CADTH

CADTH COMMON DRUG REVIEW

Patient Input

luspatercept (Reblozyl)

(Celgene Inc. / Bristol-Myers Squibb Canada Co.)

Indication: Beta-thalassemia associated anemia

CADTH received patient input from:

Thalassemia Foundation of Canada and Canadian Organization for Rare Disorders (CORD)

December 17, 2020

CADTH

Patient Input Template for CADTH CDR and pCODR Programs

Name of the Drug and Indication	**Luspatercept (Reblozyl for beta thalassemia**
Name of the Patient Group	**Thalassemia Foundation of Canada and Canadian Organization for Rare Disorders (CORD)**
Author of the Submission	[redacted]
Name of the Primary Contact for This Submission	[redacted]
Email	[redacted]
Telephone Number	[redacted]

1. About Your Patient Group

Thalassemia Foundation of Canada – http://www.thalassemia.ca/

The Mission of the Thalassemia Foundation of Canada (TFC) is to support and fund thalassemia scientific research, treatment, patient services, public awareness and education.

The organization is headed by a five-member Board of Directors. The Thalassemia Foundation of Canada has become a national organization and able to devote nearly one hundred thousand dollars per year to medical grants for research. Each year in February, the Thalassemia Foundation of Canada hosts an annual Valentine's Dinner and Dance Fundraiser to raise awareness and much-needed funds, which are completely dedicated to education, research, and to provide necessary support for patients suffering from thalassemia in Canada. It has also established a distinguished medical advisory committee headed by Dr. Douglas Templeton with the University of Toronto, and has become a member of Thalassaemia International Federation (TIF)

Canadian Organization For Rare Disorders (CORD) - https://www.raredisorders.ca/

CORD is Canada's national network for organizations representing all those with rare disorders. CORD provides a strong common voice to advocate for health policy and a healthcare system that works for those with rare disorders. CORD works with governments, researchers, clinicians and industry to promote research, diagnosis, treatment and services for all rare disorders in Canada.

2. Information Gathering

Recruitment: An initial focus group was conducted to gain qualitative feedback on the experience of treating thalassemia and opinions about Reblozyl. The focus group responses were used to develop an on-line survey. The focus group and the survey were developed and implemented by CORD in collaboration with TFC. The identification of focus group members and dissemination of the survey were done by TFC, with outreach to all TFC members through direct email outreach. The interviews and summary of feedback were conducted by CORD.

Responses: Patients provided input through a survey available on Survey Monkey from 8 to 14 December 2020. The outreach was Canada-wide. There were 8 participants in the focus group and 68 respondents to the survey.

Diagnosis: Among the survey respondents, the majority (69%) were diagnosed with beta thalassemia major; 6% were diagnosed with alpha thalassemia or thalassemia intermedia, and 22% were family members/caregivers for someone with (beta) thalassemia.

Demographic information: Overall, 73% of survey respondents identified as the person with thalassemia; 15% were a parent or guardian, and 10% said they were a family member other than parent. In total, 49% of the persons diagnosed with thalassemia identified as female; 47% as male, and 3% preferred not to say.

Of the 55 respondents who identified their place of residence 100% said they lived in Canada. Among these, 73% reside in Ontario with 11% in Alberta, 11% in Quebec, and 5% in Saskatchewan. For the purposes of the analysis, responses from all provinces were pooled; given the small numbers outside of Ontario, there was no rationale to examine provincial variations.

3. Disease Experience

“How the disease affects the patients; quality of life" were collected through open-ended questions in the focus group and one open-ended question in the survey. In addition, participants were asked to "rate" a number of symptoms and complications experienced as a result of thalassemia or treatment for thalassemia with five fixed options anchored on one end by "no problem, never" and "minor, infrequent" to "serious, frequent" and "incapacitating, life-threatening" on the other end.

The most serious and frequently experienced symptoms , "fatigue or sleepiness", with more than one-third (35%) reporting these as "serious, frequent" and only 20% said they were "minor, infrequent" or "not at all." In addition, almost half of survey respondents (47%) reported the experience of "headache, dizziness, difficulty concentrating" was “moderate” or worse.

More concerning are the serious complications due to the condition or treatment were reported. Experience of “iron overload that was not well managed by chelation” was rated as serious by one-fourth (24%) of respondents and moderate by another 30%. About 30% had had a “life-threatening” or “serious” experience of an enlarged spleen (that was subsequently removed in some cases) and another 15% said their experience was “moderate.” Other complications, in order of seriousness or frequency of impact, were “liver damage (hepatitis, fibrosis)”, “infections”, and “hearing and vision sensitivities or loss”, which reinforces the continued challenge of thalassemia despite the treatment and care availability.

In terms of psychological or emotional effects, about 14% said the experience of “anxiety, depression, panic attacks” was "serious, frequent" or worse, while about one-third (29%) said these effects were "moderate" with less than one-fourth (24% reporting these were not a problem. Moreover, most (84%) had no or only minor experience of "confusion and/or memory loss", and the remainder (16%) said this was a moderate problem,

But these ratings do not convey the overall impact on the individual and the family of living with thalassemia. These verbatim comments reflect impact on health, work, and social contexts.

IMPACT OF LIVING WITH THALASSEMIA:

“My wife requires monthly transfusions. It has prevented her from earning a fulltime income in the past, and prevented plans from us moving abroad (for work) due to lack of specialized healthcare. She has also gone through several emotional issues over the years coping with this disorder.”

“I worry about reactions during transfusions, and iron buildup over time. COVID 19 is a major added stressor now. The biggest impact is the psychological impact of Thalassemia and hearing about friends who have suddenly passed due to complications.”

"I don’t like it when I get tired because of low hemoglobin -and can’t take part in all activities in the school...."

“It’s hard to express; - my son is always trying his best to cope with his life that is different from others -he is always fighting with himself internally ....our life plan and all schedule run around him -his transfusion dates .always scared what if the haemoglobin get lower this time or the iron level gets higher"

“Thalassemia affects me on a daily basis. I am tired all time. Get sore, back pain. And then eventually depressed. Going on vacation with the family is always a treat, but prior to going it's very stressful. I need to order meds, schedule transfusions, and align everything with my health, in order to just go away for 12 days. I have never left the country for more than 15 days. It would be a dream to travel and not have to worry about a transfusion every 2 weeks.”

IMPACT OF TRANSFUSION AND IRON OVERLOAD

“My son is on two medications (desferal and jadenu). Although he doesn't like the desferal infusions, this is all he knows. Socially, my son misses school every 3 weeks. Financially there are extra gas/milage and parking expenses to go to sick kids “

“I am dependent on monthly transfusions which are not only physically taxing, they are emotionally burdensome, especially for those of us trying to balance the many competing responsibilities with our families and work or school. The transfusions also come with the need to take iron chelation therapy daily. Adherence is a challenge for me, due to a number of factors, which has resulted in my iron liver concentration to increase significantly since starting transfusions over 10 years ago. Annual monitoring of my iron liver concentration includes an MRI of my liver. I also have routine cardiac and spine MRIs, as well as bone mineral density scans, as the impact of thalassemia and iron accumulation are far reaching.”

“As Thalassemia is a life-long chronic illness, it is an ongoing difficulty. I have secondary conditions and many side effects that are difficult to deal with as a result of this illness. Maintaining my hemoglobin by having to receive life-saving transfusions so frequently is a stress and increasingly painful, as my veins are increasingly sensitive and it is very difficult for nurses to administer an IV. It is upsetting having to receive blood transfusions every three weeks. Getting older only adds to the difficulty. My energy levels fluctuate greatly. Around transfusion time, I am sometimes extremely weak, dealing with headaches and dizziness. It can sometimes take a huge amount of effort just to do normal, everyday things!”

“I started noticing my symptoms as symptoms. How tired I was, the pain I’d feel, the moodiness. I wasn’t allowed to go for sleepovers because of my desferall pump which kept me out of the loop with my friends. Once I switched to exjade sometime in high school the stomach pains and the vomiting was too much to handle so I would skip doses for years and didn’t tell anyone. I was embarrassed and ashamed of having thalassemia so I pretended I didn’t have it. I tried my hardest to fit in at school and gotten good at pretending to be someone I wasn’t but not taking my exjade caught up to me and I had extreme iron overload in my liver and my heart. I had a picc line put in me and was medicated 24/7 for 8 months. It was horrendous and really hard to go through. The site was constantly infected since I was allergic to the tape. It was always itchy and painful and took a toll on my mental health. After that I was diagnosed with depression and an anxiety disorder. Thalassemia is hard to live with and I wouldn’t wish it on anyone, however I will say I would not be the strong independent individual I am today without it.”

4. Experiences With Currently Available Treatments

Specific treatments: benefits, side effects and management: 100% of the patients represented in the survey are receiving blood transfusions. The majority (51%) receive transfusion every four weeks with another 27% transfused every three weeks and smaller percentage (13%) requiring transfusion every two weeks or more frequently. About 7% report transfusions at five or six-week intervals while one respondent is transfused “as required.”

On average, respondents have been receiving transfusions for 35 years (thalassemia major is usually diagnosed in infancy), with report of a maximum time of 57 years and minimum of three years. Overall, this sample represents patients with long-time exposure to blood transfusions and chelation. Most would have experience with iron chelation by overnight infusion, which is not only onerous but also limiting in

terms of mobility. Children are unable to do sleepovers; families are restricted in terms of travel; and adults report limitations in terms of their work, social life, and overall quality of life.

About 60% of the patients require washed (leukocyte depleted) red blood cells (RBCs) to reduce risk of reactions. Similarly, about half (51%) require special (fully) cross-matched RBCs. These procedures are important for frequently-transfused patients and require pre-planning to assure access and strict adherence to scheduling to avoid wastage.

Reactions: The majority of respondents (80%) have no or infrequent minor reactions to blood transfusions, although a "not insignificant" percentage (20%) do experience fever, chills, or itching. Importantly, none of these respondents reported experience with serious reactions (high fever, low blood pressure, infection), which is a credit to our healthcare system and the transfusion clinics.

Complications: Nearly half (47%) do experience occasional or frequent complications related to iron overload that is not resolved by chelation. This is, of course, a very serious condition that leads to organ

Improved Outcomes

The cycle of transfusion is experienced as time-consuming, interfering with work and school and a burden to normal social and home life. Moreover, prior to scheduled transfusion time, patients experience the fatigue, low energy toll and mental challenges of low hemoglobin. However, more frequent transfusions would take more time away from other responsibilities and would increase the demands on iron chelation, with iron overload already the most impactful complication of thalassemia treatment.

"Need to take the day off from work for transfusion, so there is a financial impact (not working, so not paid). Socially less active the week before receiving the transfusion since too tired to do any activity (outside of work since work already takes all the energy I have)"

"I have to explain to my employer, forfeiting my right to privacy. Transfusion takes 10-12 hours and leaves me exhausted and short of breath for 24-48 hours after, with an upset stomach and achy. My kids worry for me and are scared for my long-term health. I simply don't have the energy I should due to low haemoglobin and I miss out on activities with my kids if I am a week away from my transfusion because I'm too tired."

"We always had to take leave from office for his transfusion days and also time off for his blood work - which hampered work life and left us with almost no vacation time for the year."

"I must take personal time off work once every 4 weeks. I cannot participate in evening activities as I have to do my pump(Desferal) and keep it in for 10 hours. I cannot concentrate at work one week before blood transfusions; less oxygen to the brain."

"Transfusions are very time consuming (8-9 hours/month) which requires time off work/school (add 1-2+ hours if cross-matching the day prior depending how busy the lab is. This affects overall quality of life because a considerable amount of time is spent in hospital."

"Greatly affects. Have to be in a Montreal hospital once every 3 weeks. I'm self-employed. It's 17 extra unpaid days of work / year. It also costs me $10 / day for parking there so maybe half a gym membership additional, lol. … Affects the clients and projects I have going as well…. It stopped me from certain tours with my band, certain vacations that landed smack when I would need a transfusion mid-way. It still stops my wife and I to go away for too long to any other country as I have to be back every 3 weeks so we need to align vacation time. …attempt to experience as much of life as possible without having a specific hospital in Montreal as a pit stop that we must be near every 3 weeks."

5. Experience With Drug Under Review

About 30% of respondents reported knowing about Reblozyl (luspatercept) and 7% had direct experience. Respondents had received the drug through clinical trials. About one third (36%) reported

being unaware of the drug and about one-third (34%) had some knowledge. All of those who had received Reblozyl spoke very positively about the experience. None reported any adverse effects.

“Access to Reblozyl has allowed for less frequent transfusions.”

“The most important benefit … the ability to decrease or not require blood transfusions.”

Anything Else?

Patients were presented with information about how Reblozyl works and possible benefit to patients. Overall, 88% said it would be “very important’ to have access and 7% said it was somewhat important. Only 5% said access was neutral or somewhat unimportant. They were also asked to describe in their own words with having access would mean to them and their family.

"*This would help many patients who have relied on regular bi/weekly or monthly blood transfusions significantly by reducing the amount of blood they receive and thus reduce the deadly iron overload accumulated over time which could result in death. This would change quality of life and provide hope to patients with this new treatment."*

‘It would mean a critical improvement to quality of life. It would also mean that the effects of long-term transfusions could be greatly reduced. This is a huge break-through!"

“The need for less blood transfusions means less iron overload, less chance of exposure to blood borne diseases, less time needed to be allocated for blood transfusions, and able to take longer foreign vacations. So Reblozyl could mean better physical and mental health of the patient and their family.”

“Game changer! I am at the stage of my life where I need to think about retirement and it would be fabulous if we could move out of the city. However due to my frequent transfusions, both living in cottage country and taking long vacations are not an option.”

“Having access to this medication would substantially improve my daughter's quality of life because she would spend less time in hospital and it would reduce her exposure to donor blood. My daughter has received approximately 250 blood transfusions (so far) which translates to about 588 units of blood and over 6 months of her life spent in hospital to treat her disease.”

“Fewer hospital visits for blood transfusions(less needles to save our valuable veins, less time at hospital, or shorter visits). Less reliance on blood, which implies less iron loading, less impact on vital organs.”

Appendix: Patient Group Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH CDR and pCODR programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

Thalassemia Foundation of Canada

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 submission was completed by Thalassemia Foundation of Canada and CORD without any additional assistance.

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.

   Collection and analysis of this data was done by CORD and TFC.

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
No Company				

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: Riyad Elbard
Position: Chair
Patient Group: Thalassemia Foundation of Canada
Date: September 17, 2020

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   No, the survey and analysis were conducted by the Canadian Organization for Rare Disorders

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

   No, we have no one else entering the role.

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
BMS		x		

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: Durhane Wong-Rieger
Position: President & CEO
Patient Group: Canadian Organization for Rare Disorders
Date: 17 December 2020