CADTH

CADTH REIMBURSEMENT REVIEW

Clinician Input

idecabtagene vicleucel (Abecma)

(Celgene Inc., a Bristol Myers Squibb company)

Indication: Multiple myeloma

November 18, 2020

CADTH

CADTH Reimbursement Review
Clinician Group Input Template

CADTH Project Number	**PG0240-000**
Generic Drug Name (Brand Name)	**idecabtagene vicleucel**
Indication	**For the treatment of adult patients with multiple myeloma who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody.**
Name of the Clinician Group	**Canadian Myeloma Research Group (CMRG)**
Author of the Submission	**Dr. Donna Reece**
Contact information	Name: Donna Reece Title: Chief Medical Officer, CMRG [redacted]

1. About Your Clinician Group

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

The Canadian Myeloma Research Group (CMRG), previously named the Myeloma Canada Research Network (MCRN), is a charitable organization whose membership consists of myeloma physicians from 22 major academic medical centres in Canada. The three main purposes of CMRG consist of: 1) conducting investigator-initiated academic clinical trials to improve the outcome of myeloma patients; 2) maintenance of a national Myeloma Database, now consisting of over 7000 patients, to evaluate real-word patterns of treatment, outcomes, risk factors and areas for future research in myeloma; and 3) generation of consensus statements for myeloma management.

2. Information Gathering

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

CMRG holds monthly teleconferences, and participants agreed to submit a single document for feedback to CADTH which would be signed by the physicians who agreed with the information. The initial draft of the document was prepared by the CMRG Chief Medical Officer and sent to all members to obtain input. Comments and suggestions were incorporated as appropriate. The final draft was signed by physicians who agreed with all of the content and their Conflict of Interest obtained as required.

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:

Initial Therapy: Currently, newly diagnosed Canadian myeloma patients are still divided into those who are transplant-eligible (TE) or transplant-ineligible (TI) based on age and fitness. TE patients receive bortezomib-based induction with CyBorD (or RVD if possible) followed by high-dose melphalan + ASCT and then lenalidomide-maintenance until disease progression. TI patients receive Rd, RVd (typically "lite") with single agent lenalidomide also given until disease progression. A few patients (with renal failure, poor marrow reserve or high-risk cytogenetics if RVd not accessible) still receive CyBorD which is usually provincially funded for only 9 cycles; maintenance with a single agent proteasome-inhibitor (PI) until progression -- with compassionate ixazomib or with bortezomib outside of provincial funding--is considered optimal.

Support for these algorithms comes from phase 3 published trials as well as real-world CMRG analyses currently available as published papers or abstracts (with the full manuscripts accepted for publication). Formal practice guidelines for the above algorithms are in progress and will be posted on the CRMG website, which is undergoing revision. These will be updated on an ongoing basis as the field is rapidly evolving.

Second-line therapy (after 1 prior regimen): Second-line therapy most often consists of daratumumab and dexamethasone combined with either lenalidomide (DRd) or bortezomib (DVd), depending on first-line therapy. DRd is preferred as long as the patient has not progressed during lenalidomide. (Whether patients should undergo a second salvage ASCT as second-line therapy is uncertain and individualized after discussion with each patient; maintenance therapy after salvage transplant is not funded but is strongly advised using agents obtained through compassionate or insurance mechanisms due to better results in retrospective studies).

Third-line therapy (after 2 prior regimens): Third-line therapy is usually based on either pomalidomide (POM) *or* carfilzomib. If patients have not received daratumumab previously, the regimen of isatuximab + pomalidomide + dex (IPd) is preferred due to the unique mechanism of action of monoclonal antibodies in myeloma as well as the requirement for prior exposure to a CD38 antibody for eligibility in virtually all clinical trials in advanced disease. Other options include POM + cyclophosphamide + dex (PCd) *or* carfilzomib + dex (Kd); some provinces fund the addition of cyclophosphamide to Kd (KCd) based on results from the MCRN003/MX1 CCTG phase 2 trial. POM + dex as a doublet is usually reserved for very frail patients or those with fragile marrow function. (The selection of either a POM -or carfilzomib-based therapy is important as patients no longer have provincial funding for both in some jurisdictions). An

occasional patient may receive daratumumab as a single agent via private insurance in order to allow future trial participation.

Fourth-line therapy: Options are limited. A regimen of bortezomib +steroids can be considered but yields a short PFS. Cyclophosphamide can added to Vd or used with steroids, but cumulative lifetime exposure to cyclophosphamide is limited to about 2 years due to the risks of MDS/AML and bladder cancer from this alkylating agent. Palliation/best supportive care/local radiotherapy may be used. Clinical trials are key to improving survival of Canadian patients in this setting but are markedly limited by: 1) strict eligibility criteria such as platelets over 75 x 10^9/L or near normal renal function that may be challengi ng to meet in advanced myeloma; 2) the decision by pharma to open promising trials in only a few Canadian sites; 3) the policy of pharma to offer a time-limited trial spot for only few days so if a patient is not available immediately, the opening is removed and given to a centre in another country; 4) sl ow trial accrual to promising agents in phase 1 study as DSMB reviews need to take place before a new cohort can be opened.

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:

1) Control the disease manifestations (bone destruction/pain, renal failure, hypercalcemia, low blood counts).
2) Maintain control of myeloma and its manifestations (PFS).
3) Minimize adverse effects.
4) Minimize caregiver burden.
5) Optimize 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*
- *Treatments are needed to improve compliance*
- *Formulations are needed to improve convenience*

Response:

Myeloma remains incurable and patients eventually become refractory to all available agents. About 15% have extremely aggressive disease at diagnosis and die within 1-2 years despite all therapies; many others will experience increasingly proliferative and aggressive disease with time. At some point, all patients succumb to their disease and often have a miserable quality of life in the end stages. Some treatments are not publically funded despite Health Canada approval. In some instances, only privately insured patients can access these potentially life-extending therapies which is an ethically challenging situation for patients, their families and health care providers.

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 highest unmet need in myeloma consists of patients who have failed therapy with a PI, IMiD and CD38 monoclonal antibody as no effective therapy is available. The drug under review would address this unmet need.

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:

The drug in question would be appropriate for “triple-refractory” myeloma patients. It addresses the underlying malignancy and currently would be used in sequence after the other lines of therapy described in Section 3.1 under treatment paradigms.

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:

There are really no other effective drugs to select other than the one under review in the fourth-line setting.

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:

After failure of ide-cel, patients would most likely only be offered palliative radiotherapy and other supportive measures, as all effective and/or funded regimens have already been utilized. Moreover, many clinical trials of new immunotherapies exclude patients who have received an anti-BCMA immunotherapy-- such as ide-cel --from receiving another agent targeting BCMA. Since BCMA is the most common target of new immunotherapeutic platforms, subsequent trial participation would be limited.

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 with other poor prognosis factors such as extramedullary disease and high risk cytogenetics experience do not fare significantly worse. Older age *per se* does not seem to be an exclusion factor. From a practical point of view, patients whose disease is progressing at a rate anticipated to allow them to remain stable and relatively well during the 4-5 week waiting time for CAR-T cell processing would be the best suited for this treatment in order to avoid a significant rate of attrition.

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:

Although many myeloma patients eventually require fourth-line therapy, the identification of patients for ide-cel therapy will require careful matching of available resources with the potential numbers of patients with relapsed myeloma. Ide-cel patients require an inpatient bed for about 2 weeks (or longer if complications occur) and may require readmission. They require potentially expensive ancillary measures to treat CRS, neurotoxicity and infections, and may need ICU support. Specialized training is required for

staff, and the medical centre's infrastructure and clinical pathways must be modified to meet the safety standards for ide-cel treatment and follow-up. These realities are expected to limit the numbers of myeloma patients that can be treated. Effector Cell Therapy Committees will likely need to establish guidelines for each institution.

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

Response:

Frail patients; those with rapidly proliferating disease, ongoing infection, significant organ dysfunction and patients with pre-existing pancytopenia would be least suitable.

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:

Patients with a good performance status, organ function, minimal or no comorbidities, robust blood counts, low tumor burden and indolent disease are the most likely to have the best outcomes. However, given the similar response and PFS rates in subset analysis of the ide-cel trials, it is likely easier develop exclusion, rather than inclusion, criteria.

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:

Responses are based on the monoclonal protein marker in the serum and/or urine, bone marrow biopsy and in some instances imaging studies. These are aligned with those used in the trials, which also include the emerging parameter of marrow MRD.

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 WG*
- *Stabilization (no deterioration) of symptoms*

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

Response:

Clinically meaningful responses usually correlate with at least a partial remission by IMWG Consensus Criteria. These include improvement in symptoms (cessation of bone destruction with less pain, fractures and need for radiotherapy), improvement in energy and better ability to perform activities of daily living.

6.10. How often should treatment response be assessed?

Response:

In myeloma, responses are generally assessed every 2-3 months depending on clinical stability.

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:

Ide-cel represents a single therapy.

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

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

Response:

This therapy is appropriate for a major medical facility with expertise in other cellular therapies for hematologic malignancies. There needs to be close interaction between a specialized inpatient service, ICU familiar with immunosuppressed cancer patients, and an outpatient facility experienced in handling urgent hematologic problems. Appropriate coordination with the Emergency Department to expedite care of patients recently discharged following ide-cel treatment is also required.

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:

N/A.

7. Additional information

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

Response:

Click here to enter response.

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	*Dr. Donna Reece*
Position	*Chief Medical Officer, CMRG*
Date	*14-01-2021*

☒ **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**
BMS/Celgene	☐	☐	☒	☐
Janssen	☐	☐	☒	☐
Amgen	☐	☐	☒	☐
Sanofi	☒	☐	☐	☐
GSK	☒	☐	☐	☐
Takeda	☒	☐	☐	☐

Declaration for Clinician 2

Clinician Information	
Name	*Dr. Martha de Lacerda Louzada*
Position	*Associate professor and -Clinician Researcher (WeternU-LHSC)*
Date	*14-01-2021*

☒ **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

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BMS/Celgene	☒	☐	☐	☐
Janssen	☒	☐	☐	☐

Declaration for Clinician 3

Clinician Information	
Name	*Dr. Julie Stakiw*
Position	*Oncologist*
Date	*14-01-2021*

☒ **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

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Sanofi	☒	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐

Declaration for Clinician 4

Clinician Information	
Name	*Dr. Christopher Venner*
Position	*MD (Hematology Tumor Group lead, Cross Cancer Institute, Edmonton, Alberta*
Date	*14/01/2021*

☒ **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.

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Celgene/BMS	☒	☐	☐	☐
Takeda	☒	☐	☐	☐
Janssen	☒	☐	☐	☐
Amgen	☒			
Sanofi	☒			
GSK	☒			

Declaration for Clinician 5

Clinician Information	
Name	*Hira Mian*
Position	*Assistant Professor, McMaster University, Clinical Hematologist*
Date	*Jan 14, 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

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Celgene/BMS	☒	☐	☐	☐
Janssen	☒	☐	☐	☐
Takeda/Sanofi/GSK	☒	☐	☐	☐

Declaration for Clinician 6

Clinician Information	
Name	*Kevin Song*
Position	*Hematologist, Vancouver General Hospital*
Date	*Please add the date form was completed (14-01-2021)*

☒ **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.

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Bristol Myers Squibb	☐	☒	☐	☐
Janssen	☐	☒	☐	☐
Amgen	☒	☐	☐	☐
GlaxoSmithKline	☒	☐	☐	☐

Declaration for Clinician 7

Clinician Information	
Name	*Dr. Rodger Tiedemann*
Position	*MD, Hematologist/ Oncologist*
Date	*14-01-2021*

☒ **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

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Takeda	☒	☐	☐	☐
Amgen	☒	☐	☐	☐
	☐	☐	☐	☐

Declaration for Clinician 8

Clinician Information	
Name	*Dr. Anthony Reiman*
Position	*MD Oncologist*
Date	*14-01-2021*

☒ **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**
Nothing to Declare	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐

Declaration for Clinician 9

Clinician Information	
Name	*Dr. Heather Sutherland*
Position	*Please state currently held position*
Date	*14-01-2021*

☒ **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

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Nothing to Declare	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐

Declaration for Clinician 10

Clinician Information	
Name	*Dr. Nizar Bahlis*
Position	*Associate Professor of Medicine. Oncologist/ Hematologist*
Date	*14-01-2021*

☒ **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

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BMS/Celgene	☐	☐	☒☐	☐☒
	☐	☐	☐	☐
	☐	☐	☐	☐

Declaration for Clinician 11

Clinician Information	
Name	*Dr. Michel Pavic*
Position	*Chief of Hematology department*
Date	*14 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.

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BMS-Celgene	☐	☒	☐	☐
Amgen	☒	☐	☐	☐
Janssen	☒	☐	☐	☐

Declaration for Clinician 12

Clinician Information	
Name	*Dr. Debra Bergstrom*
Position	*Hematologist/ Assistant professor*
Date	*15 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**
Nothing to declare	☐	☐	☐	☐
	☐	☐	☐	☐
	☐	☐	☐	☐

Declaration for Clinician 13

Clinician Information	
Name	*Dr. Arleigh McCurdy*
Position	*Hematologist/Oncologist*
Date	*15 JAN 2021*

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Takeda	☒	☐	☐	☐
Amgen	☒	☐	☐	☐
Janssen	☒	☐	☐	☐
Sanofi	☒	☐	☐	☐

Declaration for Clinician 14

Clinician Information	
Name	*Dr. Darrell White*
Position	*Hematologist, QEII Health Sciences Centre, Halifax, NS*
Date	*15 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

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BMS/Celgene	☐	☒	☐	☐
Janssen	☐	☒	☐	☐

Declaration for CMRG 15

Company	Check Appropriate Dollar Rang e			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Amgen Canada Inc.				x
Sanofi				x
Janssen				x
Celgene				x
Merck Canada Inc.				x
GlaxoSmithKline Inc.				x

CADTH Drug Reimbursement Review
Clinician Group Input Template

CADTH Project Number	**PG0240-000**
Generic Drug Name (Brand Name)	idecabtagene vicleucel (TBC)
Indication	**Indications:** For the treatment of adult patients with multiple myeloma who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody. **Manufacturer Requested Reimbursement Criteria[1]:** For the treatment of adult patients with multiple myeloma who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody.
Name of the Clinician Group	**Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee (DAC)**
Author of the Submission	**Dr. Tom Kouroukis, Dr. Janet McEachern**
Contact information	Name: Dr. Tom Kouroukis Title: Provincial Head – Complex Malignant Hematology (OH-CCO) [redacted]

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.

Via email

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:

In Ontario

- Patients can be treated with pomalidomide-dexamethasone or carfilzomib-dexamethasone or other chemotherapy (e.g., cyclophosphamide)
- SAP drugs (selinexor-dex +/- bortezomib; balantamab)

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 and control disease

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 available treatments show low response rate and short duration of response

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:

Life expectancy is limited in triple-class exposed patients; idecabtagene vicleucel (ide-cel) would address the unmet need.

There may be challenges in delivering this drug in patients with comorbidities and low blood count.

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:

As per the clinical trial, in triple-class exposed multiple relapsed/refractory myeloma patients.

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:

There is insufficient information.

The risk of treating with other regimens such as carfilzomib-dexamethasone may result in patients with more organ dysfunction/treatment-related toxicities that could make delivery of CAR T-cell therapy difficult.

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:

There is no sequencing information available other than using in triple-class exposed population.

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:

There is no available information to identify any patient subgroups which are most likely to respond.

The study recruited patients with good performance status.

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:

BCMA staining is required in KarMMA – currently this is not part of routine testing.

Patients can be identified via routine criteria for myeloma relapse/progression.

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

Response:

Align with inclusion/exclusion criteria in the study.

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 is no available data

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:

Would use the standard myeloma response criteria

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:

- at least a partial response as per myeloma response criteria
- Improvement in blood counts
- Improvement in end organ function (i.e., renal function)
- Reduction in skeletal events (i.e., bone pain or fractures)
- Overall improvement in QoL

6.10. How often should treatment response be assessed?

Response:

- Every 1 to 2 months

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: Not applicable as this is usually a single treatment
6.12. What settings are appropriate for treatment with the drug under review?
Examples: Community setting, hospital (outpatient clinic), specialty clinic ***Response:*** The delivery will be at tertiary hospitals/transplant centres with expertise in cellular therapy
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:*** N/A
7. Additional information
7.1. Is there any additional information you feel is pertinent to this review?
Response: Click here to enter response.

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 submission.

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	*Dr. Tom Kouroukis*
Position	Provincial Head – Complex Malignant Hematology (OH-CCO)
Date	*10 Dec 2020*

☒ **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	*15-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/BMS	☒	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

Declaration for Clinician 3

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	☐	☐	☐	☐

Declaration for Clinician 4

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	☐	☐	☐	☐

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	☐	☐	☐	☐