

CADTH COMMON DRUG REVIEW

Patient Input

LUSPATERCEPT (Reblozyl)

(Celgene Inc., a Bristol Myers Squibb company)

Indication: Myelodysplastic syndromes-associated anemia

CADTH received patient input from:

Aplastic Anemia and Myelodysplasia Association of Canada and the Leukemia & Lymphoma Society of Canada (joint)

February 22, 2021

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CADTH 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.

CADTH Drug Reimbursement Review Patient Input Template

Name of the Drug and Indication	Luspatercept for Myelodysplastic syndromes (MDS)-associated anemia
Name of the Patient Group	The Leukemia & Lymphoma Society of Canada Aplastic Anemia and Myelodysplasia Association of Canada
Author of the Submission	██████████
Name of the Primary Contact for This Submission	██████████
Email	████████████████████
Telephone Number	██████████

1. About Your Patient Group

If you have not yet registered with CADTH, describe the purpose of your organization. Include a link to your website.

The Leukemia and Lymphoma Society of Canada (LLSC)

The mission of LLSC is: Cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of Canadians affected by all of the 137 different types of blood cancer.
<http://www.bloodcancers.ca>

Aplastic Anemia and Myelodysplasia Association of Canada (AAMAC)

AAMAC's mission is to provide a seamless support network for every Canadian patient, family member, friend, and concerned healthcare provider dealing with aplastic anemia, myelodysplasia and PNH. <http://www.aamac.ca>

2. Information Gathering

CADTH is interested in hearing from a wide range of patients and caregivers in this patient input submission. Describe how you gathered the perspectives: for example, by interviews, focus groups, or survey; personal experience; or a combination of these. Where possible, include **when** the data were gathered; if data were gathered **in Canada** or elsewhere; demographics of the

respondents; and **how many** patients, caregivers, and individuals with experience with the drug in review contributed insights. We will use this background to better understand the context of the perspectives shared.

Information was gathered through an on-line survey that was created by LLSC. The survey was created in both English and French, was made available to respondents on December 7, 2020 and closed on January 4, 2021.

Both English and French online surveys were created using Survey Monkey and promoted by LLSC and The Canadian MPN Network through various social media channels and directly by email. The survey asked for input from those with experiences with the treatments for Myelodysplastic Syndromes and luspatercept, if applicable.

There were a total of 20 respondents to the survey. 18 respondents identified as patients, 1 identified as a caregiver, and 1 identified as a friend or family member answering on behalf of a patient with MDS. None of the respondents indicated that they have taken luspatercept.

13 respondents identified as Female, 6 respondents identified as Male, and 1 respondent did not provide a gender.

All respondents identified that they live in Canada. The breakdown is as follows:

British Columbia - 10

Ontario - 4

Alberta - 3

Quebec - 2

Nova Scotia - 1

The age range of the patients are as follows:

45-54 - 1

55-64 - 7

65-74 - 5

75-84 - 7

18 of the respondents indicated the year that they were diagnosed with MDS:

2020 – 1

2019 – 1

2018 – 2

2017 – 2

2016 – 1

2015 – 2

2014 – 3

2013 – 2

2010 – 1
 2009 – 1
 2007 – 1
 2000 – 1

3. Disease Experience

CADTH involves clinical experts in every review to explain disease progression and treatment goals. Here we are interested in understanding the illness from a patient’s perspective. Describe how the disease impacts patients’ and caregivers’ day-to-day life and quality of life. Are there any aspects of the illness that are more important to control than others?

Seventeen respondents provided an answer when asked the open-ended question - “How do the symptoms associated with MDS impact your quality of life (For example: Impact on daily life, impact on social life and relationships, etc.).

Among the responses Fatigue and infections were a common theme along with transfusion schedule.

- “tiredness impacted my sporting life and day to day activities at the time.”
- “tire easily”
- “Fatigue prevents me from doing as much as I would like to.”
- “Lack of energy has me somewhat confined and doing a lot fewer things both big and small”
- “Lack of energy was my most troublesome problem.”
- “A lot of fatigue during the day, little energy to do activity, ie short periods a day. Numbness in the hands (weak) and Permanent neuropathy in both feet (deep pain, painful numbness and swelling.) Difficulty concentrating and speaking at times, poor memory at times, inattention. Almost impossible to do a simple sporting activity such as walking for more than 30 minutes without a break.”
- “Fatigue, worry about infections, worry about Eprex failing to work any longer, and having no recourse except for blood transfusions. Night sweats are a bother.”
- “impact daily life (very tired, needing many blood transfusions, rashes on my hands and feet that were open, sore and bleeding, had shingles 3x, many infections) and social life (too tired to go out or host family dinners)”
- “I get tired a lot. Also, I have to watch out for infections, e.g.:not visit grandchildren when they have a cold, etc.”
- “Severe anaemia affects what I can do in a day and makes me irritable.”
- “I have weekly transfusions and my life revolves around that.”
- “I have to sick leave from my job and now have red blood transfusion every three weeks.”

- "Impacts all aspects of my life..I can't travel any more...I only have two good weeks out of the month due to hospital visits for my monthly 7 day injections..."
- "honestly not much, other than I don't have the endurance, energy that I once had which can be frustrating at times"
- "none since I had my stem cell transplant except a bit tired, but that could be age or dealing with the pandemic."
- "the MDS itself, does not impact . GVHD, impacts lots."

One respondent reported the symptoms as having no impact

When asked if there are any aspects or symptoms that are easier to control, 10 respondents provided the following responses:

- "My main symptom is severe anaemia which is not easy to control because of an antibody making it very difficult to find compatible blood."
- "no need for control."
- "not really, maybe bruising by not bumping into things"
- "fatigue"
- "I need to be more cognoscente of not overdoing anything or not taking breaks from physical activities"
- "Fatigue"
- "Not really"
- "I listen to my body and do what I can. I try to have a rest for an hour after lunch every day and that helps increase my energy."
- "No"
- "There is no control, some days are better than others. The pain is difficult to alleviate without strong medication and therefore stupefying without eliminating it. You have to get used to living with this constant pain."

Respondents also added the following comments on how MDS affects the quality of life of their family and friends:

- "My fatigue affects what my husband and I can do. Also can't get health insurance so no visits to the US or elsewhere."
- "just needed to be more careful about too much physicality"
- "everyone is better educated"
- "my husband is my caregiver and he spends a lot of time on my appointments and care"
- "need support from family to help me do things and drive me to my many appointments/hospital"

- “My husband does a little more around the house than he used to.”
- “My family acts as if there is nothing wrong with me and expects me to carry on as normal. My husband believed there was nothing wrong with me and did not help me at all. I have tried to do things as much as possible on my own as well as run the household.”
- “Somewhat I'm sure as my Wife and I can't do some things we both did together”
- “Affects my husband.....and the things we used to do together...now he plays his golf, visits to the grandkids, curling by himself. We do not socialize because of covid 19...we do not travel anymore....because of my risk.”

4. Experiences With Currently Available Treatments

CADTH examines the clinical benefit and cost-effectiveness of new drugs compared with currently available treatments. We can use this information to evaluate how well the drug under review might address gaps if current therapies fall short for patients and caregivers.

Describe how well patients and caregivers are managing their illnesses with currently available treatments (please specify treatments). Consider benefits seen, and side effects experienced and their management. Also consider any difficulties accessing treatment (cost, travel to clinic, time off work) and receiving treatment (swallowing pills, infusion lines).

Respondents identified a variety of frontline treatments they received for MDS after diagnosis:

Chemotherapy – 9

Stem cell transplant / bone marrow transplant – 6

Drug Therapy – 8

Watch-and-wait approach – 5

Blood transfusions – 11

Blood cell growth factor therapy – 6

Anti-thymocyte globulin therapy – 1

Immunoglobulin therapy - 1

We asked respondents to describe both positive and negative experiences with frontline MDS treatment:

- “They were incredible... doctors, nurses, staff. Especially the one who volunteered to shave my head when my hair was falling out and then he made smoothies for me and made me eat/drink them. The only downside was that I am allergic to aloe vera and the nurses kept giving me wipes with aloe. I got terrible boils and sores on my bum. The nurses couldn't figure it out until I looked at the ingredients on the wipes... there it was... aloe. When I pointed it out to the nurses the reaction was "Wow. I never knew that." SO, nurses, check all the ingredients on the label.”
- I was very well taken care of and supervised by the entire hemato-onco team.

- "My treatment went fairly smoothly with only a few hiccups such as infections, some diarrhea and limited GVHD. Finding a stem cell match took almost 8 months - that felt like forever. It was important to go into the transplant as physically fit as possible as I knew I was going to get one more round of chemo and full body radiation. It was also important to be in a strong mental and spiritual state.
- "Epo stopped working after several years, ab now preventing transfusions, prednisone helps keep Hgb around 70 g/L but has caused compression fractures in 3 thoracic vertebrae and very thin, fragile skin."
- "Stem cell transplant was difficult but ultimately successful."
- unfortunately no drugs helped me. participated in clinical trial for oral decitabine but no results. transfusions more and more frequent.
- Transfusion gives me more energy for about 10 days. But it will be less later, and my ferritin is very high so that I have to take medicine daily.
- Positive: I was very lucky to have my sister as a match for my stem cell transplant. I am recovering quite well with a bit of Graft vs Host Disease (GVHD). The terrible rashes have disappeared. Negative: Chemo was bad and I had terrible mucocitis. I was an inpatient in the hospital for 31 days.....but I survived it all. The fatigue and weakness was bad. I fell several times and was unable to get up without assistance. I still have taste issues. YEA!
- positive - gave me time to come to terms with diagnosis
- I have had several infections that were hard to fight off, even with vancomycin. Took a long time to work, and my hgb dropped into the 60s, and I had to have 3 months of blood transfusions before my hgb recovered
- Negative experiences: Blood transfusions take a lot of time. Chemo requires 7 visits to the hospital per 28 days. This is inconvenient but with Covid-19 it's disturbing to have to go to a hospital where I may encounter Covid-19 patients or others with various communicable diseases while my immunity is very compromised. Furthermore, several times my chemo has had to be delayed because my blood results were too low, which meant I had to return again the following week to try again - and again to potentially expose me to others' diseases.
- The drug put my red blood count up so I no longer needed transfusions. Unfortunately I developed neuropathy in my feet, legs and hands, which has impacted my life a lot as I cannot walk as much as I used to.
- 2020 - Now taking Eprex. After 8 weeks, dose has been moved up to 60,000. Still not sure if there is a difference as I'm scheduled for another 2 unit transfusion tomorrow.
- "Positive...it is controlling mds so far. Negative...is not knowing how long the treatments will work for. Injections can be painful, the side effects"
- I developed pneumonia at the very start of treatment, which is difficult to diagnose. Then the shingles happened but it was not detected until a pustule appeared on a finger. Shingles has caused back and arm pain as well as numbness on the skin in places.

- I was treated very well by all the staff, very caring but it was still trying! I suggest encouraging the insertion of the subcutaneous catheter port at the start of chemo treatments. It is offered it but insisted upon at the beginning. We don't realize how much better it would be until the moment when we have difficulty finding a good, undamaged vein. In general, you have to be patient, it is especially long. The side effects of neuropathy types are difficult to control during treatment and above all, they gradually increase from month to month, as well as the pain among other things.

Below are the MDS treatment side effects that have impacted the quality of life of the respondents, listed in the number of classifications being identified as 5 (extremely large impact) or a 4 (large impact):

- Low blood cell counts (10)
- Extreme fatigue (9)
- Anemia (7)
- Infections (6)
- Weakness (5)
- Graft versus host disease (4)
- Diarrhea (3)
- Rashes (3)
- Hair loss (3)
- Mouth sores (3)
- Nausea and vomiting (2)
- Constipation (2)
- Tingling sensations (2)
- Lung, heart, kidney or nerve problems (2)

Respondents also added:

- "I lost my "funny" for about a year. I am a writer and write comedy and couldn't write it to save my soul. Then one day, I was writing and went "that is funny" and it was back."
- "also experienced severe sepsis at one point early on"
- "night sweats"
- "Muscle soreness, joint pain"
- "Neuropathy in the feet and mild cognitive losses"

The side effects that were experienced from frontline MDS treatment have impacted the respondents in the following ways, listed in the number of classifications being identified as 5 (extremely large impact) or a 4 (large impact):

- Change to physical activity (9)

- Anxiety (5)
- Mental health and overall happiness (4)
- Eating challenges (4)
- Social development (3)
- Educational development (2)

Respondents also shared some of the quality of life issues that were experienced due to MDS and the treatment during frontline therapy:

- "I found who my friends were and who dismissed me."
- "Couldn't enjoy softball and ice hockey early on but have returned to playing (but not now with covid). Treatment from my health team was amazing at Princess Margaret Hospital."
- "being tired alot means not able to do any extensive travelling, glad we did a fair amount prior to dignosis of MDS."
- "the watching and waiting...biopsy's, medications."
- "I have to take medicine remove more iron in my body. It makes my some kidney issues."
- "Keeping distant from those that had colds, or unknown infections, unable to do some of the volunteering that I had done previously due to possible infections"
- "Shortness of breath, now requires that I swim with a snorkel. Walking causes shortness of breath, especially uphill."
- "I often think of my potential impending death."
- "I actually appreciated life more after diagnosis as I realised just how special it is, and so the little things have not bothered me the way they did. I do not worry much about the future and take things one day at a time, so having MDS has in some ways been a very positive experience for me."
- "Mds affects all aspects of my life...I was told the treatments would give me a quality of life...it does for two weeks out of the monthly treatments...my life has changed completely.....covid 19 has not helped"
- "Dietary restrictions to be observed in relation to other pre-existing restrictions due to my state of health, cholesterol, diabetes and IBS. Isolation and precautions against germs and diseases that I had to avoid."

We asked respondents if they had any challenges accessing treatment for MDS or healthcare services and to share any positive or negative experiences:

- Most clinical trials use reduction in transfusions as an end point so not available to those who, for whatever reason, can't have transfusions. Why can't increase in Hgb be used as an end point for trials involving drugs not shown to reduce Hgb in Phase 2?

- "Not really. Now that it has been 5 years it is hard to get appointments, even a year in advance. I was supposed to be seen in Sept this year and it was Dec. Next year it is even later. I know there are lots of others, but I do wish I could get in earlier.
- No challenges with either. I had to go to emergency a few times but services were fine there as well. As an ethnic minority, Canada's stem cell database did not provide a match. I had to wait until one was found on the DKMD network. We have to do more to get the ethnic community involved in registering their stem cells.
- blood tests frequency difficult at times.
- None whatsoever. I was one week from diagnosis to treatment
- no access issues
- The hematologist that did my 3rd bone marrow biopsy told me I had MDS but nothing else. I have to wait over 1.5 months to talk to someone. I was very very happy with the leukemia/bone marrow dr when I finally got to see him. He and my sister saved my life.
- no
- No problems accessing treatment."
- I have to drive almost 30 minutes to and from the hospital for treatments but this is not a huge challenge.
- No problems or challenges. I live near the hospital where my oncologist is in the clinic and see him every three months. He had no problem getting the drug approved for me when he prescribed it.
- Oncologist Nurses, pivot nurse have taken excellent care of me....accessing other healthcare services outside of my cancer treatment is difficult. I thought I would have all aspects of my health care taken care of as a team.

5. Improved Outcomes

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

We asked respondents what are the most important factors they consider when making decisions about a new cancer treatment. The following is a list of the factors that were considered very important:

- Possible impact on disease (11)
- Physician recommendation (9)
- Quality of life (6)

- Outpatient treatment (4)
- Closeness of home (3)

Respondents shared their thoughts on improvements they would like to see in new treatments that are not available in current treatments:

- “An increase in Hgb without an initial reduction!”
- “I like that targeted chemo is more prevalent and perhaps if full body radiation less aggressive and more focused (so we aren't being exposed to more than we need)”
- “more information if possible would be beneficial.”
- “oral versions or ability to administer at home rather than hospital setting.”
- “making the available treatments available at all cancer treatment centers would be nice”
- “PMPRB should approve lusepatecept for use in Canada. In the next year or two, I will undoubtedly benefit from it, as I have MDS RARS, and have been on Eprex for 12 years, and on the highest dosage allowed for the past 3 years. Time is running out, and blood transfusions are a poorer option than lusepatercept”
- “A cure that is available to older patients, as stem cell transplant isn't always.”
- “I would like to see more new treatments become available to cure MDS, but I realise that is likely not possible at the moment. New treatments should not cause neuropathy which does impact quality of life.”
- “A way to reduce neuropathic side effects more quickly, it always seems rare, according to what I was told, and we offer drugs such as lyrika etc ... which are results without being effective enough”

6. Experience With Drug Under Review

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

How did patients have access to the drug under review (for example, clinical trials, private insurance)? Compared to any previous therapies patients have used, what were the benefits experienced? What were the disadvantages? How did the benefits and disadvantages impact the lives of patients, caregivers, and families? Consider side effects and if they were tolerated or how they were managed. Was the drug easier to use than previous therapies? If so, how? Are there subgroups of patients within this disease state for whom this drug is particularly helpful? In what ways? If applicable, please provide the sequencing of therapies that patients would have used prior to and after in relation to the new drug under review. Please also include a summary statement of the key values that are important to patients and caregivers with respect to the drug under review.

None of the respondents indicated that they have taken luspatercept

7. Companion Diagnostic Test

If the drug in review has a companion diagnostic, please comment. Companion diagnostics are laboratory tests that provide information essential for the safe and effective use of particular therapeutic drugs. They work by detecting specific biomarkers that predict more favourable responses to certain drugs. In practice, companion diagnostics can identify patients who are likely to benefit or experience harms from particular therapies, or monitor clinical responses to optimally guide treatment adjustments.

What are patient and caregiver experiences with the biomarker testing (companion diagnostic) associated with regarding the drug under review?

Consider:

- Access to testing: for example, proximity to testing facility, availability of appointment.
- Testing: for example, how was the test done? Did testing delay the treatment from beginning? Were there any adverse effects associated with testing?
- Cost of testing: Who paid for testing? If the cost was out of pocket, what was the impact of having to pay? Were there travel costs involved?
- How patients and caregivers feel about testing: for example, understanding why the test happened, coping with anxiety while waiting for the test result, uncertainty about making a decision given the test result.

8. Anything Else?

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

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.

No

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
Celgene Inc. / Bristol-Myers Squibb Canada Co.				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: Indrek Koppel
 Position: Manager, Advocacy & Partnerships
 Patient Group: The Leukemia & Lymphoma Society of Canada
 Date: January 28, 2021

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Name: Cindy Anthony

Position: Executive Director

Patient Group: Aplastic Anemia and Myelodysplasia Association of Canada

Date: January 28, 2021