sebelipase alfa (Kanuma)
(Alexion Pharmaceuticals)
Indication: Lysosomal acid lipase deficiency

CADTH received patient input for this review from:
Canadian Liver Foundation
The Isaac Foundation

November 23, 2017
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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.
1. About Your Patient Group

Founded in 1969, the Canadian Liver Foundation (CLF) was the first organization in the world dedicated to supporting education and research into all forms of liver disease. Today, the CLF continues to be the only national health charity committed to reducing the incidence and impact for Canadians of all ages living with or at risk for liver disease. The CLF is the only registered charity in Canada directing funds specifically for liver disease research in all its forms and has invested more than $29 million in the scientific search for causes, preventative measures and potential treatments for liver disease. The CLF reaches millions of Canadians through our public and professional education programs, patient support programs and other awareness, fundraising and outreach efforts. Over the past 45+ years, the CLF has invested more than $50 million in health education and prevention programs.

2. Information Gathering

To gather input for our submission, the CLF invited patients, caregivers and health care professionals from across Canada to fill out an online questionnaire modelled on the CADTH, CDR and pCODR Programs submission template. The online questionnaire was open from October 20 to November 13, 2017 and promoted on the CLF website, via CLF social media channels and to CLF patient, caregiver and health care professional contacts.

Lysosomal Acid Lipase Deficiency (LAL-D) is an ultra-rare disease in Canada (only five diagnosed cases in Canada). As such, the number of responses to this survey were expectedly low.

The responses received have been used to compile the feedback for this submission. Quotes from CLF questionnaire respondents are included in italics in various sections of this submission.

Demographic information of the respondents was requested in the questionnaire, but response was not mandatory. Below is a summary of the demographic information voluntarily provided by the respondents:

Respondent Categories:

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PATIENT Demographics:

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3. Disease Experience

Lysosomal Acid Lipase Deficiency (LAL-D) is a genetic, progressive and chronic ultra-rare metabolic disease. Infants, children and adults with LAL-D do not have a fully functioning enzyme (lysosomal acid lipase – LAL). This enzyme is responsible for the metabolism of cholesterol esters and triglycerides from low-density lipoproteins (LDLs). Without this enzyme, harmful amounts of lipid particles build up in a part of the cell known as the lysosome. This fat accumulation can lead to significant health consequences including damage to the liver and other organs.

LAL-D is extremely rare, with only an estimated five (5) LAL-D cases in Canada. LAL-D is predominantly a pediatric condition but may also be diagnosed in children and adults.

Absent or very low levels of the LAL enzyme leads to severe, early onset of LAL-D in infants. Infant LAL-D is also known as Wolman disease. Many signs of LAL-D may not be visible and can only be determined through blood tests however, some common symptoms and signs of LAL-D in infants may include:

- Failure to grow
- Difficulty absorbing nutrients from food (malabsorption)
- Persistent diarrhea and vomiting
- Swollen belly
- Jaundice (yellowing of the skin and eyes)

Sadly, the median age of death is under four (4) months of age while survival beyond one (1) year of age is very rare in infants with LAL-D.
Late onset LAL-D in children and adults is also known as cholesteryl ester storage disease (CESD). The LAL enzyme deficiency leads to a build-up of fat in the liver, spleen and other parts of the body. In children and adults, the disease may not be easily recognized, but as the liver damage progresses, symptoms may include:

- Enlarged abdomen from fluid accumulation (ascites)
- Easy bruising or bleeding
- Jaundice

In addition, high levels of lipids in the blood of children and adults with LAL-D can lead to cardiovascular complications, such as coronary artery disease and stroke.

“My liver aches, feels large and is uncomfortable. I feel lethargic. My wife and I have a 1 year old daughter so naturally I have a feeling of despair because of my concern for my family if I were to make an early departure.” – Patient 1 (adult)

“I had jaundice & severe itching for years. Abdominal pain that would come and go & bouts of extreme fatigue.” – Patient 2 (adult)

“Children with LAL-D will experience neurodegeneration, hepatomegaly and failure to thrive.” – Health Professional 1

4. Experiences with Currently Available Treatments

Because some of the signs and symptoms associated with LAL-D are similar to those of other more common disorders, it may take months or even years for people with LAL-D to get an accurate diagnosis. Diagnosis can be made with a blood spot test which measures the LAL enzyme activity level.

Current standard of care for LAL-D is mostly a matter of management, with nutritional supplements in infants and low cholesterol and reduced saturated fat diets for children and adults. These methods however have limited impact with no marked benefit on morbidity and mortality rate.

Statins have also been used in children and adults, however use of statins have shown no benefit in slowing down the progression of liver disease.

“What treatment? Statins? My liver was full of fat as found in a biopsy when I was three (3). Statin drugs will not help me and there is no link to statin drugs helping someone with LAL-D.” – Patient 1 (adult)

Beyond the limited effects of nutritional supplements and statins, stem cell therapy and liver transplantation have also been explored. While stem cell therapy has been successful in restoring normal LAL activity in a few cases, it is not an effective treatment strategy as the procedure is extremely risky. Similarly, liver transplantation is also risky and not a viable long-term solution as the newly-transplanted organ can develop liver disease from the ongoing LAL enzyme deficiency

5. Improved Outcomes

Sebelipase alfa is a new approach to treatment for LAL-D. It is the first enzyme replacement therapy that mitigates the lysosomal acid lipase deficiency by presenting a newly-created protein enzyme that reduces the accumulation of cholesterol in the body. Studies have shown that sebelipase alfa improves survival in infants with LAL-D and corrects the ALT and liver fat abnormalities in children and adults with LAL-D.

Sebelipase alfa is currently available through the Health Canada Special Access Programme so patients may have access to this medication through this mechanism. As LAL-D is an extremely rare disease however, the level of knowledge of the healthcare provider can certainly impact a patient’s access to this treatment if LAL-D symptoms are not recognized, if the
blood spot test is not utilized to make the diagnosis, if treatment options are not explored and if the Health Canada Special Access Programme is not fully understood and/or utilized to access this treatment.

As sebelipase alfa has been available through the Health Canada Special Access Programme, it is important that this treatment continues to be available to patients and their physicians, whether it remains available through the Special Access Programme or whether it is transitioned to the Canadian Public Drug Plan. With few treatment options available for LAL-D, and with studies showing improvements in quality of life and prognosis, sebelipase alfa must remain available, accessible and at zero or minimal cost.

“We need to have access to Kanuma for people in Canada with LAL-D. Please allow us access to the treatment. Thank you.” – Patient 1 (adult)

“There are no good treatments readily available for this disorder. We need more options.” – Health Professional 1

6. Experience with Drug Under Review

Sebelipase alfa is administered through an intravenous infusion and the recommended dose for infants under 6 months of age is 1 mg/kg once per week and the dose for older children and adults with late-onset LAL-D is 1 mg/kg every 2 weeks.

While this is not a long-term “cure” for LAL-D in infants, clinical studies have demonstrated a significant survival benefit with 67% of infants on sebelipase alfa surviving beyond 12 months of age, compared to zero patients without treatment. As noted earlier, children and adults with LAL-D also benefit from this new treatment option with demonstrated reductions in ALT liver enzyme levels and decreased liver fat content.

“I have been on sebelipase alfa for almost 3 years now, and rarely experience adverse effects of LAL-D anymore. I live a fairly healthy & active life. I’ve had more energy to do the things I love, and I don’t get sick (colds & flu) nearly as often as I used to. When I do get sick, it doesn’t hang on as long either.” – Patient 2 (adult)

7. Anything Else?

LAL-D is a very rare disease, but the low numbers of diagnosed patients in Canada should in no way mean that their lives don’t matter. For infants born with LAL-D, this new form of enzyme replacement therapy can improve survival rates beyond the average of 3.7 months to over 12 months. For children and adults with late-onset LAL-D diagnosis, treatment with sebelipase alfa may slow down or diminish the liver and extra-hepatic manifestations of the disease to the point where LAL-D may now be considered a treatable condition. This is life-altering and patients deserve this opportunity to experience improved quality and quantity of life.

The hope is that access to sebelipase alfa through the Public Drug Program will mean that patients and caregivers will have improved access to this new treatment. Furthermore, the hope is that the cost of treatment through the Public Drug Program does not skyrocket as this would place a significant and unexpected financial burden on families. However, if accessing sebelipase alfa is not seamlessly and readily available as part of the Public Drug Program, then there is tremendous fear and anxiety as to what impact this will have on the life of the patient with LAL-D.
Appendix: Patient Group Conflict of Interest Declaration

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 outside assistance was utilized to complete this submission. This submission was completed by CLF staff and volunteers. The only outside input for this submission came from the patients, caregivers and health care professionals who responded to the CLF’s online questionnaire.

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.

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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.

The Canadian Liver Foundation (CLF) is committed to bringing liver research to life for all Canadians through liver research, education, patient support and advocacy. The CLF receives funding from a variety of sources with the majority coming from donations from individuals across the country. We use these funds to support CLF liver awareness, education, patient support and research grant programs.

The CLF receives some program funding in the form of unrestricted educational grants from pharmaceutical companies. Grant agreements are established in support of activities initiated by the CLF and prohibit the funder from having any input or influence in program objectives or deliverables.

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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: Karen Seto
Position: Director, Professional Education & Partnerships
Patient Group: Canadian Liver Foundation
Date: November 21, 2017
1. About Your Patient Group

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 also provide support, guidance, and education for families of individuals suffering from any rare disease and advocate on their behalf to ensure government or pharmaceutical industry funding for expensive, life-sustaining treatments.

2. Information Gathering

Information for this report was obtained using one-to-one conversations with a number of patients using the current therapy, as well as parents of patients on therapy, and patients and caregivers who are hoping to gain access to treatment. An online survey was also used for Canadian and International patients. Anecdotal information was also used, gathered through conversations our organization has had with patients and families in hospitals. We also have referenced printed sources, published articles, and publicly available clinical trial data.

3. Disease Experience

LAL-D is a genetic, progressive disease that leads to multi-organ damage and premature death; patients suffering from this condition report life-altering impacts of the disease on their day-to-day life and on their quality of life. Caregivers also reported a high degree of impact on their quality of life and on their day-to-day activities while caring for a patient battling the disease.

During our one-on-one interviews, and in answers to our survey questions, it quickly became evident how much of an impact LAL-D has on the lives of these patients and family members. Constant themes mentioned by patients include the physical health impacts, disruption on school and everyday life due to chronic illness as a direct result of the disease, and the impact LAL-D has had on their mental well-being. One patient reported that they deal with “constant pains, enlarging of liver and spleen, headaches, (and) days missed of school for illness.” Not uncommon for children battling rare diseases, this patient also pointed out how important it is for them to “make sure a parent is readily available for care” at all points in time during their days and nights.

Another respondent stated that they “get sick easily, any cold or bug that was going around, and it would hang on for weeks” before they were able to begin on the only therapy possible, Kanuma. Unfortunately, for a patient without access to the drug, they continue to deal with similar illnesses, with the severity of disease progressing over time. “(I) now have cirrhosis of liver. Suffer much abdominal pain. Have had skin lesions and scarring.

The impact LAL-D has on caregivers cannot be understated, and the stress, emotional drain, and constant worry and heartache this disease leaves caregivers with was quite evident during interviews, as well as on answers to survey questions. One parent responded: “As a caregiver, it effects my life by interfering with my job, my stress levels, and overall consumes my time. I have to plan medical tests, treatments, follow ups around my work schedule, my kids school schedule, and sport schedule. I have to take the time to research treatments, symptoms, medical tests, and financial medical support. With LAL-D being such a rare disease there is no support group to attend, so I must seek others through social media, and try to reach others through our story. But the hardest thing of all as a caregiver, is knowing that your child (in my case all four children) has a rare disease and having them poked, tested, and studied. I know in heart the testing needs to be done, because it helps the doctors understand the disease. Hearing "we just don't know" is the hardest answer to accept.”

We know the toll this disease has on the body if left untreated – rapid death for patients diagnosed in infancy, and liver transplants and other severe life-threatening complications for patients diagnosed in childhood. 75% of paediatric patients
require a liver transplant within 5-14 years after diagnosis, and 50% of patients die due to liver failure if LAL-D is left untreated. The impact this has on patients and care-givers' mental well-being is unimaginable, though caregivers were able to share their stories of stress and worry with me during this process in a way that speaks to the toll LAL-D takes on everyone involved.

When the questions arose about which aspects of the disease were most important to control, parents and patients alike responded overwhelmingly about the lack of actual control they have on the progression of LALD. Without any available treatments until Kanuma, patients were left to suffer the ravages of the disease over time, and simply had to manage as best they could while liver damage, cardiovascular disease, enlarged internal organs, and gastrointestinal issues progressed. Patients and parents work to provide a strict diet to help slow the progression of LAL-D, but these severe and very life-threatening complications happen regardless of the diet, albeit, are perhaps a bit more delayed with the strict diet followed.

“Although LAL-D still effects our lives everyday, it had a lot more negative impact on our lives before Teaghan started Kanuma. The disease was always on our minds. We felt helpless, and lived in a constant state of fear. Teaghan’s school work was effected, as she was very distracted. We lived day to day, not knowing what the next day would bring. If she got a stomach ache or her head hurt, we feared the disease was progressing rapidly, and we would lose her sooner than later.”

– Caregiver Interview

4. Experiences with Currently Available Treatments

Currently, there are no available treatments to help alleviate the symptoms and progressive nature of this disease. Without treatment, multiple organs are affected, leading to life-threatening complications and early death in the majority of people with LAL-D. Some of the problems associated in the liver with untreated LAL-D include elevated ALT, elevated bilirubin, esophageal varices, microvesicular or mixed hepatic steatosis, fibrosis and cirrhosis, and a whole host of other major symptoms that impact the length and quality of life. LAL-D also leads to numerous and severe complications in the cardiovascular system, the gastrointestinal system, and the spleen. Without treatment, these symptoms progress rapidly and lead to patients requiring liver transplants and suffering from early death.

Prior to the FDA approval of Kanuma, historical care saw patients given lipid-lowering medications. Unfortunately, these medications do not reduce liver complications in patients suffering from LAL-D, nor do they address the underlying cause of the disease. In an observational study, patients taking lipid-lowering medications while battling LAL-D showed continued progression of the disease, with 56% of enrolled patients having liver biopsies showing liver cirrhosis. Of those patients, 44% had repeat biopsies showing progression of the disease, and 50% of those patients progressed to a liver transplant or had, unfortunately, died.1 Lipid-lowering medications also lead to many difficult side-effects for patients with LAL-D. Some of these side effects include, muscle pain and damage, drowsiness and dizziness, vomiting, headaches, and difficulty sleeping. More serious side-effects can include memory loss, mental confusion, high blood sugars, and, in severe cases, kidney damage or failure.

In my discussions with patients, some expressed how difficult it was to try to manage the disease with lipid-lowering medications, with many mentioning the “many negative side effects from the medicine.”

Most patients are often prescribed a low-fat diet in order to try to slow the progression of the disease. However, much like lipid-lowering medications, the disease continues to progress at a rapid rate. Some patients reported suffering from anemia due to a low-fat, meatless diet, and while they did everything they could to maintain and follow their strict diet, the disease continued to progress, with many patients reporting on our survey that they now have cirrhosis of the liver and other major complications resulting from the progressive nature of the disease.
As the disease progresses, patients are left with one final option to help alleviate some of the symptoms of the disease—a liver transplant, which still does not treat the underlying cause of the disease, nor does it deal with the symptoms experienced in the other vital organs of the body, including the heart and kidney.

Transplants are difficult for patients to endure and recover from, and come with their own very serious sideeffects. These sideeffects include, but are not limited to: bile duct complications, blood clots, transplant rejection or failure of the donated liver, and mental confusion or seizures. In addition, the new liver will continue to see the same complications as the previous liver over time, leaving patients again in life threatening positions.

When we would go for our family walks around the block, (our daughter) liked to ride her bike or use her rollerblades, but we would have to stop halfway as she would cry about how much your back hurt. We would often have to carry her home. (Our Daughter) was put on a low fat diet to try to slow down the progression of the disease. There was no other course of action. There was no other treatment available, and statins were not clinically proven to help. We had to teach (our daughter) how to read labels, and explain to her how important it was not to eat the wrong foods. That really impacted (our daughter). She was afraid that she would die, as it brought to light how serious the disease really is.

- Caregiver Interview

5. Improved Outcomes

Patients surveyed and interviewed all had high hopes for the availability of Kanuma to help treat their disease, especially considering how well the clinical trial went, how rapid the approval has been in other countries, and how well the treatment has worked in patients who are receiving access Internationally and within Canada under compassionate use requests, or from extensions to the clinical trial.

It was evident in my discussions with families that quality of life will change dramatically for everyone who is able to access therapy for themselves or their family members. One respondent said that he is “now married with a toddler daughter. I need treatment with Kanuma (so that I) might live without the threat of premature death.” This same theme was evident in all of the responses to this question posed during the survey – from both caregivers and patients alike. They simply want the chance to live, and know the only way they will get this chance is through access to Kanuma. There was nothing they wouldn’t sacrifice for the chance to gain that survival, for the chance to access treatment with Kanuma.

6. Experience with Drug Under Review

We are fortunate to have a few patients in Canada already receiving access to Kanuma through an extension of the clinical trial and, in one case, through an urgent access program, with availability of the drug provided by the company, Alexion Pharmaceuticals. There are not many patients in Canada who suffer from LAL-D, perhaps as few as 10 identified patients, much lower than the prevalence of the disease would suggest. Based on the comments and feedback we received about patients’ and caregivers’ experience with Kanuma, it should be a priority to expedite these reviews so the other patients can gain access to this life-saving treatment. Due to the limited number of patients in Canada receiving Kanuma, we also discussed the impact that this treatment has had on patients Internationally in order to get a good sense of the benefits of this treatment.

Without fail, every respondent reported a regression of their disease and their life-threatening symptoms. On mother put it simply: “My boys have had no side effects from the Kanuma. They get to live basically a normal life now and have hope for a future! I can be relieved that I don’t have to fear watching my children die!” This was echoed by every patient and every caregiver we talked with for this report.
With respect to benefits experienced, patients reported a decrease in the size of their internal organs, liver levels were normalized in all cases, muscle and joint pain disappeared, and stress levels for patients and caregivers alike were lowered. One parent, who has 4 children receiving Kanuma, reported that “The advantage over diet/Statins is that Kanuma actually works! They each progressed liver disease stages and cholesterol levels remained high with the other treatments. With Kanuma they have basically normalized.”

While the benefits of Kanuma were seen in every patient receiving access to therapy, all patients and caregivers reported very few disadvantages that impact their lives. Most comments on life-impact revolved around scheduling work and activities around bi-weekly infusions, and the time it took to travel to infusion centres. In no way were these inconveniences too much to handle in order to receive treatment for themselves or their children.

No patient on therapy reported any adverse events or side-effects from their infusions and all respondents feel the treatment should be made immediately available to all patients battling LAL-D.

We have nothing but good things to say about Kanuma. Our child has had no side effects whatsoever. She now has no issues with her back. Her headaches and stomached have significantly reduced. Her AST, ALT and Cholesterol are now within normal range, and her liver and spleen have now almost normalized. It has been an amazing experience for our whole family.

- Caregiver Interview

7. Companion Diagnostic Test

There are no companion diagnostics for this treatment – All patients battling LAL-D will exhibit a progression of their disease, which will lead to many significant life-altering and life-threatening symptoms. All patients with LAL-D can and should be considered for therapy.

8. Anything Else?

We took this opportunity to allow parents and patients the opportunity to speak directly with reviewers by leaving comments that we could cut and paste. Some patients and parents took us up on that opportunity, and these are included below. Sincere thanks to this committee for allowing the voices of our patient population to be heard during this review, a review that is critical to their long-lasting health and well-being.

“Our son has been in need of LAL enzyme for 41 years. Knowing a med is on some markets around the world yet unavailable in Canada is very upsetting, to him, his wife, daughter, we- his parents, his sister and all extended family members. He has not enjoyed a normal lifestyle; always monitoring every morsel of food he eats, every physical activity and in general tending to his health every minute of every day. He has had more blood drawn, more doctor visits, more exams of all kinds than you can imagine. As a teenager he did not grow until he was 18 years. He lived in fear that he would be stunted for life and we were certain that would happen. No explanation has ever been given, but he did eventually grow to a normal height. Those years were filled with taunts and ridicule. As his father, I worry every day.”

“THANK YOU!! The point that we are here at this time, considering approval of Kanuma in Canada, is a huge success for us. It is something that we have been dreaming about since our daughter was first diagnosed. I want to start off by saying...This drug saves lives!!!! I cannot say enough about Kanuma. It has saved our daughter’s life! It has given us peace of mind and given our child back her future.”

“Our son inherited this condition from the recessive genes of his mother and me. If I could do anything to add healthy happy years to his life at this stage - I would give mine in exchange. Once he left home and went to college he took full responsibility for his health. It was then that he fell through the cracks of the medical system. At this time he needs someone besides his mother and me to lobby for him. He only became aware of Kanuma after his mother found info online. She contacted his
childhood geneticist who was unable to do anything for him. It doesn't matter if a child is 4 or 41, a parent wants them to be healthy. Our son never was, and now with the possibility of change we are hoping and praying for treatment. If Kanuma treats LALD, he should not have to beg Health Canada to provide it. Nor should he have to wait until his health deteriorates further."

“When you first hold your child in your arms, you dream about the future. I call it the "What wills?". "What will my child look like?" "What will they be when they grow up?" When your child is diagnosed with a life threatening disease the questions change to "What if's?" "What if I can't save my child?" "What if I outlive my child?" Kanuma has given us back our "what will's?" Kanuma has saved our child's life. Kanuma has shrunk her liver and spleen, it has lowered her cholesterol, AST and ALT. Kanuma has stopped her back aches, and significantly reduced her headaches and stomach aches. Kanuma has stopped her from crying at night, telling us that she is afraid to die."

“I had jaundice & severe itching for years. Abdominal pain that would come and go & bouts of extreme fatigue. I have been on Kanuma for almost 3 years now, and rarely experience adverse effects of LAL-D anymore. I live a fairly healthy & active life. I have found, since being on Kanuma my overall health has been better. I've had more energy to do the things I love, and I don't get sick (colds & flu) nearly as often as I used to. When I do get sick, it doesn't hang on as long, either.”

“Kanuma is hope. Hope for a future where Teaghan and all others who are effected by LAL-D do not have to worry how long they will live. You should know that you will be saving lives by approving Kanuma. This drug is safe and has little to no side effects, and is the best and only treatment available for a horrible disease. Please make a life saving treatment available for those who desperately need it. For now, and in the future.”

“Thank you for reviewing this drug. I do feel it has bettered my life & health, and could do the same for others.”

“I need Kanuma! No one offered it to me. I learned about it through online research. I see Health Canada as lagging behind other progressive govs. My early geneticist, Dr. Yokoyama in Japan commented re; govt approval..."GET IT DONE! Japan has approved Kanuma!"

“The medicine has been a factor in pausing his illness. I feel it should be available to anyone with LAL-D."

“I cannot fathom why Kanuma would ever be denied!? It is proven to work! It saves the lives of those with LAL-D. Why should anyone be denied lifesaving medicine? I, as a mother, could not imagine the devastation of knowing there was a treatment available to save my child’s life, and my government said no! The fear of losing one’s child is the worst torture a parent can endure. That fear would be increased, knowing there was a way to save your child, but not allowed to do so!”

“I hope they approve this drug for Canadians, although we are currently only two people, I anticipate more diagnoses in the future. How can we help these people if we don’t have access to the proper drugs? It would also be a huge waste of my time as an individual, and I hope to see that all the turmoil I’ve had to endure (through the clinical trial) would amount to something great. I want to know that I’ve helped make this possible, and that I will help many people in the future. If you’d like for someone to speak about their journey, and what it’s like to live with LAL-D, I will gladly be a spokesperson. I aspire to help people like me to be able to live a life they want.
Appendix: Patient Group Conflict of Interest Declaration

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

The Isaac Foundation received no help in preparing this submission.

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.

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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.

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Nothing to Report

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: Andrew McFadyen
Position: Executive Director
Patient Group: The Isaac Foundation
Date: November 22, 2017