continual decline require me to adapt on a day-to-day basis. **This puts stress on me as I try to balance living a " normal" life and acknowledging my declining energy and strength**."*

*"My daughter has SMA, age 4, type 3 and 21 years old now. She is at university and **she gets over tired easily**."*

*"**The more fatigue I have, the less I can do**."*

*"**An important aspect of SMA is mental health.** Our son is starting to question his abilities and why SMA limits his "leg muscles". He will cry and ask why SMA affects his legs and if this is permanent or if this will change."*

*"Mobility limitations **takes a toll on mental health and happiness**, it makes you **feel shameful**. I cannot enjoy my children's hockey games and I feel excluded from social events and sporting events."*

*"I've lost 27 friends because when you grow up in the hospital, you meet kids and sometimes they die. While I love my life, SMA2 has not only affected me physically, it's **affected me psychologically**."*

Increased Falls and Fear of Falling (Basophobia)

*"I now **fear falling** (have fallen four times since August)."*

*"I was diagnosed at the age of 2 when I could no longer bear weight and **began falling down a lot**."*

*"SMA affects her safety: to be able to walk and **sit without falling out of a chair**."*

*"I **worry he may fall**. He will **fall sometimes** and I will limit some activities."*

*"My SMA definitely slows me down. It doesn't allow me to do a lot of things that I normally should be able to do, like using stairs. **I have falls because of my SMA** and then I can't get up on my own."*

*"My movements are restricted I **fear I will fall**. I cannot go up and down stairs or hug a small child. It embarrasses. me, I avoid situations. I avoid stands or steps because I cannot access steps. I cannot do sports. **I fall so easily in the winter as I do have the balance and stability to walk**."*

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).

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 4 key themes emerged: **difficulty accessing treatments due to age; importance of method of delivery; anxiety related to maintaining access to treatment; positive changes and side effects observed; cost and time lost are significant barriers.** For individuals who did not have access/exposure to treatments, they noted that they managed SMA with frequent massages for nerve and muscle pain, rehabilitation with occupational and physical therapists, supplements, aquatic therapy and taking medications and oils for pain management.

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, mental health and access perspective.

Difficulty Accessing Treatments Due to Age

*"I am **not currently managing my SMA with any treatments**. Being well into my forties the benefit to me is minimal compared to someone younger and stronger."*

"I do **not have any treatments or therapies** at the moment."

*"**At my age, I am not currently receiving any active treatment for SMA** (i.e. Spinraza). However, managing the secondary effects of my condition, such as respiratory exams, neurology appointments, etc. does interfere with my work. I am in private practice so I do not have the ability for sick or vacation time being that I am self-employed."*

*"I am not currently on any specialized treatment for SMA. This is due to the fact that there are very **few treatments for SMA and they are difficult to access**. This is because of **prohibitive costs, lengthy and restrictive approval processes, invasive or difficult route of administration, and travel to medical facilities."***

"Provincial limitations in BC - as someone whose 54 years there are less meds and treatments for a person with SMA."

*"I don't have any access to treatments right now. **Spinraza is not available to adults**. For adults it is approved on a case-by-case basis and **I've never been able to qualify**."*

*"**I'm excluded from treatment because of my age**."*

*"I am **still under review for Spinraza (because of my age)** even though all documentation has been provided."*

*"My neurologist and I shared concern about Spinraza for me because of the **trade-off with an invasive treatment delivered via spinal fluid and all of the secondary complications** that can arise from that versus the benefit for **someone of my age**."*

Method of Delivery is Important

*"A pill sounds like an improvement over the current, more **invasive**, methods."*

*"Not able to access Spinraza because of **need of lumbar puncture** and I have spine fusion."*

*"The **downfall of Spinraza is definitely the need of having a spinal injection**. I'm definitely one of those people that is not easy to give the injection too. I struggle with **multiple pokes** and **struggles from the doctor to be able to find the correct place in my lumbar area**. As a result I end up dealing with **spinal headaches every time** and am forced to have to be in bed two to three days to recuperate. On an ongoing basis, because of the many pokes, I deal with **severe back pain** constantly."*

*"**Injections in spine is challenging."***

"Having a treatment in form of an oral drug - concerns about swallowing mechanism - needs to be reflected upon."

*"**Any form intravenous delivery of drug can be challenging** because getting IV lines is like winning the lottery - veins are hard to get to."*

*"**My son requires an IV injection to sleep, limited movement for Spinraza.** He has side effects and the most heartbreaking is when he wakes up and doesn't recognize his parents. Spinraza has a negative effect for 2-3 days following injection."*

***"**Some of the issues with **Spinraza is how invasive** it is and it being stressful for children."*

*"I can't access Spinraza because **my spine is curved**."*

*"She is not a candidate for **Spinraza because of the rods in her back**."*

"Complicated to do the Spinraza treatment."

*"I have **scoliosis** so I can't get Spinraza treatment. This is why an oral drug is so exciting."*

*"**Receiving meds in the spine is not ideal**!"*

*"For the **frequent lumbar punctures**, we don't know what will be the long term impact on our son."*

*"Given my **spinal surgery as a child, the injections are not done in my lumbar spine area,** which is the recommended approach, and instead the injection goes between C1 and C2. This makes the procedure more risky with potential side effects that could be deadly."*

*"Since Spinraza is a **spinal injection, it is a rather painful and stressful procedure** that requires a full day of being at the hospital and recovery time. This is especially an issue since so many with SMA including myself have had spinal fusion surgeries, making the procedure much more complicated and risky."*

Access and Fear/Anxiety Related to Maintaining Access

*"Accessing Spinraza initially was a rollercoaster. Without the recommendation for adults, Saskatchewan has determined approval on a case-by-case basis. It took a long time to get provincial approval. There was a lot of meetings held and people met and letters written. But then not only that, **maintaining access to treatment** is almost just as difficult. Testing needs to be done with the Hammersmith test and upper extremity test every four months. And the **fear of having your abilities change within a point, is extremely worrisome**. One-point difference from the previous testing and I could no longer qualify for Spinraza. That is a **constant worry**.*

*"Provincial government must prove not getting worse must do continue tests - which is time away from work and travel, the **tests are stressful** - **my life depends on the results of tests - strain on the mental health, testing is so important and must be done frequently** - and it's never going to stop - **incredibly stressful**."*

*"**Getting access of treatment was stressful and to keep the access of treatment** is extremely stressful to prove that you continually to need this treatment."*

*"Spinraza was approved so it was easier to access, but Zolgensma was very difficult to get, the cost was impossible. With the cut-off date due to age, **it was very stressful**."*

*"One of the other issues we had with Spinraza is that our daughter had to be tested before each dose which puts **stress and fear of not knowing she could continue to received his life saving drug**."*

*"**We fear her ability to be renewed for Spinraza**. We worry how she will be covered once she is off our insurance."*

*"For Spinraza, she has to be put under for in order to do the treatment, **repeated blood draws are hard** - hard to find a vein, anesthetic is hard on her she is not herself, it's a traumatic experience to get her treatment. It affects her perception and feelings towards medical staff - tears start. After she has a headache. The day is of is hard to say the least."*

*"Three month doses of Spinraza - it's been a ride - the last load was bad **- pain, anxiety, melt down, he felt every bit of it** - now he will only take it if he is put under."*

*"**My child has developed anxiety** – especially right before every treatment of Spinraza."*

*"Spinraza **led to her anxiety** - if she seeing blood or a doctor – she panics. She cries. She isn't well three days post Spinraza."*

*"She always **gets extremely agitated** following her Spinraza dose. It is an **emotional challenge** on all of us."*

Positive Changes & Side Effects Observed

*"I currently receive Spinraza every four months. I am incredibly thankful for access to this treatment, but there are certain **downfalls with this specific drug** that would be rectified with alternate forms of treatment such as Risdiplam."*

*"My daughter has had Spinraza since she was 2 (she is now 7). This treatment has allowed her to **gain strength since beginning**, even while the natural progression of SMA would have meant she would have otherwise been losing strength."*

*"Currently, I am one of the fortunate few adults in our country who has access to Spinraza. I have been on Spinraza since July of 2019. There have been **so many benefits to me being on treatment**! My **energy level has gone higher than it's ever been**. I have more trunk control and strength and I'm doing things that I haven't been able to do in 10 years or more. Driving is easier, baking is easier, getting through the day is easier and I no longer need a nap halfway in between."*

*"Spinraza has resulted in her **ability to reach while sitting and walking using walker**. She can roll more. **Sitting without flopping, can sit on her knees with control.** She can now lift a cup of water. Has manual wheelchair - can now get over small humps on her own. But Spinraza also caused **spinal headaches**."*

*"Spinraza- benefits, **alive, maintained ability to swallow**, was seeing gains, working on standing, and sitting. She does have scoliosis .. biggest concern right now. side effects = scoliosis.. child frustrated with **not being able to sit**.. very soft food, but was orally fed."*

*"My daughter received Zolgensma through lottery at 22 months. Benefits = **a lot more interactive, lift cup herself, a lot more vocal, talking more, most notable, eating abilities, was very puree before, now a lot more textures, aspiration a lot less.** Side effects, just a continuation of the scoliosis. Maybe too soon to see. She did have a hard time with the after treatment: **steroids were very bitter, irritated stomach, some vomiting, blood work biweekly now**."*

*"My daughter had her first loading dose of Spinraza at 2 months of age, we did see **a turn-around** in her, and I truly believe it **saved her life**. It meant **moving her arms more** than she could before, and some the muscle function she was losing stopped."*

*"Zolgensma –We moved to Boston for many reasons during the start of the Covid -19 pandemic (we are since back in Canada) one of the main reason was so that our daughter would be able to access Zolgensma. But it was difficult to have to move away from family, friend and supports. The day after she had her infusion she was **able to sit unassisted for over 30 minutes** which is something that she had never been able to do before. We **saw gains almost right away** and we have seen prolonged improvement as well as more energy and movement. The only side effect we had was that she had to go on some steroids because of some liver issues but she is better now."*

*"My son is on Spinraza, and that is making a great difference for him with keeping him at his baseline and **preventing further atrophy**."*

*"She was diagnosed at 7 months and couldn't move, her breathing was laboured – now because of Spinraza she is **able to sit, knee, talks, drinks, arm movement can move her head can use a manual wheelchair , she can use walker, improved breathing, can cough when she gets sick** and importantly she **can be at home instead of the hospital**. She is able to do the things she wants to do, **she's alive**, that's a big one!"*

*"Because of Spinraza, she has **more energy**. She is able to go down the stairs assisted. She can now hang onto the railing and can pull herself partially up the stairs. Before Spinraza she wouldn't attempt the stairs at all. Less falls."*

*"Our son is currently receiving Spinraza (nusinersen) since 2018 and has received 11 injections via lumbar punctures to date. Benefits seen: Our son **has increased endurance when walking and running short distances.** We have not seen any progression of the disease since treatment and our son has had significant growth spurts and weight gains. We have also seen a **decrease in the frequency that he will "fall" without warning** due to SMA. He is **also able to alternate legs when going up stairs.** These were all very weak prior to receiving treatment. Side effects have been none that we can associate with the medication; however, our son has had **some dizziness** due to being sedated for the lumbar puncture, which is required to administer the drug. Our son's confidence in his abilities has also increased since receiving treatment."*

Cost and Time Lost Are Significant Barriers

*"The **costs** associated with available treatments, like Spinraza and Zolgensma, put them **out of reach for me** and most like me."*

*"**Cost** is the big issue but travelling far distances is another problem."*

*"I am hoping my neurologist can get me on Spinraza. That is not proving to be very fruitful. Yes, I mean it is **cost prohibitive.** The province I live in is **not covering it** for anyone. I think they are considering covering it for people under 12. It is not accessible to me for those reasons."*

*"I cannot take Spinraza due to physical complications and **insurance won't cover it**."*

*"I am currently not receiving any treatments for SMA. This is due to the **current costs of treatments being well outside my financial means and local government not funding treatment for people over 18 currently."***

*"I require other people to **take a day off work** just to bring me to a doctor's appointment in another city. Sometimes this requires a hotel stay, which is even more exhausting for everyone involved, as I require extensive equipment to make hotel rooms work. I also **cannot bathe when I have to travel because hotel bathrooms are not conducive to my needs**, as I typically use a monorail lift system at home. So there are always possible secondary skin issues that result from having to travel and not being able to manage my hygiene as effectively as I can when I am home. And it impacts my caregivers as well, who **have to take time off work to support me**."*

*"In terms of difficulties accessing treatment, **cost is a major issue**. The only viable treatment for my condition, **Spinraza, is not funded by my provincial government** and therefore I cannot access it."*

*"Receiving Spiniraza for a year and a half, not idea **have travel 3 hours one way,** may need to stay **overnight at a hotel** - could be missing two days of work missing every month. Costs of hotel - **minimal two days down time**."*

*"Spinraza: Dose at Children's every 4 months. **Involves time off work for both parents on day of dose**, and normally time spent beforehand."*

"I have access to travel but knowing others individuals may not have access to travel. Taking a pill means I don't need to travel because I can access at home."

*"I had to **pay for physiotherapy** as extended health benefits would only provide so much. I take her to the pool 2-3 x a week for public swim - she can walk with a noodle."*

*"In order to receive Spinraza, we **have to fly in the night before treatment**, have treatment for next day and then the day after treatment must fly back home. This also forces us to get appointments done in a short period of time – **huge stress and loss of time**."*

*"**The cost of treatments are so high**."*

*"We've been thankful - we were apart of the early access program for Spinraza then transferred to our government - without this we **couldn't afford it**. There is no way we could afford this treatment if it was not covered. We're lucky the hospital is only 20 minutes away - we had to delay one treatment due to a cold and the treatment was a month - these were delays in her function - we've had to **take a day off work -** it's an **all-day event**."*

*"**Huge costs , travel to clinic and time off work**, we live 5 hours away from the hospital. Our daughter is so young – a day trip is too hard – so we need to take time off work, book a hotel - she comes with so much equipment - machines - we need to take a number of days off work for treatment."*

*"Parking at the hospital is **expensive**. I don't want to be near hospital but we have to go. We are lucky enough we have a short commute."*

*"If Spinraza was approved, the treatment is 4 hours one way which means **time off work, travel costs, hotel accommodations**. The treatment is not offered where I live."*

*"he main barrier is the **high cost of the treatments currently**, which makes them practically inaccessible unless one is very wealthy or in a life-or-death situation. If the therapies help even to ensure that a patient like me is able to live independently with minimal required support as an adult, then that alone is a major life changing impact; however, the steep costs simply preclude this."*

*"At first, for the first 4 loading doses, we traveled from NB to Ottawa to receive his treatment which **accumulated significant expenses (flights, hotels, meals, etc.).** Subsequent to these doses, we were able to receive the remaining treatment at our local hospital. Difficulties accessing treatment is due to OR time and physician schedule. We do need to take our son out of school and take time off work for the entire day of the procedure."*

*"I am one of the lucky adults in Canada who has been able to have coverage for Spinraza. As a Federal public servant my medical plan covers some of this in Ontario and the pharmaceutical company is covering the remainder of the costs. The Covid-19 situation has impacted the schedule of my injections, but I have had the initial 4 and am moving into my quarterly injection schedule. This process includes **taking a day off work**, and having the injection in the hospital under the CT scan. I have had no serious adverse reactions to the injections aside from some dizziness the following day and some pain/discomfort during the procedure. However, there is **at least a day or two of recuperation and depending on what day of the week the procedure happens this can influence further days off from work**. Again, I am lucky that I live in an urban centre that has Eastern Canada's neuromuscular Centre at the civic Hospital so I do not need to travel."*

*"At **current prices**, treatments for SMA remain **unattainable**."*

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 muscle strength, motor and respiratory functions; and (3) maintain skills and abilities/slow down rate of progression of disease.

Improved Independence and Quality of Life

*"I walked until age 10. If an effective treatment were available to me then…**life would have been much different and much, much easier**. Never needing a wheelchair would have saved me and my family (not to mention the government and various charities) hundreds of thousands of dollars—wheelchairs are expensive, as are wheelchair vans, not to mention retrofitting home to be wheelchair friendly."*

*"I could just very basically shower and **go to the bathroom by myself**. From that basic to travel easier, to be able to take up cooking again and **other things outside of my job**. **Normal life stuff."***

*"For quality of life, I just want an opportunity to have enough strength that will **allow me to be independent**. I'm all about **living a normal lifestyle** (both in appearance and actions), and I would be very accepting of any potential method that would enable me to do that."*

*"This treatment could **improve independence** if abilities could improve in general."*

*"As long as I can, I would like to stay in my own home, and it is cost effective to stay at home. **Maintain as much independence** as possible."*

*"To be **less reliant** on others."*

*"To **prolong my life expectancy**, but would **keep my quality of life up**."*

*"Any benefit even a marginal benefit can be huge for someone with SMA, and bring so much **happiness and independence**. It would be great if with treatments if my daughter could play with her siblings in ways that she could not do now."*

*"If he would need fewer assistive devices. He would experience fewer frustrations and **greater acceptance from others**."*

Improvements with Muscle Strength, Mobility and Respiratory Function

***"**Ideal treatment would be to completely reverse this and to start building up strength."*

"It would be great if a treatment would stop progression and allow me to rebuild muscle and strength and give me everything I desire to do."

*"Treatments that could help **grow muscle mass** and reverse the effects of SMA would be ideal."*

*"All I would like is **muscle strength** back to use the computer and my wheelchair more easily, like I use to."*

"Improvements in muscle tone."

*"To **improve respiratory ability**, I would love to have this medication improve my lungs enough so that I don't need these machines. My biggest fear is that I will get to a point where I need a trach, so if this therapy/treatment can provide that help for my lung I think that would be huge."*

*"Help to **reduce muscle loss**. If I could have a treatment to help with my muscle loss it would help a lot."*

*"I would be thrilled at any **slowing of the progression and any small improvements**, any added function in my upper body. any **improvement in my swallowing, so I don't choke**. If I could have any ability gains, any **support to my pulmonary system**."*

*"**Respiratory function, improvement in upper body and hand strength**. Swallowing is huge. **Upper body strength is everything. His arm and hands maintaining and improvement strength is massive**."*

*"To experience an **improved ability to swallow and manage secretions**."*

*"The **need to monitor his airway 24/7 would be decreased**, as would his risk of aspiration."*

Maintenance of Skills and Abilities/Slow Down Progression

*"**Maintaining limited function** in hands and breathing are important to control/maintain and a bit of strength back in core and neck would be nice; this would allow the ability to plan for **less future progression** and allow for **more independence and safety** which is always a risk. Maintaining or enhancing limited hand control would lead to continued independence. Imagine what it would be like to touch your partner, have a drink or play a hand in poker. Even the **smallest things could make a difference**."*

*"I would love to **regain some strength** but would settle for **the slowing (or outright stopping)** of SMA's progression."*

*"Ideally, I would love to see **regeneration of muscle strength**. Given that I am in my thirties, this may not be medically practical so even stability of the strength I currently have would be a benefit."*

"I would like to regain some strength, but ultimately, I am looking for a way to cease progression of my condition."

*"I would like to **stop the progression** at the very least. Has been shown to **get some small functional gains** would be amazing, hand strength, not looking to be able to walk again but to not live with the daily fear of what next week or year looks like. small gains would make a difference to do things easier. like holding a pen has changed a little bit in the last week, **stopping the progression** or **getting a little gain would make so much difference.**"*

*"**Stopping the progression is critical**, I can still drive a little bit, I love writing and would love to be able to gain a bit of ability to be able to do that. Maintain my eating, would love to be able to stay in my own home and die there, not have to go to LTC."*

*"**Halt the progression** of the disease in its tracks."*

*"I don't care so much about Improvement as they do about being **stable**."*

*"**Halting progress** is really important."*

"I want to see me not get worse, I want to see me get some power back."

In terms of trade-offs – many agreed they would "give up a lot to be able to have the ability to breathe on my own." It was consistently noted that low invasiveness, limited hospital visits, safety/low side effects and low costs were highly valued when considering a treatment. Not requiring the hospital to administer the drug via lumbar puncture and not requiring a child/family member to be sedated every time was noted as very important. Having the ability to take medication at home would simplify the process by allowing persons affected to have more control. A treatment that has continuous presence in the system may provide with a more constant response to treatment. Less time in hospitals was indicated as highly valued and welcomed especially in the era of COVID-19. If families were faced with the decision to choose a different therapy, they would consider potential side effects reported by the "new" versus "current" therapy. They would consider the ease of accessibility of treatment and whether private/provincial insurance would cover costs.

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 4 had been treated with risdiplam.

Benefits following risdiplam were:

"My son has been using Ridisplam for 2.5 years, he was very fortunate to be accepted into a clinical trial for the drug. There is ***no cost to us*** *as we are being provided the treatment due to his participation in the Ridisplam Clinical Trial. We have seen him* ***improve greatly*** *with the use of Ridisplam, in every aspect* ***(physical, mobility, energy levels, weight gain, appetite, etc****). There is data that suggests that Ridisplam would work great for older people with SMA."*

*"****All of our experiences have been positive with this treatment****. His* ***health has improved*** *in way that we didn't think it would. He has a easier time eating and is not as dependent on his feed tube which means he is getting to eat more healthier food which has contributed to his weight gain. We have noticed with Spinraza that there are peaks and lows between doses, which isn't the case with Risdiplam. it is nice that we can administer it at home and pick up the drug at our pharmacy. Some other benefits would be for people like my son who have had spinal fusion surgery and other who can't get Spinraza through a traditional spinal tap."*

*"****There is no decline or loss between doses like with Spinraza."***

"No headaches *that can come like with the Spinraza spinal tap."*

"It is ***wonderful that we can take this at home****, so we don't have to do to the hospital and book a OR.***"**

"Our son had special approval to receive Risdiplam even though it is not approved yet in Canada. He receives compassionate dosing, which if we had to pay for it would be in the neighbourhood of $180,000 per year. The main reason we switched to Risdiplam was on the advice of our neuromuscular specialist. He had read the research on both Spinraza and Risdiplam and had noted that Risdiplam had a more global effect in all muscle tissues of the body, whereas Spinraza seemingly settled in the lower extremities. It was a long shot that we might see improvement in his core strength (breathing, and esophageal strength) and in his tongue movement, swallow and head control. He advised that Risdiplam delivered at least the same benefit as Spinraza, but had greater potential benefits. The other recommendation to make the switch to Risdiplam is that it could be administered via his feeding tube and would not require lumbar punctures. The progression of our son's scoliosis was making lumbar punctures more difficult and his doctors were concerned at some point they might not be able to deliver the Spinraza intrathecally, potentially leaving him without treatment. They were also concerned about the potential risks and long term consequences of repeated lumbar punctures."

"It is early to determine the benefits of Risdiplam. It's hard to separate out what is a benefit of the Risdiplam and what is a continued progression of benefit of the Spinraza. We also got some other painful digestive system issues under control recently, so he may just be feeling better and up to more activity because of his GI issue resolution. What we do know is that in July of 2020 prior to Risdiplam he was able to sit unassisted out of his brace for 10-15 seconds on occasion, and in his brace for between 30 seconds to 1 minute. Now, in November 2020, he can sit unassisted without his brace for 1-2 minutes on occasion, and in his brace he can sit unassisted for anywhere from 15-30 minutes routinely. His head and trunk control have improved immensely in the past few months, which do coincide with when he started Risdiplam. His respiratory status continues to improve as well, for his night time invasive ventilation his settings are about as low as anyone on a vent would typically go with a PIP of 10 and a PEEP of 5. We have not (yet) seen significant changes to his ability to swallow or in his tongue movement. He hasn't experienced any side effects at all from Risdiplam. We are very happy that he is experiencing huge (for a kid with SMA Type 1) gains in his strength and quality of life because of Risdiplam."

"*I am on Risdiplam, I'm the first one in Manitoba to use it and I'm trying to get it here for others. I have not experienced any side effects and I've already noticed gains in ability. It's simple to take, it's a liquid medication that's taken once a day.* ***Risdiplam has shown amazing results in both adults and children****. The only thing that is halting access, to my knowledge, is the government funding the drug."*

"I got access to the drug via the Sunfish clinical trial. I suspect I was on the placebo for the first year, as I still got sick frequently and was getting weaker. During the second year, when everyone was guaranteed access to the drug, ***I put on over a quarter of my body weight (80lbs-105lbs). This is a good thing****. When I get sick, I can struggle to eat as it is too tiring. As a result, my body pulls nutrients from my muscles and I often end up permanently weaker. I also* ***haven't been sick since*** *I started on the real drug (over 14 months.* ***Considering I could expect a minimum of one hospital stay a year plus 2-3 smaller illnesses, this is massive.*** *I haven't noticed meaningful gains in strength, but I also* ***haven't lost any****."*

Disadvantages following risdiplam were:

"There is a ***longer time to get to you to the point where you feel the effects*** *of the drugs (6 months) compared to Spinraza."*

*"****We haven't seem any bad side effects with Risdiplam****, unlike with Spinraza with headaches and peaks and lows in energy levels. When the option to switch to Spinraza came available, we opted to keep him on Risdiplam and we have never questioned that decision."*

"As I've said, I ***haven't experienced any side effects*** *and I'm already noticing gains. "*

"Our son began Risdiplam in August 2020. While there have been reduced food and accommodations costs, we must drive to McMaster (about an hour each way) to pick up the medication from their pharmacy every 50 days. With gas and parking that adds up to about $100 every two months. There is also some additional stress on myself, my husband and our respite workers. We have to refrigerate, and administer this gene therapy at home. It's a big responsibility for families. Still the benefits of not having to go through frequent lumbar punctures and sedation make it a more tolerable risk."

Although only a small number have received risdiplam, others that were interviewed mentioned that they would "do anything" to get access for the treatment. It was repeatedly mentioned that they hope this drug is approved, before it *"becomes too late:"*

"No child or adult should have to wait. It's a literal matter of life and death for them. The benefits to these SMA patients are enormous too and, ***if not life-saving, certainly life-changing****."*

"I belong to a group from around the world and it is really hard to see people in other countries and not being able to have access to it here, and the longer it takes the weaker we get.

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.

84 out of the 92 (91.3%) 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. The only barrier noted was having other family members tested. Below are quotes that further highlight the experiences of patients and caregivers with the testing:

"Yes, the ***access was pretty straight forward****, don't remember any barriers or challenges, just an appointment for a blood test."*

"Yes, it ***was fine getting access to it****, no barriers."*

"Yeah I've had genetic testing for SMA, and then again maybe 6-7 years ago again, to determine my SMA diagnosis and ***confirmed type*** *2."*

"We have had a genetic testing, we found it ***simple and straight forward****, helpful and we will have our children tested when they are older. We would really recommend people getting this testing done."*

"I believe I have at least twice once when I was 2 years old via a muscle biopsy, and this past year via a blood test was ***really easy****."*

"Yes. ***No barriers - the genetic counsellor was awesome****. It was great!* ***Only barrier - I wanted my children tested at an earlier age - but that wasn't allowed.*** *I'm ok with that. My husband did not carry the gene when planning a family - worried about having children to be passed along. "*

"Yes. We live in a rural community - at three months old we noticed there was something wrong - went to family doctor who agreed something was wrong - referred to pediatrician resident recognized the signs - referred to a neurologist. ***Was diagnosed immediately.*** *She was able to receive Spinraza - neurologists*

was excellent with information even provided private cell number - there was a ***rush on their genetic testing and within a week she was scheduled to receive Spinraza****. The* ***testing was beneficial it went very smoothly****."*

"Prior to starting on Risdiplam, his neuromuscular specialist did a physical exam testing his muscle movement and did tests with sensors on him to take readings of his muscles responses to electrical impulses. He was able to compare those to the records he had for him from December 2017 prior to receiving any treatment at all. He also had ***his genetic test results that confirmed his diagnosis of SMA*** *Type 1 on file already (0 copies of SMN1, 2 copies of SMN2)."*

"We were open to the testing. ***There were no costs for the tests and we had no barriers to accessing them.*** *We did have to travel to McMaster for a single day appointment, the full cost was around $****50-70 for gas, food, and parking that day****. There were no adverse effects other than my son, who is 3, did not like having the sensors on his skin for the test."*

"Genetic Testing was completed which include a blood sample at our local hospital. Results were provided to us by our physician approximately 4 weeks after blood test was sent."

"I live in an urban centre where blood work testing to evaluate biomarkers is easily available. This has not delayed any treatment that I have had thus far and this work did not incur any additional costs. Since I am 1 of the few adults in Eastern Canada receiving Spinraza, my blood work is also provided for research purposes. ***I have no concerns or anxieties about this type of testing.*** *This is been much easier part of the procedure."*

"The length of time to have to wait for an appointment is important. I feel that if testing was required and it delayed access to the drug in any way, that would definitely not be a good thing. ***Time is of the essence*** *when you are dealing with a disability that is progressive and sometimes moves quite quickly. Having a physical disability is definitely not an expensive. There are many costs that arise from medication to medical supplies to vehicles and two equipment in order to provide quality of life. If there needed to be any type of charge required to get this testing done, that would charge required to get this testing done, that would definitely be a hindrance for our community. That is something that I feel needs to be covered by either the government or the drug company itself****. I know for sure there would definitely be anxious feelings while waiting for the testing results****. We already deal with so many issues surrounding testing. This just adds to the pile. It definitely would be ideal if the decision came back after the test results, notifying that the drug would not be ideal for that particular patient."*

"I have 3 other small children, and since there is a 97 percent chance my husband and I are both carriers (as per my neurologist, we have been tested and are awaiting our results), a 1 in 4 chance any of my other kids could also have a milder or later onset version of SMA. Obviously I pushed for testing for them as well, and this proved to be extremely frustrating and time consuming for me. ***SickKids said they could not do the tests for my others children because technically only my affected daughter was their patient. My family doctor had absolutely no idea how to order the test and took a month to come up with requisitions.*** *Then, it turned out the* ***lab in my physician's building does not perform this test.*** *After phoning around I discovered a few other labs in my area would do it, but with a* ***$300*** *price tag for each of my other children. I ended up talking to my nurse at SickKids who apologized for the run around since it was not her policy, and she ended up facilitating new requisitions so I could take them all to* ***SickKids and have them tested there in the end without charge****. We do not yet have those results. I still do not understand why I encountered so much resistance trying to get these tests performed, especially since SMA testing is has been part of newborn screening since 2020 (3 years after my affected daughter's birth)."*

8. Anything Else?

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

"Having access to a drug like risdiplam would be life changing for our family. Our daughter would no longer be subjected to long trips and stays in-hospital, pre procedure COVID swabs, the effects of frequent sedation/anesthesia, frequent needles and lumbar punctures, and all of the trauma that goes with anticipating these things and not understanding why the people who love her are allowing other people to cause her pain. My other kids would not have to deal with being left with other people while I take her to treatments, and I would be way less stressed and better able to better distribute myself among them, avoiding the hypervigilance and focus on my affected child after each treatment that disrupts our family dynamic. ***Risdiplam would mean WAY less trauma and anxiety for my family and a better quality of life for my daughter, my spouse and I, and for my other 3 small children.*** *I would have fewer appointments to attend, and more time to spend improving myself and working towards my own personal and professional goals that have all taken a backseat to managing my daughters condition."*

*"****Access to Risdiplam would give people with SMA a tremendous amount of freedom and strength, and help so many of the people who cannot currently access the other limited treatments that are available.*** *Access to this treatment would allow us to live fuller, healthier, and longer lives without having to worry about what abilities we might lose tomorrow."*

"Don't want any families in Canada to have to go through this and ***I wish that this drug is available right away*** *to all that need it."*

"Every child with SMA should have a chance with this drug. ***Nobody should be forgotten.*** *Why is there an age restriction when other provinces do not cap an age group. BC does. Try to put yourself in a child shoes - and being told you are too hold to access a drug. He cannot have access to a drug because of his age and the province he lives in. "*

*"****Dying wish.*** *As someone that is nearing the end of their journey in life while being consumed by SMA; I feel it is imperative to help younger generations so they don't have to endure the same struggles that I have."*

"In general, living life with Spinal Muscular Atrophy presents significant challenges in all aspects of my life. Having a drug that would assist me in getting stronger, even if just a little bit, would provide immense benefits to the quality of my life. I am consistently dreaming and wishing for drugs and treatments to become available / be invented that could help myself and others with SMA overcome the hardships we deal with on a regular basis."

*"****Parents who have children with SMA are excited about the possibility of having more than one treatment option. Our kids are intelligent, and deserve a chance at a life with greater mobility, and easier breather, and speaking. Given the opportunity to make it to adulthood they will become major contributors to our society****."*

" I urge two things: ***Don't discriminate and prevent treatment for people with SMA due to ventilator status.*** *Invasive ventilation may be temporary, or it may be chronic. but people with SMA who receive treatment live longer and are able to have a high quality of life.* ***My son plays with his sister, he uses his iPad to communicate, he draws and builds with blocks, and loves Paw Patrol just like every other three year old. His doctors believe (thanks to Spinraza and now Risdiplam) that he will live into his teenage years and beyond.*** *Please do not count kids like this out. Do not limit treatment because a child is "invasively ventilated". He has shown that he can make huge improvements with compassionate access to these drugs, but without compassionate access he would have been locked out of any provincially funded options because he is invasively ventilated (even though with these drugs he is steadily weaning off the vent). I know costs have to be considered, but* ***lives are priceless****, and going forward there are a very small number of children who will be seeking treatment who have not received newborn screening.* ***Streamline processes****. Quality of life and life itself hang in the balance for many while CADTH, and then the provinces make their decisions and negotiations on who can have access, and who can have funded access. Children die who could otherwise live. This thought should always be front of mind in your decision making processes and timelines."*

*"**I appeal to your sense of empathy and humanity**, if you or someone you loved, would you not secure this medication or treatment, to help stop the progression, and help them gain some independence. I live with the knowledge that I am getting worse and to know that there is something that might help, and I appeal for access to it."*

*"**Please approve risdiplam as fast as possible!** I would be willing to try this new drug today if I could. It's so hard when these drugs are available but are not affordable and they can make such a difference for many lives."*

*"There's a lot of costs and efforts - **SMA without treatment is a life limiting disease**. Using costs only to make a decision is not right - **need to look at the whole patient.** Do not limit age group - if you are in an age group - if over 18 how can you determine who can have treatment. Many patients are not getting treatment because of their age. "*

*"I hope that you understand and appreciate the urgency in their decision to approve this - the nature of SMA - **I can't wait for this treatment to be held up or financial pay for the treatment myself. I am relying on you to help me."***

*"**These are exceptional people that have the ability to be contributing members of society and by making an investment in their health that will ultimately lead to giving greater contribution to society.** The gains made by only a slight improvement in his independence would spill over into all aspect of his life, and could really mean an entirely different future for my son that would include a world of successes he would otherwise not be able to achieve."*

*"Lack of access is frustrating - it can't happen fast enough. I want it to relevant to us (SMA community). I want to be active productive member of society. I hate that I can't do simple things. **I can't hunch down to hug my kids. I don't want to lose anymore, I don't want to be too afraid to travel or sit on the side lines, I want to participate**."*

"I understand these drugs are very expensive, but what I would like them to consider is that cover the expense of this treatment is actually going to save money long term because these machines will not be needed, same with health care."

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
Roche				**X** ($103,592.50 in the last 2 years, which includes $47,500 for a SMA Summit (Medical and Scientific Conference sponsorship), $40,000 for education initiatives (webinars, task force) and $15,000 for Walk sponsorship**. <u>No amount was offered to allow the completion of this questionnaire.</u>**

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: Dr. Homira Osman
Position: Director of Knowledge Translation & External Engagement
Patient Group: Muscular Dystrophy Canada
Date: December 10, 2020

MUSCULAR DYSTROPHY CANADA
DYSTROPHIE MUSCULAIRE CANADA

Homira Osman

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