Canada's Drug Agency
L'Agence des médicaments du Canada

CDA-AMC REIMBURSEMENT REVIEW

Patient and Clinician Group Input

cipaglucosidase alfa with miglustat (TBC)

(Amicus Therapeutics Canada Inc.)

Indication: Cipaglucosidase alfa: Indicated for use in combination with the enzyme stabilizer miglustat for long-term treatment in adult patients with late-onset Pompe disease (acid α glucosidase deficiency). • Miglustat: An enzyme stabilizer indicated for use in combination with the enzyme replacement therapy cipaglucosidase alfa for long-term treatment in adult patients with late-onset Pompe disease (acid α glucosidase deficiency).

December 13, 2024

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CDA-AMC in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings. **If your group has submitted input that is not reflected within this document, please contact Formulary-Support@cda-amc.ca.**

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CADTH

CADTH Reimbursement Review Patient Input

Name of the Drug and Indication	**cipaglucosidase alfa and miglustat** **Pompe disease** **SR0871-000**
Name of Patient Group	**Muscular Dystrophy Canada**
Author of Submission	**Homira Osman, PhD**

1. About Your Patient Group

Describe the purpose of your organization. Include a link to your website.

Muscular Dystrophy Canada is registered with CDA.

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 is a sophisticated network of informed professionals, service specialists, and volunteers who deeply understand neuromuscular disorders. 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.

MDC has a full spectrum of programs, services, and supports for the thousands of Canadians of all ages living with a neuromuscular disorder 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. Plus, MDC invests in transformative research to work towards more answers, therapies, and hopefully, potential cures.

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.

At the MDC, we follow the principle *Nothing About Us Without Us* closely. Individuals with Pompe disease and their circle of support are actively involved in every aspect of our organization - from leadership and decision-making roles to serving on committees and participating in collaborative research efforts. By integrating the perspectives and experiences of those affected by Pompe disease, we strive to ensure that our efforts are aligned with the needs and priorities of the patient community

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.

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, information on clinical trials) 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 reached out to adults with late-onset Pompe disease (acid α-glucosidase deficiency) and parents of children over 16 to participate in a healthcare experience survey (available in both English and French) as well as semi-structured virtual interviews (via phone or Zoom). The survey was distributed through e-blasts, personalized invitations, and Canadian patient online communities. Additionally, the Canadian Association of

Pompe played a key role in promoting the opportunity and helping to ensure strong participation and engagement.

MDC also conducted the Pompe Canadian Journey Mapping project, aimed at capturing the comprehensive lived experiences of both children and adults with Pompe disease. The project focused on understanding the entire healthcare journey, highlighting the challenges faced, and exploring the profound impacts of the disease on individuals and their families. Through this initiative, we collected valuable insights into various aspects of the Pompe experience, including delays in diagnosis, gaps in available treatments, emotional and social impact, and difficulties related to accessing appropriate care and support systems.

The following submission presents data from 41 individuals (24 males, 17 females) diagnosed with Pompe disease, all of whom have received a confirmed diagnosis through clinical reports. Additionally, 15 caregivers or family members of individuals with Pompe disease participated, bringing the total number of respondents to 56. This is a notable sample, especially considering there are approximately 60 individuals with Pompe disease in Canada. Due to privacy concerns and the rarity of the condition, we do not report the number of respondents by province, as some provinces had only one respondent. However, we can confirm that the participants were from Ontario, Alberta, British Columbia, Quebec, Saskatchewan, Nova Scotia, and New Brunswick.

A qualitative descriptive approach, utilizing the constant comparison method, was employed to conduct a thematic analysis of the data. This approach allowed us to identify key themes and patterns within the experiences shared by participants. To ensure that patients' voices are authentically represented, we have incorporated direct quotes throughout the report, offering valuable context to complement the quantitative data. Additionally, a separate, comprehensive report containing all patient comments is available for review, providing further insight into the individual perspectives and experiences of those impacted by Pompe disease.

2. 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?

We asked participants to describe how Pompe disase affects their daily life and quality of life, as well as which aspects of the condition are more important to manage. Based on the responses, we identified 5 key themes that were frequently reported, listed in order of frequency: 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.

On average, individuals with late-onset Pompe disease first noticed symptoms at **age 23.**
"*I was a competitive athlete and my performance was starting to decline. It was a real hit to my self-confidence and increased frustration. I was exhausted all of the time, it made it impossible to get through the day without falling asleep. I was napping constantly and had difficulty staying up later to hang out with friends like most typical teens."*

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 has definitely impacted my ability to be the parent I'd hoped to be. Severely limited participation in sports and other outdoor activities I once enjoyed. I'm still able to work, but my years as a cook are numbered..."

"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."*

3. 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).

When MDC inquired about how Pompe disease is managed with the available treatments or

therapies, all respondents noted that intravenous enzyme replacement therapy (ERT) is the primary treatment, with some also mentioning the inclusion of physiotherapy.

One respondent shared their experience*: "It took months before ERT started, which was nerve-wracking because we didn't know how much muscle degeneration was occurring daily. After starting ERT, we had to travel two hours every two weeks for the infusions over the course of three months. Now, the nurses administering the home ERT are fantastic. My husband also began an exercise and nutrition clinical trial at McMaster about two months ago, where he takes vitamin supplements and follows a prescribed exercise plan."*

Another respondent described their journey: *"For many years, no treatments were available, so I could only have check-ups with my neurologist to monitor my condition. In 2012, my neurologist told me about the Adult Metabolic Diseases Clinic at a different hospital and referred me there. I visited them in early 2013 and was introduced to ERT. They made arrangements for me to begin receiving treatment at my local hospital."*

One participant shared some challenges they encountered: *"During the first year, treatments were given at the hospital, and it was very time-consuming. Not all nurses were trained to administer the treatment, which often led to delays due to pharmacy backups, staff shortages, and other issues. Once treatments were moved to home care, we faced challenges finding skilled nurses who could successfully insert IVs, and there were problems with equipment, such as broken IV pumps, a reluctance to try new technologies, and limited resources."*

When asked whether patients applied for funding to access ERT:

- Majority mentioned that the cost of treatment was already covered, or their doctor managed the coverage.
    - "Funding was applied for so I could receive ERT treatments. The doctors at the clinic assisted with the application process, so it went fairly smoothly."
    - "Yes, it was very straightforward and mostly handled by my healthcare team. All I had to do was take a few tests and sign some forms."
- Those who did apply for funding stated that while the process was easy to understand, it was still lengthy and difficult, with a lot of paperwork involved.
    - "Trillium funding… the initial application was long, but it's easy to renew each year."
    - "Applying for funding is a very tedious process."
- Some expressed frustration with insurance companies in trying to get coverage approved, including being denied multiple times.
    - "We applied for ERT through insurance. The Rare Together program and the genetics doctor's receptionist were very helpful, but the insurance companies were terrible. That's what took 3 months—fighting with insurance and going to many doctor appointments for tests to show them."
- Patients also discussed advocating for drug funding approval.
    - "I tried to meet with the Health Minister of NB but was redirected to the Drug Program, where I was told it wasn't funded and there was no money for it."
    - "It was funded through the Special Access Program under compassionate use, and I'm still under that today because I'm on a ventilator. The company and the government agreed to keep me on compassionate use."

4. Improved Outcomes

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

Despite approved therapies for Pompe disease in Canada, there are significant unmet treatment needs. Patients with Pompe expressed a strong need for better management and control over their condition. They seek treatments that not only minimize the impact of symptoms but also reduce side effects and prevent exacerbations that can severely disrupt their lives. Effective therapies would help patients maintain their independence, reduce the frequency of serious medical interventions or hospitalizations, and ultimately improve their overall quality of life.

Improvements that patients and caregivers reported from treatments or therapies was increased strength and energy, followed by a slower progression of the disease, with one participant noting improved mental health and also a subset observing no benefits as of yet. **Participants indicated that while the treatment worked, disease progression continued.**

"Myozyme - I am still alive I guess. I wasn't supposed to be. It slows down the progression of my disease. My lungs should be a lot worse than they are. It is slowing the degradation of my organs, heart, lungs. I am slowly getting worse, but Myozyme is slowing it down at a good rate."
"Within the first 6 months, it was amazing. It was a life saver, I went from bed ridden to going outside. I got my GED, went to university. I have a daughter. It surprised a lot of doctors. They took my charts around the world to show everyone how well it worked. I gained a lot more independence."

When asked, what they 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. 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.

When asked about how decisions were made regarding their current therapy or treatment, the most common response was that there was no choice, as only one treatment was available. Additionally, the time commitment required for infusion treatments and the financial cost and affordability of the treatment were important factors in the decision-making process.

- "There was no choice. It was the only treatment available."
- "To be honest, I didn't think of anything as a trade-off. I was excited to participate in the clinical trial once I learned the new drug had much better benefits."
- "I had to choose between going to a clinic with skilled nurses and better resources, but the treatment took over 5 hours, and I couldn't breastfeed or bring my baby. Or, I could do it at home, but then I had to deal with nurses who couldn't start an IV after several attempts, and I had to use IV pumps that weren’t battery-operated, meaning I had to stay plugged into a wall. None of the options were ideal. Plus, I had to miss work every two weeks."
- "I made the best of it by getting a gaming laptop and having some 'me time' during my infusions."

- "I miss school for ERT and can't move closer to family because the treatments aren't available in that town. It feels like we have to stay in Vancouver. I won't miss any more school for physical therapy, occupational therapy, or speech therapy."
- Did you try multiple treatments? Why did you switch? (N=22)
- Yes, multiple treatments: 1
- No, only 1 treatment: 21
- For those who said no, they all started with and continue with ERT.
- The one participant who tried multiple treatments mentioned, "It was due to an early misdiagnosis, but once I was diagnosed with Pompe, I was switched to Myozyme."

5. Experience With Drug Under Review

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

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways? 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.

N/A

6. 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.

The diagnostic journey was prolonged and challenging: it took an average of 7.69 years from the onset of bothersome symptoms to a confirmed diagnosis. On average, individuals were 30 years old when they finally received a diagnosis.Many had received misdiagnoses such as

Polymyositis, fatty liver, asthma, liver issues, limb girdle muscular dystrophy, muscular dystrophy, Becker muscular dystrophy, thyroid issues, FSHD and pneumonia.

"I was told I was lazy, and my mom was lazy too. We kept being dismissed about my symptoms, with doctors suggesting I would eventually catch up."

"I underwent numerous tests before the biopsy. Pompe wasn't even considered at first."
"Our family doctor referred him to a neurologist locally, but the appointment took months. Then we had to wait for the results. The neurologist acknowledged something was wrong but didn't know what, so we were referred to another neurologist in downtown Toronto. After more waiting, we were told it would take three months for the test results to come back. When we didn't hear anything after three months, we called them every week. Four months later, they told us they lost his blood work and we had to redo the test. It took a total of seven months from that last appointment to get the results. From the initial family doctor visit, it was a whole year before we got the Pompe diagnosis. And when we finally got the diagnosis, it wasn't from the doctor over the Zoom call—it was from her assistant, who couldn't answer any of our questions. She said she needed to consult with the doctor and would get back to us. It was an incredibly frustrating experience."

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**."*

7. Anything Else?

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

There's a pressing need for treatment options to address the ongoing challenges faced by patients with adult onset Pompe disease. We request the CDEC Committee to watch this Canadian patient testimonial: https://www.youtube.com/watch?v=AgeMvBUtays .

From our engagement with Canadians affected by Pompe, we learned that the experiences shared by individuals with Pompe reflect a range of emotional, physical, and logistical challenges:

- Many find living with Pompe to be both physically and emotionally draining. Feelings of isolation and lack of support from healthcare providers are common, with some expressing frustration over limited time and assistance from their specialists.
- The process of getting treatment approved can feel like a battle, with some patients describing it as begging for their lives. While some have received respectful treatment from health officials, the approval process remains a significant obstacle for many.
- Positive developments in Pompe awareness are seen as beneficial, especially in securing access to life-saving treatments, therapies, and mental health support for both patients and their caregivers.
- The challenge of an "invisible disability" is a recurring theme, with patients struggling to navigate daily life while appearing outwardly healthy, making it difficult for others to understand their daily struggles.
- For some, access to healthcare services has been a source of relief. Having local support makes the experience somewhat easier.
- Navigating insurance approvals for treatment can be a lengthy and difficult process.
- Many patients appreciate the ongoing research and hope for quicker action regarding treatments. The example of countries like the Netherlands is cited as a model for faster responses in offering treatments.
- Connecting with others who have Pompe is seen as vital for emotional support.

- Participating in clinical studies has been described as morally rewarding. However, there is a desire for better communication with neurologists, as some feel they lack sufficient knowledge.

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.

   No.

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

   We collaborated with the Canadian Association for Pompe to ensure we gathered the perspectives and experiences of Canadians impacted by Pompe. The Association played a key role in distributing the survey to their members and referring individuals to Muscular Dystrophy Canada.

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
Amicus				X No funds were directed toward Muscular Dystrophy Canada's operations or staff salaries. All funding received was through a single restricted educational grant, with no involvement from Amicus

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: December 13, 2024

Clinician Group Input

No Clinician Group Input was received for this review.