CADTH REIMBURSEMENT REVIEW

Patient and Clinician Group Input

ELRANATAMAB (Elrexfio)

(Pfizer Canada ULC)

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.

October 30, 2023

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

CADTH Reimbursement Review Patient Input

Name of Drug: elranatamab (ELREXFIO)

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.

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 the disease can enter periods of remission, but myeloma will ultimately always return, and require new treatment. Myeloma patients also become refractory to treatments, 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 patient and caregiver surveys regarding elranatamab, a BCMA targeted, t-cell engaging, bispecific antibody therapy for the treatment of relapsed refractory multiple myeloma. Both patient and caregiver surveys were available from September 26, 2023, to October 23, 2023, and were shared across Canada and internationally, via email and social media by Myeloma Canada. The Leukemia and Lymphoma Society of Canada also agreed to share our survey. Sixty-

seven complete responses to the patient 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. Thirty-two caregivers responded to the caregiver survey, 12 were removed from the data due to incomplete responses, and 7 due to ineligibility. 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. All patients (38) and caregivers (11) 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 (24**)** who would currently be eligible for treatment with elranatamab, herein referred to as Subset E. Respondents were from Alberta (2), British Columbia (5), New Brunswick (1), Manitoba (1), Ontario (7), Quebec (6), and 2 from outside of Canada (France). Of 24 Subset E respondents, 12 identified themselves as assigned male at birth (further referred to in this report as male'), and 12 as assigned female at birth (further referred to in this report as female'). 10 Subset E patients were in an urban area, 8 in a suburban area, and 6 were in a rural area. One Subset E patient was between '40–49' years of age, 5 were '50–59' years of age, 8 patients were between '60–69' years, 10 patients between '70–79' years.

2. Patients **(14)** who have received or are currently receiving treatment with elranatamab, herein referred to as Subset T. Respondents were from Alberta (5), British Columbia (1), Quebec (2), Ontario (5), Saskatchewan (1), and 8 respondents identified themselves as female, 6 as a male. Responding patients (14) were equally located in urban (5) and rural areas (5), with the additional 4 patients living in a suburban area. One Subset T patient was between the ages of '40–49', 3 patients between '50–59', 8 patients between '60–69' and 2 patients

between “70–79’ years of age.

3. Caregivers **(8)** of patients who would currently be eligible for treatment with elranatamab, herein referred to as Subset Ec. Of 8 respondents, two caregivers were from British Columbia, one from New Brunswick, 4 from Ontario and one from Quebec. Seven responding caregivers were located in a suburban area, and one was in an urban area. Four caregivers were female, three were male, and one preferred not to answer. One caregiver was ‘30–39’ years of age, one was ‘40–49’ years, two were between ‘50–59’, two were between ’60–69’, and two were between ’70–79’ years of age. Six responding caregivers were caring for a spouse/partner, and two indicated they were caring for a family member (i.e., parent, sibling, other relatives).

4. Caregivers (3) of people who have received or are currently receiving treatment with elranatamab, herein referred to as Subset Tc. Respondents **(3)** were from Alberta (1), British Columbia (1), and Ontario (1). All three were located in an urban area. Two caregivers identified themselves as females, and one as male. Two responding caregivers indicated they were caring for a spouse/partner, and one indicated they were caring for a family member (i.e., parent, sibling, other relatives). One Subset Tc caregiver was between the ages of ‘40–49’ and two were between’60–69’.

3. Disease Experience

All patients were asked, “*How do symptoms associated with myeloma impact or limit your day-to-day activities and quality of life. Please rate on a scale of 1–5 where 1 is “No impact” and 5 is ‘Extreme impact.’*”; by weighted average rating, responding patients (38) indicated that their ability to work (3.3) was most significantly impacted, followed by ability to travel (3.1), and to exercise (3.0).

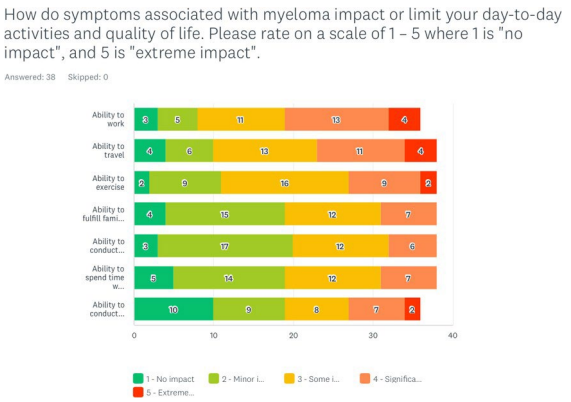


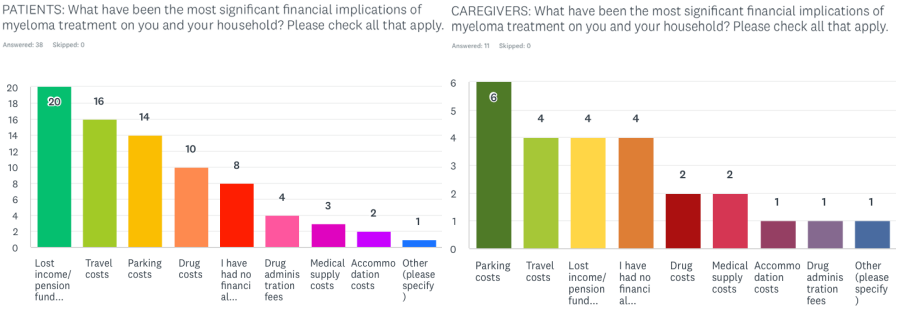
Figure 1—Impact of myeloma on everyday life and activities (patients; 38)

All patients (38) and caregivers (11) were asked how often they, or the person they care for, visit their hospital or cancer centre for treatment. Patient respondents selected, ‘once a month’ (28.9%; 11) and ‘once a week’ (28.9%; 11) with equal frequency, followed by every two weeks (26.3%; 10). Four respondents chose ‘Other’ (twice a week, once a month, twice a week for two weeks followed by once every two weeks, once a week) one chose ‘N/A’, and one chose 'Never'. Caregivers most frequently chose ‘Once a week’ (5), followed by ‘Once a month’ (3), and three chose ‘Other’ (two indicated the person they care for takes treatment at home, and one said, ‘*Sometimes twice a week, often once a week’*.

When all patients were asked, “*How long does it take you to make a round-trip (to and from) the hospital/cancer centre where you receive treatment?”* most respondents, 50.0% (19), indicated “Less than 1 hour one way”,10 respondents chose “1–2 hours (30 min—1h one way)”, 6 chose “3–4 hours (1h—2hrs one way)”, one responded “5 hours or more (2.5 hours or more one way)”, and two final respondents chose ‘Other’ but their comments indicted they would fall under “Less than 1 hour one way” and “3–4

hours (1–2 hrs one way)”. When caregivers (11) were posed the same question, 7 chose “Less than 1 hour one way”, 2 respondents chose “1–2 hours (30 min—1h one way)”, 2 chose “3–4 hours (1h—2hrs one way)”.

When patients (38) and caregivers (11) 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"*; patient respondents indicated 'lost income/pension funds due to absence from work, disability, or early retirement' 52.6% (20), and travel costs 42.1% (16) were the most significant financial implications of



myeloma treatment. Followed by parking costs 36.8% (14) and drug costs 26.3% (10). For caregivers (11), 'parking costs' (6), 'travel costs' (4), and 'lost income/pension funds due to absence from work, disability, or early retirement' (4) were the most significant implications.

Figure 2(A)—Financial implications of myeloma treatment (patients; 38); figure 2(B)—Financial implications of myeloma treatment (caregivers; 11)

All patients were asked, "*Has living with multiple 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 (38) felt that that "Interruption of life goals/accomplishments (career, retirement, etc.) (3.7; 38) had the greatest impact on quality of life, and it was the option most frequently rated '5 — Severe impact'. Patients also indicated 'Loss of sexual desire' (3.3; 38) and 'Anxiety/worry' (3.1; 38) to have more significant impacts on quality of life, with all other options receiving a weighted average rating of 2. Caregivers (11) similarly felt that caring for someone with myeloma had the most impact on 'Interruption of life goals/accomplishments (career, retirement, etc.)' (4.1; 10), followed by 'anxiety/worry' (4.0; 11), and 'loss of sexual desire' (3.3;11), all but two options listed received a weighted average rating of 3 — Minor impact' or above.

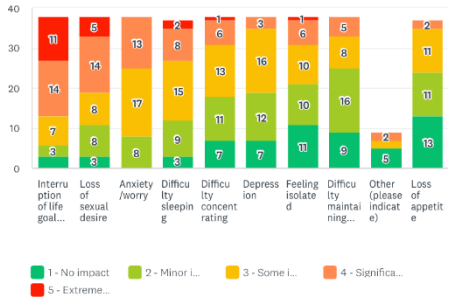
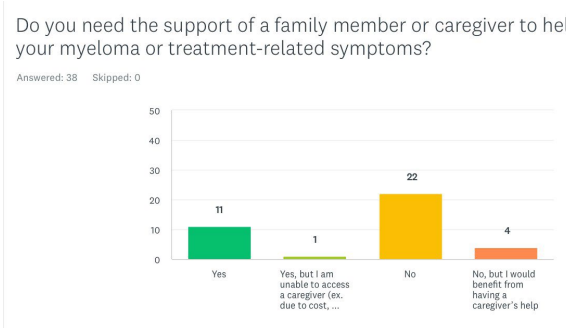


Figure 3—Psychological/social difficulties caused by living with myeloma, and their impact on quality of life. (Patients; 38)

When patients (38) were asked, "*Do you need the support of a caregiver or family member to help you manage your myeloma or your treatment-related symptoms?"* 57.8% (22) responded 'No' they did not need a caregiver, 29.0% (11) chose 'Yes' they do require a



caregiver, 4 patients answered 'No, but I would benefit from a caregiver's help', and 1 chose 'Yes but I am unable to access the help I need'.

Figure 4—Need or desire for a caregiver (all patients; 38)

All patients (38) and caregivers (11) were asked to identify the factors they consider to be most important to (any) myeloma treatment. Respondents (37, 11) 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:

- *"Results. I have had great results from elranatamab when all previous chemotherapy have not worked"*
- "*Ability to still function on my day-to-day life, ability to focus and exercise. Ideally, I would prefer less frequent visits to the hospital [currently going once a week, three weeks on, one week off, which is very limiting."*

- *"Good communication with Doctors and Nurses to allow understanding and gain knowledge of side effects and options available. And why some treatments are not recommended due to possible issues."*
- *"Effectiveness of treatment, infections, quality of life, side effects, cost."*
- *"My physical and mental well-being. I want to be able to continue to write (I am a published author) and I want to be able to do aerobic and weight training exercises."*
- *"Patient's wellbeing"*
- *"Efficacy against the cancer paired with quality of life"*

4. Experiences With Currently Available Treatments

All patients (38) 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' (4.4) was the most important aspect to control and was rated '5—extremely important' most frequently (33; 55%). Patients also felt mobility (4.2), kidney problems (4.1), were slightly more important to control. After rounding, all options listed other than fatigue (3.9) received an average rating of '4—very important'. Patients also left comments (6) that mentioned gastrointestinal issues (nausea), and graft versus host disease.

All patients (38) and caregivers (11) were asked, "*How many prior lines of therapy have you/the person you care for received?"* 13 patients and 3 caregiver respondents indicated 3 lines of therapy, 6 patients and 5 caregivers responded '4 lines of therapy', 6 patients and one caregiver chose '1 line of therapy'; 5 patients and 2 caregiver respondents indicated they or the person they care for had received '5 lines of therapy or more'. In total, respondents most frequently indicated 3 lines of therapy (13), followed by 4 lines of therapy (11), while 7 respondents each chose 1, 2, and 5+ lines of therapy.

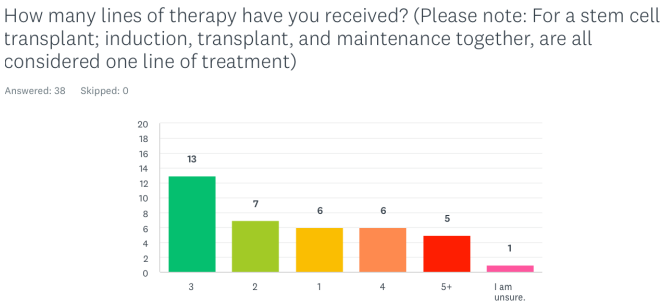


Figure 5—Number of lines of therapy received (patients, 24)

When asked, "*Have you/the person you care for, received an autologous stem-cell transplant (ASCT) to treat your myeloma?"* 34 of 37 patient respondents and 8 of 11 caregiver respondents said "Yes", while 2 patients and 3 caregivers indicated they/the person they care for was not eligible for an ASCT. One additional patient was preparing to have an ASCT soon.

Patients (38) and caregivers (11) were asked if they or the person they care for had received any BCMA- targeted therapy. Twelve patients chose 'Yes', 21 chose 'No', and 5 indicated they were not sure. Two caregivers chose 'Yes', 6 chose 'No', and 2 indicated they were not sure.

5. Improved Outcomes

Subset E (24) 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'*.", 52.2% (12) of 23 respondents felt it was 5 — Extremely important, while 20.1% (6) answered '4 — Very important', and 21.7% (5) chose 3 — Somewhat important. When asked, "*When considering a myeloma treatment for yourself, how important is it for the treatment to extend your life? Rate on a scale of 1 — 5, 1 is 'Not important' and 5 is 'Extremely important'",* 73.9% (17) indicated it was '5 — Extremely important', and 17.4% (4) chose '4 — Very
important', and 8.7% (2) chose '3 — Somewhat important'.

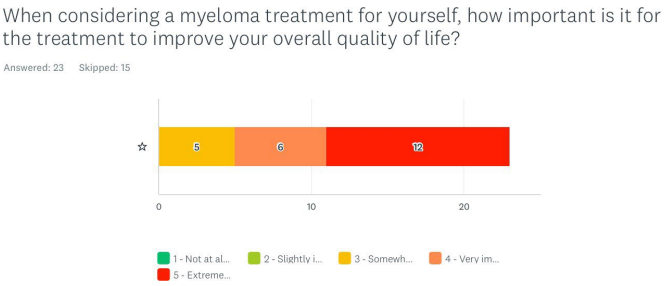


Figure 6— A) Desirability of extended life

Subsets E (24) and Ec (8) were presented information about common side effects of elranatamab: 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 elranatamab, patients may not drive for 48 hours following administration of the step-up doses and may be admitted to the hospital overnight for monitoring.

Subset E was asked, "*Amongst the most common side effects in patients who receive elranatamab, 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 perceived pneumonia (2.4) ICANS (2.5), upper respiratory tract infections (2.5) cytokine release syndrome (2.6), and infections (2.9) to be the least tolerable side effects, followed by peripheral neuropathy, other infections and COVID-19, with all three receiving a weighted average rating of 2.7.

Subset Ec (8) was asked, *"Amongst the most common and/or serious side effects in patients who receive elranatamab, do you expect any to require increased care/assistance from you? Please check all that apply."* Respondents most frequently indicated that 'Neutropenia' (6) and 'Upper respiratory tract infections' (6) would require increased care.

When Subset E (24) was asked, "*Compared to other treatment options available to you, how worrisome is the overall side effect profile for elranatamab? 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' (62.5%; 15), followed by '2 — Slightly worrisome' (20.8%; 5), '4 — Significantly worrisome'

(12.5%; 3) and ‘1—Not at all worrisome’ (4.7%; 1). Responding to the same question, 50% (4) of Subset Ec caregivers (8) chose ‘3 — Somewhat worrisome’, 3 chose ‘2 — Slightly worrisome’, while one chose ‘4

— Significantly worrisome’.

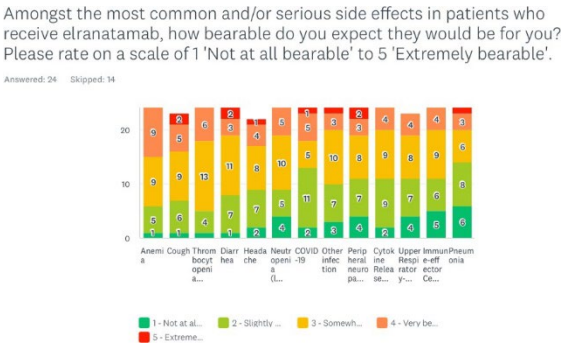


Figure 7—Perception of elranatamab side effects (Subset E; 24)

Subsets E and Ec were asked, “*Just over half of patients (57%) in the clinical trial experienced cytokine release syndrome (CRS) but for all patients it was either Grade 1 or 2 (i.e. less severe). As well, all cases of CRS but one, occurred following the first three doses, with 46% occurring after the first dose of elranatamab, and each subsequent dose corresponding to fewer cases of CRS. Zero patients experienced CRS of Grade 3 severity or higher, and zero patients died or discontinued treatment due to CRS. Does knowing this information impact your level of concern/worry about experiencing/the person you care for experiencing CRS due to elranatamab treatment?”* Patient respondents (24) most frequently chose ‘Yes, I am less worried’ (62.5%; 15), followed by ‘No, my level of concern/worry remains the same’ (20.8%; 5), and ‘Yes, I am more worried’ (16.7%; 4). Subset Ec caregivers (8) most often chose “No, my level of concern/worry remains the same’ (3) followed by ‘Yes, I am more worried’ (2) and ‘Yes, I am less worried’ (2), one caregiver indicated they were unsure.

Subsets E and Ec were posed the question, “*Does traveling to and from your hospital/cancer centre for treatment usually involve you driving*?” to which 16 of 24 patient respondents said “Yes” and 8 chose “No”. As a follow-up question, Subset E was asked “*If yes, do you have a caregiver or family member who could drive you to appointments if*

needed?" 15 responding patients chose 'Yes', two patients chose 'No', and two patients chose 'I am unsure'. Subset Ec (8) was similarly asked if they usually drive the person they care for to treatment, 7 responding caregivers chose 'Yes', 1 chose 'No', and 4 subsequently indicated 'Yes' they would be able to drive the person they care for to treatment when needed.

The dosing schedule was presented and explained to Subset E patients, after which they were asked, '*Compared to other treatment options available to you, would the dosing schedule described above (weekly injections for at least 24 weeks, with the possibility of then switching to every two weeks) have an impact on your quality of life?"* Respondents (24) most often chose "Negative impact" (11), followed by "Positive Impact" (7) and "No impact" (6). Comments provided indicated it would limit patients' ability to travel, and/or require that they relocate to an urban area (near their cancer centre) for the duration of treatment.

Subset E (24) was asked, "*If you were required to stay in the hospital for 24–48 hours following one or both step-up doses, do you expect this would cause any significant issues for you? (Ex. with transportation, time away from work/family, etc.) If yes, please explain."* All but one patient respondent (95.8%; 23) chose 'No', and the one patient who selected 'Yes' commented '*Would rather not have a hospital stay'.* When posed the same question, Subset Ec caregivers (8) largely chose 'No' (7) while 1 respondent chose 'Yes' providing the comment, *"Patient mental and physical comfort".*

Subset E was asked, "*If you were eligible to receive elranatamab treatment for your myeloma, what do you believe the advantages and/or disadvantages would be for you?*" Respondents (24) 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: 10, No change: 5, Decreased: 1, I'm not sure: 8) Control of myeloma and its symptoms' (Increased: 11, No change: 1, Decreased: 2, I'm not sure: 10), Frequency of trips to the hospital or cancer centre for treatment (Increased: 17, No change: 4, Decreased: 2, I'm not sure: 1), Tolerability of the treatment's mode of administration (Increased: 6, No change: 11, Decreased: 2, I'm not sure: 5), Quality of life (Increased: 8, No change: 4, Decreased: 4, I'm not sure: 9). Many patients were unsure of the impact elranatamab would have on all factors, while there was the greatest consensus on elranatamab requiring more frequent trips to the hospital (17).

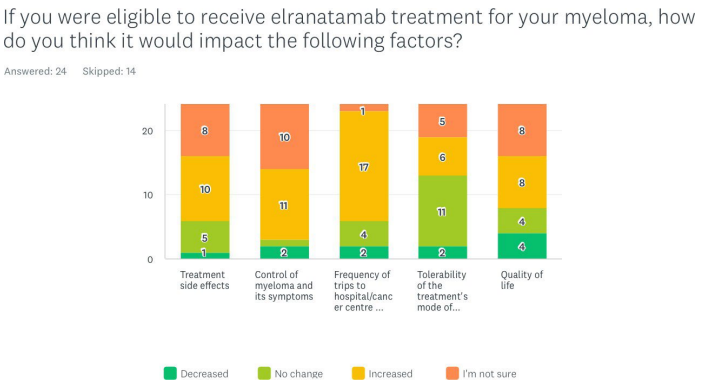


Figure 8—Perceived advantages/disadvantages of treatment with elranatamab; Subset E (patients; 24)

To the question, "*With what you know today, would you consider elranatamab as an option for your next treatment? (Presuming you are eligible, and your doctor agrees).*" 54.2% (13) of Subset E patient respondents (24) indicated 'Yes', while 29.32 (6) said they were unsure, and 4 additional patients
indicated they would need more information to decide and indicated they would need to hear their oncologist's perspective on the treatment.

When given the opportunity to share any further thoughts about potential treatment with elranatamab, 10 Subset E patients left comments, of which many described the importance of speaking with their hematologist/oncologist about elranatamab, as well as expressing hope that this treatment will be available to them when they relapse, and their desire to see updated data on survival/duration of response with elranatamab and how it compares to other treatments. Some comments are as follows:

- *"I would like for it to be available at a hospital near to where I live. In Gatineau Quebec"*
- *"As my paraprotein numbers are beginning to increase while being treated with daratumamab, I am relieved to know there will be other therapies available. Thank you."*
- *"I'm concerned with the low response rate and the low time to relapse in the trials so far."*
- *"Son efficacité (et implications générales) vs les autres traitements, par le daratumumab."*
- *"Durée moyenne d'efficacité de ce traitement ? "*

Subset Ec caregivers were similarly asked if they had any additional comments about the person they care for potentially receiving treatment with elranantamab. Three caregivers provided comments, indicating they were concerned that the person they care for may not be in good enough health to be eligible for elranatamab. For example:

- *"Eligibility due to age and current health"*
- *"Mobility issues post surgery hip replacement surgery new cancer diagnosis coupled with pre existing MM diagnosis."*

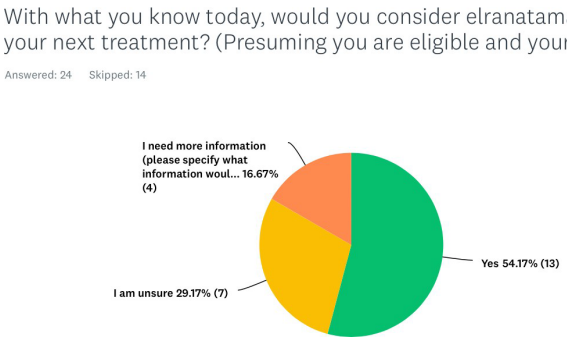


Figure 9—Would you consider elranatamab for your next treatment? (Subset E patients; 24)

6. Experience With Drug Under Review

As noted previously, there were 14 patients with elranatamab experience who responded to the survey, and 3 caregivers, and they are referred to herein as Subset T and Tc respectively. When asked to " … *indicate when you began treatment with elranatamab*.", 3 Subset T patients (14) chose "Less than three months ago", 3 chose "Over a year ago", 4 chose "Between 3–6 months ago", 4 chose "Between 6–12 months ago" and 2 respondents chose "Other" and their comments indicated they could be classified as "Over a year ago" and "Less than three months ago". When asked if they had relapsed since receiving elranatamab, 12 Subset T respondents (14) chose 'No, I have not yet relapsed and am still receiving elranatamab', one chose 'Yes, I have relapsed and am no longer receiving elranatamab' and one chose 'Other' indicating it was too soon to tell. Almost all Subset T respondents (13) are still currently undergoing treatment with elranatamab. The one patient who has relapsed and no longer receives elranatamab indicated they relapsed after 4–6 months of treatment. One Subset Tc caregiver (3) indicated that the person they

care for had relapsed within 1–3 months of starting elranatamab, one chose “No, they have not relapsed, and are still receiving elranatamab”, and one was unsure.

When asked if they were “ *… receiving elranatamab alone, or in combination with another drug? If applicable, please indicate the drug you were/are receiving alongside elranatamab.”,* 10 Subset T respondents (14) selected ‘Elranatamab alone (as monotherapy)’, and 4 chose ‘In combination with another drug’ and provided the drug name. Of these 4 patients, two are receiving daratumumab alongside elranatamab, and two patients are receiving dexamethasone in combination with elranatamab. Two Subset Tc caregivers (3) indicated that the person they care for was receiving elranatmab alone, and one was unsure.

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.*” All 14 Subset T respondents chose ‘Yes’ and indicated the length of their stay. The amount of time patients spent in-hospital ranged from 4 nights to 2 weeks with the most frequently reported stay length falling between 4 and 7 nights. Of three responding Subset Tc caregivers, 2 chose “Yes” the person they care for had been admitted to the hospital (4 and 10 nights), and one chose “No”. [All responses: 4 nights (4), 5 nights (4), 6 nights (1); 7 nights (3); 10 nights
(2), 2 weeks/14 nights (1)].

When asked, “*How often do you visit a hospital/ cancer centre for elranatamab treatment since the step- up dosing period ended?*”, 7 Subset T respondents (14) chose ‘Once a week’, 5 chose ‘every two weeks’ and, 1 patient indicated they were still in the step-up dosing period and one chose ‘other’ and commented they had recently shifted to every 4 weeks from every 2 weeks. Two Subset Tc caregivers chose ‘Once a week’ and one indicated the person they care for is no longer receiving elranatamab.

Subset T (14) was asked, ‘*Which of the most frequent elranatamab side effects listed below have you 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, 14 responding patients rated

'Cough' (3.0) as the least bearable side effect, followed by 'Cytokine Release Syndrome' (3.2), 'Neutropenia' (3.2), and 'Upper Respiratory Tract Infections' (3.3). Similarly, the median response to all other listed side effects was 4—Very bearable or higher. One patient left the following comment "*Significant burning of the skin on my face, chest, back and groin areas. Muscle and bone pain, primarily in the legs. Fatigue. Oral Thrush. Muscle atrophy in my legs, resulting in significant walking, mobility and balance issues. Rashes on my hands and feet, with corresponding peeling of the skin*."

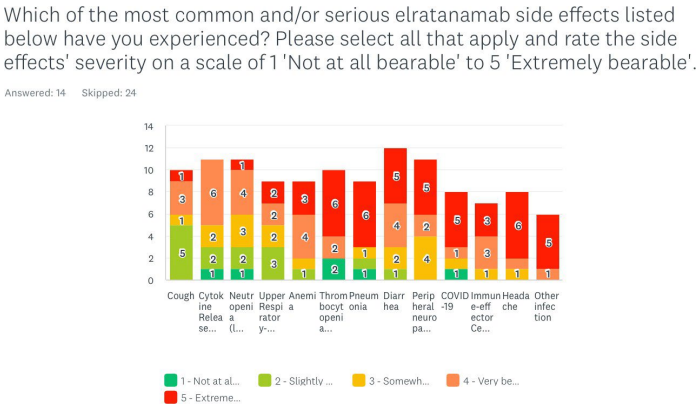


Figure 10—Experience of elranatamab side effects (Subset T patients; 14)

When asked, "*Compared to how your previous treatments were administered, did the mode of administration by which you received elranatamab 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 (14) most frequently selected 1—No impact (7), 2 patients chose "2—A little impact", 3 patients selected "3—some impact", one patient chose "4—significant impact" and one patient chose "5—severe impact".

Responding to the question, "*How effective was the supportive care you received in managing your side effects from elranatamab 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 (14) chose "5 — extremely effective', 6 patients chose '4 — Significantly effective', 3 chose '3 — Somewhat effective', while one patient chose 2 — Sightly effective' and none chose

‘not at all effective’. Responding to the same question, two Subset Tc caregivers chose “4—significantly effective” and one chose “3—somewhat effective”.

Subset T respondents (14) were asked, “*Compared to past treatments you received, do you think elranatamab 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: 6, No change: 4, Decreased: 3, Too soon to tell: 1) Control of

myeloma and its symptoms (Increased: 8, No change: 0, Decreased: 2, Too soon to tell: 4); Frequency of trips to the hospital or cancer centre for treatment (Increased: 7, No change: 5, Decreased: 1, Too soon to tell: 1); Tolerability of the treatment’s mode of administration (Increased: 5, No change: 8, Decreased: 1, Too soon to tell: 0); and Quality of life (Increased: 8, No change: 3, Decreased: 2, Too soon to tell: 1).

Following the instructions “*Please answer each of the following questions on your overall perception of treatment with elranatamab, by rating them on a scale of 1–5, where 1 is Not at all and 5 is Completely”",* Subset T patients (14) responded to the questions:

—“*Did elranatamab treatment improve your overall quality of life?*” (Completely: 3; Mostly: 3, Somewhat: 1; Slightly: 1; Not at all: 2; Too soon to tell: 4).

—“*Were the overall side-effects you experienced while receiving elranatamab manageable?* (Completely: 5, Mostly: 5, Somewhat: 2; Slightly: 1; Too soon to tell: 1)

—*Was elranatamab effective in controlling your myeloma?* (Completely: 8, Mostly: 3, Somewhat: 1; Too soon to tell: 2),

—“*Did elranatamab meet your expectations in treating your myeloma?*” (Completely: 8, Mostly: 2, Slightly: 1; Too soon to tell: 3).

Comments (8) provided by patients were predominantly positive (6), some comments of note were as follows:

- "*I say completely because I had gone through available treatments prior to this trial. I was going downhill fast. The effects of this treatment were immediate and positive.!"*

- *"After the first month of treatment they could already see improvement in my bloodwork. After 2 months my bloodwork had improved so much. I am going to the hospital once a week now but they are going to try me at every 2 weeks and watch to make sure it stays under control. My Oncologist ordered a bone marrow aspiration about a month ago. I have my monthly follow-up appointment with the Oncologist next week to find out the results. it was a test to see what was happening at the molecular level. unofficially I have heard they could not detect Myeloma cells."*

- *"My treatment program has been effective in controlling myeloma, however, the number and severity of side effects during the first three cycles has been particularly difficult and had a significant detrimental impact on my quality of life."*
- "*Elranatamab only showed a minor benefit in controlling my myeloma for a couple of months. Concurrent to this, my red blood cells, neutrophils and platelets all dropped to dangerously low levels."*

- *"In combination with Daratumumab, Elranatamab has been extremely effective for me."*

- *"First treatment since SCT that has given me a complete response."*

Subsets T (14) and Tc (3) were asked to indicate how they were or are accessing elranatamab, 11 patients indicated through a clinical trial (ongoing) 1 patient chose through a clinical trial (complete), and 1 patient selected through compassionate access, and 1

patient was unsure. 2 caregivers indicated through a clinical trial (ongoing) and 1 chose ‘through compassionate access’.

Finally, when asked if there was anything else they would like to share about their experience with elranatamab, 8 Subset T patients provided comments regarding their experience, relevant comments are as follows:

- “*It has been very successful for me. I am so thankful for the drug and how quickly it worked. I feel like it is a miracle. I wish I could thank the people who developed the drug. I hope the results will last and hope moving to every 2 weeks will keep the Myeloma under control. Thank you for the opportunity to provide feedback.*”

- "*In discussions with my treatment team, I have experienced a number of side effects that are very different from other trial patients. I would have very second thoughts about participating in the trial if I had known about the effect that these side effects would have on my quality of life currently and into the future. That being said, I have had seven previous therapies over the past eight years and I am running out of alternatives to control my myeloma. Elranatamab and another phase 1 trial were provided as treatment options and I selected Elranatamab as there was a known list of potential side effects based upon the previous phase 1 trial.*"

- *“I am grateful this treatment is available.”*

- “*It is difficult to know the cause (Elranatamab, Daratumumab, or the combination of the two) but I had extreme fatigue for months. My physicians couldn’t pinpoint the cause, and I certainly wouldn’t care to venture a guess, but it was a side effect of my treatment early on, then it went away and reappeared after about 6 or 7 weeks. Currently I do not suffer from the same extreme fatigue. I thought I should mention it just in case it is related and/or other patients report this*

also."

- "*I'm very grateful to receive this treatment. I had a wonderful summer on my "bonus time". I'm not sure how long this will work for me but I'm making the most of this time."*

Subset Tc caregivers were similarly asked if they had any further comments to share, 2 of 3 respondents provided the following responses:

- *"Of all the treatments this has been the easiest for coping with side effects. The treatment has been effective for 6 months with no signs of waning … she has only had 1 infection that being a cough that has lasted for 3 weeks'*

- *'Hard for me to comment on side effects as this drug didn't work at all for my husband.'*

7. Anything Else?

As the therapeutic landscape for myeloma is ever evolving, and treatment regimens that combine drugs from different therapeutic classes are more commonly used, more patients will be triple class exposed by their first or second line of therapy. In our survey data, 7 patients who are triple-class exposed and thus would be eligible for elranatamab indicated they were on their first (3) or second (4) line of therapy, and 7 patients indicated they were on their second line of therapy. Similarly, elranatamab would be one of few currently available options outside a clinical trial for patients who have previously received anti-BCMA targeted therapies. It is notable that, if approved for the manufacturer submitted indication, elranatamab could fulfill an unmet need for these subpopulations of patients.

Subset E patients (24) 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?"* 15 patients respondents chose 'Yes', 2 chose 'Yes, but I'm not sure what they are', 5 respondents chose 'No', and two indicated they were unsure. When the 17 patients with previous awareness were asked where they learned of BCMA-targeted T-cell engaging therapies, 10 respondents chose 'Through my own research', 8 chose 'Through Myeloma Canada,' 5 chose 'Through my support group/other people with myeloma', 8 chose 'Through my oncologist/care team',

and 3 ‘Through another organization’. Subset E was asked, “*Have you heard of B-cell maturation antigen (BCMA)-targeted bi- specific antibodies to treat myeloma? (Ex. Elranatamb, Teclistamab)”,* 14 respondents chose ‘Yes’ while 1 chose ‘Yes, but I’m not sure what they are’, 6 chose ‘No’, and 3 were unsure. When asked where they learned about BCMA-targeted bispecific antibodies, 9 respondents chose ‘Through Myeloma Canada’, 10 chose ‘Through my own research’, 9 respondents chose ‘Through my oncologist/care team’, 7 indicated ‘Through my support group/other people with myeloma’ while the final 3 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* 12 of 24 respondents correctly identified the answer was ‘all of the above’, and 12 respondents gave a partially correct answer. Overall, it appears most surveyed patients who would be eligible for elranatamab have at least some knowledge of anti-BCMA targeted t-cell engaging bispecific antibodies (like elranatamab) 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 to this effect are as follows:

- *“I have been doing treatment for 19 yrs and am aware that must continue with treatment in order to keep my myeloma in remission”;*

- *“I have learned to live with MM and consider it a chronic disease and not necessarily (praise be to God) a terminal illness. I am anxious to learn when car-T cell therapy will be approved in Canada for the treatment of MM. It has been described to me by one of my physicians as 'close to a complete cure' for MM. Thank you and kind regards.”*

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 around the same time of year, made available for a similar length of time, and of 91 patient responses received, 14 were from Canadians with elranatamab experience. This is indicative of the comparative ease with which elranatamab 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, and equally from rural and urban areas. Overall, the data (though limited) show there is already relatively widespread uptake of elranatamab by Canadian doctors treating myeloma, though special consideration must be given to rural/remote patients, ensuring there is equal access to elranatamab *within* provinces, as well as across provinces.

Finally, when considered together, comments from patients currently receiving elranatamab were largely 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, though two patients described significant difficulty with side effects. (See original comments in Treatment Under Review section).

Clinician Input

CADTH Project Number: PC0315-000
Generic Drug Name (Brand Name): Elranatamab (TBC)
Indication: For the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 3 classes of prior therapies, including a proteasome inhibitor (PI), an immunomodulatory agent, and an anti-CD38 monoclonal antibody
Name of Clinician Group: Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Author of Submission: Dr. Tom Kouroukis, Dr. Jordan Herst, Dr. Selay Lam, Dr. Lee Mozessohn, Dr. Pierre Villeneuve, Dr. Joanna Graczyk, Dr. Guillaume Richard-Carpentier

1. About Your Clinician Group

OH-CCO's Cancer 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

Information was gathered via videoconferencing.

3. Current Treatments and Treatment Goals

Current treatments include Pd, Kd, SVd, chemotherapy, CAR-T (not yet funded), and clinical trials.

Goals are to prolong life, 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.

With elranatamab, there is 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?

Another option for triple class exposed patients, most likely to be used in third and fourth line.

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 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 as well as 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, with availability of tocilizumab. There may be 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 a 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 each clinician 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, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date: 21-09-2023

☒ **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

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. Jordan Herst
Position: Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date: 21-09-2023

☒ 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**
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 3

Name: Dr. Selay Lam

Position: Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date: 21-09-2023

☒ 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

	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 4

Name: Dr. Lee Mozessohn
Position: Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date: 21-09-2023

☒ 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**
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 5

Name: Dr. Pierre Villeneuve

Position: Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date: 21-09-2023

☒ 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**
Add company name				

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

Declaration for Clinician 6

Name: Dr. Joanna Graczyk
Position: Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date: 21-09-2023

☒ 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 6

	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				

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

Declaration for Clinician 7

Name: Dr. Guillaume Richard-Carpentier
Position: Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date: 21-09-2023

☒ 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 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
Pfizer	X			
Add company name				

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

CADTH Project Number: PC0315-000
Generic Drug Name (Brand Name):Elranatamab
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

- Our view of the current Canadian therapeutic space within which elranatamab would be used is similar to the recent feedback submitted for both the cilta-cel and teclistamab indications.
- 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 “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 when funded), which represents a high-priority for virtually all patients. Until recently, the only funded antibody has been daratumumab and, in the relapsed setting, only for patients relapsing after 1-3 prior lines of therapy and in combination with either bortezomib or lenalidomide. Thus, prior to the funding of frontline daratumumab combinations in TI patients, the majority of patients receive daratumumab and dexamethasone combined with bortezomib (DVd) as

second-line therapy. The minority of patients who did not progress on first-line therapy with a lenalidomide-containing regimen have been preferentially treated with DRd.

- Several relevant novel 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). (The availability of IsaPd and IsaKd has allowed patients who "missed" the opportunity to receive an anti-CD38 antibody as part of second-line therapy to access it as part of third-line treatment, as discussed below.)
- 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, which 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 consists of 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. It is important to note that, given the widespread use of anti-CD38 containing regimens early in treatment along with early usage of PIs and IMIDs, most patients will be triple class-exposed--if not refractory--by the end of their second line of treatment. This is earlier than the proposed 3-prior line indication for elranatamab as well as the previously submitted teclistamab and cilta-cel. Canadian hematologists are concerned about the anticipated need to offer unnecessary/ineffective therapy in triple class-exposed/refractory patients simply to allow give another “line of therapy” and qualify for enranatamab or other novel immunotherapeutics.

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. Similar to the recently endorsed product cilta-cel and recently submitted product teclistamab, the latest data for elranatamab are expected to exceed that of any previous standard of care regimen for this group of “triple class-exposed/refractory” patients. Bispecifics such as elranatamab also addresses 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.

Since, based on the proposed indication, elranatamab will be used late in the current lines of myeloma treatment (i.e., after failure of multiple agents), its introduction 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 elranatamab will complement access to the recently endorsed the 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. It is expected to fill a similar void as would teclistamab if both were to be made available.

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 reserve 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 elranatamab 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 elranatamab.

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, elranatamab 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]?

Similar to the previous feedback submitted for teclistamab, we suggest that elranatamab 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. This feature has been present on the previous submissions for cilta-cell and teclistamab. We feel this is 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 also the much earlier use of anti-CD38-containing regimens. As noted above, most recently patients will be triple class-refractory/exposed after 2 lines of treatment. 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, with little difference in these two patient groups.. 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 established in a previous era of myeloma therapy. 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 elranatamab should exclude the "requirement of 3 prior lines of therapy" and focus on the specific previous agents received. We would propose the following: **Elranatamab 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 elranatamab 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 patients eligible for anti-BCMA agents. for the foreseeable future). For example, Cohort C from the MajesTEC1 trial (using the other approved anti-BCMA antibody teclistamab) 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 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) be allowed access to enranalamab.

7. Conflict of Interest Declarations

Declaration for Clinician 1

Name: Dr. Anthony Reiman
Position: Professor, Department of Oncology, Saint John Regional Hospital
Date: 25-10-2023

☒ 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 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
Nothing to Declare				

Declaration for Clinician 2

Name: Aljama Mohammed
Position: Hematologist, Oncologist
Date: 25-10-2023

☒ 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		
Pfizer	X			
Beigene	X			
Sanofi	X			
Forus	X			

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

Declaration for Clinician 3

Name: Stephen Parkin
Position: Hematologist, Clinical Assistant Professor
Date: 25-10-2023

☒ 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. Darrell White
Position: Hematologist, Dalhousie University and QEII Health Sciences Centre
Date: 29-10-2023

☒ 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

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		X		
Janssen			X	

Declaration for Clinician 5

Name: Dr. Alexander Keith Stewart
Position: Professor, Division of Hematology-Oncology Princess Margaret Cancer Centre
Date:29-10-2023

☒ 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**
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 6

Name: Dr. Annette Hay
Position: Professor, Queen's University, Head, Division of Hematology, Kingston Health Sciences Centre
Date: 29-10-2023

☒ 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

	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 7

Name: Dr. Donna Reece
Position: Chief Medical Officer, CMRG
Date: 30-10-2023

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

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

Declaration for Clinician 8

Name: Dr. Christopher Venner
Position: Hematologist Lymphoma and Myeloma Program, BC Cancer Vancouver Centre
Date: 30-10-2023

☒ 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

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	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 9

Name: Dr. Sathish Gopalakrishnan
Position: Oncologist and Hematologist
Date: 30-10-2023

☒ 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**
Nothing to declare				

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

Declaration for Clinician 10

Name: Dr. Rami Kotb
Position: Hematologist, Oncologist, Cancer Care Manitoba
Date: 30-10-2023

☒ 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
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 11

Name: Dr. Michael Pavic
Position: Hematologist
Date: 30-10-2023

☒ 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
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 12

Name: Dr. Jason Hart
Position: Medical oncologist and hematologist, BC Cancer, Victoria
Date: 30-10-2023

☒ 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 12: Conflict of Interest Declaration for Clinician 12

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				

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

Declaration for Clinician 13

Name: Dr. Nicole Laferriere
Position: Hematologist/ Chief of Oncology
Date: 29-10-2023

☒ 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

Company	Check appropriate dollar range*			
	$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 14

Name: Dr. Julie Stakiw
Position: Oncologist
Date: 30-10-2023

☒ 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

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

Declaration for Clinician 15

Name: Dr. Bethany Monteith
Position: Hematologist
Date: 30-10-2023

☒ 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
Sanofi	X			
Pfizer	X			
Forus	X			

Declaration for Clinician 16

Name: Dr. Kevin Song
Position: Hematologist, Vancouver General Hospital
Date: 28-10-2023

☒ 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

Company	Check appropriate dollar range*			
	$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 17

Name: Dr. Martha L. Louzada
Position: Hematologist, London Reginal Cancer Program
Date: 30-10-2023

☒ 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

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	X			
Janssen	X			

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

Declaration for Clinician 18

Name: Dr. Heather Sutherland
Position: Hematologist, BC Cancer-Frasey Valley Site Lymphoma/Myeloma
Date: 26-10--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

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

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

Declaration for Clinician 19

Name: Dr. Richard LeBlanc
Position: Hematologist and medical oncologist
Date: 26-10-2023

☒ **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

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 20

Name: Dr. Suzanne Trudel
Position: Oncologist
Date: 30-10-2023

☒ 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**
Sanofi	X			
BMS			X	

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

Declaration for Clinician 21

Name: Dr. Vishal Kukreti
Position: Hematologist / Oncologist
Date: 30-10-2023

☒ 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**
Amgen	X			
Kirin/Kyoto	X		X	

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

Declaration for Clinician 22

Name: Dr. Alfredo de la Torre
Position: Hematologist
Date: 30-10-2023

☒ 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. Christine Chen
Position: Hematologist
Date: 30-10-2023

☒ 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

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	X			
Janssen	X			

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

Declaration for Clinician 24

Name: Dr. Arleigh Mccurdy
Position: Hematologist, Oncologist
Date: 30-10-2023

☒ 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**
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 25

Name: Dr. Victor Zepeda
Position: Hematologist, Oncologist
Date: 30-10-2023

☒ 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

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 26

Name: Dr. Nizar A. Samad
Position: MD Hematology
Date: 30-10-2023

☒ 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 26: Conflict of Interest Declaration for Clinician 26

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				

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