CADTH

CADTH REIMBURSEMENT REVIEW

Stakeholder Feedback on Draft Recommendation

luspatercept (Reblozyl)

(Celgene Inc., a Bristol-Myers Squibb Company)

Indication: for the treatment of adult patients with very low- to intermediate-risk myelodysplastic syndromes (MDS)-associated anemia who have ring sideroblasts and require red blood cell (RBC) transfusions.

August 26, 2021

August 25, 2021

To CADTH review committee,

Please consider feedback from the Alberta Myeloid Malignancies Tumour Group regarding the recent conditional recommendation for luspatercept in patients with lower risk myelodysplastic syndromes. The renewal recommendation, which reads, "At 16 weeks patients should be red blood cell transfusion independent" does fully reflect the patient group that would benefit clinically from this drug. As clinicians, we have endorsed treatments that would reduce transfusion requirements by 50% or result in transfusion independence. For many patients, the reduction in frequency of lab tests, reduction in frequency and volume of blood transfusions ie from every 2 weeks to every 4 weeks, as well as the reduction in associated fatigue and symptoms of anemia that preceed the need for transfusion is a clinically important outcome and reflects a partial response to treatment. This outcome was used in studies assessing erythropoietin stimulating agent efficacy. In addition, this would reduce the burden of chair time and nursing time required by cancer centres and hospitals to provide transfusion support.

It is also not infrequent for a patient who is doing well and requiring infrequent tranfusions, or who has become transfusion independent, to have an intercurrent illness ie pneumonia or a bleed related to low platelets, require hospitalization and need a transfusion during this acute illness. They may then become transfusion independent again afterwards. Using this criteria for renewal would then exclude these patients from ongoing treatment with luspatercept and does not reflect the reality of treating MDS patients. This can be seen in the swimmer plots from this study where some patients had a period of transfusion independence, lost the transfusion independence, and become independent again.

This study and the newer IWG criteria do try to capture this by classifying patients as low transfusion burtden or has having higher transfusion burden.

We would ask you to consider altering the renewal recommendation to reflect clinical practice. It would be clinically appropriate to renew luspatercept referral if the patients are transfusion independent, improve from a high transfusion burden group to low transfusion burden group, or reduce red cell requirements by 50%

Dr. Michelle Geddes, MD
On behalf of the Alberta Myeloid Malignancies Tumour Group

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0670
Brand name (generic)	Roblozyl (luspatercept)
Indication(s)	MDS related anemia
Organization	OH-CCO Hematology Cancer Drug Advisory Committee
Contact information[a]	Name: Dr. Tom Kouroukis [redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐
Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.		

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐
If not, what aspects are missing from the draft recommendation?		

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification. Contact information will not be included in any public posting of this document by CADTH.

Appendix 2. Conflict of Interest Declarations for Clinician Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
- This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the feedback from patient groups and clinician groups.
- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.
- For conflict of interest declarations:
  - Please 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.
  - Please note that declarations are required for each clinician that contributed to the input.
  - If your clinician group provided input at the outset of the review, only conflict of interest declarations that are new or require updating need to be reported in this form. For all others, please list the clinicians who provided input are unchanged
  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☐
	Yes	☒
If yes, please detail the help and who provided it. OH-CCO provided secretariat support to the Hem DAC.		
3. Did you receive help from outside your clinician group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☒
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Dr. Tom Kouroukis • Dr. Janet MacEachern (DAC term completed in March 2021) • Dr. Lee Mozessohn • Dr. Pierre Villeneuve		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
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**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
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**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
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**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐

Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 4	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 5	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

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**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	
Brand name (generic)	Luspatercept
Indication(s)	Transfusion dependent MDS with ring sideroblasts
Organization	Odette Cancer Center
Contact information[a]	Name: Rena Buckstein

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☐
	No	☒

Please explain why the stakeholder agrees or disagrees with the draft recommendation. Whenever possible, please identify the specific text from the recommendation and rationale.

I disagree with the renewal prerequisite of TI at 16 weeks. This should be renewal after 16 weeks of exposure at the highest recommended dose of 1.75 mg/kg. Since ramp up only occurs every 6 weeks, patients don't reach that dose for a minimum of 12 weeks. You need another 16 weeks at highest dose to know if it is working or not. This requirement for TI also discounts the 50% reduction in transfusion needs achievable with this agent which is clinically important. In addition, there are new emerging data that late responders are observed as well.
So I would change renewal criteria to state:
Renewal contingent on one of the following:

1. Achievement of transfusion independence for 16 weeks or more within the first 28 weeks of drug exposure
2. A 50% reduction in transfusion needs for 12 weeks or more within the first 28 weeks of drug exposure.

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☒

If not, what aspects are missing from the draft recommendation?
It is not addressing the importance of reducing transfusion frequency with luspatercept of 50% or more in patients with high transfusion burden which is clinically important in addition to the achievement of transfusion independence.

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☒

If not, please provide details regarding the information that requires clarification.

The @ 16 weeks, patients should be red blood cell transfusion independent is unclear. This should clarify, at 16 weeks of maximal drug dose 1.75 mg/kg, not 16 weeks from start of therapy. I would also clarify the duration of transfusion independence to be called TI. In the IWG 2018 criteria, Hematologic improvement erythroid different according to burden of transfusion dependence:
For low transfusion burden: (3-7 units in 16 weeks in at least 2 transfusion episodes): HI-E in LTB patients corresponds to transfusion independence, defined by the absence of any transfusions for at least 8 wk in an observation period of 16-24 wk with the same transfusion policy (defined below) compared with 16 wk prior to treatment; only a response duration of at least 16 wk, however, is considered clinically meaningful

For High transfusion burden (>=8 units RBCs in 16 weeks, >= 4 in 8 weeks): there are both major and minor responses that are clinically meaningful

Major response: Major HI-E response in HTB patients corresponds to transfusion independence, defined by the absence of any transfusions over a period of minimum 8 wk in an observation period of 16-24 wk with the same transfusion policy (defined below) compared with 16 wk prior to treatment; only a response duration of at least 16 wk, however, is considered clinically meaningful

Minor response: Minor HI-E response in HTB patients is defined as a reduction by at least 50% of RBCs over a minimum of 16 wk with the same transfusion policy (defined below) compared with 16 wk prior to treatment

5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☒
	No	☐

If not, please provide details regarding the information that requires clarification.

[a] CADTH may contact this person if comments require clarification.

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  - Please add more tables as needed (copy and paste).
  - All new and updated declarations must be included in a single document.

A. Assistance with Providing the Feedback		
2. Did you receive help from outside your clinician group to complete this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
3. Did you receive help from outside your clincian group to collect or analyze any information used in this submission?	No	☒
	Yes	☐
If yes, please detail the help and who provided it.		
B. Previously Disclosed Conflict of Interest		
4. Were conflict of interest declarations provided in clinician group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section C below.	No	☐
	Yes	☒
If yes, please list the clinicians who contributed input and whose declarations have not changed: • Clinician 1 • Clinician 2 • *Add additional (as required)*		

C. New or Updated Conflict of Interest Declarations

New or Updated Declaration for Clinician 1	
Name	*Rena Buckstein*
Position	*Head, Hematology Site Group, Chair, National MDS registry*
Date	*Please add the date form was completed (24-08-2021)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.
Conflict of Interest Declaration	

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	☐	☐	☐	☒
	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 2	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
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**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 3	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
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**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review

Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0670
Name of the drug and Indication(s)	Reblozyl (luspatercept) for the treatment of adult patients with very low- to intermediate-risk myelodysplastic syndromes (MDS)-associated anemia who have ring sideroblasts and who have failed or are not suitable for erythropoietin-based therapy.
Organization Providing Feedback	FWG

1. Recommendation revisions Please indicate if the stakeholder requires the expert review committee to reconsider or clarify its recommendation.		
Request for Reconsideration	**Major revisions:** A change in recommendation **category** or patient **population** is requested	☐
	Minor revisions: A change in reimbursement **conditions** is requested	X
No Request for Reconsideration	**Editorial revisions:** Clarifications in recommendation **text** are requested	☐
	No requested revisions	☐

2. Change in recommendation category or conditions Complete this section if major or minor revisions are requested
N/A

3. Clarity of the recommendation Complete this section if editorial revisions are requested for the following elements
a) Recommendation rationale
N/A
b) Reimbursement conditions and related reasons
Initiation Condition 2. was not included as a condition in the CDEC recommendation for the beta-thalassemia indication, despite PM indicating: *Consider the risk of use of Reblozyl® in β-thalassemia patients who were excluded from clinical trials i.e., patients with uncontrolled hypertension, a deep vein thrombosis or stroke in the previous 24 weeks, or use of an erythropoiesis-stimulating agent (ESA) within the previous 24 weeks*

These exclusions do not appear to be listed in the PM similar to the above for the MDS population. Should this condition be removed for consistency with the *β-thalassemia* recommendation?

For Renewal Condition 3, FWG requests clarification on the duration that is recommended to consider a patient red blood cell transfusion-independent. Additionally, FWG would like to understand if patients need to be completely transfusion-independent to stay on therapy. FWG suggests that discontinuation conditions be developed to identify situations where the drug should be stopped.

c) Implementation guidance

Could implementation guidance on what would be considered failure or not suitable for ESA (per Initiation Condition 1.) be added?

CADTH

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CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0670-000
Brand name (generic)	Reblozyl (luspatercept)
Indication(s)	Myelodysplastic syndromes-associated anemia
Organization	The Leukemia & Lymphoma Society of Canada / Aplastic Anemia & Myelodysplasia Association of Canada
Contact information[a]	Indrek Koppel: [redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐
While we agree with the committee's recommendation to reimburse this treatment, we are concerned with the renewal condition that patients should be red blood cell transfusion independent at 16 weeks. We feel this condition may leave a significant number of patients without access.		

Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☐
	No	☐
If not, what aspects are missing from the draft recommendation?		

Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☐
If not, please provide details regarding the information that requires clarification.		

[a] CADTH may contact this person if comments require clarification.

Appendix 1. Conflict of Interest Declarations for Patient Groups

- To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest.
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- CADTH may contact your group with further questions, as needed.
- Please see the *Procedures for CADTH Drug Reimbursement Reviews* for further details.

A. Patient Group Information	
Name	*Please state full name*
Position	*Please state currently held position*
Date	*Please add the date form was completed (DD-MM-YYYY)*
☐	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.

B. Assistance with Providing Feedback		
1. Did you receive help from outside your patient group to complete your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		
2. Did you receive help from outside your patient group to collect or analyze any information used in your feedback?	No	☐
	Yes	☐
If yes, please detail the help and who provided it.		

C. Previously Disclosed Conflict of Interest		
1. Were conflict of interest declarations provided in patient group input that was submitted at the outset of the CADTH review and have those declarations remained unchanged? If no, please complete section D below.	No	☐
	Yes	☐

D. New or Updated Conflict of Interest Declaration

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**
Add company name	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review
Feedback on Draft Recommendation

Stakeholder information	
CADTH project number	SR0670-000
Brand name (generic)	REBLOZYL® (luspatercept)
Indication(s)	For the treatment of adult patients with RBC transfusion-dependent anemia associated with very low- to intermediate-risk MDS who have ring sideroblasts
Organization	Celgene Inc., a Bristol Myers Squibb company
Contact information[a]	[redacted]

Stakeholder agreement with the draft recommendation		
1. Does the stakeholder agree with the committee's recommendation.	Yes	☒
	No	☐
Bristol-Myers Squibb Canada agrees with the CDEC initial recommendation for luspatercept (REBLOZYL®) for the treatment of adult patients with RBC transfusion-dependent anemia associated with very low- to intermediate-risk MDS who have ring sideroblasts. The CDEC acknowledged that treatment with luspatercept in addition to best supportive care (BSC) was associated with a statistically significant reduction in transfusion burden compared with placebo. For the key secondary efficacy outcomes of RBC-TI of 12 weeks at week 48 and week 24, a greater proportion of patients in the luspatercept treatment group achieved RBC-TI than the placebo group.		
Expert committee consideration of the stakeholder input		
2. Does the recommendation demonstrate that the committee has considered the stakeholder input that your organization provided to CADTH?	Yes	☒
	No	☐
Comments on stakeholders input in regards to reimbursement conditions are provided under question 5 below.		
Clarity of the draft recommendation		
3. Are the reasons for the recommendation clearly stated?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
4. Have the implementation issues been clearly articulated and adequately addressed in the recommendation?	Yes	☒
	No	☐
If not, please provide details regarding the information that requires clarification.		
5. If applicable, are the reimbursement conditions clearly stated and the rationale for the conditions provided in the recommendation?	Yes	☐
	No	☒
• In alignment with the evidence provided from the pivotal trial (Medalist), with the input provided by clinicians and patients on the reimbursement submission of luspatercept for patients with myelodysplastic		

syndromes (MDS), as well as with the 2018 IWG guidelines, BMS kindly requests a minor reconsideration to the proposed renewal criteria to add reduction in transfusion burden to the list of reimbursement conditions.

- There is an undeniable unmet need for MDS patients for treatment that reduces transfusion burden. In the CADTH Reimbursement Recommendation, the clinicians from Alberta indicated the lack of effective treatment options other than long term transfusions and iron chelation to help manage the related iron overload with associated side effects of chelation. (Page 7, Clinician Group Input, paragraph 3)

- Patient input indicated that transfusion frequency has a detrimental impact on their quality of life, with one patient stating, "I have weekly transfusions and my life revolves around that". (Page 5, Patient Input, paragraph 3)

- Clinicians input from Ontario Health (Cancer Care Ontario) Hematology Disease Site Drug Advisory Committee (OH- Hematology DAC) and the Alberta Tumour Board Myeloid Physicians Group (ATB-MPG), agreed that a clinically meaningful response to treatment include a reduction in transfusions. (Page 7, Clinician Group Input, paragraph 4)

- In the renewal criteria of luspatercept in the pivotal trial (Medalist), evidence of clinical benefit including a decrease in red blood cells transfusion requirements had to be confirmed. (Page 8, Clinical evidence, paragraph 3)

- The 2018 IWG guidelines highlight that a reduction in red blood cells transfusion is a meaningful response criterion.

- Also, a study based on the MDS-Canadian patients registry showed that a 1-unit increase in the red blood cell transfusions per 8 weeks was associated with a greater mortality risk and increased odds of hospitalization. Buckstein et al., 2020[1]

- Therefore, a reduction in transfusion burden should be added to the renewal criteria in the reimbursement conditions of luspatercept for MDS patients in order to align with the treatment renewal criteria from the pivotal trial (Medalist) and the clinical meaningful benefit of the reduction in transfusion burden highlighted by the clinicians' and the patients' input provided on this reimbursement submission.

Buckstein, R., et al. (2020, May 14). The burden of red blood cell transfusions on overall survival, healthcare resource utilization, and quality of life in patients with lower-risk myelodysplastic syndromes and ring sideroblasts [Electronic Poster 827]. European Hematology Association 2020. https://library.ehaweb.org/eha/2020/eha25th/294744/heather.leitch.the.burden.of.red.blood.cell.transfusions.on

[a] CADTH may contact this person if comments require clarification.