Common Drug Review
Patient Group Input Submissions

galsulfase (Naglazyme) for long-term enzyme replacement therapy in patients with a confirmed diagnosis of Mucopolysaccharidosis VI

Patient group input submissions were received from the following patient groups. Those with permission to post are included in this document.
The Isaac Foundation for MPS Treatment and Research/ The Canadian Society for Mucopolysaccharide and Related Diseases Inc. (The Canadian MPS Society) — permission granted to post.

CADTH received patient group input for this review on or before June 16, 2015
CADTH posts all patient input submissions to the Common Drug Review received on or after February 1, 2014 for which permission has been given by the submitter. This includes patient input received from individual patients and caregivers as part of that pilot project.

The views expressed in each submission are those of the submitting organization or individual; not necessarily the views of CADTH or of other organizations. While CADTH formats the patient input submissions for posting, it does not edit the content of the submissions.

CADTH does use reasonable care to prevent disclosure of personal information in posted material; however, it is ultimately the submitter's responsibility to ensure no personal information is included in the submission. The name of the submitting patient group and all conflict of interest information are included in the posted patient group submission; however, the name of the author, including the name of an individual patient or caregiver submitting the patient input, are not posted.

The Isaac Foundation for MPS Treatment and Research/ The Canadian Society for Mucopolysaccharide and Related Diseases Inc. (The Canadian MPS Society)

Section 1 — General Information

Name of the drug CADTH is reviewing and indication(s) of interest	NAGLAZYME – (Galsulfase) – MPS VI Maroteaux- Lamy Syndrome
Name of the patient group	The Isaac Foundation for MPS Treatment and Research/ The Canadian Society for Mucopolysaccharide and Related Diseases Inc. (The Canadian MPS Society)
Name of the primary contact for this submission:	[redacted]
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Patient groups' contact information: Email	[redacted]
Telephone	[redacted]
Address	[redacted]
Website	http://www.theisaacfoundation.com http://www.mpssociety.ca
Permission is granted to post this	Yes

1.1 Submitting Organization

The Isaac Foundation's mission is to fund innovative research projects that aim to find a cure for MPS, a rare, debilitating, and devastating disease. We provide support for families of individuals suffering from MPS and advocate on their behalf to ensure government funding for expensive, life-sustaining treatments are covered by the health care system.

Founded in 1984, The Canadian Society for Mucopolysaccharide and Related Diseases Inc. (The Canadian MPS Society) is committed to providing support to individuals and families affected with MPS and related diseases, educating medical professionals and the general public about MPS, and raising funds for research so that one day there will be cures for all types of MPS and related diseases.

1.2 Conflict of Interest Declarations

The Isaac Foundation

1. BIOMARIN PHARMACEUTICALS: The Isaac Foundation has received sponsorship funds from Biomarin Pharmaceuticals over the course of the past 6 years. Sponsorship has been granted
2. to our Annual GALA FOR A CURE, an event designed to raise funds to find a cure for MPS VI. Biomarin has been a sponsor of this event since its inception 6 years ago.
3. SHIRE PHARMACEUTICALS: The Isaac Foundation has received sponsorship funds from Shire Pharmaceuticals for various events over the past two years. These sponsorship grants go directly to our MPS II Research program, with all dollars raised funding research projects that aim to find a cure for MPS II (Hunter Syndrome).
4. JANSSEN PHARMACEUTICALS: Janssen Pharmaceuticals, a division of Johnson and Johnson, began supporting our GALA FOR A CURE in 2013 and 2014, and has committed to supporting our event again in 2015. All money provided by Janssen goes directly toward funding research projects aimed at finding a cure for MPS.

The Canadian MPS Society

The Canadian Society for Mucopolysaccharide and Related Diseases Inc. (Canadian MPS Society) provides support to individuals and families affected by MPS. They also provide education to medical professionals and the general public about MPS and raise funds for research. The Society receives unrestricted grants and event sponsorships from Genzyme Canada, Shire Canada, and Biomarin Pharmaceuticals. It declared no conflict of interest in the preparation of this submission.

b) We have the following declaration(s) of conflict of interest in respect of those playing a significant role in compiling this submission:

The Isaac Foundation and the Canadian MPS Society has no conflict of interest to declare with respect to anyone playing a significant role in compiling this submission. All work, interviews, and drafting of this submission was supported and completed by our organizations alone.

Section 2 — Condition and Current Therapy Information

2.1 Information Gathering

Information for Section 2 was obtained using one-to-one conversations with a number of patients using the current therapy, as well as parents of patients on therapy. An online survey was also used for Canadian and International patients currently receiving therapy. Personal information was used, as our organization helps and supports numerous families suffering from Maroteaux-Lamy Syndrome (MPS VI). We also have referenced printed sources, published articles, available clinical trial data, and discussed the condition and experiences using this therapy with the lead investigator responsible for the initial NAGLAZYME clinical trial in Oakland, California.

2.2 Impact of Condition on Patients

Maroteaux-Lamy Syndrome is a disease that has numerous life-altering, life--threatening, and very progressive symptoms. These symptoms include but are not limited to bone and joint disease, heart and airway disease, progressive stiffening of the joints, spinal cord compression, corneal clouding, hearing loss, and decreased endurance.

All patients/parents that were interviewed for this submission reported that Maroteaux-Lamy Syndrome affects all aspects of their/their child's lives. One parent noted the far-ranging effects the disease has on her child, including serious impacts on ***"fine motor skills, gross motor skills, stiffness and pain in joints, low energy level overall, lethargy, poor appetite, general "sick" feeling, toileting, dressing, self-grooming, sleeping issues, pain at night due to carpal tunnel, corneal clouding, nearsightedness, surgeries, and numerous doctor appointments."***

A parent of an affected individual expressed similar experiences dealing with the disease: ***"Every aspect of the body is affected in some way. We are lucky to have a treatment for this disease to slow down or stop the progression of these symptoms, but the symptoms that appeared prior to starting treatment are***

debilitating. For instance, his hands are incredibly impacted, which leads to difficulty gripping objects, opening jars, dressing himself and tying his shoes. His shoulders became very stiff and range of motion in his shoulders decreased rapidly before treatment began and this has prevented him from being able to raise them over his head very effectively. This impacts his ability to wash his hair and dress himself. We feel blessed that this deterioration slowed down or stopped after treatment began because further disability would lead to even more complications in his life than he already has."

Maroteaux-Lamy Syndrome is a very progressive disease, and all parents of patients suffering from the condition that were interviewed reported numerous activities that they could not do that used to be a "normal" part of their life. Examples of lost abilities include bike riding, running, team sports, playing musical instruments that require fine motor skills, handwriting and drawing. Dressing themselves was reported as a major difficulty for all patients we connected with.

"Some of the basic activities that our daughter can't do include team sports, anything with high risk of injury due to fragility of her neck, spine and hips. She has other activities which are more of a challenge to her as a result of some impaired flexibility such as reaching light switches. Handwriting, drawing, anything utilizing her fingers is becoming increasingly more challenging for her." – Caregiver Interview

In addition to the ultimate goal of prolonging life, the aspects of this condition that are most important to control are endurance and bone and joint disease. These two symptoms seem to play a crucial role in maintaining independence and quality of life of affected individuals. Improved endurance has an impact on all facets of life and endurance is a good measurement of how well a patient's body is performing. From heart to bones to pulmonary function, increased endurance indicates that those systems are working better. With respect to bone and joint disease, the stabilizing or improvement of this aspect of the disease leads to a better quality of life, reduced reliance on mobility devices, and the potential for pain reduction in all affected joints.

All patients and caregivers interviewed expressed a desire to see the disease stabilized or the progression of the disease slowed down or halted. ***"A progressive disease is heartbreaking for families, and it's always our hope to find a cure for this disease someday. For now, having a treatment that slows down the progress of MPS VI is incredibly hopeful. It's a lifeboat for our son until we find that cure. Stabilizing a progressive disease is so important, and we've been able to do that with ERT."***

2.3 Patients' Experiences With Current Therapy

Before the FDA approved Naglazyme in 2006, patients suffering from Maroteaux-Lamy Syndrome had no access to treatment. Prior to Naglazyme, treating the disease was done by managing symptoms as they appeared and essentially a long-term palliative approach to managing the disease was taken. This is still true for patients who do not gain access to treatment with Naglazyme. Patients who do not have access to enzyme replacement therapy (ERT) face a pain-filled and relentless deterioration of every bone, tissue, muscle, and organ in their body and must undergo numerous surgical interventions, with more severe effects being seen as the disease progresses. In Canada, 14 patients have been fortunate to access treatment with Naglazyme, the first patient being infused in Ontario in 2006. Every patient and parent of the patients that I interviewed has seen dramatic improvements in their condition and general quality of life since treatment began.

One caregiver noted the impact she has seen on her daughter since treatment with Naglazyme began: ***"Naglazyme is the only treatment for treating MPS VI, and although it is not a cure, it is a vital treatment to halt the progression and damage that this disease does to an affected child. Our daughter is a prime example of the benefit of ERT with Naglazyme, without it she would have numerous health issues as a result of non-treatment, her quality of life would be greatly diminished and her life expectancy shortened substantially. With weekly infusions of Naglazyme there is hope, there is renewed health and energy in our girl and there is a chance of her body being healthy enough for a cure in the future. She is able to count on having a future with her weekly infusions of Naglazyme. It is sustaining her life, it is working!"***

A consistent theme that showed in all interviews was how stable patients were since undergoing treatment with Naglazyme. All reported a marked stabilization of the condition, which is the goal when dealing with a progressive disease. One caregiver remarked at how great the improvements and stability have been and what it means to them: ***"Her energy increased dramatically. Her stamina and endurance increased dramatically. Her strength is improved; her mood is better (due to better sleeping and being able to do more physical activities). Her Maroteaux-Lamy symptoms have been slowed down dramatically. All medical appointments this past 12 months have been encouraging.***
She has shown improvements in all aspects of her health, including growth."

Current treatment with Naglazyme is very effective in controlling aspects of this disease. Clinical trial data and the recent 10-year resurvey data compiled by Dr. Paul Harmatz showed a dramatic increase in endurance for patients participating in the clinical trial. This increase in endurance has the potential to manifest improvements in all aspects of disease progression. Endurance is a good indicator on how well the body is working, and any such increase works to improve overall quality of life.

"I hate to thing where we'd be right now if we didn't have (early) access to Naglazyme. I believe Naglazyme is saving our son's life right now and maintaining his quality of life."

– Caregiver Interview

The resurvey data published by Dr. Harmatz and his colleagues is groundbreaking data regarding the efficacy of ERT with Naglazyme due to the sheer volume of the clinical trial patients they were able to follow over the 10-year period. This publication should be the starting point for any team reviewing the potential impact and efficacy of therapy for individuals suffering from Maroteaux-Lamy Syndrome. In short, the conclusion of this in-depth study concretely shows that **"long-term galsulfase ERT results in improved survival, continued growth, improvement in endurance and pulmonary function, and stabilization of cardiac and quality of life measures in MPS VI patients. Even in patients with more severe disease, galsulfase ERT results in stabilization of endurance and pulmonary function as well as improved survival. Clinical benefits of galsulfase ERT are likely to be enhanced by early initiation of the therapy in MPS VI patients."**

However, treatment using ERT for this condition does not come without some level of hardship. While none of the patients interviewed experienced any adverse reactions during their infusions or afterward, Biomarin Pharmaceuticals does indicate on their labeling that anaphylaxis, or a severe life threatening reaction, can occur during the infusion process.

Primarily, the hardships reported during interviews centered on location and travel time associated with receiving infusions. Many patients have to travel multiple hours to and from infusion sites, which makes the process take the better part of one or two days. Added travel to an already tiring infusion process creates an exhaustion level for patients that is difficult to recover from. Many patients and their caregivers express a keen desire to have home-infusions. This will cut travel time for infusions down to zero, allow families to better schedule their lives around infusion timelines, and allow patients and caregivers the ability to lead a more normal life.

2.4 Impact on Caregivers

Caregivers face significant challenges caring for patients with Maroteaux-Lamy Syndrome. First and foremost, the stress of diagnosis of a child is unquantifiable, and as many supports as possible should be put in place to help all caregivers of patients suffering from Maroteaux-Lamy Syndrome.
Patients suffering from Maroteaux-Lamy Syndrome require significant medical interventions, long hospital stays, many surgical procedures, and repeated appointments with a host of specialists. This is further compounded if they do not have access to treatment. These visits, operations, and appointments cannot be done alone, and caregivers sacrifice a lot of their own time to ensure patients receive company and support during these visits.

Many caregivers must leave the workplace for all or a portion of the workweek in order to care for their loved ones battling this disease. With ERT infusions, this may still be the case due to the current need to infuse in a hospital

setting. This leaves parents and partners of those affected bringing their loved ones into infusion centres for the day or two-day long treatment (depending on travel time).
None of the caregivers or patients interviewed reported any serious or life-threatening adverse effects related to therapy with Naglazyme and thus could not comment on what challenges, if any, they would have if such adverse- affects were to be experienced. A few caregivers reported that their children suffered some mild infusion-associated reactions and that those reactions were tolerable considering the immense impact the treatment has had on slowing down or halting the disease progression in their children.

No patients in Canada have discontinued ERT despite the hardships identified.

Section 3 — Information about the Drug Being Reviewed

3.1 Information Gathering

Information for Section 2 was obtained using one-to-one conversations with a number of patients using the current therapy, as well as parents of patients on therapy. Personal information was also used, as our organization helps and supports numerous families suffering from Maroteaux-Lamy Syndrome. We also have referenced printed sources, published articles, available clinical trial data, and discussed the condition and experiences using the new therapy with the lead investigator responsible for the initial Naglazyme clinical trial in Oakland, California.

3.2 What Are the Expectations for the New Drug or What Experiences Have Patients Had With the New Drug?

a) Based on no experience using the drug:

It has been shown very concretely that the lives of patients will be improved significantly by receiving treatment with Naglazyme drug. First and foremost, and much like ERT being used for other types of MPS diseases, stabilization of the disease is expected to occur in all individuals, regardless of when treatment begins. Clinical trial data and the 10-year resurvey data also point to increased endurance and a decrease in overall glycosaminoglycan (GAG) accumulation in the urine of Maroteaux-Lamy Syndrome patients. The decrease in this GAG accumulation indicates a lower storage of these GAGs in the bones, tissue, organs, and muscles of patients. Accumulation of these GAGs results in the clinical symptoms that individuals experience and a reduction in the body would indicate a slowing-down of the disease progression. The resurvey data also shows that treatment with Naglazyme ***"results in improved survival, continued growth, improvement in endurance and pulmonary function, and stabilization of cardiac and quality of life measures in MPS VI patients."***

Currently, there are no other treatments available for patients so there is a tremendous unmet need for ERT. The adverse effects that were experienced in the clinical trial setting were very minor compared to the benefit that this treatment offered patients. The opportunity to see improvement in endurance, bone and joint disease, and heart and pulmonary function far outweighs the relatively minor allergic reaction that can sometimes occur during the infusion process. In addition, such reactions during infusion are rare and easily managed by slowing down the infusion process or halting it until the reaction has been corrected and maintained.

Any improvement in this condition can have a profound effect on the quality of life for patients suffering from this disease. All such improvements lead to fewer hospital visits, fewer medical interventions, and fewer doctors' appointments. This results in less time off work, less time away from school, and less stress for all family members. While these benefits are unquantifiable from a socio-economic perspective, they are incredibly important to the wellbeing of patients and their families.

b) Based on patients' experiences with the new drug as part of a clinical trial:

This drug underwent its clinical trial over 10 years ago and we did not interview patients that were part of the original clinical trial. However, much of that data collection and the follow up can be found in the 10- year resurvey data and should be used by the CDR panel when reviewing this drug for use here in Canada. It should

also be noted that numerous provinces throughout the country have already noted efficacy and tremendous unmet need for this drug for patients suffering from Maroteaux-Lamy Syndrome. As such, they have provided reimbursed therapy for all patients in the country that would benefit from treatment with Naglazyme. This includes reimbursed therapy in BC, Alberta, Saskatchewan, Ontario, Quebec, and New Brunswick.

The impact of this treatment on the patients and families battling Maroteaux-Lamy Syndrome cannot be understated. All patients and caregivers discussed the improved quality of life they have experienced since treatment began for them. Caregivers expressed the joy and hope that this treatment provides their family, while others talked about the future more than they would have prior to beginning treatment. This was a common theme amongst interviewees, and is summed up nicely by this caregiver: ***"It is essential to the health and well-being of the MPS VI patient - positive effects become very evident and it can truly alter the path of the patient's life to give them a new lease on life. It is important to start treatment as early as possible."***

"Naglazyme has done everything we could have hoped it would and then some. He is growing at a somewhat steady pace, his organs are normal size and the amount of GAG in his urine is very close to 'normal'. His skeletal deformities have not worsened at all since beginning treatment. He has had no adverse affects from the treatments whatsoever!

– Patient Interview

Section 4 – Additional Information

The questions included in this template were very clear and helpful. It would be helpful to families and patients if they could provide direct input to your review team, rather than having to direct that input through an organization. We appreciate your time and consideration of this document and look forward to watching Naglazyme work its way through the CDR process in a timely fashion.