CADTH REIMBURSEMENT REVIEW

Patient and Clinician Group Input

teclistamab (Tecvayli)

(Janssen Inc.)

Indication: For the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 3 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

September 11, 2024

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CADTH in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings.

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Patient Input

Name of Drug: teclistamab (Tecvayli)

Indication: Adult patients with relapsed-refractory multiple myeloma who have received at least 3 prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody; and with no previous exposure to BCMA targeted therapies.

Name of Patient Group: Myeloma Canada

Author of Submission: Aidan Robertson

1. About Your Patient Group

Multiple myeloma, also known as myeloma, is the 2nd most common form of blood cancer. Myeloma affects plasma cells, which are a type of immune cell found in the bone marrow. Every day, 11 Canadians are diagnosed with myeloma, yet despite its growing prevalence the disease remains relatively unknown. People with myeloma experience numerous relapses; with successful treatment it can enter periods of remission, but myeloma will always ultimately return and require further treatment. Myeloma patients also become refractory to a treatment, meaning it can no longer control their myeloma, and they require a new regimen. Myeloma Canada has existed for over 15 years to support the growing number of Canadians diagnosed with myeloma, and those living longer than ever with the disease access new and innovative therapies. Over the years, as a part of this mission Myeloma Canada has collected data on the impact of myeloma and its treatments on patients and caregivers by conducting surveys. The compiled data are then presented to the pERC.

www.myeloma.ca

2. Information Gathering

Myeloma Canada is sharing the input received from a patient and caregiver survey regarding teclistamab, a BCMA targeted, t-cell engaging, bispecific antibody therapy for the treatment of relapsed refractory multiple myeloma. Our patient and caregiver survey was available from August 28 to September 6, 2023, and was shared across Canada and internationally, via email and social media. Fifty-four complete responses to the survey were received, 4 incomplete responses wherein a respondent did not finish answering survey questions, and 16 disqualified responses wherein the respondent's answers indicated they did not meet the eligibility requirements, were removed from the dataset. Survey eligibility was determined by patient and caregiver self-report of their experience with myeloma, that they (or the person they care for) have relapsed/refractory myeloma, received at least three prior lines of therapy including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody, with no previous exposure to BCMA targeted therapies. All patients (32) and caregivers (3) were initially asked similar questions regarding disease experience. Upon verifying their eligibility for, or experience with, the treatment under review, respondents were divided

into three subsets, and correspondingly posed different questions. The subsets and their demographic characteristics are as follows.

1. Patients who would currently be eligible for treatment with teclistamab, herein referred to as Subset E.1. Respondents **(22)** were from Alberta (1), British Columbia (5), New Brunswick (1), Saskatchewan (1), Ontario (8), Quebec (5), and 1 from outside of Canada (France). Of 22 E.1 respondents, 12 identified themselves as assigned male at birth (further referred to in this report as male'), and 9 as assigned female at birth (further referred to in this report as female'). Eleven Subset E.1 patients were located in an urban area, 7 in a suburban area, and 4 were located in a rural area. One Subset E.1 patient was between '50–59' years of age, 10 patients were between '60–69' years, 10 patients between '70–79' years, and one final patient was between '80–89' years old.
2. Caregivers **(3)** of patients who would currently be eligible for treatment with teclistamab, herein referred to as Subset E.2. One caregiver was from Alberta, one from British Columbia, and one from Quebec. All responding caregivers were located in an urban area and were female. One caregiver was '40–49' years of age, one was between '60–69', and one was between '70–79' years of age.
3. Patients who have received or are currently receiving treatment with teclistamab, herein referred to as Subset T. Respondents **(11)** were from Alberta (2), British Columbia (1), Quebec (2), Ontario (3), Saskatchewan (2), and 6 respondents identified themselves as female, 5 as male. Responding patients (11) were predominantly located in urban areas (8), with two living in a suburban area, and one living in a rural area. One Subset T patient was between the ages of '40–49', one patient between '50–59', 2 patients between '60–69' and 7 patients between '70–79' years of age.

   (*Note: no caregivers with teclistamab experience responded to the survey)*

4. *Disease Experience*

When all patients (33) were asked to "*Rate on a scale of 1–5 (1 is No impact and 5 is Extreme impact'), how symptoms associated with myeloma impact or limit your day-to-day activities and quality of life."*; by weighted average rating, patients indicated that their ability to travel (3.82) was most significantly impacted, followed by ability to work (3.56),

and to exercise (3.36).

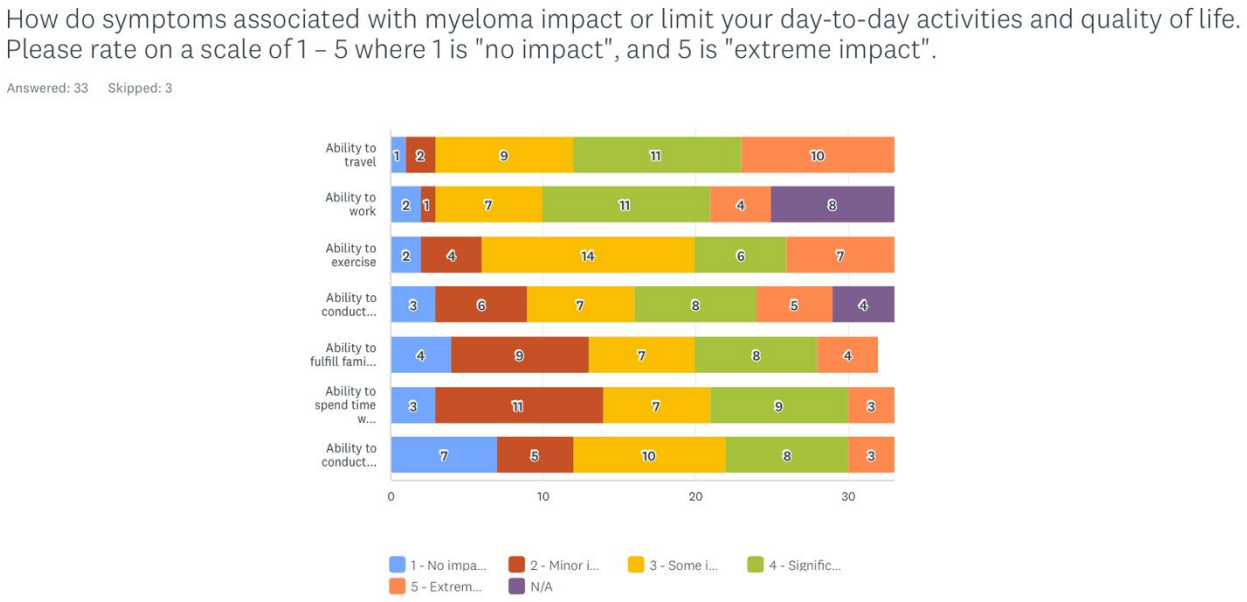

Figure 1—Impact of myeloma on everyday life and activities (patients; 33)

When all respondents (36) were asked "*How long does it take you to make a round-trip (to and from) the hospital/cancer centre where you, or the person you care for, receives treatment?"* most respondents, 55% (20), indicated 'Less than 1 hour one way',10 respondents chose '1–2 hours (30mins – 1h one way)', 3 chose '5 hours or more (2.5 hours or more one way)', and 2 chose '3–4 hours (1h – 2hrs one way)', while one respondent chose Other and commented "*N/A*".

When all patients and caregivers (36) were asked how often they, or the person they care for, visit their hospital or cancer centre for treatment, respondents most frequently selected, once a month 53% (19), followed by once a week 19.4% (7), and every two weeks 11% (4).

When patients and caregivers (35) were asked, "*What is the most significant financial implication of myeloma treatment on you and your household? If there is more than one implication, please check all that apply"*; respondents indicated lost income/pension funds due to absence from work, disability, or early retirement 34.3% (12), and travel costs 34.3% (12) were the most significant financial implications of myeloma treatment. Followed by parking costs 25.7% (9) and drug costs 14.3% (5).

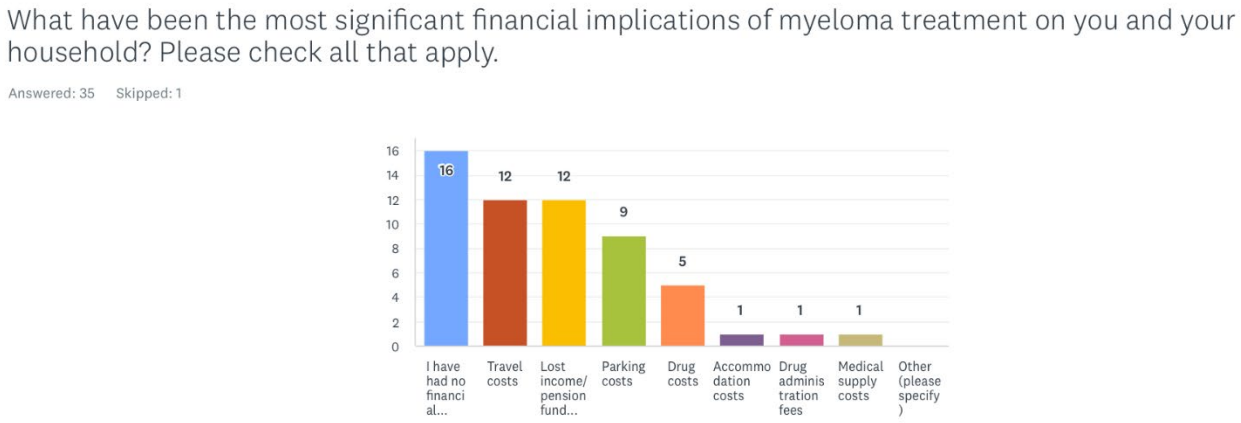

Figure 2—Financial implications of myeloma treatment (patients and caregivers; 35)

All patients and caregivers were asked *Has multiple myeloma, or caring for someone with myeloma, resulted in any of the following psychological / social difficulties for you? Please rate on a scale of 1–5 how severely they impacted your quality of life (1 – No impact and 5 – Severe impact)'*. By the weighted average of responses, patients (33) felt that that 'loss of sexual desire' (3.42) had the most impact on quality of life, and it was the option most frequently (9; 27%) rated 5 – Severe impact. Patients also indicated 'Anxiety/worry' and 'Interruption of life goals/accomplishments (career, retirement, etc.)' to have more significant impacts on quality of life, with each receiving a weighted average rating of 3.33. Caregivers (3) felt that caring for someone with myeloma had the most impact on 'anxiety/worry' (3.25), followed by 'Interruption of life goals/accomplishments (career, retirement, etc.)' (3.00), no other option listed received a weighted average rating above 2 – minor impact'.

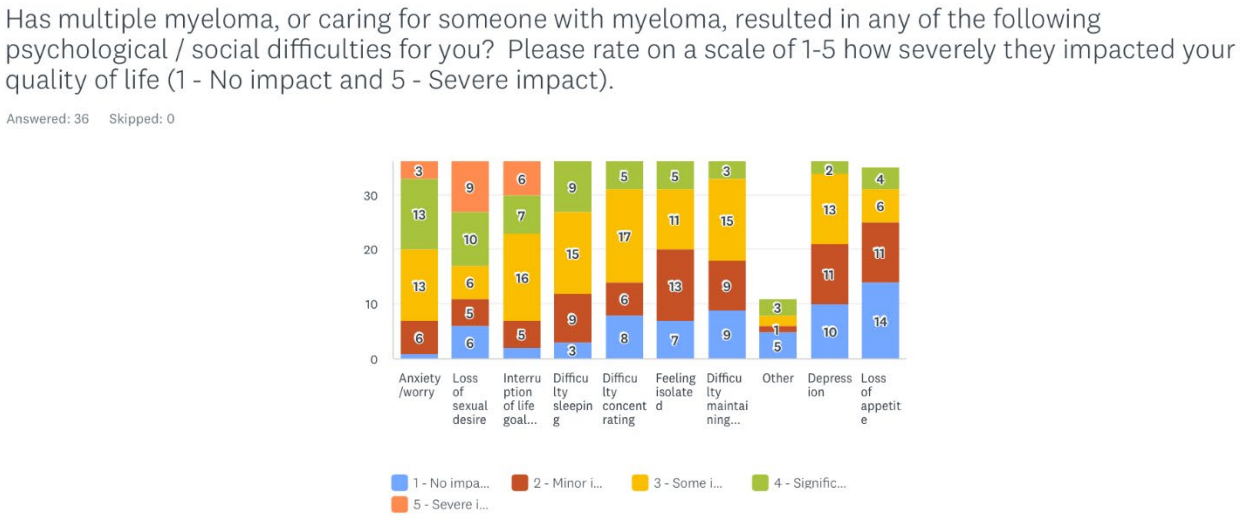

Figure 3—Psychological/social difficulties caused by living with or caring for someone with myeloma, and impact on quality of life. (Patients and caregivers; 36)

When patients (33) were asked "*Do you need the support of a caregiver or family member to help you manage your myeloma or your treatment-related symptoms?"*, 55% (18) responded 'Yes' they required a caregiver, 39.4% (13) answered 'No' they did not need a caregiver, and 6.1% (2) chose 'No', but I would benefit from a caregiver's help.

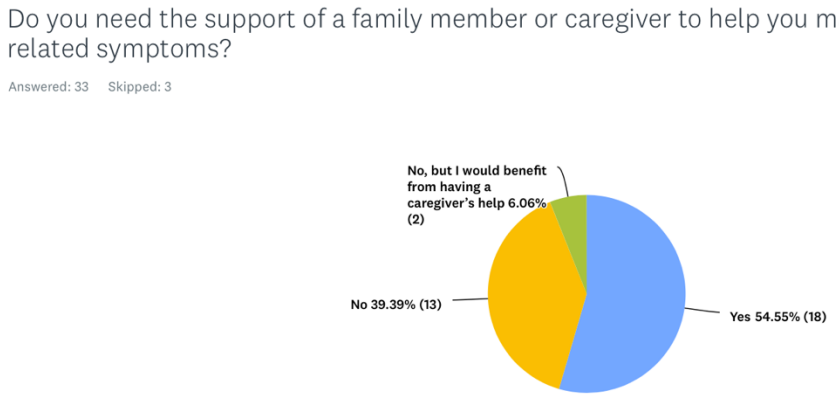

Figure 4—Need or desire for a caregiver (all patients; 33)

All patients and caregivers were asked to identify the factors they consider to be most important to (any) myeloma treatment. Respondents (35) most frequently mentioned quality of life and making side effects manageable, along with the effectiveness of treatment, especially in achieving remission and having a long, durable, response, accessibility/portability of treatment (including fewer/minimal visits to the hospital/cancer centre), to be key factors. Some responses of relevance are as follows:

"*Long term protection of kidney function and ability to travel.";*

"It is important to me that the side-effects do not unduly affect my quality of life.";

"Son efficacité avec le moins d'effets secondaires possible";

"Le mode d'administration et le temps d'administration du médicament qui nécessite pas de se rendre à l'hôpital par exemple des comprimés oraux car on ne se déplace pas et c'est dans le confort de notre foyer. Si pas possible des injections au lieu de l'intraveineuse car c'est plus rapide et moins d'inconfort.";

"Remission that is deep and hopefully long lasting. Side effects that are not debilitating, such as peripheral neuropathy.".

5. *Experiences With Currently Available Treatments (eligible population Subsets E.1, E.2)*

All patients (33) were asked "*How important it is for you to control various aspects of myeloma? (Please rate on a scale of 1 'Not important' to 5 'Extremely important')".* By the weighted average of responses, 'infections' (4.56) was the most important aspect to control and was rated '5 – extremely important' most frequently (22; 68.8%). Patients also felt

kidney problems (4.50) and mobility (4.34), were slightly more important to control, though all options listed received an average rating of '4 – very important'. Patients also left comments that mentioned gastrointestinal issues, relapse, and secondary cancers were important.

Subsets E.1 and E.2 (25) were asked "*How many prior lines of therapy have you or the person you care for received?",* 12 respondents (48%) indicated they received 3 lines of therapy, 10 (40%) responded 4 lines of therapy, and 3 respondents indicated they or the person they care for, had received 5 lines of therapy or more.

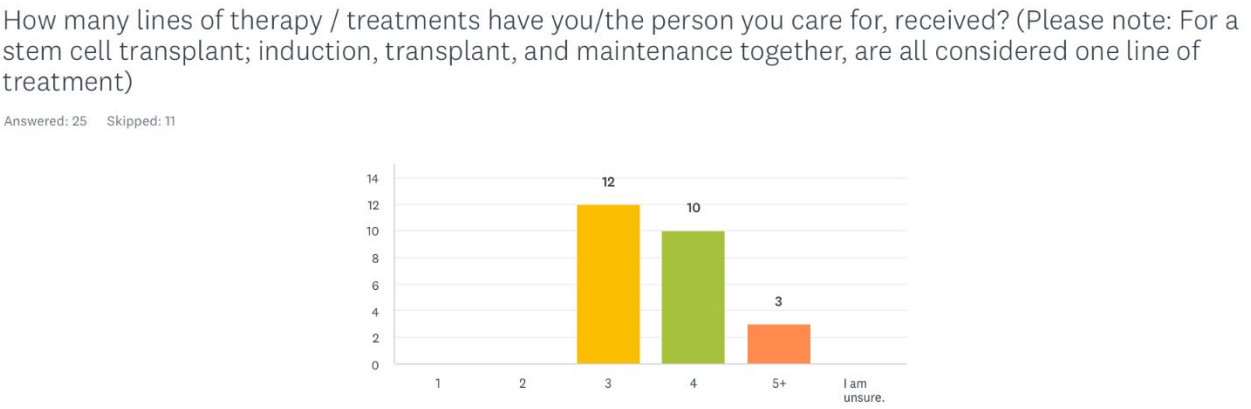

Figure 5 – Number of lines of therapy received (Subsets E.1 & E.2; 25)

When asked, "*Have you/the person you care for, received an autologous stem-cell transplant (ASCT) to treat your myeloma?"* 88% of Subsets E.1 and E.2 respondents (25) said yes, and 12% (3) indicated they/the person they care for was not eligible for an ASCT.

6. *Improved Outcomes*

Subset E.1 (22) was posed the question, "*When considering a myeloma treatment for yourself, how important is it for the treatment to improve your overall quality of life? Rate on a scale of 1 – 5, 1 is 'Not important' and 5 is 'Extremely important'*.", 59.1% (13) of respondents felt it was 5 – extremely important, while 27.3% (6) answered '4 – very important', and 13.6% (3) chose 3 – somewhat important.

Subset E.1 (22) was asked how desirable an estimated minimum 1 year to 21 months of extended life is to them at this stage in their myeloma journey, 77.3% (17) indicated it was '5 – extremely desirable', and 22.7% (5) chose '4 – very desirable'.

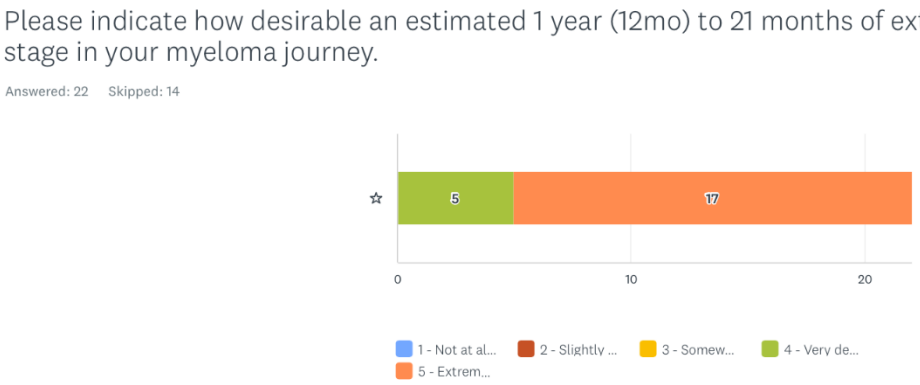

Figure 6–Desirability of 1–2 years extended life (Subset E.1; 22)

Subsets E.1 (22) and E.2 (3) were presented information about common side effects of teclistamab: Cytokine Release Syndrome, Infections, Neutropenia, Immune Effector Cell Associated Neurotoxicity Syndrome (ICANS). As well the step-up dosing period, and dosing schedule (weekly) were described, and respondents informed that after starting treatment with teclistamab, patients must remain within 48 hours of their treatment centre for the duration of the step-up dosing period, and may not drive for 48 hours following administration of the step-up doses.

Subset E.1 was asked "*Amongst the most common side effects in patients who receive teclistamab, how tolerable do you expect they would be for you? Please rate on a scale of 1 Not at all tolerable to 5 Extremely tolerable'".* Ordered by weighted average of responses Subset E.1 perceived ICANS (2.5), cytokine release syndrome (2.8), and infections (2.9) to be the least tolerable side effects, followed by thrombocytopenia (3.0) and neutropenia (3.1). Overall, the median tolerability rating was 3 – Somewhat tolerable for all side effects except ICANS (2) and fatigue (4).

When Subset E.1 (22) was asked, "*Compared to other treatment options available to you, how worrisome is the overall side effect profile for teclistamab? Please rate on a scale of 1–5 where 1 is 'Not at all worrisome' and 5 is 'Extremely worrisome'.*" respondents most frequently chose '3 – Somewhat worrisome' (68.2%; 15), followed by '4 – Significantly worrisome' (18.2%; 4) and '2 – Slightly worrisome' (13.6%; 3). Responding to the same question, two Subset E.2 caregivers (3) chose '2 – Slightly worrisome' (2), while one chose '3 – Somewhat worrisome'.

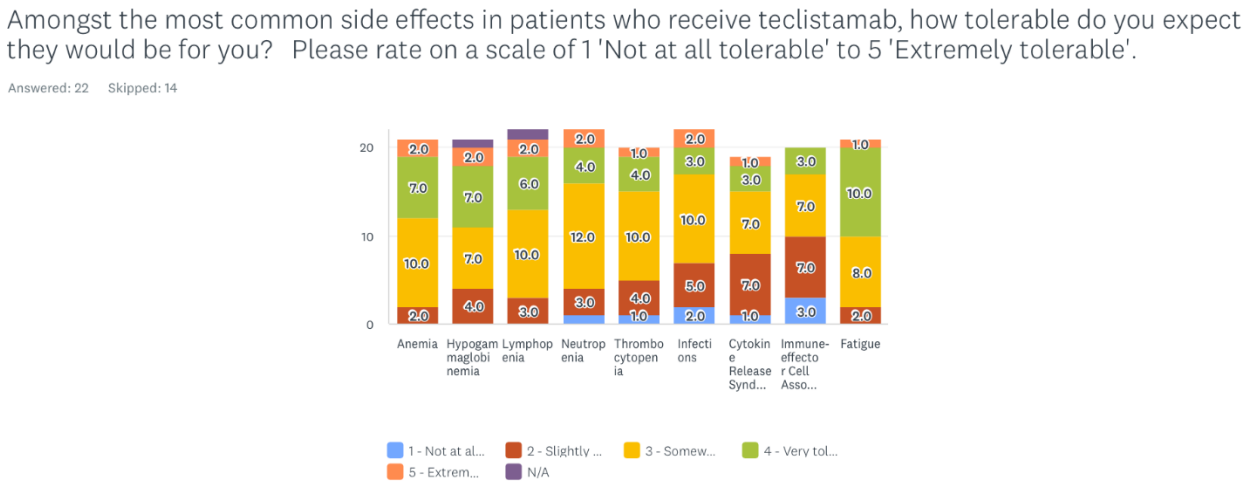

Figure 7–Perception of teclistamab side effects (Subset E.1; 22)

Subset E.1 was asked *Most patients in the MajesTEC-1 trial experienced CRS (72%), and for almost all patients it was either Grades 1 or 2 (i.e. less severe). 0.6% of patients experienced grade 3 CRS and there were NO grade 4 or 5 CRS events. Does knowing this information impact your level of concern/worry about experiencing CRS due to teclistamab treatment?".* Respondents (22) most frequently chose No, my level of concern/worry remains the same (68%; 15), followed by Yes, I am less worried (18%; 4), and 'Yes', I am more worried (14%; 3).

When asked "*If you were eligible to receive the treatment under review, do you expect to need accommodation near your hospital/cancer centre for the duration of the step-up dosing period?",* the majority of Subset E.1 respondents (22) chose 'No' (82%;18), while 2 patients chose 'Yes' and two additional patients indicated they were unsure. When asked the same question, two Subset E.2 caregivers (3) chose 'No' and one chose 'I am unsure'.

Subset E.1 was posed the question, "*Does traveling to and from your hospital/cancer centre for treatment usually involve you driving*?" to which 17 of 22 respondents said 'Yes' and 5 chose No'. As a follow-up question, Subset E.1 was asked "*If yes, do you have a caregiver or family member who could drive you to appointments if needed?"*, 18 of 20 responding patients chose 'Yes', one patient chose 'No', and one patient chose I am unsure'. Subset E.2 was similarly asked if the person they care for usually drives to treatment, all three responding caregivers chose 'Yes' and subsequently indicated 'Yes' (3) they would be able to drive the person they care for to treatment when needed.

Subset E.1 was asked "*If you were eligible to receive teclistamab treatment for your myeloma, what do you believe the advantages and/or disadvantages would be for you?*". Respondents (22) were provided the following list of factors and asked to indicate if they felt there would be an increase or decrease in that area; Treatment side effects (Increased: 6, No change: 4, Decreased: 0, I'm not sure: 9) Control of myeloma and its symptoms'(Increased: 12, No change: , Decreased: 0, I'm not sure: 9), Frequency of trips to the hospital or cancer centre for treatment (Increased: 10, No change: 9, Decreased: 0, I'm not sure: 6), Tolerability of the treatment's mode of administration (Increased: 1, No change: 13, Deacreased: 0, I'm not sure: 6), Quality of life (Increased: 7, No change: 6, Decreased: 0, I'm not sure: 9).

Many patients indicated they were unsure of the impact teclistamab would have on all factors, while there was the greatest consensus on teclistamab providing increased control of myeloma and its symptoms (12), and there being no change (13) in the tolerability of teclistamab's mode of administration (compared the last treatment they received or are currently receiving).

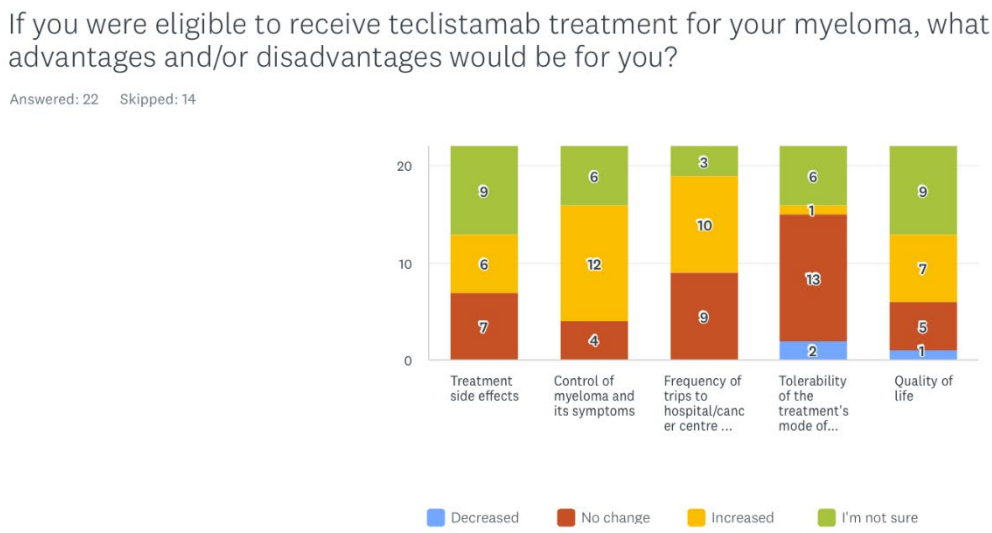

Figure 8–Perceived advantages/disadvantages of treatment with teclistamab; subset E.1 (patients; 22)

To the question "*With what you know today, would you consider teclistamab as an option for your next treatment? (Presuming you are eligible, and your doctor agrees).*" 59.1% (13) of Subset E.1 patient respondents (22) indicated 'Yes', while 27.3% (6) said they were unsure, and 3 additional patients indicated they would need more information to decide .

When given the opportunity to share any further thoughts about potential treatment with teclistamab, 9 E.1 respondents left comments, of which many described the importance of speaking with their hematologist/oncologist about teclistamab, one comment noted they were about to start treatment with teclistamab in the next few weeks.

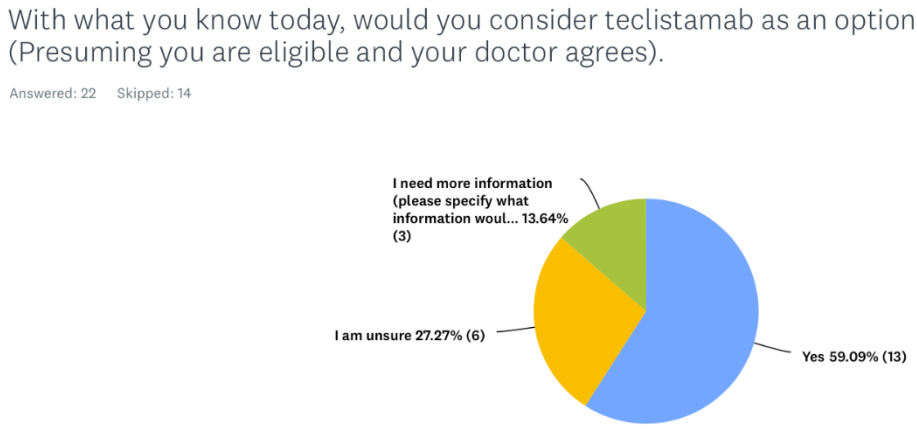

Figure 9—Would you consider teclistamab for your next treatment? (Subset E.1 patients; 22)

7. *Experience With Drug Under Review*

As noted previously, there were 11 patients with teclistamab experience who responded to the survey, no caregivers, and they are referred to as Subset T. When asked to "…*indicate when you began treatment with teclistamab*.", 3 Subset T patients (11) chose 'Less than three months ago', 3 chose 'Over a year ago', 2 chose 'Between 3–6 months ago', 2 chose 'Over 2 or more years ago' and one respondent indicated they did not remember. All Subset T respondents (11) are still currently undergoing treatment with teclistamab. When asked if they had relapsed since receiving teclistamab, 10 Subset T respondents (11) chose 'No, I have not yet relapsed and am still receiving teclistamab' and one chose 'Other' indicating they had just started their treatment with teclistmamab very recently (Aug. 25, 2023).

When asked if they were "*…receiving teclistamab alone, or in combination with another drug? If applicable, please indicate the drug you were/are receiving alongside teclistamab.",* 5 Subset T respondents (11) selected 'Teclistamab alone (as monotherapy)', one patient indicated they were unsure, and 5 chose in combination with another drug and provided the drug name(s). Of these 5 patients, two are receiving daratumumab alongside teclistamab, one patient is receiving talquetamab in combination with teclistamab, while the remaining two described supportive care drugs not a combination therapy (IVIG, steroids, Benadryl) and their responses were subsequently added to the teclistamab as monotherapy category. The final count was thus 7 Subset T respondents (11) receiving teclistamab alone, one unsure, and 3 receiving teclistamab in combination with another drug.

When asked, "*Were you… admitted to the hospital at any point in the initial step-up dosing period? If yes, please indicate how many nights you spent in the hospital.*" 10 of 11 Subset T respondents chose 'Yes' and indicated the length of their stay, while one respondent chose 'I'm not sure'. The amount of time patients spent in-hospital ranged

from 4 nights to 4 weeks with the most frequently reported stay length falling between 9 and 10 nights. [All responses: 4 weeks/30 days (1), 23 (1),10 (2); 9 (2); 8 (1), 6 (1), 4 (1), 0 (1)].

When asked, "*How often do you visit a hospital/ cancer centre for teclistamab treatment since the step-up dosing period ended?*", 6 Subset T respondents (11) chose Once a week, 2 chose every two weeks and, 3 respondents chose other all of whom commented they received treatment once a month. Of these three, one is receiving teclistamab in combination with another drug, one was unsure if they were receiving a combination therapy, and one was located in France. In comparison, all of the 5 patients who initially reported receiving weekly treatment, also reported receiving teclistamab as a monotherapy.

Subset T (11) was asked, "*Which of the most frequent teclistamab side effects listed below have you/the person you care for experienced? Please select all that apply and rate the side effects severity on a scale of 1 Not at all bearable to 5 Extremely bearable'.".* By weighted average of responses, 10 responding patients rated Respiratory Infections (2.50) as the least bearable side effect, followed by COVID-19 (2.8), Fungal Infections (2.9) and Immune-effector Cell Associated Neurotoxicity Syndrome (2.9). Similarly, the median response to all listed side effects was 3 – Somewhat bearable or higher, except for Respiratory Infections (median 2 – Slightly bearable').

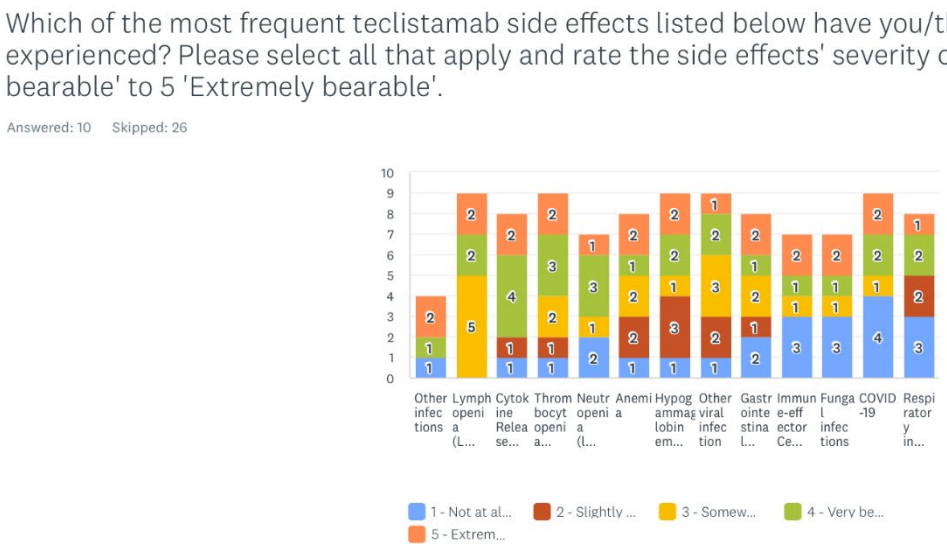

Figure 10 — Experience of teclistamab side effects (Subset T patients; 11)

When asked, "*Compared to how your previous treatments were administered, did the mode of administration by which you received teclistamab have any impact on your quality of life? (Please rate on scale of 1 – 5 where 1 is No impact and 5 is Severe impact').",* Subset T respondents (11) most frequently selected 1 – No impact (5), 3 patients selected 3 – some impact 2 patients chose 4 – significant impact and 1 patient chose 2 – A little impact'. Responding to the question "*How effective was the supportive care you received in managing your side effects from teclistamab*

treatment? Please rate on a scale of 1–5 where 1 is Not at all effective and 5 is Extremely effective", 4 Subset T respondents (11) chose 5 – extremely effective 3 patients each chose 4 – Significantly effective (3) and 3 – Somewhat effective (3), while one patient chose 2 – Sightly effective'.

Subset T respondents (11) were asked "*Compared to past treatments you received, do you think teclistamab treatment had any of the following advantages and/or disadvantages?",* and were provided the following list of factors and asked to indicate if they felt there had been an increase or decrease in that area; Treatment side effects (Increased: 1, No change: 2, Decreased: 5, Too soon to tell: 3) Control of myeloma and its symptoms (Increased: 6, No change: 0, Decreased: 2, Too soon to tell: 3); Frequency of trips to the hospital or cancer centre for treatment (Increased: 4, No change: 4, Decreased: 2, Too soon to tell: 1); Tolerability of the treatment's mode of administration (Increased: 2, No change: 5, Decreased: 3, Too soon to tell: 1); and Quality of life (Increased: 7, No change: 2, Decreased: 1, Too soon to tell: 1).

Following the instructions "*Please answer each of the following questions on your overall perception of treatment with teclistamab, by rating them on a scale of 1 – 5, where 1 is Not at all and 5 is Completely'",* Subset T patients (10) responded to the questions:

– "*Did teclistamab treatment improve your overall quality of life?*" (Completely: 2; Mostly: 4, Somewhat: 1; Not at all: 3).

–"*Were the overall side-effects you experienced while receiving teclistamab manageable?* (Completely: 4, Mostly: 3, Somewhat: 2; Slightly: 1)

–*Was teclistamab effective in controlling your myeloma?* (Completely: 7, Mostly: 1, Slightly: 2),

–"*Did teclistamab meet your expectations in treating your myeloma?*" (Completely: 6, Mostly: 2, Slightly: 2). Comments provided by three patients indicated it was too soon in their treatment to effectively answer most of these questions, while some other comments of note were as follows:

"*My Stem Cell transplant did not work well, as I went into remission for only 6 monthes [sic], the chemo treatments worked to reduce the spread, but of course had chemo/steroid side effects that brought on bad side-effects. Teclistamab has been far & away the best treatment for me so far!";*

"didn't expect such severe side effects";

"one of the best myeloma treatments I've had".

Subset T (11) was asked to indicate how they were or are accessing teclistamab, 6 patients indicated through a clinical trial (ongoing) 1 patient chose through a clinical trial (complete), and 4 patients selected through compassionate access.

Finally, when asked if there was anything else they would like to share about their experience with teclistamab, 8 Subset T patients provided comments, one indicated they were unable to answer the final questions of the survey because they had not been on teclistamab long enough, and two simply responded 'No'. Further comments of relevance are as follows:

"*Very thankful to have received it. Hope it will benefit many others*.";

"*Nous aviser qu'il peut prendre plus de 3 cycles avant de faire effets et que l'on devra être à l'hôpital 2 fois par semaine."*

"*Jusqu'à aujourd'hui, meilleure solution médicamenteuse appliquée. A voir la tenue dans le temps mais ce qui est pris est pris*."

"*It is the first drug since diagnosis 3 1/2 years ago that has allowed me to feel human again. I can take it without the premeds that have caused me so many severe side effects in the past."*

8. *Anything Else?*

Subset E.1 and E.2 patients and caregivers (25) were posed questions to gauge their awareness and understanding of anti-BCMA targeted t-cell engaging therapies, and anti-BCMA targeted bispecific antibody therapies. When asked "*Have you heard of B-cell maturation antigen (BCMA) targeted t-cell engaging therapies to treat myeloma?"* 11 survey respondents chose 'Yes', 7 chose 'Yes, but I'm not sure what they are', and 7 respondents chose 'No'. When the 18 patients with previous awareness were asked where they learned of BCMA-targeted T-cell engaging therapies, 12 respondents chose 'Through my own research', 12 chose 'Through Myeloma Canada', 5 chose 'Through my support group/other people with myeloma', and 4 respondents each chose 'Through my oncologist/care team' (4) and 'Through another organization' (4). Subset E.1 and E.2 (25) were asked "*Have you heard of B-cell maturation antigen (BCMA)-targeted bi-specific antibodies to treat myeloma? (Ex. Elranatamb, Teclistamab)",* 13 respondents chose 'Yes' while 6 chose 'Yes, but I'm not sure what they are', and 6 chose 'No'. When asked where they learned about BCMA-targeted bispecific antibodies, 15 respondents chose 'Through Myeloma Canada', 9 chose 'Through my own research', 5 respondents each chose 'Through my oncologist/care team' and 'Through my support group/other people with myeloma' while the final 4 respondents indicated 'Through another organization'. For both questions, the organization most frequently mentioned by those who chose 'Through another organization' was the International Myeloma Foundation. When Subsets E.1 and E.2 were asked to identify the correct definition for *B-cell maturation antigen*

targeted (BCMA), t-cell engaging, bispecific antibody therapies 17 of 25 respondents correctly identified the answer was ‘all of the above’, and 8 respondents gave a partially correct answer. Overall, it appears most surveyed patients and caregivers who would be eligible for teclistamab have at least some knowledge of anti-BCMA targeted t-cell engaging bispecific antibodies (like teclistamab) for the treatment of multiple myeloma. A persistent fear for this sub-population of myeloma patients (triple-class exposed, relapsed/refractory, on third line+ of treatment) is the availability of further treatments when their current regimen becomes no longer effective. As a result, some patients seek information on new drugs, even more are exposed to the information in their environment, and many are looking forward to having this option available to them when they are inevitably in need of a new treatment. Comments provided by Subset E.1 to this effect are as follows:

“Right now I’m doing ok on Dara /rev/dex . I’m interested in finding out more about teclistamab in case the above becomes ineffective. I’ve been on it now for 48 months”;

“*I am 10 years post diagnosis and about to start a 4th line of treatment Pom/Dex with unknown results. I am hoping this protocol will keep me stable enough until Tecv is approved and funded by my Provincial authority.”*

It was notable that cytokine release syndrome (CRS) despite causing significant concern for Subset E.1 (second least tolerable side effect; weighted average rating 2.8), was considered the third most bearable side effect for Subset T patients who had actually received teclistamab (weighted average 3.63), and no other option listed received as many ratings of ‘4– Very bearable’ (4) or above from Subset T.

From August 28 to September 30, 2022, Myeloma Canada conducted a different survey about a CAR T-cell therapy which received 200+ responses; yet only one Canadian patient and one caregiver reported experience with said therapy. The present survey was distributed at the same time of year, and despite a significantly shorter period of data collection, and narrower eligibility requirements, received responses from 11 Canadians with teclistamab experience. This is indicative of the comparative ease with which teclistamab can and has been made accessible to Canadians with triple-class-exposed relapsed/refractory myeloma. Supporting this idea is the fact that Subset T patients were from multiple provinces, though nearly all were from an urban or suburban area, with only one rural patient currently receiving teclistamab. Similarly, the survey data showed that since Health Canada’s recent approval of teclistamab, 3–4 patient respondents have started receiving teclistamab (or soon will be) through compassionate access. Overall, the data (though limited) show there is already relatively widespread uptake of teclistamab by Canadian doctors treating myeloma, though special consideration must be given to rural/remote patients, ensuring there is equal access to teclistamab *within* provinces, as well as across provinces.

Finally, when considered together, comments from patients currently receiving teclistamab were largely very positive, with multiple patients indicating at different points in the survey that this was the ‘best’ treatment they had received for their myeloma so far. (See original comments on pages 12 and 13).

Clinician Input 1

CADTH Project Number: PC0332

Generic Drug Name (Brand Name): Teclistamab

Indication: Teclistamab injection is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least three prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

Name of Clinician Group: Ontario Health (CCO) Hematology Cancer Drug Advisory Committee

Author of Submission: Dr. Tom Kouroukis, Dr. Pierre Villeneuve

1. *About Your Clinician Group*

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.

Information Gathering

Information was gathered via videoconferencing and email.

3. *Current Treatments and Treatment Goals*

Current treatments include Pd, Kd, SVd, chemotherapy and CAR-T (future).

Goals are to delay progression, improve symptoms and quality of life.

4. *Treatment Gaps (unmet needs)*

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

Other than Car-T cell therapy, there is no other substantial treatment available for triple class exposed patients.

Ease of administration (subcutaneous injection, no need for apheresis)

5. *Place in Therapy*

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

This is another option for triple class exposed patients.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

As per the clinical trial

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

Standard myeloma response measures

CRS and ICANS toxicity grading scales

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

Loss of response, progression, significant toxicities

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

Centers skilled in managing CRS and ICANS. There is some inpatient component required for monitoring purposes.

6. *Additional Information*

N/A

7. *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 function to the group.

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> who 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

Name: Dr. Tom Kouroukis
Position: Lead, OH-CCO Hematological Cancer Drug Advisory Committee
Date: 31-08-2023

☒ **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.

Table 1: Conflict of Interest Declaration for Clinician 1

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				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Dr. Pierre Villeneuve
Position: Member, OH-CCO Hematological Cancer Drug Advisory Committee
Date: 27-07-2023

☒ 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.

Table 2: Conflict of Interest Declaration for Clinician 2

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				

* Place an X in the appropriate dollar range cells for each company.

Clinician Input 2

CADTH Project Number: PC0332-000
Generic Drug Name (Brand Name): Teclistamab

Indication: Relapsed or refractory multiple myeloma
Name of Clinician Group: The Canadian Myeloma Research Group
Author of Submission: Dr. Christopher Venner

1. About Your Clinician Group

The Canadian Myeloma Research Group (CMRG) is a Canada-wide network of researchers aiming to develop better treatments for extending life of myeloma patients, enhancing the quality of life for those living with myeloma and related diseases and working to find a cure for these diseases and other plasma cell disorders. 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 10 000 Canadian 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.

Website: cmrg.ca

2. Information Gathering

CMRG holds monthly physician 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 in consultation with 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 and Treatment Goals

- Regardless of the line of therapy the overall treatment goals in patients are to: 1) control the disease and its associated sequalae (bone destruction/pain, renal failure, hypercalcemia, low blood counts) by achieving an anti-myeloma response; 2) maintain control of myeloma and its manifestations for as long as possible given the current incurable nature of the disease (i.e. maximize progression-free survival); 3) Improve overall survival; 4) minimize adverse effects of treatment; and 5) optimize QOL by adequately controlling the disease and minimizing toxicity with the aim to tailor the treatment approach to the individual patient.
- 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 RVD or CyBorD followed by high-dose melphalan + ASCT and then lenalidomide maintenance until disease progression. TI patients have previously most often received Rd or RVd (typically “RVd Lite”) followed by single-agent lenalidomide (also given until disease progression); more recently daratumumab-based combinations such as DRd or Dara-CYBORD/VMP are preferred and include provisions for long-term continuous administration of selected agents. Support for these algorithms comes from published phase 3 trials as well as real-world CMRG analyses. These approaches have also been endorsed by CADTH in the recent Provisional Funding Algorithm.
- Second-line therapy (after 1 prior regimen): Second-line therapy depends on whether patients have progressed on lenalidomide (currently, this includes most ASCT and TI patients). Key in second-line therapy is the inclusion of an anti-CD38 antibody such as daratumumab or isatuximab, which represents a high-priority for virtually all patients. Presently daratumumab is funded in the relapsed setting only for patients relapsing after 1-3 prior lines of therapy. Thus, prior to the relatively recent funding of frontline daratumumab combinations in TI patients, most patients receive daratumumab and dexamethasone combined with bortezomib (DVd) as second-line therapy. Very recently, isatuximab has been funded in some provinces, with some patients now being treated with isatuximab, carfilzomib and dexamethasone (Isa-Kd) after 1-3 prior lines. The minority of patients who did not progress on first-line therapy with a lenalidomide-containing regimen have been preferentially treated with DRd.
- Other relevant anti-CD38 monoclonal antibody-containing regimens have been approved by Health Canada and could be used in second line and beyond. Ideally, such patients would receive daratumumab/isatuximab with dexamethasone and POM (DPd, IsaPd), or daratumumab/isatuximab with dexamethasone and carfilzomib

(DKd, IsaKd). (Presently, only the isatuximab-containing regimens are approved and **funded** in Canada and are incorporated into the recent CADTH funding algorithm).

- As more TI patients progress after anti-CD38 containing regimens as initial therapy, second-line therapy will need to be based on combinations of either proteasome inhibitors (bortezomib or carfilzomib) **or** pomalidomide [POM]. Funded options include bortezomib + dex +/- cyclophosphamide [Vd or CyBorD], selinexor + bortezomib + dex (SVd), carfilzomib + dex +/- cyclophosphamide [Kd or KCd] and POM + dex +/- cyclophosphamide [PCd]. However, provincially funded regimens often restrict access to POM-based therapy in second line and require exposure to both a PI and lenalidomide first. Triplet regimens are generally preferable to doublets. Of note, there is no publicly reimbursed access to any BCMA-targeted agents.
- Third-line therapy (after 2 prior regimens): If patients have not yet received an anti-CD38 monoclonal antibody by the time of third-line treatment is needed, every effort is made to procure a combination containing such agents. This is a dwindling population of patients. Otherwise, third-line therapy is usually based on either POM or carfilzomib with less efficacious partners. Funded options include POM + dex +/- cyclophosphamide (PCd) or carfilzomib + dex +/- cyclophosphamide (Kd or KCd). For patients still bortezomib-sensitive the agent can be used again. As above, the more recently funded regimen SVd is also an option. Again, triplet regimens are generally preferable.
- Fourth-line therapy: Options are extremely limited. A POM- or carfilzomib-based regimen such as Pd or Kd may be utilized if not used earlier in the third line. Bortezomib-based regimens can be explored but only if patients are still PI-sensitive which is rare by that stage. Although cyclophosphamide can be added to many regimens--or even used with steroids as a doublet (CyDex)--the cumulative lifetime exposure to cyclophosphamide is limited to 1 to 2 years for each patient due to the risks of secondary MDS/AML and bladder cancer from this alkylating agent. The risk of secondary MDS/AML may also further restrict use of alternative alkylating agents like melphalan. As such, palliation/best supportive care/local radiotherapy are often all that can be pursued within the confines of the publicly funded system.
- While antibody drug conjugates, bispecific antibodies and cellular therapy are positioned to fill this triple class refractory space none are available currently in Canada. Cilta-cel has been endorsed by CADTH but at present negotiations are still ongoing to establish provincial pricing. Even once this is achieved, we expect ongoing bottlenecks due to production limitations and challenges with capacity at the institutional level.
- Clinical trials are key to improving survival of Canadian patients through early access to promising agents in this setting but access is markedly limited by: 1) strict eligibility criteria, such as the need for good hematologic reserve and adequate renal function, may be challenging 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) slow trial accrual to promising agents in a phase 1 study as DSMB reviews need to take place before a new cohort can be opened.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

Myeloma remains incurable and patients eventually become refractory to all available funded agents. The highest unmet need in myeloma is patients with advanced disease who have received multiple lines of treatment and have already received the three major classes of drugs ("triple-class exposed/refractory") including an IMID, PI and anti-CD38 monoclonal antibody. Outcomes in this patient population are dismal in the Canadian landscape due to the lack of access to additional novel agents, including anti-BCMA therapy. This is supported by recent data from our CMRG group examining outcomes in these triple-class refractory patients. The ORR to subsequent line of treatment was approximately 40% with the median PFS from start of subsequent therapy being 4.4 months, and the median OS being 10.5 (95% CI 8.5-13.8) months (LeBlanc, R et al. 2023; *Eur J Haematol* and Visram A, et al. American Society of Hematology Annual Meeting, 2022). The clinical features associated with advanced disease and short duration of responses lead to a poor quality of life, significant caregiver burden and a shortened patient lifespan. Thus, this situation represents one of the most pressing unmet needs in Canada for patients with multiple myeloma.

5. Place in Therapy

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

Bispecific and CAR-T cell therapies are presently positioned to address the unmet need in the “triple-class exposed/refractory” myeloma patients. Like the recently endorsed product cilta-cel, the latest data for teclistamab are expected to exceed that of any previous standard of care regimen for this group of “triple-class refractory” patients. Teclistamab also addresses the myeloma in an entirely novel way, thus overcoming resistance mechanisms to the more traditional approved approaches. Currently, it would be used in sequence after the other lines of therapy described in Section 3. per the available information from CADTH

As there are very few options in patients with triple-class refractory disease, the issue of intolerance to other treatments or contraindications to other treatments is less relevant. Specifically, all other options that are currently available in this setting yield markedly inferior results.

As teclistamab will be used late in the current lines of myeloma treatment, i.e. after failure of multiple agents, it is not expected to impact the sequencing of agents earlier in the disease course, or lead to a major change in treatment algorithms prior to patients becoming “triple-class exposed/refractory”. However, given its impressive efficacy in terms of both a high response rate and durability of response, it is expected to lead to a major shift in the current treatment paradigm for those with advanced disease. It will provide an additional, more readily accessible T-cell redirecting therapy for patients refractory to the most commonly used agents. Availability of teclistamab will complement access to the recently endorsed cilta-cel T-cell platform, broadening access to such new therapeutic strategies, and ensuring that logistical bottlenecks do not become a barrier for delivery of these novel products to Canadian patients.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

The least suitable patients would include frail patient with poor functional and organ reserve. Patients receiving T-cell redirecting therapies should have the fitness to contend with the rigours of the initial treatment period, which include the risks of CRS and ICANS. Additionally, those with rapidly proliferating disease, ongoing infection, significant organ dysfunction and/or with pre-existing pancytopenia represent challenging clinical situations, although it should be noted that teclistamab does not require the lengthy preparation time inherent in the generation of CAR-T cells.

Conversely, patients with a good performance status, minimal or no comorbidities, relatively low tumor burden, adequate organ function and satisfactory blood counts are the most likely to have the best outcomes. It is, however, important to note that the rates of immune-related complications are lower with bispecific antibodies in general-making them more broadly applicable to patients and more amenable to patients with more comorbidities (be they disease- related or otherwise). Moreover, they represent an “off the shelf” treatment which can be administered quickly even in the face of rapidly proliferative myeloma. Chronological older age alone *per se* does not seem to be an exclusion factor. Overall, patients with poor disease-related prognostic factors, such as extramedullary myeloma and high-risk cytogenetics, do not fare significantly worse and should be eligible for teclistamab.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

Responses are based on the monoclonal protein markers in the serum and/or urine, bone marrow biopsy and, in some instances, by imaging studies (standardized International Myeloma Working Group Criteria (IMWG)). These parameters are aligned with those used in the clinical trials, which also included the emerging parameter of marrow minimal residual disease (MRD).

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. In myeloma, responses are generally assessed every 1-3 months depending on clinical stability and regimen used for therapy.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

Similar to more conventional myeloma therapies, teclistamab is presently given until disease progression. Treatment is continued based on ongoing efficacy, as measured above, and, additionally, long-term tolerability is required. Late effects that are of note include immune suppression and recurrent infections. While supportive care paradigms are emerging to minimize these complications, recurrent or life-threatening infections despite maximal supportive care may require a cessation of therapy despite disease control.

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

We suggest that teclistamab be administered and monitored by hematologists/oncologists who have the knowledge and expertise to manage the potential short- and long-term adverse events that can be associated its use. We also recommend administration of the initial dosing in centers with, or the commitment to develop, the necessary infrastructure, experience and supports to safely administer T-cell redirecting therapies, for example, clinical assessment tools for CRS/ICANS grading/treatment, ICU support, and ready tocilizumab availability.

6. Additional Information

Two other points are worth considering with respect to implementation:

1) Presently, the focus on number of lines of therapy--in addition to the actual classes of prior agents received--are both included in the indication. We feel this may be too restrictive, especially with the widespread use of triplet-containing regimens including both a PI and an IMID for frontline induction therapy pre-ASCT and the much earlier use of anti-CD38-containing regimens. In addition, some Canadian patients are already able to access a quadruplet induction regimen with an IMiD, PI and anti-CD38 antibody via clinical trials or private insurance, as such regimens represent the current standard of care for induction in the US and some other countries. Both the Canadian RWE as well as results published by others indicates the triple-class exposure/refractoriness, regardless of the numerical line of therapy, confers a poor outcome. The field of myeloma is moving away from the “lines of therapy” concept as a reliable measure of disease resistance, in order to avoid giving patients ineffective regimens to meet a target number of combinations. An important recent recommendation from other expert group has suggested that “refractoriness to drugs/drug classes is a more consistent/scientific definition of prior therapies as compared to prior lines” (Goel U, et al. *Blood Cancer J* 2023; 13:11).

   Therefore, we feel that the final indication for teclistamab should exclude the “requirement of 3 prior lines of therapy” and focus on the specific previous agents received. We would propose the following: **Teclistamab is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least three prior therapies, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression after the last therapy.**

2) One other consideration in developing the implementation strategy is to address usage of teclistamab in patients who have previously received anti-BCMA therapy. There is mounting evidence of efficacy in this population with phase 2 data maturing. Currently there are a number of anti-BCMA therapies that have been used in Canada. This includes bispecific antibodies as well as antibody drug conjugates accessed through either Health Canada SAPs or clinical trials.

As we have stated in previous submissions for other anti-BCMA approaches, Canada has led a large phase I/II trial with pomalidomide, belantamab mafodotin and dexamethasone (Trudel S, et al; ASH 2022) in which over 100 Canadian patients have been treated to date. Our experience with these agents indicates that there are clearly patients who have been exposed to prior anti-BCMA therapy—and responded well—but had the anti-BCMA agent discontinued for reasons other than disease progression and hence are not refractory. This is particularly true for the currently available agents in which issues such as ocular toxicity (in the case of belantamab mafodotin). With CAR-T therapy, the finite, single infusion approach leading to durable remissions without continuous therapy will result in a cohort of patients who remain anti-BCMA sensitive at relapse. In both cases, the disease recurrence is related to loss of the immune response through T-cell exhaustion of CAR-T depletion rather than loss of the BCMA target. Such patients would be expected to remain sensitive to future anti-BCMA approaches.

In general, there is an evolving body of literature for this group of patients (which will still reflect the minority of teclistamab usage for the foreseeable future). Cohort C from the MajesTEC1 trial specifically examined patients with prior anti-BCMA therapy. A 40% ORR response rate was noted with CRs achieved in approximately 20% of patients. At the time of the last analysis the median PFS of this cohort has not yet been reached indicating durable responses (Touzeau, C *et al* 2023, *HemaSphere* 2022;6: 85-86.)

Given that prior anti-BCMA exposure does not preclude responsiveness to subsequent anti-BCMA CART therapy, we would recommend that patients with prior anti-BCMA therapy who did not progress during it (i.e., non-refractory to anti-BCMA therapy other than anti-BCMA CAR-T) be allowed access to teclistamab.

7. Conflict of Interest Declarations

Declaration for Clinician 1

Name: Dr. Darrell White
Position: Hematologist, Dalhousie University and QEII Health Sciences Centre
Date: 08-09-2023

☒ 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.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
BMS		X		
Janssen			X	

Declaration for Clinician 2

Name: Dr. Alexander Keith Stewart
Position: Professor, Division of Hematology-Oncology Princess Margaret Cancer Centre
Date:08-09-2023

☒ 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.

Table 2: Conflict of Interest Declaration for Clinician 2

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Janssen			X	
Amgen		X		
Pfizer	X			
Sanofi	X			
GSK	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 3

Name: Dr. Stephen Parkin
Position: Hematologist, Clinical Assistant Professor
Date: 08-09-2023

☒ 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.

Table 3: Conflict of Interest Declaration for Clinician 3

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Janssen (speaker, consultancy fees)	X			
Add company name				
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 4

Name: Dr. Jason Hart

Position: Medical oncologist and hematologist, BC Cancer, Victoria
Date: 08-09-2023

☒ 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.

Table 4: Conflict of Interest Declaration for Clinician 4

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Nothing to declare				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 5

Name: Dr. Annette Hay
Position: Professor, Queen's University, Head, Division of Hematology, Kingston Health Sciences Centre
Date: 08-09-2023

☒ 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.

Table 5: Conflict of Interest Declaration for Clinician 5

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Roche				X
Merck				X
Seattle Genetics				X
Abbvie				X
Incyte				X
Janssen				X
Karyopharm				X

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 6

Name: Dr. Donna Reece

Position: Chief Medical Officer, CMRG
Date: 08-09-2023

☒ 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.

Table 6: Conflict of Interest Declaration for Clinician 6

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			X	
Janssen			X	
Amgen			X	
Sanofi	X			
GSK	X			
Takeda	X			

Declaration for Clinician 7

Name: Dr. Anthony Reiman
Position: Professor, Department of Oncology, Saint John Regional Hospital
Date: 08-09-2023

☒ 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.

Table 7: Conflict of Interest Declaration for Clinician 7

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 8

Name: Dr. Heather Sutherland
Position: Hematologist, Vancouver General Hospital
Date: 09-09--2023

☒ 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.

Table 8: Conflict of Interest Declaration for Clinician 8

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Forus	X			

Declaration for Clinician 9

Name: Dr. Hira Mian
Position: Assistant Professor
Date: 09-09-2023

☒ 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.

Table 9: Conflict of Interest Declaration for Clinician 9

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Takeda, Jansen, BMS, Sanofi, Amgen, GSK (advisory board fees)		X		
Jansen Research Funding				X
Add or remove rows as required				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 10

Name: Dr. Richard LeBlanc
Position: Hematologist and medical oncologist
Date: September 9th 2023

☒ **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.

Table 10: Conflict of Interest Declaration for Clinician 10

Company	Check appropriate dollar range*			
	$0 to $5,000	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Janssen – advisory boards and honoraria		X		
Pfizer – advisory board and honoraria		X		
BMS – advisory boards	X			
Amgen – advisory boards	X			
Sanofi – advisory boards	X			
FORUS Therapeutics – advisory boards	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 11

Name: Dr. Arleigh Mccurdy
Position: Hematologist, Oncologist
Date: 09-09-2023

☒ 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.

Table 11: Conflict of Interest Declaration for Clinician 11

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	X			
Takeda	X			
Amgen	X			
Janssen	X			
Sanofi	X			

Forus Therapeutics	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 12

Name: Dr. Christopher Venner
Position: Hematologist Lymphoma and Myeloma Program, BC Cancer Vancouver Centre
Date: 11-10-2022

☒ 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.

Table 12: Conflict of Interest Declaration for Clinician 12

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Celgene/BMS	X			
Takeda	X			
Janssen	X			
Amgen	X			
Sanofi	X			
GSK	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 13

Name: Dr. Jean Roy
Position: Full professor, Université de Montréal, hematologist, Maisonneuve-Rosemont Hospital
Date: 11-09-2023

☒ 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.

Table 13: Conflict of Interest Declaration for Clinician 13

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**

Nothing to declare				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 14

Name: Dr. Sita Bhella
Position: Hematologist, Princess Margaret Cancer Centre
Date: 11-09-2023

☒ 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.

Table 14: Conflict of Interest Declaration for Clinician 14

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Gilead	X			
Novartis	X			
Sanofi	X			
Amgen	X			
Celgene/Bristol Myers Squibb	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 15

Name: Dr. Victor Zepeda
Position: Hematologist, Oncologist
Date: 11-09-2023

☒ 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.

Table 15: Conflict of Interest Declaration for Clinician 15

Company	**Check appropriate dollar range***

	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Janssen		X		
BMS	X			
Takeda	X			
Amgen	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 16

Name: Dr. Sindu Kanjeekal
Position: Hematologist, Oncologist
Date: 11-09-2023

☒ 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.

Table 16: Conflict of Interest Declaration for Clinician 16

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Nothing to declare				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 17

Name: Dr. Kevin Song
Position: Hematologist, Vancouver General Hospital
Date: 11-09-2023

☒ 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.

Table 17: Conflict of Interest Declaration for Clinician 17

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Bristol Myers Squibb		X		

Janssen		X		
Amgen		X		

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 18

Name: Dr. Nizar A. Samad
Position: MD Hematology
Date: 14-09-2023

☒ 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.

Table 18: Conflict of Interest Declaration for Clinician 18

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Nothing to declare				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 19

Name: Dr. Sathish Gopalakrishnan
Position: Oncologist and Hematologist
Date: 14-09-2023

☒ 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.

Table 19: Conflict of Interest Declaration for Clinician 19

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Nothing to declare				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 20

Name: Dr. Rami Kotb
Position: Hematologist, Oncologist, Cancer Care Manitoba
Date: 14-09-2023

☒ 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.

Table 20: Conflict of Interest Declaration for Clinician 20

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
BMS, Amgen, JNJ		X		
Takeda	X			
Sanofi, Merck				X
Karyopharm				X

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 21

Name: Dr. Michael Pavic
Position: Hematologist
Date: 14-09-2023

☒ 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.

Table 21: Conflict of Interest Declaration for Clinician 21

	Check appropriate dollar range*			
Company	**$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				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 22

Name: Dr. Marc Lalancette
Position: Hematologist
Date: 14-09-2023

☒ 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.

Table 22: Conflict of Interest Declaration for Clinician 22

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Nothing to declare				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 23

Name: Dr. Suzanne Trudel
Position: Oncologist
Date: 14-09-2023

☒ 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.

Table 23: Conflict of Interest Declaration for Clinician 23

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Sanofi	X			
BMS			X	

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 24

Name: Dr. Nicole Laferriere
Position: Hematologist/ Chief of Oncology

Date: 14-09-2023

☒ 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.

Table 24: Conflict of Interest Declaration for Clinician 24

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Astra Zeneca, AMGEN Canada, ROCHE, Abbvie, Sanofi Canada, Lundbeck, Janssen, Celgene, Teva Pharm, Novartis, KiTE, AbbVie, Incyte	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 25

Name: Dr. Alfredo de la Torre
Position: Hematologist
Date: 14-09-2023

☒ 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.

Table 25: Conflict of Interest Declaration for Clinician 25

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Nothing to declare				

* Place an X in the appropriate dollar range cells for each company.