CADTH Drug Reimbursement Review
Clinician Group Input Template

CADTH Project Number	SR0670-000
Generic Drug Name (Brand Name)	**Luspatercept (Manufacturer: Celgene)**
Indication	**Indications:** 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. **Manufacturer Requested Reimbursement Criteria[1]:** 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.
Name of the Clinician Group	Ontario Health (Cancer Care Ontario) Hematology Disease Site Drug Advisory Committee
Author of the Submission	**Dr. Tom Kouroukis, Dr. Pierre Villeneuve, Dr. Janet MacEachern, Dr. Lee Mozessohn**
Contact information	Name: Dr. Tom Kouroukis Title: Provincial Head – Complex Malignant Hematology (OH-CCO) Email: [redacted] Phone:

1. About Your Clinician Group

Please describe the purpose of your organization. Include a link to your website (if applicable).

OH-CCO's Drug Advisory Committees provide timely evidence-based clinical and health system guidance on drug-related issues in support of CCO's mandate, including the Provincial Drug Reimbursement Programs (PDRP) and the Systemic Treatment Program.

2. Information Gathering

Please describe how you gathered the information included in the submission.

3. Current treatments

3.1. Describe the current treatment paradigm for the disease

Focus on the Canadian context.

Please include drug and non-drug treatments.

Drugs without Health Canada approval for use in the management of the indication of interest may be relevant if they are routinely used in Canadian clinical practice. Are such treatments supported by clinical practice guidelines?

Treatments available through special access programs are relevant.

Do current treatments modify the underlying disease mechanism? Target symptoms?

Response:

Patients are currently treated by transfusion support. Patients with presence of del[5q] MDS may be treated with lenalidomide.

In cases with low endogenous epo level (Epo < 500) – they will get erythropoietin stimulating agent (ESA) injections. However, invariably, patients fail ESAs and become transfusion-dependent again with no good option besides disease/modifying therapies (e.g. hypomethylating agents, Revlimid, etc.).

For some intermediate-risk patients, they may be treated with azacitidine based on IPSS score.

Oral azacitidine/decitabine can potentially be accessed compassionately/or self-paid by some patients.

4. Treatment goals

4.1. What are the most important goals that an ideal treatment would address?

Examples: Prolong life, delay disease progression, improve lung function, prevent the need for organ transplant, prevent infection or transmission of disease, reduce loss of cognition, reduce the severity of symptoms, minimize adverse effects, improve health-related quality of life, increase the ability to maintain employment, maintain independence, reduce burden on caregivers.

Response:

Transfusion independence, reduction in transformation to AML, improvement in QOL

5. Treatment gaps (unmet needs)

5.1. Considering the treatment goals in Section 4, please describe goals (needs) that are not being met by currently available treatments.

Examples:

- *Not all patients respond to available treatments*
- *Patients become refractory to current treatment options*
- *No treatments are available to reverse the course of disease*
- *No treatments are available to address key outcomes*

- *Treatments are needed that are better tolerated*
- *Treatment are needed to improve compliance*
- *Formulations are needed to improve convenience*

Response:

Currently there are no other treatment options other than transfusion, ESAs for some patients, and for a small subset of patients – hypomethylating agents (e.g. azacitidine or decitabine/cedazuridine).

5.2. Which patients have the greatest unmet need for an intervention such as the drug under review?

Would these patients be considered a subpopulation or niche population?

Describe characteristics of this patient population.

Would the drug under review address the unmet need in this patient population?

Response:

The patients with the greatest unmet need will be the ones ineligible for azacitidine, which constitute the majority of patients with lower-risk (≤ int-1 as per IPSS).

6. Place in therapy

6.1. How would the drug under review fit into the current treatment paradigm?

Is there a mechanism of action that would complement other available treatments, and would it be added to other treatments?

Is the drug under review the first treatment approved that will address the underlying disease process rather than being a symptomatic management therapy?

Would the drug under review be used as a first-line treatment, in combination with other treatments, or as a later (or last) line of treatment?

Is the drug under review expected to cause a shift in the current treatment paradigm?

Response:

Luspatercept is largely a symptomatic therapy to reduce transfusion and their consequences (i.e., iron overload).

6.2. Please indicate whether or not it would be appropriate to recommend that patients try other treatments before initiating treatment with the drug under review. Please provide a rationale from your perspective.

If so, please describe which treatments should be tried, in what order, and include a brief rationale.

Response:

No other treatment available other than azacitidine/decitabine-cedazuridine or ESAs for eligible patients.

6.3. How would this drug affect the sequencing of therapies for the target condition?

If appropriate for this condition, please indicate which treatments would be given after the therapy has failed and specify whether this is a significant departure from the sequence employed in current practice.

Would there be opportunity to treat patients with this same drug in a subsequent line of therapy? If so, according to what parameters?

Response:

Provide new therapeutic option to have patients become transfusion-independent for patients who have failed ESA

6.4. Which patients would be best suited for treatment with the drug under review?

Which patients are most likely to respond to treatment with the drug under review?

Which patients are most in need of an intervention?

Would this differ based on any disease characteristics (e.g., presence or absence of certain symptoms, stage of disease)?

Response:

The trial included patients who were unlikely to respond to an ESA, with IPSS-R very low, low, and intermediate. The forest plot showed all groups benefit, irrespective of age, degree of transfusion-dependence, gender, time since diagnosis.

6.5. How would patients best suited for treatment with the drug under review be identified?

Examples: *Clinician examination or judgement, laboratory tests (specify), diagnostic tools (specify)*

Is the condition challenging to diagnose in routine clinical practice?

Are there any issues related to diagnosis? (e.g., tests may not be widely available, tests may be available at a cost, uncertainty in testing, unclear whether a scale is accurate or the scale may be subjective, variability in expert opinion.)

Is it likely that misdiagnosis occurs in clinical practice (e.g., underdiagnosis)?

Should patients who are pre-symptomatic be treated considering the mechanism of action of the drug under review?

Response:

The MEDALIST trial enrolled patients with IPSS-R very low, low or intermediate who have ringed sideroblasts, failed EPO and have EPO < 500. The study also used revised IPSS whereas azacitidine eligibility is based on IPSS.

The trial excluded patients with del[5q] or secondary MDS.

6.6. Which patients would be least suitable for treatment with the drug under review?

Response:

Patients with low EPO levels or higher risk patients.

6.7. Is it possible to identify those patients who are most likely to exhibit a response to treatment with the drug under review?

If so, how would these patients be identified?

Response:

No (see Figure S3 in the MEDALIST publication)

6.8. What outcomes are used to determine whether a patient is responding to treatment in clinical practice?

Are the outcomes used in clinical practice aligned with the outcomes typically used in clinical trials?

Response:

Transfusion frequency, hemoglobin level.

6.9. What would be considered a clinically meaningful response to treatment?

Examples:

- *Reduction in the frequency or severity of symptoms (provide specifics regarding changes in frequency, severity, and so forth)*
- *Attainment of major motor milestones*
- *Ability to perform activities of daily living*
- *Improvement in symptoms*
- *Stabilization (no deterioration) of symptoms*

Consider the magnitude of the response to treatment. Is this likely to vary across physicians?

Response:

Reduction in transfusions

6.10. How often should treatment response be assessed?

Response:

Every 3 to 4 weeks

6.11. What factors should be considered when deciding to discontinue treatment?

Examples:

- *Disease progression (specify; e.g., loss of lower limb mobility)*
- *Certain adverse events occur (specify type, frequency, and severity)*
- *Additional treatment becomes necessary (specify)*

Response:

Worsening of MDS, progression to a higher risk category, or transformation to AML

6.12. What settings are appropriate for treatment with the drug under review?
Examples: Community setting, hospital (outpatient clinic), specialty clinic ***Response:*** Outpatient clinic
6.13. For non-oncology drugs, is a specialist required to diagnose, treat, and monitor patients who might receive the drug under review?
If so, which specialties would be relevant? ***Response:*** Not applicable.
7. Additional information
7.1. Is there any additional information you feel is pertinent to this review?
Response: None

8. Conflict of Interest Declarations

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 clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

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

   OH-CCO provided secretariat support to the DAC in completing this input.

2. Did you receive help from outside your clinician group to collect or analyze any information 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. **Please note that this is required for <u>each</u>**

clinician that contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.

Declaration for Clinician 1

Clinician Information	
Name	*Dr. Tom Kouroukis*
Position	*Please state currently held position*
Date	*18-Feb-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				
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	☐	☐	☐	☐

Declaration for Clinician 2

Clinician Information	
Name	*Dr. Janet MacEachern*
Position	*Hematologist/Oncologist*
Date	*05-Feb-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				
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	☒	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Declaration for Clinician 3

Clinician Information	
Name	*Dr. Pierre Villeneuve*
Position	*Hematologist/Oncologist*

Date	*18-Feb-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

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	☐	☐	☐	☐

Declaration for Clinician 4

Clinician Information	
Name	*Dr. Lee Mozessohn*
Position	*Hematologist/oncologist*
Date	*15-Feb-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

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	☐	☐	☐	☐

Declaration for Clinician 5

Clinician 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 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

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
Clinician Group Input Template

Instructions

Input from clinicians is submitted to CADTH by **groups or associations of health care professionals**. Individual clinicians who wish to provide input are encouraged to work with a group that represents their profession to prepare a group submission.

CADTH will accept input from individual clinicians only when there is no relevant group or association that could provide input for the drug under review. Individuals who wish to submit input for a drug review should first contact CADTH (at requests@cadth.ca) to confirm the absence of a relevant group or association.

Completing the Template

Please complete all applicable sections of the clinician input template.

Ensure that all contributing clinicians have completed the conflict of interest declaration in the clinician input template. Input **will not be accepted without the conflict of interest section** completed for all contributors.

Complete the template by the deadline given on the Open Calls page.

Filing the Completed Template:

Send the completed template by using the *Submit* link next to the drug listed on the Open Calls page. The input must be filed as a Microsoft Word document by the posted deadline date for the information to be used by CADTH.

CADTH Reimbursement Review
Clinician Group Input Template

CADTH Project Number	**SR0670-000**
Generic Drug Name (Brand Name)	**luspatercept**
Indication	**Myelodysplasia related anemia**
Name of the Clinician Group	**Alberta Tumour Board Myeloid Physicians Group**
Author of the Submission	**Dr. Michelle Geddes**
Contact information	Name: Dr. Michelle Geddes Title: Clinical Associate Professor, Hematology, University of Calgary Email: [redacted] Phone: 403-944-8047

1. About Your Clinician Group

Please describe the purpose of your organization. Include a link to your website (if applicable).

We are a group of physicians who treat myeloid malignancies and acute leukemias (myelodysplastic syndromes, myeloproliferative neoplasms, acute myeloid leukemia and acute lymphoblastic leukemia) within Alberta and function as a group within the Alberta Hematology Tumour Group. We meet as Edmonton and Calgary groups regularly to discuss patient cases and upcoming and open clinical trials on a regular basis, and provincially we meet every 3 months and also annually to update treatment guidelines for Alberta for care of these diseases.

2. Information Gathering

Please describe how you gathered the information included in the submission.

Members of the Alberta myeloid tumour group are hematologists who work in academic and community based settings to treat patients with hematologic disease. We review data for new drugs as publications come out and review evidence for optimal patient treatment in an Alberta context as we develop guidelines for patient care in a formal setting every year. We review literative and have group discussions around care. Written guidelines are reviewed in a group setting, modified based on written and oral discussion and edits, and approved by the group before publication on the website.

3. Current treatments

3.1. Describe the current treatment paradigm for the disease

Focus on the Canadian context.

Please include drug and non-drug treatments.

Drugs without Health Canada approval for use in the management of the indication of interest may be relevant if they are routinely used in Canadian clinical practice. Are such treatments supported by clinical practice guidelines?

Treatments available through special access programs are relevant.

Do current treatments modify the underlying disease mechanism? Target symptoms?

Response:

The current treatment for patients with lower risk myelodysplasia and symptomatic anemia involves transfusion support with red cell transfusions, and erythroid stimulating agents (ESAs). ESAs are most effective in patients with low transfusion requirements and erythropoietin levels, and are variably funded across the country. For example, there is currently no funding for erythroid stimulating agents in Alberta and although these are very commonly used and considered standard of care. They are funded entirely through compassionate funding sources through their pharmaceutical company. Other provinces fund ESAs for all MDS patients or have specific criteria for funding. Our online Alberta clinical practice guidelines recommend erythropoietin for patients with lower risk MDS.

For most patients who have not responded or lost response to ESAs, there are no current treatment options outside of transfusion support, with the exception of the approximately 10% of patients with deletion 5q who are treated with lenalidomide. Transfusions can be lifesaving and improve quality of life, however the hemoglobin levels of patients can vary drastically over weeks depending on whether patients have recently had transfusion, making a marked impact on their function in their lives. Some patients with schedule activities around when they expect to have anticipated transfusions. In addition, patients will become transfusion overloaded and many require chelation therapy with associated costs and side effects. Canadian guidelines recommend chelation for patients who have a life expectancy of at least a year, 20 units of blood or ferritin >1000.

ESAs can be effective to keep patients with a stable hemoglobin (avoiding large fluctuations) and are well tolerated, however they lose their response at a median of about 18 months and there are no other treatment options available.

Current treatments with transfusions and ESAs target symptoms but do not impact underlying disease mechanisms or prevent progression of disease. However, there is significant evidence that patients with higher transfusion needs have increased mortality, possibly related to differences in underlying disease pathology, but also that increases in ferritin and iron load are associated with increased mortality especially of cardiac sources thought to be related to cardiac iron loading. This is especially important in patients with lower risk disease who have a relatively long median survival of years.

4. Treatment goals

4.1. What are the most important goals that an ideal treatment would address?

Examples: Prolong life, delay disease progression, improve lung function, prevent the need for organ transplant, prevent infection or transmission of disease, reduce loss of cognition, reduce the severity of symptoms, minimize adverse effects, improve health-related quality of life, increase the ability to maintain employment, maintain independence, reduce burden on caregivers.

Response:

Prolong life, delay disease progression, reduce severity of symptoms and improve health related quality of life, maintain independence, reduce burden on caregivers (including bringing patients for frequent and lifelong transfusion support) including reducing burden on the health care system and facilities. In this case we hope to improve symptoms, reduce need for frequent labwork (CBCs, type and screens, iron monitoring) and long times in infusion chairs getting blood transfusions at hospitals and cancer centres.

5. Treatment gaps (unmet needs)

5.1. Considering the treatment goals in Section 4, please describe goals (needs) that are not being met by currently available treatments.

Examples:

- *Not all patients respond to available treatments*
- *Patients become refractory to current treatment options*
- *No treatments are available to reverse the course of disease*
- *No treatments are available to address key outcomes*
- *Treatments are needed that are better tolerated*
- *Treatment are needed to improve compliance*
- *Formulations are needed to improve convenience*

Response:

Not all patients respond to ESAs and all patients eventually progress on ESA therapy and become transfusion dependent again if they have an initial response. We need an additional treatment option to avoid or reduce red blood cell transfusions and concomitant iron loading, as well as provide stable hemoglobin that reduces times of major anemia symptoms, as well as visits to health care facilities for transfusions. In addition, in Alberta, many patients live in rural areas where travel to labs and health facilities for transfusions (consider many of these sites do not have blood banks on site and require blood products to be shipped to them with some delays before infusion) is difficult for this patient population of largely elderly patients. This application does not provide additional benefit to patients with lower risk MDS without ring sideroblasts, however the patient group with ring sideroblasts is the patient group that tends to have highest transfusion needs and long overall survival (generally years) warranting effective therapy that can avoid significance iron overload.

5.2. Which patients have the greatest unmet need for an intervention such as the drug under review?

Would these patients be considered a subpopulation or niche population?

Describe characteristics of this patient population.

Would the drug under review address the unmet need in this patient population?

Response:

Patients with the greatest unmet need are those who have not responded to ESAs or have lost their response to ESAs, and those who have a higher erythropoietin level and are unlikely to respond to ESAs.

6. Place in therapy

6.1. How would the drug under review fit into the current treatment paradigm?

Is there a mechanism of action that would complement other available treatments, and would it be added to other treatments?

Is the drug under review the first treatment approved that will address the underlying disease process rather than being a symptomatic management therapy?

Would the drug under review be used as a first-line treatment, in combination with other treatments, or as a later (or last) line of treatment?

Is the drug under review expected to cause a shift in the current treatment paradigm?

Response:

Luspatercept would be an additional line of therapy for symptomatic anemia for patients who have progressed on ESAs, have not responded to ESAs, or have a high erythropoietin level precluding response to ESA therapy. This would be expected to cause a shift in the current treatment paradigm and keep a significant number of patients from requiring regular transfusion support at our health care facilities. This would be helpful at all times and especially in these current pandemic times as this is a significant nursing, facility and time burden for the treating facilities as well as for patients who are coming in for transfusions.

6.2. Please indicate whether or not it would be appropriate to recommend that patients try other treatments before initiating treatment with the drug under review. Please provide a rationale from your perspective.

If so, please describe which treatments should be tried, in what order, and include a brief rationale.

Response:

This drug indication is for patients who have failed or are not suitable for ESAs, and this is the appropriate order of treatments in clinical practice. For patients with higher erythropoietin levels and >2 units red cell transfusions per month, response rates to ESAs are extremely low and these patients should appropriately be targeted to receive luspatercept. In other patients with <2u red cells per month and low epo levels, ESAs have a good response rate and would be the appropriate first therapy with luspatercept available if there is no response or there is progression.

6.3. How would this drug affect the sequencing of therapies for the target condition?

If appropriate for this condition, please indicate which treatments would be given after the therapy has failed and specify whether this is a significant departure from the sequence employed in current practice.

Would there be opportunity to treat patients with this same drug in a subsequent line of therapy? If so, according to what parameters?

Response:

This allows for an additional line of effective therapy for anemia in MDS; there are no other treatment options at this time for patients who do not respond to luspatercept after either progressing on ESAs or being inappropriate for ESA therapy. Patients who do not respond to luspatercept or progress would require long term transfusion support.

6.4. Which patients would be best suited for treatment with the drug under review?

Which patients are most likely to respond to treatment with the drug under review?

Which patients are most in need of an intervention?

Would this differ based on any disease characteristics (e.g., presence or absence of certain symptoms, stage of disease)?

Response:

Patients best suited are lower risk MDS patients with symptomatic anemia who have failed ESAs or are inappropriate for ESA therapy. Patients in this group have no other effective treatment options other than long term transfusions and iron chelation to help manage the related iron overload, with associated side effects of chelation.

Patients with higher risk MDS would be better served with hypomethylating agents and are not included in this application.

6.5. How would patients best suited for treatment with the drug under review be identified?

Examples: *Clinician examination or judgement, laboratory tests (specify), diagnostic tools (specify)*

Is the condition challenging to diagnose in routine clinical practice?

Are there any issues related to diagnosis? (e.g., tests may not be widely available, tests may be available at a cost, uncertainty in testing, unclear whether a scale is accurate or the scale may be subjective, variability in expert opinion.)

Is it likely that misdiagnosis occurs in clinical practice (e.g., underdiagnosis)?

Should patients who are pre-symptomatic be treated considering the mechanism of action of the drug under review?

Response:

Patients are given an IPSS-R prognostic score at diagnosis based on bone marrow aspirate results ie blast count, cytogenetics risk and degree of cytopenias, and this identifies the presence of ringed sideroblasts along with next generation sequencing (NGS) of DNA for the SRSF1 mutation seen in ringed sideroblast disease. Patients are identified by the morphologic diagnosis, results of the scoring scale for that patients, and commonly available lab tests such as erythropoietin levels. Most patients requiring regular transfusions would be investigated and have a clear diagnosis as long as they are willing to undergo bone marrow aspiration.

NGS sequencing is available in Alberta and much of the country although this is variable and it would be required more frequently to confirm a ringed sideroblast diagnosis in patients with 5-15% ringed sideroblasts. Currently we do this on all newly diagnosed MDS patients in Alberta, and we anticipate this will become standard of care as funding for the testing becomes available across the country. It can be requested as needed across the country currently for diagnostic purposes.

6.6. Which patients would be least suitable for treatment with the drug under review?

Response:

Those with allergies to the medications. Otherwise it would be appropriate for the patients for which it is being requested in this applicaiton.

6.7. Is it possible to identify those patients who are most likely to exhibit a response to treatment with the drug under review?

If so, how would these patients be identified?

Response:

There can be improved rates of response with lower erythropoietin levels however this is not highly discriminative and would not be a reason to exclude patients from treatment eligibility.

6.8. What outcomes are used to determine whether a patient is responding to treatment in clinical practice?

Are the outcomes used in clinical practice aligned with the outcomes typically used in clinical trials?

Response:

Improvement in hemoglobin levels, reduction in transfusion requirements.

6.9. What would be considered a clinically meaningful response to treatment?

Examples:

- *Reduction in the frequency or severity of symptoms (provide specifics regarding changes in frequency, severity, and so forth)*
- *Attainment of major motor milestones*
- *Ability to perform activities of daily living*
- *Improvement in symptoms*
- *Stabilization (no deterioration) of symptoms*

Consider the magnitude of the response to treatment. Is this likely to vary across physicians?

Response:

Improvement in hemoglobin by 15 g/L, reduction in transfusion requirements of at least 25%

6.10. How often should treatment response be assessed?

Response:

CBC done monthly; would initially be done weekly with type and screen in patients who are currently transfusion dependent, and if they are stable off of transfusions expect CBC could be done less frequently.

6.11. What factors should be considered when deciding to discontinue treatment?

Examples:

- *Disease progression (specify; e.g., loss of lower limb mobility)*
- *Certain adverse events occur (specify type, frequency, and severity)*

- *Additional treatment becomes necessary (specify)*

Response:

Decrease in hemoglobin without an alternative cause, increase in transfusion requirements or need to introduce regular transfusions in patients who have been transfusion independent.

If a patient becomes ill for other reasons ie infection, or bleeding, both of which are more common in MDS patients, they may transiently require transfusion again while the reason for deterioration is treated. This shouldn't preclude ongoing therapy if it is effective except for the effect of the intercurrent illness.

6.12. What settings are appropriate for treatment with the drug under review?

Examples: Community setting, hospital (outpatient clinic), specialty clinic

Response:

Community setting ie pharmacy administration, outpatient clinic, specialty clinic.

6.13. For non-oncology drugs, is a specialist required to diagnose, treat, and monitor patients who might receive the drug under review?

If so, which specialties would be relevant?

Response:

Yes – hematology, medical oncology

7. Additional information

7.1. Is there any additional information you feel is pertinent to this review?

Response:

There are limited treatment options in this group of patients with otherwise good risk MDS and often long life expectancies; the benefit to patients who can become transfusion independent (or remain so after developing symptomatic anemia) is very significant and can reduce a significant burden both to patients and to the health care institutions who provide regular transfusion support over very long time periods to these patients.

8. Conflict of Interest Declarations

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 clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

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

No

2. Did you receive help from outside your clinician group to collect or analyze any information 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. **Please note that this is required for <u>each clinician</u> that contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Clinician Information	
Name	Michelle Geddes
Position	Hematologist, Foothills Medical Centre and Tom Baker Cancer Centre
Date	Jan 29, 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				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Pfizer	☒	☐	☐	☐
Jazz	☒	☐	☐	☐
Celgene/BMS	☐	☒	☐	☐
Taiho	☒	☐	☐	☐
Novartis	☒	☐	☐	☐
Abbvie	☒	☐	☐	☐
Amgen	☒	☐	☐	☐
Astellas	☒	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐

Declaration for Clinician 2

Clinician Information	
Name	Kareem Jamani
Position	Hematologist, Tom Baker Cancer Centre & Clinical Assistant Professor, University of Calgary
Date	29-01/2021
☒	**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

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Pfizer	☒	☐	☐	☐
Jazz	☒	☐	☐	☐
Novartis	☒	☐	☐	☐
Paladin	☒	☐	☐	☐

Declaration for Clinician 3

Clinician Information	
Name	*Dr. Aniket Bankar*
Position	*Hematologist and Assistant Professor, University of Alberta Hospital, Edmonton, AB*
Date	*29 Jan 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

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	☒	☐	☐	☐
Novartis	☒	☐	☐	☐
AbbVie	☒	☐	☐	☐
Pfizer	☒	☐	☐	☐

Declaration for Clinician 4

Clinician Information	
Name	Dr. Deirdre Jenkins
Position	Clinical Associate Professor
Date	29-Jan-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				
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 disclosures to declare	☐	☐	☐	☐
	☐	☐	☐	☐

Declaration for Clinician 5

Clinician Information	
Name	Joseph Brandwein
Position	Hematologist, Director (Division of Hematology), and Professor (Medicine), University of Alberta, Edmonton
Date	18-01-2021
☒	**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				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Pfizer	☒	☐	☐	☐
Astellas	☒	☐	☐	☐
Amgen	☒	☐	☐	☐
Celgene/BMS	☒	☐	☐	☐
Taiho	☒	☐	☐	☐
Abbvie	☒	☐	☐	☐
Jazz	☒	☐	☐	☐
Roche	☒	☐	☐	☐
Teva	☒	☐	☐	☐
Novartis	☒	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐

Declaration for Clinician 6

Clinician Information	
Name	Mary Lynn Savoie
Position	Hematologist, Tom Baker Cancer Centre, and Associate Professor (Medicine), University of Calgary, Calgary
Date	20-01-2021
☒	**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

Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Amgen	☐	☒	☐	☐
Novartis	☐	☒	☐	☐
Pfizer	☐	☐	☒	☐
Merck	☒	☐	☐	☐
Astellas	☒	☐	☐	☐
Jazz	☒	☐	☐	☐
Celgene	☒	☐	☐	☐
Abbvie	☒	☐	☐	☐
BMS	☒	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐

Declaration for Clinician 7

Clinician Information	
Name	Sonia Cerquozzi
Position	Clinical Assistant Professor
Date	29-01-2021
☒	**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				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Novartis	☐	☒	☐	☐
Celgene/Bristol Myers Squibb	☒	☐	☐	☐
Pfizer	☒	☐	☐	☐

Declaration for Clinician 8

Clinician Information	
Name	*Adam Bryant*
Position	*Clinical Assistant Professor*
Date	*29 Jan 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				
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 conflicts of interest to disclose	☐	☐	☐	☐

Declaration for Clinician 9

Clinician Information	
Name	Dr. Minakshi Taparia
Position	Clinical Associate Professor, University of Alberta and Cross Cancer Institute, Edmonton
Date	22/02/21
☒	**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				
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 conflicts of interest to declare	☐	☐	☐	☐

Declaration for Clinician 10

Clinician Information	
Name	*Nancy Yan Zhu*
Position	*Assistant Clinical Professor, Department of Medicine, University of Alberta*
Date	*22Feb2021*
☒	**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				
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	☒	☐	☐	☐
Takeda	☒	☐	☐	☐