CADTH

CADTH Reimbursement Review
Patient Input Template

Name of the Drug and Indication	**avalglucosidase alfa (Nexviazyme)**
Name of the Patient Group	**Muscular Dystrophy Canada**
Author of the Submission	**Homira Osman**

1. About Your Patient Group

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 19,155 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.

Pompe disease is one of the neuromuscular disorders that falls under MDC's umbrella.

Pompe disease is caused by the lack or deficiency of a single enzyme, lysosomal acid alpha-glucosidase, leading to severe respiratory and skeletal muscle myopathy due to progressive accumulation of glycogen, which builds up to abnormal levels in tissues, particularly in muscles, ultimately causing the disease's symptoms. It is a rare condition that is identified in about 1 in 40,000 births. Pompe disease occurs from a defect in the GAA gene leading to the accumulation of lysosomal glycogen and, depending on the form and severity, can result in cardiomyopathy, progressive muscle weakness, respiratory failure, and heart failure.

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.

The Neuromuscular Service Support Staff identified and contacted parents whose child (children) have Pompe disease or adults living with Pompe disease to participate in a healthcare experience survey (available in English and French) and semi-structured virtual (phone, Zoom) interviews. The Canadian Association for Pompe (CAP) was instrumental in supporting the dissemination of the survey and call for feedback. CAP has 50 parent/patient society members affected by Pompe; they shared the survey with their constituents by e-blasts and personalized invites.

The following submission reflects data from a total of 41 individuals impacted by Pompe disease; this is remarkable as there is expected to be 60 Canadians affected by Pompe disease at present. Our submission reflects 68% of the population under consideration, and 2 individuals had been treated with Nexviazyme. The respondents included 12 males between ages 26 to 81; 14 females between ages 23 to 75; and 11 parents/caregivers of individuals between the ages of 4 to 63 (7 males; 4 females).

We sought the opinion on the value of having Nexviazyme 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 in the MDC survey: "Can you describe how Pompe disease impacts your (or your child's) day-to-day life and quality of life? Are there any aspects of Pompe disease that are more important to control than others?" - the following 5 key themes were identified (in order of frequently reported): 1- significant impact on mobility, strength, balance and energy levels; 2- significant impact on breathing; 3- negative impact on mental health; 4- reduced ability to participate in daily activities; 5- negative impact on the family. The below quotes from individuals affected by Pompe disease highlight that the impact of Pompe is not purely physical, but that the condition impacts mental health, quality of life and the well-being of families.

Significant Impact on Mobility, Strength, Balance and Energy Levels

*"Having Pompe has caused me to **struggle with my movements and balance**. I am currently dependant on a wheelchair for mobility. I currently experience a lot of pain mostly in my hips, back and shoulders. I have **experienced lots of falls** and can not help myself off the floor. This has affected my respiratory system whereas I have been very fatigued. I use to require a trach but no longer require this. But I am dependant on oxygen and require a c-pap machine. I also get frequent headaches. I am required to exercise regularly to keep my strength and range of motion."*

*"Pompe disease has **caused some mobility issues for me**. The most obvious symptom is that my **knees are weak**, I get **very tired from climbing stairs**, and I cant stand up without using my hands if I'm sitting on the ground. I also can't do sit ups. My arms are also weaker, so I can't carry heavy things."*

"I have some mobility issues which makes some things more challenging. I still try to continue to do as much as I can but it can be frustrating."

*"It affects the **strength of my proximal muscles**. In consequence, my **balance is affected**; my breathing while laying down; my **overall strength especially when using stairs and walking uphill**."*

*"I need a walker as I have **poor balance.** I can't do things in the kitchen as I have to hold onto the counter with one hand."*

*"As a Pompe patient with mild to moderate symptoms, I am no longer able to take part in most physical activities as I **no longer have the body strength** necessary to do so."*

*"The largest impact Pompe has on my day to day life is related to my **mobility** and confidence."*

*"I am not able to move my body in ways that most others find easy. **Walking a flight of stairs can be taxing**, having to stand up quickly isn't an option, **my balance is not great**, and I suffer from sore muscles daily."*

*"With the **limited movement range and relatively low energy**, I am unable to do simple tasks such as long period of standing and walking, physical tasks like heavy lifting, any chores that requires moderate core and lower back strength, even simple chore such as bring laundry up and down a few flights of stairs proved to be difficult."*

*"I am bound to a wheelchair and on a ventilator due to late onset Pompe (diagnosed at 28 months old) Pompe hinders my **day-to-day life by limiting my ability to move** and do the simplest of things. I need assistance with all my personal care but still have the ability to drive my chair, eat and drink on my own."*

*"Daily activities **tax stamina** and they must pick and choose so as not to over-expend their energy, which affects their social lives."*

*"My son and daughter both have Pompe... they require a lot of sleep. Each day requires planning of activities so as not to over-do things and pay the price after. A **too high energy expenditure** results in several days of **extreme fatigue**...the inability to do much at all. Appetite is an issue. Both struggle to eat enough to keep weight on...both extremely thin and always trying to put on weight."*

*"I'm fortunate not to have significant pain, but I do have **frequent fatigue**. It causes me to take longer to do anything more than basic tasks. I avoid doing things that I know I won't be able to handle."*

*"Muscle weakness affects **breathing and walking**, two basics of being able to have **energy** to accomplish basic tasks."*

*"**General fatigue** means an inability to plan ahead....never knowing how they will feel each day. Often having to cancel social plans. Limited ability to engage in physical activities and hesitance to divulge to their peers their health issues."*

Significant Impact on Breathing

*"Both my children affected by Pompe battle **anxiety and depression**, muscle pain, spasms and weakness."*

*"I am limited in what I can do with my children (unsteady on my feet, can't run, **can't lie on my back without breathing assistance**, can't swim in deep water) and at work (I'm a cook, I have a hard time lifting things and get pretty worn out being on my feet all day)."*

*"I have **breathing issues** and my **diaphragm muscle don't work**. My posture is very bent as well."*

*"**Breathing is labored** most of the time and always using a BPAP at night."*

*"I use a **Bi-Pap machine** for sleeping at night."*

*"Pompe has **affected my breathing**, I have to **wear a respirator at night to help me breathe** when laying down. I cannot sleep without it. Because of poor muscle strength, I wake each time I move in my sleep. My quality of sleep is definitely worse than it was before the onset of symptoms. If I sleep too long I get quite sore, so it's a balance. I take care when getting out of bed or I might strain a leg, hip or abdominal muscle. I take that kind of care when I do many things."*

Negative Impact on Mental Health

*"There are also days where my **mental health is affected** as I do feel down from time to time that I have to deal with this illness."*

*"It **negatively impacts my self-esteem** to know that I am not going to be able to be the one that helps my children with a lot of things in their life."*

*"The biggest negative effect that disease has on me is **unavoidable stress** linked to "There are a few things I'm unable to do such as sweeping and washing floors and walking with a walker all the time. Need help all of the time."*

*"Pompe impacts my confidence to perform daily tasks, attempt athletic activities or try things like hiking with those I don't know well. I sometimes **feel like a burden** when friends want to do physical activities or colleagues participate in a sports based activity."*

*"The physical limitations and challenges that comes with Pompe disease has also created a **negative impact on my mental health**. Having to second guess and be careful of what I can and cannot do limits my past time activities, ability to go out and hanging out with friends, and having to carefully*

plan ahead every time I want to leave the house can really make me shy away from being outside so much, or partake in any activities and accept invitations from friends."

*"Pompe has brought an **extra layer of stress into my life**. As a female hoping to start a family I question my ability to carry a child. I wonder for how long will I be able to keep up with them, will I be able to play with them outside, etc."*

*"He is doing virtual school right now but he is **very conscious of the way he looks**. He is sitting in a wheelchair during school and worries about what others think about him."*

*"Because of Pompe, I suffer from stomach issues which I have heard many others with this disease complain about. The unpredictability and urgency of bowel movements can be **extremely nerve wracking.** This impacts my ability to do leisure activities such as hike or boat as I need to ensure I can get to a washroom quickly should I experience a flair up."*

*"On any given day I don't feel good. Family has accepted but **emotionally it's hard**."*

*"Because of the disease, I always see flaws in things I do. I always wonder how it would be if I was born without the disease and it **makes me sad** to think about it."*

"*It has changed everything in my daily routines and can't do the things I use to do. I can no longer work and help people like I use to. I have **struggled with depression and suicidal thoughts**. It has impacted my personal relationships and I feel that nobody will want to be in an intimate relationship with me as a result of my disease."*

*"Both battle **anxiety and depression** to varying degrees, off/on. They both live with a sense of not knowing what kind of future they have, how long they will live. For their age, they do quite well with this, but sometimes it weighs heavier than others."*

*"The **frustration** that comes with being limited in what I can do with my children."*

*"For me it is just that sometimes I **feel down** and when I do I don't much feel like being social."*

*"He has been significantly affected from a social perspective. He would get **teased** because of the way he walks. He would be **called "weird"** a lot He hates being in a wheelchair and this causes him much distress He doesn't want to leave the house because he is in a wheelchair. When he was not as verbal, his **mental health was exhibited through irritable behaviors**. He tends to get agitated more because he can't do what others kids can do."*

Reduced Ability to Participate in Daily Activities

"It takes time to do everything. We went to a farm this past weekend, but I had to stop and research the different farms to find which ones are most accessible - one that can maneuver his wheelchair. As his mother, I have to assist him in the shower because he is using a bath chair. Independence is very limited and this ***impacts a lot of what he can on a daily basis*** *."*

"It definitely ***affects every aspect of everyday life****. Just being able to use the toilet can be a challenge, being able to shower, brush your teeth and just begin able to get out bed."*

*"****It impacts my life*** *and quality of life negatively in almost every way possible."*

"Pompe disease has ***impacted my day-to-day life tremendously****. It limited my movement ability and the energy I have throughout the day. There are days I feel very tired even with adequate amount of rest, this has been made worse by the COVID pandemic, preventing me from visiting the gym, which is essential for keeping myself healthy and slowing down the progression of Pompe."*

"I no longer work, I can not do stairs, ***basic every day chores are getting harder*** *to do."*

"All activities must be planned. ***There is no spontaneity in life****."*

Impact on the Family

"My mother is a Pompe patient. As a result, I ***assist her in her day-to-day activities****, attend doctor appointments, and assist in lifting her up after falls and being an advocate when needed in respect to the healthcare system."*

"I am able to get around by using walkers, wheel-chairs, and scooters. I have ***a partner who is able and willing to assist me whenever needed****. I have a personally modified bathroom, stairs, and chairs in our home."*

"Have to ***be with someone 24/7*** *in case something happens to my ventilator."*

"My son is 4 years old. He has low muscle tone, he cannot run or jump or keep up with his peers. He has low oral muscle tone which makes eating more challenging, sometimes he gags and/or vomits. He is hyper-nasal which makes it difficult for people to understand him so I need to translate for him. We have also experienced delays in potty training (he isn't fully trained yet). We are ***more isolated from socializing for fear of him getting sick****. I am his* ***full-time care giver****. We are busy with appointments either at the hospital or virtual, homework from physiotherapy, speech therapy and occupational therapy as well as weekly 7 hour long infusions (not including prep and wait times). We need to adapt for his lack of stamina which changes the way we go for walks, bike rides, has limited our ability to hike and removed the possibility for other sports."*

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: "How are you managing Pompe 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: no treatment experience, but focus on rehabilitation; minimal (or plateau) effect of Myozyme observed; positive benefits of enzyme-replacement therapy with minimal side effects observed.

The below quotes from individuals affected by Pompe highlight that while enzyme replacement therapy (Myozyme) has contributed to positive health outcomes, there remains significant concerns over long-term/sustained benefits.

No treatment experience, but focused on rehabilitation

*"I am allergic to the standard IV treatment for Pompe and could not take it due to a rash and swelling. I complete **physical therapy** regularly which helps."*

*"I didn't have significant symptoms when diagnosed but declined in a few years. I have received enzyme replacement therapy for over 11 years. At the time I started that treatment, my breathing and mobility were declining rapidly. The decline stopped and I my breathing and mobility both improved. 11 years later they are still better than before treatment. I have experienced gradual decline in the last 5 years, but not as rapid as before. The only side effect that I've seen is difficulty sleeping the day of and some fatigue the next day. I've tried **inspiratory muscle training** but had to discontinue. My diaphragm is partially paralyzed so I experienced too much discomfort. I've tried **CoEnzyme Q10** with no benefit. I've tried **salbutamol**, which was studied at Duke University and found to help with strength for those treated with Myozyme. Unfortunately, severe muscle cramps caused me to discontinue."*

Minimal (or plateau) effect of Myozyme observed

*"I was put on the Myozyme for 18 months all together drugs and stopped them partially because of my decision because they **didn't have a big effect**. It was expensive and I **did not think it was worthwhile carrying on.** I am not currently on any medication for Pompe. Not since 2015."*

*"I am Myozyme patient with zero side effect. It worked really well in the beginning but I **plateaued** and I've been regressing since."*

*"I follow Myozyme treatment. To my understanding it is supposed to slow down progression of the disease. I have **not experienced improvement in my condition** and the effect on progression reduction are impossible to evaluate as there are no baselines. I have not experienced any side*

effects that I am aware of other that the stress related to the infusion procedure as I am have a severe fear of needles."

"He has received ERT. We find that in the first few years, he was thriving but now he has ***plateaued****. We don't see any improvements but also not much decline."*

"Myozyme is the only treatment that's been available in our area, it definitely slowed the down progression of his disease but ***the longer he was on it the more it affected his mental health****. The only way to manage it was to stop the Myozyme."*

"I tried enzyme replacement therapy. It seemed to make me more tired and I didn't get any stronger or even stop the weakness from progressing much, if at all. I'm on a ***high protein, low carb diet****. I am hoping a new treatment will work for me before I die."*

"Before the development of Myozyme doctors had only suggested dietary changes to my mother (patient) which ultimately changed my diet as well. Once Myozyme was developed and available, we saw a slight improvement in her mobility (less falls and could walk greater distances before fatigue). However after a few years the ***results started to plateau*** *and falls were happening more frequently. Vibration therapy was another therapy suggested by her doctor. This therapy requires her to stand on a teeter-totter style vibration plate for a few minutes every day. This therapy improved muscle tone present already, and increased the bone density back to normal levels. However, this therapy requires consistent use and for safety measures requires someone to be present while she completes it in case of falls which is not always possible with mine and my father's work schedules."*

"I am currently doing Myozyme treatment, just finished #4, go to the hospital every two weeks. It's a 13hour day, I get very exhausted and drained. Haven't gotten any side effects and ***no results yet****. Can't wait till I can do the treatments at home because getting to hospital and the environment makes me really tired."*

"Since I had a robust physical exercise program which started prior to my diagnosis in 2011 and lasted until 2020, there was no dramatic impact that ERT provided when I was approved for it in 2016. I believe that ERT provided initial support for my general condition, though ***it did not improve my mobility****. I have not experienced any side effects. I am very pleased with the availability of Home infusions and would like to see infusions also available internationally which would allow more flexibility in travel."*

Positive benefits to enzyme-replacement therapy with minimal side effects

"*Prior to starting ERT I would have several downfalls a month, now I have one or two a year."*

*"****Drastically reduced inflammation*** *in my back and legs."*

"I have experience with Myozyme for 10+ years No side effects ***Benefits*** *- I find my face starts to droop before my infusion and once I have it, I am tired, but it gives me a boost. It was so good at the beginning, but now not going to the gym or rehab, has not made the effects as good. I have lost a lot of muscle. Hard to tell if Myozyme effect is wearing off or if it's the time/progression/ageing."*

"My treatments seem to be going okay. I have port that is accessed. The treatments are ***helping me*** *as I do as much as I can each day and it helps me to keep moving, Side effects are on the following day my face gets red and hot around 10:00 in a.m. and is cleared up by about 4:00p.m. I take a Benadryl, an allergy pill and 2 Tylenol for it."*

"The treatment I have been receiving has helped tremendously. I do notice a steady, but slow negative progression of the symptoms and impacts, which in my knowledge is as good as it can get. There were not many side effects I have experienced with the current treatment, with only one mild reaction to the medication which seems to have been caused by a dramatic increase in infusion speed."

*"****ERT had been amazing****. I do wish that it took less time as it can feel like you lose a day every second week and to a young teacher that can seem like a lot. I luckily haven't experienced any negative side effects from my treatment but have found my exhaustion level decreased significantly."*

"Besides exercise the only real treatment I have been on is Myozyme, and well that saved my life, so I think that has been a ***huge benefit****."*

"Very fortunate that ERT has ***worked well, few side effects****; I received them in the hospital which is 10 minutes away. I now have access with Handi-Trans."*

"My son has only been on Myozyme. First 20mg every 2 weeks, then weekly, now 40mg weekly. With the increased doses he has shown an ***increase in energy and oral capability****. He was initially failure to thrive leading to tube feeding which increased his energy. His left lung was collapsed by his enlarged heart so he was on BiPap for a while until his heart returned to a relatively normal size. That also increased his energy however it disrupted his sleep and caused him to vomit if he was sick."*

"I have been fortunate to have experienced ***excellent treatment*** *in the two ways I have received treatment. The first was with hospital care in which I would go to the hospital to receive my infusion on a designated day every two weeks. The care was exemplary and professional. I could arrive at the hospital at a regular time and be done at a regular time. This was during my first 10 years. When the pandemic required home infusions, I received excellent care there as well. Everything went well and was professional. I had no side effects which made management unnecessary."*

*"My **treatment experience has always been great** I had have no complications through my whole life I have been receiving the treatments."*

*"Treatment is keeping me **somewhat stable**, at the beginning, I would get itchy but that has gone away. I get a bit tired after treatment but the next day I am good."*

*"I have been on ERT since 2004 and was stable for a while but find myself declining. Treatment has made **great and huge improvement to me**, my ability to do sports has increased and I have more strengths in both legs and arms. I haven't have much side effects yet."*

*"Getting **treatment has been great**. When I was more mobile I was at a clinic and they were great. Now I'm getting home infusions and that's been great so far. I've been able to access physicians and help when needed."*

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) promote strength and breathing function; (2) slow down progression without a plateau effect; and is (3) delivered in a different mode that saves time.

Regaining strength and breathing function

"*I would like to be able **to stand again**."*

*"Continue to improve with **muscle strength** and keep my lung function as is without any decrease."*

"Compared to Myozyme, I need this to give me better strength I know this drug is not a cure, but I need it to help with my fatigue and give me muscle strength."

"Regaining strength."

"I would like to see more strength and easier breathing."

"Muscle strengthening breathing improvement."

"Breathing capacity , additional leg muscle mobility."

"Independence. Breathing. Being able to walk. Being able to work. Being able to mother."

"Recovery of muscle strength and respiratory capacity would be wonderful but, realistically, I'd like to see a more effective halt in decline. I would consider that a win."

"I would like to get better with my breathing and walking."

"I would like to see positive improvement in muscle strength."

"I would love to see something that got rid of the glycogen from my muscles and repaired the damage to them so I could get stronger again. So the muscles around my arteries could repair themselves."

"Stronger effectiveness for oral muscles."

Slow down progression without plateau effect

"Realistically, I would like to see even further slowing of the negative impacts and progression of the disease. Optimistically, I would like to see it preventing any further impacts or damage cause by the disease. Very optimistically, I hope for it to reverse the damages caused by the disease."

"I would love to see a treatment that stops all deterioration and my dream would to see one that rejuvenates your muscle to become normal."

"If possible get some of the muscle loss back and not decline after a few years."

"It would be particularly beneficial to me if the new treatment would specifically slow the progression of the Pompe disease, and especially my legs and core muscles."

Different mode of drug delivery

"Something in pill form."

"Faster infusion time would be great!"

"Any other mode of treatment other than infusion."

"Something that could be taken orally or doesn't take hours to infuse."

"A more rapid method of delivery."

"Maybe less process time the medicine needs to get in the body not really sure."

"Less time involvement, effective at addressing general fatigue."

"General greater effectiveness that would lead to fewer infusions and shorter infusion times."

"Better absorption into the muscle tissue, longer active periods in the body (current medications only last 72 hours before excretion), no plateau in chronic usage, assistance in regenerating muscular tissue to replace that which is degenerated already."

When considered therapy, patients, families and caregiver consider mode of delivery, side effects, time, frequency of treatments, convenience and impact on finances (cost). 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. 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. 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.

Two adults indicated they received the drug under review as part of the clinical trial. Detailed video interviews were conducted with both individuals where they shared their treatment experiences (please see links attached to this submission). In short, the individuals shared:

*"I am on the clinical trial. I have not done any other therapies. I have **not had any side affects** I have seen **huge improvements**."*

*"I was in the clinical trial for it. It was my first treatment so I don't have any comparison. It gave me a **huge improvement with my muscle strength** however the site is out of my province so it is very time consuming for me to go there (and my caregiver). There were **no side effects** for me."*

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.

100% reported that they did have diagnostic testing completed with at least a blood test; but many also had biopsies to confirm diagnosis. The vast majority found it to be a cost-effective but lengthy process. Below are quotes that further highlight the experiences of patients and caregivers with the testing:

Simple blood test and/or muscle biopsy

*"I had to see a specialist in my hometown and went for **blood work**. I then went to Hamilton to see a specialist after being diagnosed here. I was able to access treatments at my local hospital. I received travel grants for any travel."*

*"I believe it was paid for my Ontario Medicare. Testing was set up for me and it was all requested by the doctor at the hospital. I did not have any concerns with the testing. It was **no worse than having blood taken.** I was diagnosed with **muscle biopsy after having elevated liver enzymes**. It took few months."*

*"The doctor that diagnosed a family member organized a **genetic blood test** for me that confirmed my diagnosis; I was not exposed to any costs."*

*"It only took a **blood test**. The family later had genetic testing done. There was no out of pocket costs except for recommended yearly visits to Halifax (5 hours' drive) to a rare disease specialist."*

*"Government covered all costs, **genetic testing was blood tests** done at the doctors request. We also completed muscle biopsy at this point. No delay in treatment from testing."*

"I had back pain was lucky to have a great walk in clinic who got the process going fast once I had been sent to children's had a biopsy right away to collect piece of my thigh, after that I was diagnosed with Pompe and go on the list for treatment hoping to get approved and I did!"

"I just did some blood tests; we went to many doctor's and finally got a referral to a specialist. After hearing my symptoms, the specialist was pretty sure I had Pompe disease."

Misdiagnoses

*"Testing was part of the diagnostic process from the get-go. Was **initially diagnosed with muscular dystrophy, but got correct diagnosis within a few week** waiting period for test to be done at lab in Quebec."*

*"I had **repeated misdiagnoses**. I kept getting worse and worse. Tests upon tests."*

*"I was **diagnosed with Muscular Dystrophy at first**, however, my (at the time) pediatric specialist was not satisfied with the result and did further testing. I was then scheduled to have a muscle biopsy, which properly diagnosed me with Pompe."*

*"Biggest delay in **diagnosis was being ignored**. Misdiagnosed as B12 deficient due to being vegan (B12 was fine), blood came back hypo-thyroid, abdominal ultrasound showed enlarged heart; finally sent to Metabolics after 2 weeks. Blood was sent from BC to Quebec and South Carolina but 14 days from meeting Metabolics we had the first treatment. Testing was covered by BC."*

"I was diagnosed with Limb Girdle Muscular Dystrophy *at age 12. Because I was getting different symptoms I asked my doctor to have me retested. They did muscle testing, bloodwork and it came back as Pompe Disease."*

*"Spent years thinking **I had Limb Girdle Muscular Dystrophy**. New symptoms lead to new testing. Breathing test led to muscle bi posy. Hospital for breathing local (20km), main testing Ottawa (60km). Appointment for genetics was easy to get. No cost for test. Just travel, gas and parking."*

*"Following a rigorous physical examination in my doctor's office in 2010, I began a series of tests which while inconclusive by Dec 2010, suggested that I had **Limb Girdle Muscular Dystrophy**. When my younger brother was properly diagnosed with Pompe Disease in February 2011, I immediately was given*

*a **blood spot test and had a muscle biopsy done** to confirm my Pompe disease in late February 2011. At the time I was living in the Lower mainland of BC so I had no difficulty in travelling to the VGH for testing. I had a **5 year delay in receiving ERT due to the report from the provincial health rare disease committee that I was too healthy**. All the costs associated with testing for Pompe Disease were covered by my BC health plan."*

Lengthy diagnostic process: multiple tests

*"It took **a long time to get diagnosed** I kept going to the doctor. It wasn't until I went to Physiotherapy that they told me more was going on. After **much more testing** with a neurologist they finally **did a biopsy** to diagnose Pompe. There was no cost to me."*

*"I had an awful genetic testing experience. **It took them almost 30 years**. Delay in diagnosis. Took them about a year and half until finally I got the right test. I got bloodwork. I was tested with leukemia and had to get bone marrow. The tests were paid for but lots of travel to different docs."*

"I travelled from Thunder Bay to Hamilton for testing, Because they diagnosed my brother with Pompe, they called me and asked me to go down with him as he was already having his first treatment

"They covered all cost for me to go. It was about a month after being diagnosed that I started my treatments. I was identified as a potential patient because a family member was **diagnosed after a great length of time**."

*"It took about **3.5 weeks to diagnose him**. There was **a lot of testing and process of elimination**. There was bloodwork. There wasn't much information given along the way. We didn't pay for any of the testing, it was conducted through the testing. The results were explained...but NOT well. I was at a loss for words. Unexpected diagnosis. I had never heard of Pompe."*

"We had to travel about 90 minutes for testing and doctors' appointments; he had a few blood tests done and a MRI done for the diagnosis. Our provincial health insurance covered all the appointments and tests, social assistance helped with mileage and meals."

*"The doctors **did tons of tests** for a myriad of different diseases before they found out what it was. I was the first diagnosed juvenile in Canada. I'm in Canada so we didn't have to pay for anything out of pocket. I was 14 when diagnosed, so I was still with my parents."*

*"It was my mother that fought for the diagnosis as I was 28 months old. She went to **many doctors for many tests**; most just pushed her away saying things like she was a lazy mother. It was the muscle biopsy that helped with making the right diagnosis."*

*"It **took years** to finally be referred to the proper doctor and department. But once we were, testing and diagnosis went fairly smoothly and was expedited as fast as possible. Still took many months to receive clear answers. Cost covered by Alberta Health Care."*

*"Testing took a **very long time**."*

*"I was **misdiagnosed** for a while but after seeing a few physicians they got to the bottom of it. Being persistent with my family doctor helped. I had a muscle biopsy and then seen another doctor who said I didn't have Pompe so ordered a DNS test. It **took about 2 years for the final result**. Treatment was not available to me at first and the provincial government refused to pay for it. **Took 10 years from diagnosis until getting treatment**."*

*"I was referred to a metabolic specialist to look at **unusual blood test results**. I was also seen by a neuromuscular specialist in the clinic as well. I was otherwise healthy. I was tested for many things, eventually being **diagnosed with Pompe disease after about four years**. I had so many tests, some taking some time to get results for. I've had a **liver biopsy and a muscle biopsy**. Both were painful for a few days. Genetic testing wasn't done. It was never made clear to me which test method they used. When I was diagnosed I was still mostly asymptomatic, so the **delay in diagnosis** didn't delay treatment for me. For the last two years of testing, I was living about 400kms from the clinic, so there were travel costs. I can imagine that for some people that would have been an issue."*

*"I saw a doctor in Toronto who **wasted 10 months testing** and not reporting the results quickly. After the dry blood test she said it might be Pompe and she walked away. She came back and said we might go to see a doctor in Hamilton but it would take a long time to get an appointment and it would be very expensive. We already had an appointment for the next day. He diagnosed me on the spot and my first infusion was 2 weeks later. We didn't pay for anything except one test which was $75 and that was with the first doctor."*

Emotional experience

"It was an **extremely stressful** *and **emotional time**. A lot of uncertainty."*

*"It was probably the **most stressful decision** in my life as to this day it remains one that is mostly based on hope and faith."*

*"A **shocking** and **overwhelming** process."*

*"I wasn't fully aware of the impact of what happened at the time, and I cannot recall many of the **negative feelings** I experienced."*

*"I was **overwhelmed** and don't remember much but we had a great team who helped us through everything."*

*"I had a muscle biopsy with the first doctor and an intern did it. He hit a nerve which was horrible. It was some time before we got the results, and that was **cause for anxiety**. The whole time was very tense as we didn't know what to expect."*

*"Lots of anxiety waiting for results and then knowing the results with no cure **led to depression**. Then when there was a treatment here and couldn't get it, **it made me furious**."*

8. Anything Else?

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

"Anything that can help us is so important to our quality of life."

"I hope this new medication will be available to everyone and that it will improve everyone's well-being."

"This disease SUCKS for lack of better terms. It is devastating. While we can frame it in positives such as appreciating life, but the challenges it comes with - it's difficult as a single parent. It's a lot. The financial support is limited but the needs are a lot. Any drug or therapy that can reduce the impact is worthwhile. It not only takes a toll on the person diagnosed, but on family members: I had to quit my job, my daughter had to pick and choose where she works because she is mindful of her brother's condition and all the choices we make."

“I think this drug under review really changed my life. I cannot imagine after being diagnosed and knowing that my muscle will weaken as I age, but having no solution to it. Even though the drug is not a cure for the disease, it slows down the process and even had a huge improvement for me. I am really thankful and I really hope this drug can be approved in Canada so all patients can have access to it.”

“From what I've been able to gather, Nexviazyme looks like an improvement over the current enzyme replacement therapy. Even modestly reducing decline can be very significant over a patient's lifetime. I am looking forward to access to this drug myself.

“This new drug offers a window of opportunity to positively affect my health. If the drug effectively slows the progression of the disease, I will be pleased.”

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH reimbursement review process, 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.

   None.

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.

   We worked in partnership with the Canadian Association for Pompe to ensure we captured the voices and experiences of Canadians affected by Pompe. The Canadian Association for Pompe was instrumental in sharing the survey with their members and helping to refer individuals to MDC for semi-structured phone interviews.

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
Sanofi-Genzyme				X $101, 500 – all for educational initiatives: Roundtables Webinars Awareness video on Pompe disease

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, PhD
Position: VP, Research & Public Policy
Patient Group: Muscular Dystrophy Canada
Date: October 25, 2021