CADTH REIMBURSEMENT REVIEW

Patient and Clinician Group Input

Isatuximab (Sarclisa)

(Sanofi-Aventis Canada Inc.)

Indication: Sarclisa (isatuximab for injection) is indicated in combination with bortezomib, lenalidomide and dexamethasone, for the treatment of patients with newly diagnosed multiple myeloma who are not eligible for autologous stem cell transplant (ASCT) or with no intent for ASCT as initial therapy.

November 12, 2024

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

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CADTH

CADTH Reimbursement Review Patient Input

Name of Drug: isatuximab (Sarclisa) – in combination with bortezomib, lenalidomide, and dexamethasone.

Indication: Adult patients with newly diagnosed multiple myeloma, ineligible for autologous stem cell transplant (ASCT) or not undergoing ASC.T

Name of Patient Group: Myeloma Canada

Author of Submission: Aidan Robertson ([redacted])

1. About Your Patient Group

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

www.myeloma.ca

2. Information Gathering

Myeloma Canada is sharing the input received from a patient and caregiver survey regarding isatuximab in combination with bortezomib, lenalidomide, and dexamethasone (IsaVRd) for the treatment of newly diagnosed multiple myeloma patients receiving an autologous stem cell transplant. Our patient and caregiver survey was available from October 11 – November 10, 2024, and was shared via email and social media by Myeloma Canada, and the Leukemia and Lymphoma Society of Canada. Of 43 total responses to the survey, 19 incomplete or ineligible responses were removed from the dataset, leaving 24 complete and eligible responses. Survey eligibility was determined by patient and caregiver self-report of their experience with myeloma, that they (or the person they care for) were ineligible for autologous stem cell transplant at the time of diagnosis, and/or did not receive an ASCT as their first the first line of therapy.

All respondents were initially asked similar questions regarding disease experience. Upon verifying their line of therapy, or experience with, the treatment under review, respondents were divided into two subsets, and correspondingly posed different questions. The subsets and their demographic characteristics are as follows:

Note: No survey respondents were currently eligible for the treatment under review (ineligible for stem cell transplant and had not yet started first line therapy).

1. **Subset C:** Patients who were ineligible for or did not receive first-line treatment with an autologous stem cell transplant (ASCT) and their caregivers.
    i. Respondents **(22)** were from British Columbia (11), Quebec (3), Alberta (2), Ontario (2), Manitoba (1), Newfoundland and Labrador (1). and 2 from outside of Canada (Belgium, Ivory Coast).
    ii. 10 respondents were patients, and 1 was a caregiver.
    iii. 7 respondents identified themselves as female, 15 as male.
    iv. 19 respondents were located in an urban area, and 3 in a rural area.
    v. 15 respondents were between '70—79' years of age, 3 respondents were between '80-89', 2 between '60–69' and 1 respondent was between '50–59' years of age.
2. **Subset T:** Patients who have received treatment with IsaVRd isatuximab + bortezomib + lenalidomide + dexamethasone as first line therapy in place of an ASCT
    i. Respondents **(2)** were both patients, from Ontario, living in an urban area, and between the ages of 70-79. 1 respondent identified themselves as female, and 1 as male.

3. Disease Experience

All patients and caregivers were asked "*How important it is to control various symptoms related to myeloma? Please rate on a scale of 1 - Not important to 5 - Extremely important"*, respondents (24) most frequently rated 'Bone issues (fractures, breaks, bone pain)' (12; average rating 4.32) as '5 – extremely important' to control, followed by 'Infections' (10; 4.25), 'Mobility' (9; average rating 4.10), and 'Neuropathy' (8; 4.13).

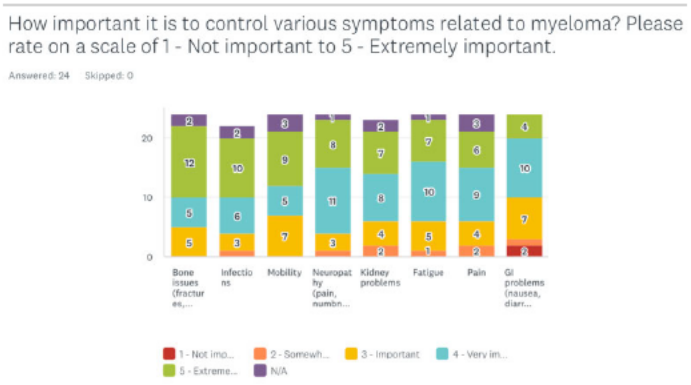


Figure 1 – Importance of controlling myeloma symptoms. (All respondents, 24)

When asked "*Do symptoms associated with myeloma, or caring for someone with myeloma impact or limit your day-to-day activities and quality of life? Please rate on a scale of 1 - No impact to 5 - Extreme impact."*, by weighted average rating, respondents (24) most frequently indicated that myeloma had a '5 - Extreme impact' on their 'ability to travel' (5; 3.33) 'ability to work' (4; average rating 3.28), and 'ability to conduct household chores and responsibilities' (3; 2.83).

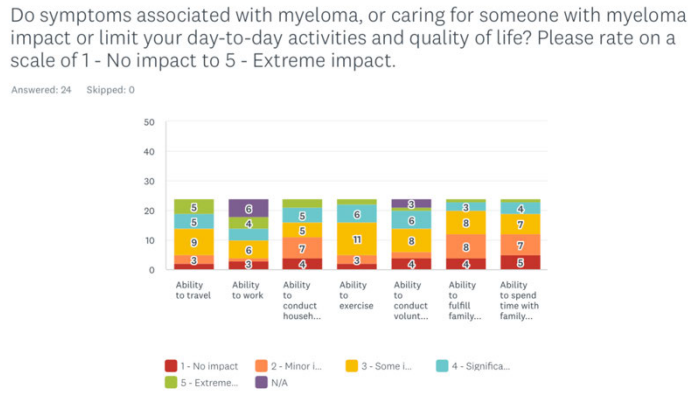


Figure 2 – Impact of myeloma or caring for someone with myeloma on quality of life. (All respondents, 24)

When asked "*If you are currently receiving active treatment for your myeloma, or you care for someone who is, please indicate how often you/they visit a hospital/cancer centre for treatment."* respondents (23) most frequently selected, 'once a month (19), 1 chose 'every two months', 1 chose 'every two weeks', and 2 respondents selected 'other', one of whom commented 'once every two weeks', and the other commented "*Une foi en 2021 intraveineuse de dexametazone plus un supplément d un autre associé*".

When all respondents (24) were asked "*How long does it take you to travel to the hospital/cancer centre where you, or the person you care for, receive(s) treatment?",* 46%(11) of respondents indicated 'Less than 30 minutes', 9 respondents chose '30 mins – 1 hour', 3 chose '1 hour - 2 hours', and 1 respondent chose 'Other'; commenting "*Transport en commun".*

When patients and caregivers (23) were asked, "*What have been the most significant financial implications of myeloma treatment on you and your household? Please check all that apply"*; respondents indicated 'parking costs' (8), 'drug costs' (5), and drug administration fees (3) were the most common significant financial implications of myeloma treatment.

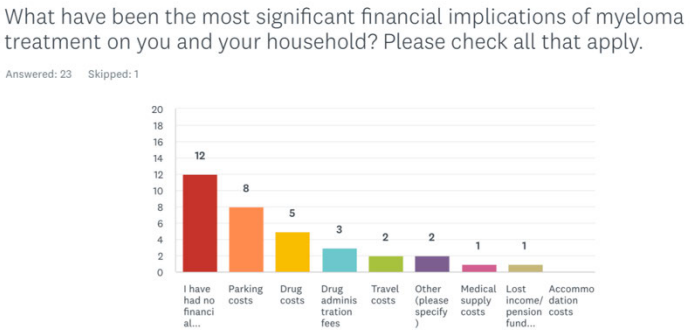


Figure 3 – Financial implications of myeloma treatment (All respondents, 23).

All patients and caregivers were asked "*Have you experienced any of the following psychological / social difficulties due to multiple myeloma, or caring for someone with myeloma? Please rate how severely they impacted your quality of life on a scale of 1 - No impact to 5 - Extreme impact.".* Respondents (24) most frequently indicated that 'Loss of sexual desire' (4; 3.18) had a '5 – extreme impact' on quality of life, followed by 'Difficulty sleeping' (3; 3.13), and 'Anxiety/worry' (2; 2.96),

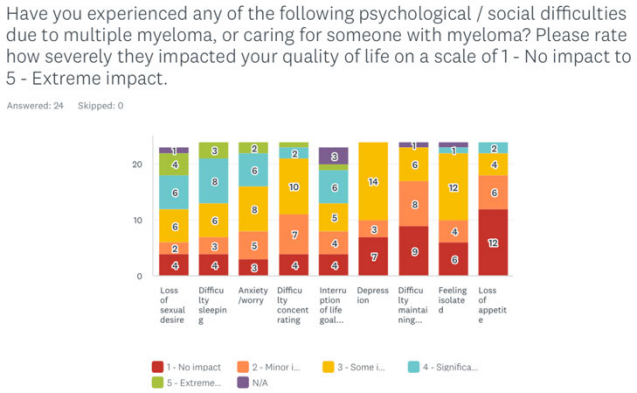


Figure 4 –Psychosocial impacts of myeloma/caring for someone with myeloma. (All respondents, 24)

When all patients (21) were asked "*Do you need the support of a caregiver or family member to help you manage your myeloma or your treatment-related symptoms?"*, 8 answered 'No' they did not need a caregiver, 11 chose 'Yes', and 2 chose 'No, but I would benefit from a caregiver's help'.

All patients and caregivers were asked to identify the factors they consider to be most important to (any) myeloma treatment. Respondents (22) frequently mentioned A) effectiveness of treatment and achieving a long remission, B) maintaining quality of life (including mental health) and making side effects manageable, C) portability of treatment to achieve fewer/minimal visits to the hospital/cancer centre & minimize impact on day-to-day activities, and D) the cost and accessibility of treatments to be key factors. Responses to this effect are as follows:

- *"De pouvoir avoir accès a un traitement disponible et remboursé.... D avoir accès au service médical qui puisse le proposer en dehors des essarts cliniques pas accessible. De ne pas rester sans soins ..ce qui m est un peu arrivé. La disponibilité du traitement sur le marché, du coup l accès plus facile, du coup être soignée et aller mieux ..c est un réel espoir pour nous tous."*
- *"Quality of life. Comfort availability of treatment facilities Access to doctors and pharmacy Control my back pain Participation of our family doctor in requesting & reviewing test results. Helping us to understand what's happening and what we should be doing to get a diagnosis ."*
- *"I can get the best possible treatment. Least amount of side effects. Receiving treatment close to home"*

4. Experiences With Currently Available Treatments (Subset C - Received 1st line treatment with drug regimens other than IsaVRd)

Of Subset C respondents (22), 18 indicated they were ineligible for ASCT at the time of diagnosis, and 4 indicated they were eligible but did not receive a transplant and do not plan to. Subset C (22) was asked

to indicate what treatment(s) they received as first line therapy, responses indicated that dexamethasone (21) was the most widely used drug followed by lenalidomide (18) and daratumumab (13). DRd was the most common treatment combination (11), followed by Rd (3).

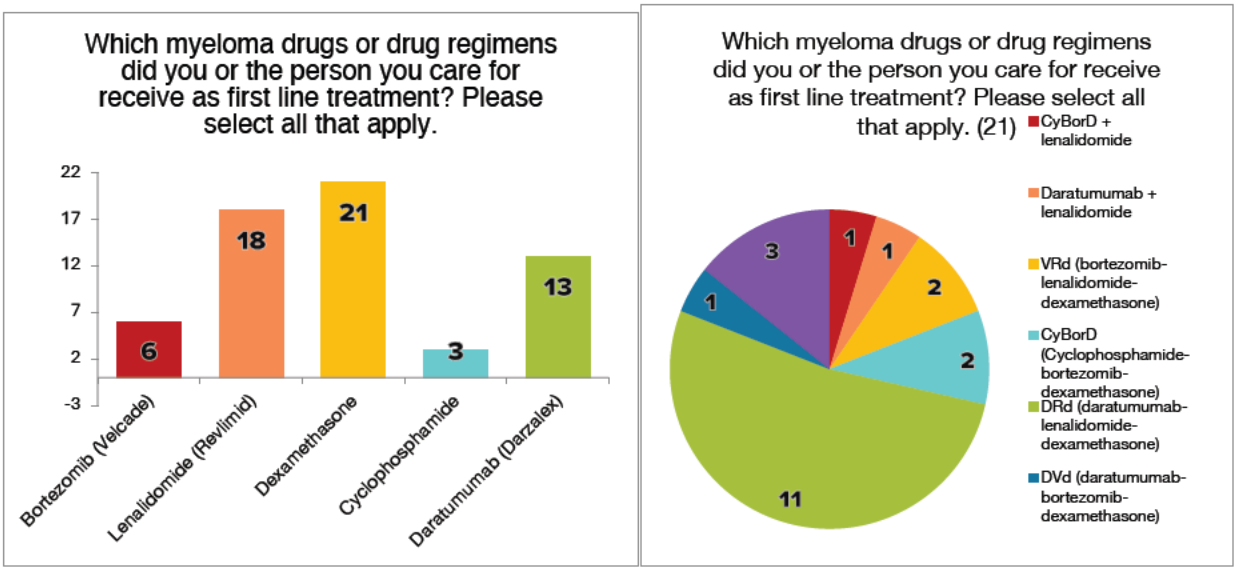


Figure 5.1 – Drugs received in first line of therapy(Subset C, 22) & Figure 5.2 – Treatment combinations received as first line therapy (Subset C, 21)

Following the instructions "*Please respond to the following questions on your overall experience with the first line treatment you or the person you care for received, by rating them on a scale of 1- Not at all to 5 - Completely",* Subset C respondents (22) responded to the questions:

- "*Did the treatment improve overall quality of life for you or the person you care for?*" (Completely: 5, **Mostly: 6,** Somewhat: 6; Slightly: 1, Not at all: 5).
- "*Were the treatment's side-effects manageable?* (Completely: 3, **Mostly: 10**, Somewhat: 6; Slightly: 3, Not at all: 0).
- "*Was the treatment effective in controlling myeloma for you/the person you care for?"* (Completely: 7; **Mostly: 11**, Somewhat: 4; Slightly: 0; Not at all: 0).
- "*Did the treatment meet your expectations in treating myeloma?*" (**Completely: 4**, Mostly: 12, Somewhat: 3; Slightly: 2, Not at all: 0).[Note one person did not respond to this question].

Responses to the above questions by treatment combination received is included in the final section of this report.

5. Improved Outcomes (Subset C)

Respondents in Subset C were presented information about the efficacy of IsaVRd vs VRd from the IMROZ trial, common side effects, and the dosing schedule at both stages of treatment (induction, maintenance).

Subset C was asked "*How bearable do you expect most common side effects of IsaVRd (isatuximab-bortezomib-lenalidomide-dexamethasone) would be for you or the person you care for? Please rate on a scale of 1 - Not at all bearable to 5 - Extremely bearable."* Respondents (21) most frequently rated 'infections' (4; 2.62) and 'cataracts' (4; 2.71) as '1 – Not at all bearable', followed by 'neutropenia' (2; 2.9) and 'fever' (2; 2.90).

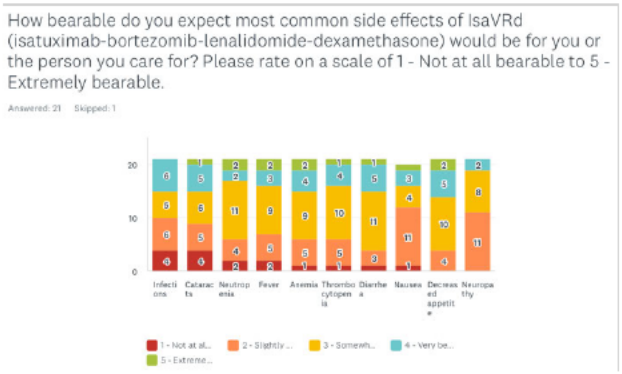


Figure 6 – Perception of IsaVRd side effects (Subset C; 21)

When **Subset C** was asked, "*How worrisome is the overall side effect profile for IsaVRd (isatuximab-bortezomib-lenalidomide-dexamethasone), compared to the treatment you or the person you care for received? Please rate on a scale of 1 – Not at all worrisome to 5 – Extremely worrisome'.*" Respondents (20) most frequently chose '3 – Somewhat worrisome' (7), followed by '2 – Slightly worrisome' (6), '1 – Not at all worrisome' (4) and '4 – Very worrisome' (3).

When asked, "*What do you believe the advantages and/or disadvantages of first line treatment with IsaVRd (isatuximab-bortezomib-lenalidomide-dexamethasone) would have been be compared to the treatment you or the person you care for received?*". **Subset C** respondents (21) 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: 4, No change: 6, Decreased: 1, I'm not sure: 10
- Control of myeloma and its symptoms – Increased: 7, No change: 5, Decreased: 2, I'm not sure: 7),
- Frequency of trips to the hospital or cancer centre for treatment – Increased: 14, No change: 2, Decreased: 2, I'm not sure: 3).
- Tolerability of the treatment's mode of administration – Increased: 3, No change: 8, Decreased: 2, I'm not sure: 8.
- Quality of life (20) – Increased: 2, No change: 9, Decreased: 4, I'm not sure: 5.

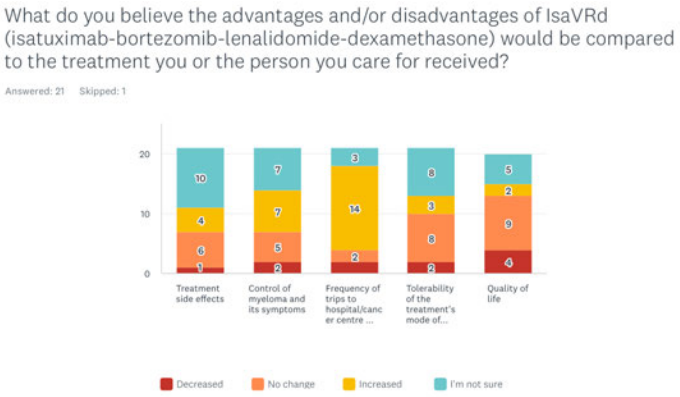


Figure 7 – Perception of IsaVRd advantages/disadvantages compared to treatment received (Subset C; 21)

To the question "*Based on what you know today, would you have been interested in receiving IsaVRd (isatuximab-bortezomib-lenalidomide-dexamethasone) as first line treatment for yourself or the person you care for? (Presuming you were eligible and your doctor agreed).*" **Subset C** respondents (22) most frequently indicated 'Yes' (9), 5 said they were unsure, 4 chose 'No' and 4 additional respondents indicated they would need more information to decide.

When given the opportunity to share any further thoughts about IsaVRd (isatuximab-bortezomib-lenalidomide-dexamethasone) in comparison to their first line treatment, 11 **Subset C** respondents left comments, 3 of which described that they would not want a treatment with dexamethasone, additional comments of note are as follows.

- "*Je pense que l accès au traitement qui sont susceptibles d améliorée la qualité de vie du patient atteint de myélome est un espoir réel car c est une maladie actuellement incurable et agir des que possible au cas par cas le paraît capital ....plus je gagne du temps pour vivre stable et auprès de mes proches et plus belle est la vie .. Espoir. Merci. Courage a tous et toutes.*"
- *"I received cybortdex as first line, isavrd sounds like an improvement. I am 3 years on treatment, now on daralendex to control protein and light chains. Seems to be helping."*
- *"Daratumumab has been a miracle drug for me. The key issue at diagnosis was whether my private insurance would cover it ((YES!) as it wasn't covered by OHIP at the time. I was quite worried about the Vrd side effects and am glad Zi didn't have to deal with them"*
- *"The increased trips and increased dexamethasone would not be tolerable"*

6. Experience With Drug Under Review – Subset T

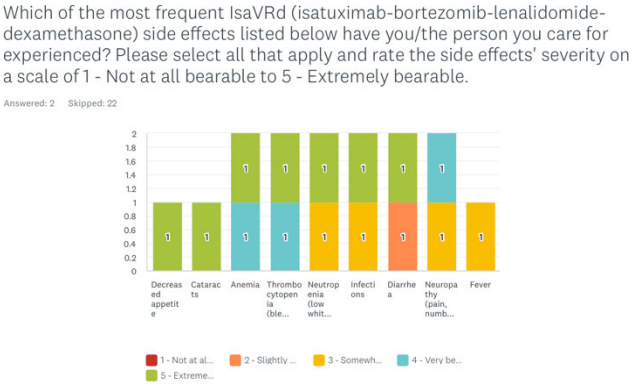
As noted previously, there were 2 individuals with IsaVRd (isatuximab-bortezomib-lenalidomide-dexamethasone) experience who responded to the survey, and they are referred to as Subset T.

When asked "*When did you or the person you care for start treatment with IsaVRd (isatuximab-bortezomib-lenalidomide-dexamethasone)?*", both Subset T respondents (2) chose '2 years ago'.

1 Subset T respondent indicated they had relapsed and were at the induction stage of a new treatment, 1 is currently receiving maintenance treatment.

When Subset T respondents were asked "*How long were you/the person you care for receiving IsaVRd (isatuximab-bortezomib-lenalidomide-dexamethasone)?"*, 1 chose '1 year', and 1 chose '2 years'.

Subset T was asked, "*Which of the most frequent IsaVRd (isatuximab-bortezomib-lenalidomide-dexamethasone) side effects listed below have you/the person you care for experienced? Please select all that apply and rate the side effects severity on a scale of 1 Not at all bearable to 5 Extremely bearable'.".* Respondents (2) did not rate any side effects as '1 – Not at all bearable', 'diarrhea' (1) was the only side effect rated '2 – Slightly bearable', followed by 'infections' (7; 3.17), and 'neuropathy' (7; 3.20).



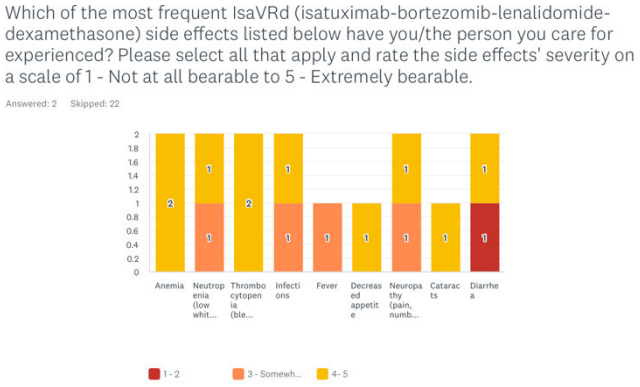


Figure 8.1— Experience of IsaVRd side effects (Subset T; 2) & Figure 8.2 — Experience of IsaVRd side effects, recoded (Subset T; 2)

When asked "*How effective was the supportive care you received in managing your side effects from IsaVRd (isatuximab-bortezomib-lenalidomide-dexamethasone) treatment? Please rate on a scale of 1–5 where 1 is Not at all effective and 5 is Extremely effective",* Subset T respondents (2) chose '4 – Very effective'.

Subset T was asked "*While receiving treatment with IsaVRd (isatuximab-bortezomib-lenalidomide-dexamethasone), how did the following factors negatively impact your quality of life?"* and were provided three factors. Respondents (2) felt that:

- 'Treatment side effects' '3 – somewhat' and '2 – slightly' negatively impacted their quality of life;
- Frequency of trips to the hospital or cancer centre for treatment had '3 – somewhat' and '2 – slightly' negatively impacted their quality of life;
- Tolerability of the treatment's mode of administration had '1 – not at all' (2) negatively impacted their quality of life.

Following the instructions "*Please answer each of the following questions on your overall experience with IsaVRd (isatuximab-bortezomib-lenalidomide-dexamethasone), by rating them on a scale of 1- Not at all to 5 - Completely",* Subset T (2) responded to the questions:

- "*Did IsaVRd (isatuximab-bortezomib-lenalidomide-dexamethasone) treatment improve overall quality of life for you or the person you care for?*" (**Completely: 1**; Mostly: 1).
- "*Were the overall side-effects of IsaVRd (isatuximab-bortezomib-lenalidomide-dexamethasone) manageable?* (**Mostly: 2**).
- "*Was IsaVRd (isatuximab-bortezomib-lenalidomide-dexamethasone) effective in controlling myeloma for you/the person you care for?"* (**Completely: 2**).
- "*Did IsaVRd (isatuximab-bortezomib-lenalidomide-dexamethasone) meet your expectations in treating myeloma?*" (**Completely: 1**, Mostly: 1)

1 respondent provided the following comment:

- *"I have become stronger and more mobile my last PET scan showed no active myeloma cells."*

Subset T (2) was asked to indicate how they were or are accessing IsaVRd, 1 indicated 'through a clinical trial (ongoing)', and 1 chose through 'private insurance'.

7. Anything Else?

Considering the scarcity of effective treatment options for transplant-ineligible myeloma, access to IsaVRd will help meet an important need for this population of patients.
It is critical that if recommended for reimbursement, the indication includes both patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant (ASCT) and those **"with no intent for ASCT as initial therapy"** (as applied for). This is particularly important as it allows patients to have additional choice in deciding their course of treatment, especially considering ASCT's significant impact on quality of life, accommodation/travel costs, and disruption of everyday life and routines. In a survey conducted by Myeloma Canada from August 26 – October 10, 2024 regarding the two treatment combinations including belantamab mafodotin currently under review (BPd & BVd), respondents who indicated they had not received an ASCT were asked "*Why did you, or the person care for, not receive an autologous stem cell transplant (ASCT)?".* Of 87 respondents, 53 indicated 'Age', 8 chose 'Was not offered', 6 indicated 'Chose not to', and 2 indicated 'I am unsure'. 18 selected 'Other' and provided comments, most of which described comorbidities (heart, kidneys, amyloidosis) that precluded them from ASCT. Two additional comments illuminate reasons patients and caregivers may choose not to undergo an ASCT.

- *"Is special needs(dev. ch) - would be too traumatic, doing well with meds & chemo"*
- *"The newer drugs equaled the advantages of the Stem Cell Transplant but without the complications."*

As well, when asked "*What have been the most significant financial implications of myeloma treatment on you and your household?"* the proportion of respondents to this survey who selected 'I have had no financial implications related to myeloma' was higher than typically seen in our previous surveys. Upon examining responses to this question from the aforementioned belantamab mafodotin survey, the same

trend was present. Transplant ineligible respondents (87) most frequently selected 'I have had no financial implications' (41), followed by parking costs (21), whereas transplant eligible respondents (200) most frequently selected 'Lost income/pension funds due to absence from work, disability, or early retirement' (81) followed by 'travel costs' (66). This may be due to a number of factors including that patients ineligible for ASCT are usually older, and thus have access to different insurance, and are less likely to be employed and lose their source of income due to myeloma. Similarly, the cost of travel and accommodation for ASCT can be significant for patients, some who may live a mere kilometer outside the distance required for certain travel reimbursements, and ASCT is likely to necessitate more time off of work for patients who rely heavily on their monthly income. There may be significant advantages of choosing not to undergo a stem cell transplant for certain patients, and access to IsaVRd at the first line for patients both ineligible for and not intending to undergo an ASCT will provide additional choice for all newly diagnosed myeloma patients and their physicians.

For additional specificity in understanding transplant ineligible patients' experience with currently available first line treatments, the results of questions from section 4 are presented in the table below.

Table 1: *Overall experience with first line treatment (Subset C; 22)*

Drug Combination	Did the treatment improve overall quality of life for you or the person you care for?	Were the treatment's side effects manageable?	Was the treatment effective in controlling myeloma for you or the person you care for?	Did the treatment meet your expectations?
CyBorD (Cyclophosphamide-bortezomib-dexamethasone)	4 - Mostly	4 - Mostly	4 - Mostly	4 - Mostly
CyBorD (Cyclophosphamide-bortezomib-dexamethasone)	1 - Not at all	4 - Mostly	5 - Completely	4 - Mostly
CyBorD + lenalidomide	3 - Somewhat	2 - Slightly	3 - Somewhat	3 - Somewhat
Daratumumab + lenalidomide	4 - Mostly	4 - Mostly	4 - Mostly	4 - Mostly
DRd (daratumumab-lenalidomide-dexamethasone)	1 - Not at all	2 - Slightly	3 - Somewhat	2 - Slightly
DRd (daratumumab-lenalidomide-dexamethasone)	2 - Slightly	2 - Slightly	4 - Mostly	2 - Slightly
DRd (daratumumab-lenalidomide-dexamethasone)	4 - Mostly	3 - Somewhat	4 - Mostly	4 - Mostly

DRd (daratumumab-lenalidomide-dexamethasone)	5 - Completely	5 - Completely	5 - Completely	3 - Somewhat
DRd (daratumumab-lenalidomide-dexamethasone)	5 - Completely	4 - Mostly	5 - Completely	5 - Completely
DRd (daratumumab-lenalidomide-dexamethasone)	1 - Not at all	3 - Somewhat	3 - Somewhat	4 - Mostly
DRd (daratumumab-lenalidomide-dexamethasone)	3 - Somewhat	4 - Mostly	4 - Mostly	4 - Mostly
DRd (daratumumab-lenalidomide-dexamethasone)	5 - Completely	4 - Mostly	5 - Completely	5 - Completely
DRd (daratumumab-lenalidomide-dexamethasone)	4 - Mostly	3 - Somewhat	4 - Mostly	4 - Mostly
DRd (daratumumab-lenalidomide-dexamethasone)	3 - Somewhat	4 - Mostly	4 - Mostly	4 - Mostly
DRd (daratumumab-lenalidomide-dexamethasone)	4 - Mostly	4 - Mostly	4 - Mostly	4 - Mostly
DVd (daratumumab-bortezomib-dexamethasone)	1 - Not at all	5 - Completely	4 - Mostly	5 - Completely
Rd (lenalidomide-dexamethasone)	3 - Somewhat	3 - Somewhat	3 - Somewhat	4 - Mostly
Rd (lenalidomide-dexamethasone)	3 - Somewhat	3 - Somewhat	5 - Completely	
Rd (lenalidomide-dexamethasone)	1 - Not at all	3 - Somewhat	5 - Completely	4 - Mostly
VRd (bortezomib-lenalidomide-dexamethasone)	5 - Completely	5 - Completely	5 - Completely	5 - Completely
VRd (bortezomib-lenalidomide-dexamethasone)	3 - Somewhat	4 - Mostly	4 - Mostly	4 - Mostly

Appendix: Patient Group Conflict of Interest Declaration

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

   No

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it.

   The Leukemia and Lymphoma Society of Canada assisted with data collection by sharing the link to our survey.

No help was received from outside Myeloma Canada for data analysis.

3. List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.

Table 2: Financial Disclosures

Company	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Abbvie	☐	☒	☒	☒
AstraZeneca	☐	☐	☒	☐
Apotex	☐	☐	☐	☒
Amgen	☐	☐	☐	☒
The Binding Site	☐	☐	☐	☐
BMS	☐	☐	☐	☒
FORUS Therapeutics	☐	☐	☐	☒
GSK	☐	☐	☐	☒
IMC	☐	☒	☐	☒
JAMP	☐	☐	☒	☐
Janssen	☐	☐	☐	☒
Merck	☐	☐	☒	☐
Pfizer	☐	☐	☐	☒
Rapid Novor	☐	☐	☐	☒
Roche	☐	☐	☒	☐
Sanofi	☐	☐	☐	☒
Sebia Diagnostics	☐	☐	☒	☐
Takeda	☐	☐	☒	☐

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Aidan Robertson
Position: Advisor, Health Policy and Advocacy
Patient Group: Myeloma Canada
Date: 11-06-2024

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: **PC0378-000**
Brand Drug Name (Sarclisa)
Generic Drug Name (Isatuximab)
Indication: multiple myeloma not eligible for ASCT
Name of Clinician Group: Canadian Myeloma Research Group (CMRG)
Author of Submission: Dr. Alissa Visram

1. About Your Clinician Group

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

The Canadian Myeloma Research Group (CMRG) 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 disorders 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 7000 patients, to evaluate real-word patterns of treatment, outcomes, risk factors and areas for future research in myeloma; and 3) generation of consensus statements for myeloma management.

Website: cmrg.ca

2. Information Gathering

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

CMRG holds monthly teleconferences, and participants agreed to submit a single document for feedback to CADTH which would be signed by the physicians who agreed with the information. The initial draft of the document was prepared 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

Please describe the current treatment paradigm for the disease.

- Focus on the Canadian context.
- Please include drug and non-drug treatments.
- Drugs without Health Canada approval for use in the management of the indication of interest may be relevant if they are routinely used in Canadian clinical practice. Treatments available through special access programs are relevant. Are such treatments supported by clinical practice guidelines?
- Do current treatments modify the underlying disease mechanism? Target symptoms?
- What are the most important goals that an ideal treatment would address?

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

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 (previously CyBorD) followed by high-dose melphalan + ASCT and then lenalidomide-maintenance until disease progression. TI patients preferentially daratumumab-based regimens, typically DRd until disease progression; a small proportion with renal compromise or poor marrow reserved may commence treatment with Dara-CYBORD. Less often, frailer TI patients may receive Rd or RVd (typically “lite”) with single- agent lenalidomide also given until disease progression. 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.

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.

Please describe goals (needs) that are not being met by currently available treatments. Examples of unmet needs:

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

Please describe limitations associated with current treatments (e.g., adverse events, administration, etc., if applicable).

Myeloma remains incurable despite the introduction of new agents over the last 2 decades. While options exist for multiple lines of therapy as the disease waxes and wanes, much of the success and improvements in longterm survival is contingent upon maximizing disease control with the first line of treatment. It is in this line that the majority of patients will have their longest period of disease control. Maximizing response durability is contingent on maximizing response depth. This includes rates of complete response by conventional serologic, urine and marrow assessments as well as by more sensitive minimal residual disease (MRD) testing. If MRD negativity is achieved, especially if durably so (>12 months), such patients are predicted to have a very durable remission lasting many years. The importance of optimizing the depth and duration of response in first line therapy is underscored by the fact that 19% of Canadian TI patients do not go on to receive a second line of therapy due to either death or progression without treatment (McCurdy *et al*., BCJ 2023).

5. Place in Therapy

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

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

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

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

Would the drug under review be reserved for patients who are intolerant to other treatments or in whom other treatments are contraindicated?

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

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

Based on the IMROZ trial (Facon *et al.* NEJM 2024), isatuximab would be added to VRD in the first-line treatment of patients with TI NDMM. Isatuximab, like daratumumab, is an anti CD38 monoclonal antibody with comparable efficacy and tolerability to daratumumab. If a quadruplet regimen was implemented in the frontline setting, patients would be exposed to the three main classes of agents for MM allowing for deep and durable responses. The IMROZ trial was a phase 3 randomized control trial which demonstrated that the quadruplet regimen significantly increased both the 60-month PFS (63.2% with Isa-VRD versus 45.2% with VRD) and the proportion of patients with a complete response and MRD negative status (55.5% with Isa-VRD versus 40.9% with VRD). Though VRD is not the current standard of care regimen for TI-NDMM, the phase 3 BENEFIT trial (Leleu *et al.* Leukemia 2024) has similarly shown that Isa-VRD significantly increases the rate of MRD negativity at 18 months compared to Isa-RD (53% versus 26%, respectively). Both the BENEFIT and IMROZ trial showed that the Isa-VRD is well tolerated and the expected adverse effects (particularly infections and neutropenia with an anti-CD38 monoclonal antibody, and peripheral neuropathy due to bortezomib) are similar to Isa-RD and VRD, respectively. Therefore, we advocate that in fit TI-NDMM patients Isa-VRD should become the first-line standard of care regimen.

The primary shift in the current treatment paradigm would be the addition of bortezomib to anti-CD38 mAb, lenalidomide, and steroid backbone that is the current standard of care. If Isa-VRD is used similarly to the dosing schedule of the IMROZ trial, bortezomib would only be used in the first 24 weeks (~6 months) of treatment, and following that the treatment would be Isa-RD. Currently, patients relapsing on DRD are eligible are proteasome inhibitor unexposed and therefore can be treated with Selinexor-bortezomib-dexamethasone (XVD), CyBorD, or carfilzomib regimens. Extrapolating from the Kaplan-meier curve in the IMROZ publication, only ~6% of patients on Isa-VRD progressed (or died) within 6 months of treatment and therefore would likely be bortezomib refractory and ineligible for CyBorD or XVD. Patients refractory to bortezomib in the frontline setting could still be treated with a carfilzomib based regimen in second line. Therefore, implementation of Isa-VRD in the first line setting is unlikely to substantially alter the relapsed treatment landscape.

Another consideration for implementing Isa-VRD in first line is that Isatuximab is an intravenous infusion that requires a longer duration of administration compared to subcutaneous daratumumab, which has implications on the healthcare resource utilization. However, a shorter 30-minute infusion time for patients on maintenance Isatuximab without infusion reactions has shown to be feasible and well tolerated (Ocio *et al.* Blood 2023), and would significantly reduce the chair time required for administering this therapy.

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?

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

Which patients are most in need of an intervention?

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

How would patients best suited for treatment with drug under review be identified (e.g., clinician examination/judgement, laboratory tests (specify), diagnostic tools (specify))

Are there any issues related to diagnosis?

Is a companion diagnostic test required?

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

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

It's important to recognize that TI-NDMM encompasses a large spectrum of patients ranging from frail to fit irrespective of chronological age. While there are numerous scores that estimate a patient's frailty, both the IMROZ (Isa-VRD vs VRD) and BENEFIT (Isa-VRD vs Isa-RD) studies included TI-NDMM patients who were quite fit with minimal comorbidities. In both studies, patients above age 80 were excluded, and the majority of patients treated with Isa-VRD had a baseline ECOG performance status of 0-1 (88.7% patients in IMROZ and 88% of patients in BENEFIT). Therefore, frailer patients may be best suited for DRD, VRD, or RD alone. Given that there is no unified definition of frailty in multiple myeloma, assessing frailty status is left to the discretion of the treating physician.

In fit TI-NDMM, treatment with Isa-VRD should be the standard of care given the efficacy compared to VRD and Isa-RD and tolerability of this regimen. The treatment workup and diagnosis of multiple myeloma will be unaffected by the incorporation of this regimen in the front line treatment setting.

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?

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

What would be considered a clinically meaningful response to treatment? Consider the magnitude of the response to treatment. Is this likely to vary across physicians?

Examples: improved survival; reduction in the frequency/severity of symptoms (provide specifics regarding changes in frequency, severity, etc.); attainment of major motor milestones; ability to perform activities of daily living; improvement of symptoms; and stabilization (no deterioration) of symptoms.

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?

Examples: disease progression (specify, e.g. loss of lower limb mobility); certain adverse events occur (specify type/frequency/severity); or additional treatment becomes necessary (specify).

Unacceptable intolerance or toxicity as a result of the addition of bortezomib to the standard approach may require discontinuation. In the pivotal trial that compared DRD (the current standard of care) to RD, the most common grade 3 or 4 adverse events with DRD were due to neutropenia (50% patients) and infections (32.1% patients), particularly pneumonia (13.7%). The quadruplet Isa-VRD is relatively well tolerated, with expected grade 3 or 4 neutropenia and infectious complications (neutropenia 54.4% in IMROZ and 45% in BENEFIT, pneumonia 20.2% in IMROZ and respiratory infections 40% in BENEFIT). Not surprisingly, Isa-VRD is associated with peripheral neuropathy due to the addition of bortezomib. Rates of overall peripheral neuropathy were numerically lower in the BENEFIT trial (any grade: IMROZ 54.4% versus BENEFIT 28%; grade 3 or 4: 7.2% IMROZ vs 10% BENEFIT), likely due to the use of weekly bortezomib rather than twice weekly bortezomib in the IMROZ trial. However, the relative dose intensity for bortezomib in the IMROZ trial was 90% for patients treated with Isa-VRD, and patients treated with Isa-VRD and VRD had similar rates of peripheral neuropathy (54.4% versus 60.8%, respectively), showing that the use of Isa-VRD is tolerable despite the peripheral neuropathy.

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]?

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

If a specialist is required, which specialties would be relevant?

This therapy is appropriate for delivery in all settings with current experience delivering isatuximab and bortezomib. We suggest that Isa-VRD be administered and monitored by hematologists/oncologists who have the knowledge and expertise to manage the potential AEs that can be associated its use. This includes community oncology clinics and tertiary medical facilities with expertise in other cellular therapies for hematologic malignancies.

6. Additional Information

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

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.

   <Enter Response Here>

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.

   <Enter Response Here>

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for <u>each clinician</u> who contributed**

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

Declaration for Clinician 1

Name: Jesse Shustik
Position: Medical Oncologist, BC Cancer-Surrey
Date: 12-11-2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

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

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

Declaration for Clinician 2

Name: *Hira Mian*
Position: *Assistant Professor*
Date: 12-11-2024

☒ 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

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
Takeda, Jansen, BMS, Sanofi, Amgen, GSK		x		
Jansen Research Funding				x

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

Declaration for Clinician 3

Name: *Dr. Bethany E. Monteith*
Position: *Hematologist, Kingston Health Sciences Center*
Date: 12-11-2024

☒ 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**
Forus	x			
Sanofi	x			
Pfizer	x			

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

Declaration for Clinician 4

Name: *Dr. Anthony Reiman*
Position: *Professor, Department of Oncology, Saint John Regional Hospital*
Date: 12-112024

☒ 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. Alfredo de la Torre*
Position: *Hematologist/Oncologist, Halifax*
Date: 12-11-2024

☒ 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

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.

New or Updated Declaration for Clinician 6	
Name	*Dr. Guido Lancman*
Position	*Hematologist/Oncologist, Toronto*
Date	*12-11-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Janssen	☐	☐	☒	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 7	
Name	*Dr. Ibraheem Othman*
Position	*Hematologist/Oncologist, Regina*
Date	*12-11-2024*

☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Nothing to Declare	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 8	
Name	*Dr. Darrell White*
Position	*Hematologist, Dalhousie University and QEII Health Sciences Centre*
Date	*12-11-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
BMS	☐	☒	☐	☐
Janssen	☐	☐	☒	☐
Add or remove rows as required	☐	☐	☐	☐

New or Updated Declaration for Clinician 9	
Name	*Dr. Kevin Song*
Position	*Hematologist/Oncologist, Vancouver*
Date	*12-11-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
BMS	☐	☒	☐	☐
Janssen	☐	☒	☐	☐
Amgen	☐	☒	☐	☐

New or Updated Declaration for Clinician 10	
Name	*Dr. Christopher Venner*
Position	*Hematologist/Oncologist, Vancouver Centre*
Date	*12-11-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Celgene/BMS	☒	☐	☐	☐
Takeda	☒	☐	☐	☐
Janssen	☒	☐	☐	☐
Amgen	☒	☐	☐	☐
Sanofi	☒	☐	☐	☐
GSK	☒	☐	☐	☐

New or Updated Declaration for Clinician 11	
Name	*Dr. Donna Reece*
Position	*Chief Medical Officer, CMRG*
Date	*12-11-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
BMS/ Celgene	☐	☐	☒	☐
Janssen	☐	☐	☒	☐
Amgen	☐	☐	☒	☐
Sanofi	☒	☐	☐	☐
GSK	☒	☐	☒	☐
Takeda	☒	☐	☐	☐

New or Updated Declaration for Clinician 12	
Name	*Dr. Arleigh McCurdy*
Position	*Hematologist/Oncologist, Ottawa*
Date	*12-11-2024*
☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration				
List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.				
Company	**Check Appropriate Dollar Range**			
	$0 to 5,000	**$5,001 to 10,000**	**$10,001 to 50,000**	**In Excess of $50,000**
Janssen	☐	☒	☐	☐
Sanofi	☒	☐	☐	☐
GSK	☒	☐	☐	☐
Pfizer	☒	☐	☐	☐
Forus	☒	☐	☐	☐
Amgen	☒	☐	☐	☐

New or Updated Declaration for Clinician 13	
Name	*Dr. Sindu Kanjeekal*
Position	*Hematologist/Oncologist, Windsor*
Date	*12-11-2024*

☒	**I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Conflict of Interest Declaration

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Nothing to Declare	☐	☐	☐	☐
Add company name	☐	☐	☐	☐
Add or remove rows as required	☐	☐	☐	☐

CADTH

CADTH Reimbursement Review

Clinician Group Input

CADTH Project Number: PC0378-000
Generic Drug Name (Brand Name): isatuximab (Sarclisa)
Indication: In combination with bortezomib, lenalidomide and dexamethasone, for the treatment of patients with newly diagnosed multiple myeloma who are not eligible for autologous stem cell transplant (ASCT) or with no intent for ASCT as initial therapy.
Name of Clinician Group: Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Author of Submission: Dr. Tom Kouroukis and members of the OH-CCO Hematology Cancer Drug Advisory Committee

1. About Your Clinician Group

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

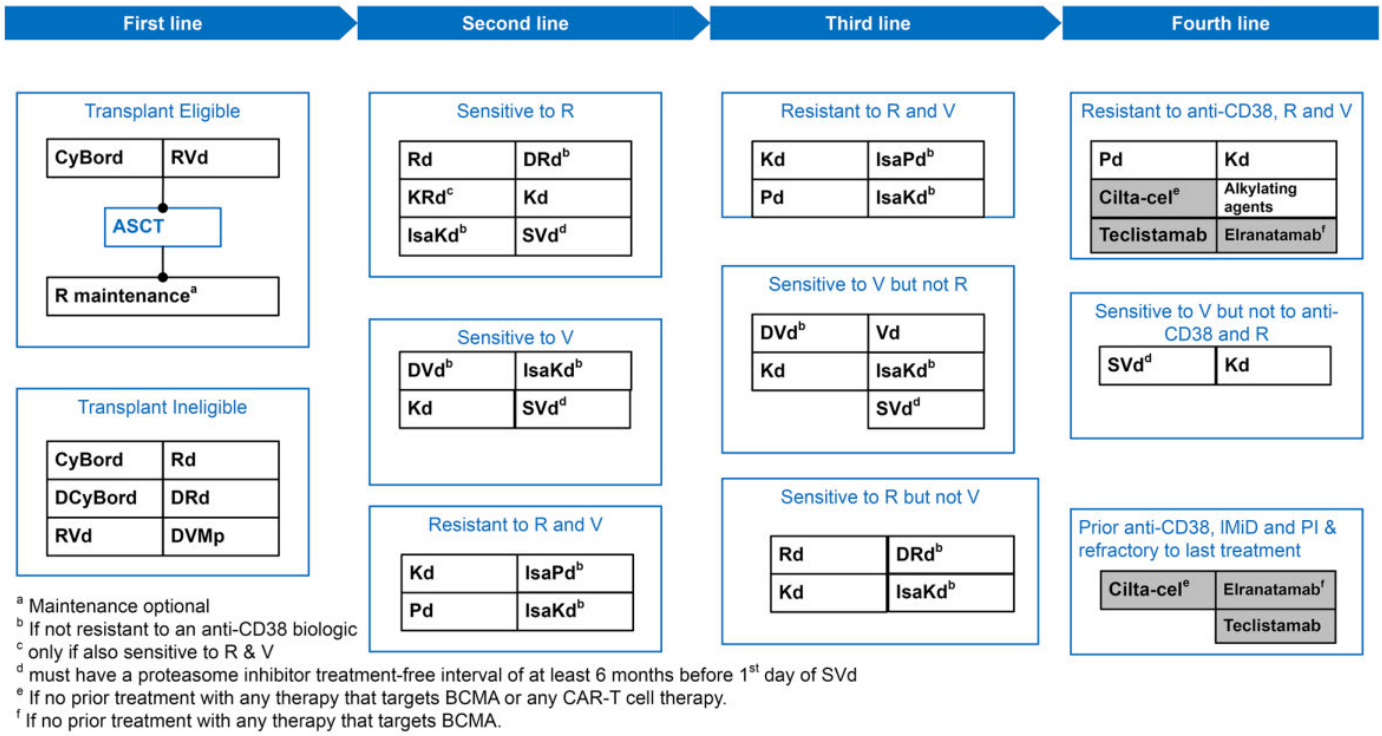
2. Information Gathering

Information was gathered via email and teleconference meeting.

3. Current Treatments and Treatment Goals

Current treatments include DRd, Dara-CyBord, CyBord, Rd and RVd. (Please refer to CDA provisional funding algorithm below for first-line transplant ineligible population.)

Goals are to achieve disease remission, improve symptoms, minimize organ damage, prolong survival.



[a] Maintenance optional
[b] If not resistant to an anti-CD38 biologic
[c] only if also sensitive to R & V
[d] must have a proteasome inhibitor treatment-free interval of at least 6 months before 1st day of SVd
[e] If no prior treatment with any therapy that targets BCMA or any CAR-T cell therapy.
[f] If no prior treatment with any therapy that targets BCMA.

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 is not curable, thus prolongation of remission and survival are still required.

5. Place in Therapy

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

It would provide an anti-CD38 antibody option for first line as a quadruplet. There is no comparative evidence of this regimen to the widely used DRd.

Isatuximab requires IV administration which may not be appealing to some patients, compared to daratumumab.

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

As per the clinical trial, those not intending to proceed to ASCT.

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?

Commonly used myeloma response criteria.

Progression-free survival is an accepted standard outcome measure in myeloma.

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

Significant intolerance or disease progression.

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]?

Systemic therapy centres.

6. Additional Information

In clinical practice, bortezomib once weekly is felt to be as effective as given twice a week with fewer side effects and more convenient for patients.

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

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

   OH-CCO provided secretariat support to the group.

2. Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

   No.

3. List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for <u>each clinician</u> who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Tom Kouroukis

Position: Lead, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date: 07-11-2024

☒ **I hereby certify** that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
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. Christopher Cipkar
Position: Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date: 07-11-2024

☒ 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

	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 3

Name: Dr. Joanna Graczyk
Position: Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date: 07-11-2024

☒ 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
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: 07-11-2024

☒ 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
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. Selay Lam
Position: Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date: 07-11-2024

☒ 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

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	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 6

Name: Rami El-Sharkaway
Position: Member, Ontario Health (Cancer Care Ontario) Hematology Cancer Drug Advisory Committee
Date: 07-11-2024

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 6: Conflict of Interest Declaration for Clinician 6

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Add company name				
Add company name				
Add or remove rows as required				

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