Canada's Drug Agency
L'Agence des médicaments du Canada

Reimbursement Recommendation

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(Draft)

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)

Sponsor: Sanofi-Aventis Canada Inc.

Recommendation: Reimburse with Conditions

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Recommendation

The CDA-AMC pCODR Expert Review Committee (pERC) recommends that isatuximab be reimbursed in combination with bortezomib, lenalidomide and dexamethasone (IsaVRd), for the treatment of patients with newly diagnosed multiple myeloma who are not eligible for autologous stem cell transplant (ASCT) only if the conditions listed in Table 1 are met.

Rationale for the Recommendation

One ongoing, randomized, open-label, parallel-group phase III trial (IMROZ; N = 446) demonstrated that treatment with IsaVRd resulted in added clinical benefit when compared to bortezomib, lenalidomide, and dexamethasone (VRd) in adult patients with newly diagnosed multiple myeloma who were ineligible for ASCT. At the second, planned interim analysis, IsaVRd resulted in a statistically significant and clinically meaningful improvement in progression-free survival (PFS) compared to VRd (hazard ratio [HR] = 0.596; 95% confidence interval [CI], 0.406 to 0.876), as well as a significant improvement in MRD negative CR rate (55.5% vs. 40.9%). Additional analyses of PFS at landmark 18-month (88.2% [95% CI, 83.5 to 91.6] vs. 79.6% [95% CI, 72.6 to 85.0]), 36-month (76.1% [95% CI, 70.2 to 80.9] vs. 66.4% [95% CI, 58.3 to 73.2]), and 60-month (63.2% [95% CI, 56.2 to 69.4] vs. 45.2% [95% CI, 35.6 to 54.2]) timepoints were supportive of the progression-free advantage demonstrated by IsaVRd. pERC could not draw definitive conclusions on the impact of IsaVRd on overall survival (OS) as the data were immature and median OS was not reached at the interim analysis.

Despite the number of available publicly funded treatments for newly diagnosed multiple myeloma in Canada, there is a lack of direct comparative evidence for IsaVRd and other treatments, particularly daratumumab, lenalidomide and dexamethasone (DRd), which pERC considered the most relevant comparator. Per the sponsor-submitted indirect evidence, there was no difference detected between IsaVRd and DRd for PFS or OS at 1-year or 5-years; however, pERC noted several limitations including the immaturity of the IMROZ trial data, the inability to adjust for important effect modifiers, and small sample sizes, with most estimates affected by significant imprecision due to wide 95% CIs, reducing the ability to draw firm conclusions on the comparative efficacy of IsaVRd from the ITCs.

Multiple myeloma is an incurable disease and pERC agreed that there is an unmet need for additional therapies that effectively delay first relapse. Patients identified a need for treatments with manageable side effects that control the disease, prolong remission, and maintain quality of life in comparison to currently available treatments. Given the totality of the evidence, pERC concluded that IsaVRd meets some of these needs by delaying progression and controlling the disease. Though the results suggested no detriment to health-related quality of life (HRQoL) compared to VRd, pERC was unable to draw definitive conclusions on the effect of IsaVRd on patients' quality of life due to limitations of the evidence.

Using the sponsor submitted price for isatuximab and publicly listed prices for all other drug costs, the incremental cost-effectiveness ratio (ICER) for IsaVRd was $311,681 per quality-adjusted life-year (QALY) compared with DRd. In the absence of direct comparative evidence and given the limitations of the indirect clinical data, there is considerable uncertainty regarding the cost-effectiveness of IsaVRd relative to DRd. As such, the total cost of IsaVRd should not exceed the total cost of treatment with DRd for adult patients with newly diagnosed multiple myeloma who are not eligible for ASCT.

Table 1: Reimbursement Conditions and Reasons

Reimbursement condition	Reason	Implementation guidance
Initiation		
1. Treatment with IsaVRd should only be initiated in adult patients with previously untreated multiple myeloma who are ineligible for ASCT.	In the IMROZ trial, treatment with IsaVRd demonstrated a clinical benefit in adult (≥ 18 years) patients with symptomatic multiple myeloma, as defined by the IMWG criteria who were ineligible to undergo ASCT due to their age (65 years or older) or to coexisting conditions.	—
2. Patients must have good performance status.	The IMROZ trial excluded adults with an ECOG performance status greater than 2. Overall, only 48 patients (10.8%) enrolled in the IMROZ trial had an ECOG performance status score of 2, and 1 patient had an ECOG of 3.	Patients with an ECOG performance status greater than 1 may be treated at the discretion of the treating clinician.
3. Patients must not: 3.1. Have received prior systemic therapy or SCT for multiple myeloma 3.2. Have left-ventricular ejection fraction < 40%.	The IMROZ trial excluded patients with these characteristics. As such, the potential benefit of IsaVRd in these patients has not been demonstrated.	—
Discontinuation		
4. Treatment should be discontinued upon the occurrence of either of the following: 4.1. Evidence of disease progression according to IMWG criteria 4.2. Unacceptable toxicity	Patients in IMROZ trial discontinued treatment upon progression or unacceptable toxicity, consistent with clinical practice.	—
Prescribing		
5. IsaVrd should be prescribed by clinicians with expertise in managing transplant-ineligible newly diagnosed multiple myeloma.	This is meant to ensure that IsaVrd is prescribed for appropriate patients and that adverse effects are managed in an optimized and timely manner.	—
Pricing		
6. The total cost of IsaVRd should be negotiated so that it does not exceed the total cost of treatment with DRd for adult patients with newly diagnosed multiple myeloma who are not eligible for ASCT.	Based on public list prices, the ICER for IsaVRd is $311,681 per QALY gained when compared with DRd. Given the lack of head-to-head evidence and limitations with the indirect clinical evidence, the cost-effectiveness of IsaVRd relative to DRd remains highly uncertain. Hence, there is insufficient justification for a price premium for IsaVRd over DRd. To align with the available clinical evidence,	—

Reimbursement condition	Reason	Implementation guidance
	the total cost of IsaVRd should not exceed that of DRd.	
Feasibility of adoption		
7. The organizational feasibility of delivering IsaVRd must be addressed.	IsaVRd includes intravenous administration of isatuximab, which requires infusion chair time, patient monitoring at treatment centres, and sterile compounding. These requirements are expected to place greater demands on health system resources compared with DRd, which includes subcutaneous administration of daratumumab. As such, IsaVRd may impact infusion capacity, staffing, and infrastructure at cancer treatment centres.	—

ASCT = autologous stem cell transplant; DRd = daratumumab, lenalidomide, and dexamethasone; ECOG = Eastern Cooperative Oncology Group; ICER = incremental cost-effectiveness ratio; IMWG = International Myeloma Working Group; IsaVRd = isatuximab, bortezomib, lenalidomide, and dexamethasone; QALY = quality-adjusted life-year.

Discussion Points

- **Unmet Need:** Multiple myeloma is an incurable cancer that is associated with significant impairment to patients' quality of life because of both the disease and the toxicity of treatment. pERC discussed the input from patient and clinician groups as well as the clinical experts, all of whom noted that despite the treatments available today, most patients progress and continue to experience myeloma symptoms, and even death. pERC discussed the need for more effective first-line therapies that delay first relapse and progression. As noted, the committee felt that IsaVRd may meet some of these needs, providing an additional treatment with clinically meaningful and durable responses. However, pERC was unable to ascertain whether IsaVRd met the unmet needs identified versus DRd — the most relevant comparator for patients with newly diagnosed multiple myeloma who are ineligible for or decline to receive ASCT — due to a lack of direct comparative evidence and limitations associated with the submitted indirect evidence.
- **Relevant Comparators and Place in Therapy:** pERC discussed the relevance of the comparator in the IMROZ trial (VRd), noting that daratumumab-based regimens, specifically DRd, are the most relevant and widely used treatments in newly diagnosed multiple myeloma patients who are ineligible for or decline to receive ASCT in the Canadian clinical setting. pERC also discussed the place in therapy of IsaVRd given the current treatment landscape and considering the differences between IsaVRd and DRd that are often considered when choosing treatment options (e.g., mode of administration [IV vs. SC], ease of access, chair time, hospital visits, etc.). pERC also noted the potential change in therapeutic landscape considering the recently published results of the CEPHEUS trial of daratumumab plus RVd for this indication.
- **Certainty of Evidence:** pERC discussed the pivotal evidence submitted for this review which consisted of 1 phase III, open-label RCT (IMROZ). pERC noted that compared to VRd, IsaVRd resulted in statistically significant and clinically meaningful improvements in PFS, which was associated with a moderate level of certainty per the CDA-AMC Grading of Recommendations, Assessment, Development and Evaluation (GRADE) assessment. For the outcomes of OS and HRQoL, the certainty of evidence was rated as low. For OS, this was primarily due to the immaturity of the results (median OS not reached, and only 26.0% vs 32.6% of patients experienced OS events in the IsaVRd and VR groups, respectively). pERC also noted that longer follow-up for OS is likely to be confounded by subsequent treatments. Overall, this precluded the committee from drawing conclusions on the effect of IsaVRd on OS. For HRQoL, pERC noted that despite the low certainty rating, there did not appear to be detriment to HRQoL, though there was a substantial amount of missing data due to attrition.
- **Indirect Evidence:** pERC discussed the sponsor-submitted indirect evidence, which included unanchored matching adjusted indirect comparisons (MAICs) comparing IsaVRd to DVMP, DRd, Rd, and DCybord; and a non-randomized comparison using IPTW methods to compare IsaVRd to CyBord using real-world individual patient data (IPD) from Flatiron. pERC highlighted that for the comparison to DRd from the MAIC, there was no difference detected between IsaVRd and DRd for PFS at 1-year (HR, [redacted]) and 5-years (HR, [redacted]), as well as for OS at 1-year (HR, [redacted]) and 5-years (HR, [redacted]). pERC noted that compared to other daratumumab-based regimens (DVMP and DCybord), results for PFS generally favoured IsaVRd at 1 year, but there was no difference between IsaVRd and DCyBord at 5-years, while there was no difference for OS at either timepoint. pERC also highlighted the limitations with the indirect evidence, noting the immaturity of the IMROZ efficacy data, the inability to adjust for various effect modifiers due to lack of reporting and dichotomization of effect modifying categories, as well as the small effective sample sizes after matching with reductions ranging from [redacted] to [redacted] across analyses, which could render the results unstable and imprecise. Additionally, the ITCs did not assess HRQoL or safety outcomes, precluding pERC from drawing conclusions on these important outcomes.
- **Generalizability:** pERC discussed the eligibility criteria of the IMROZ trial, which excluded patients over 80 years of age, and patients with an ECOG PS greater than 2. No patients over 80 years were enrolled and most patients enrolled had an ECOG PS of 0 or 1 (89.0%), though few patients with ECOG PS of 2 (10.8%) were enrolled. pERC noted that patients aged 80 years and older, and those with ECOG performance status greater than 1 may be treated on a case-by-case basis at the discretion of the treating clinician. This clinical decision may be based on, among other factors, a patient's frailty assessment, and whether frailty is considered due to symptoms of the disease rather than other characteristics such as age, or cognitive or physical conditions, though pERC and the clinical experts noted the lack of evidence for these patients. The clinical experts also noted that for patients with renal impairment, the quadruplet of IsaVRd may be a good option, with the potential to adjust dosing of individual drugs as needed, noting that the VRd backbone, particularly lenalidomide and dexamethasone, is the most toxic component of the regimen.
- **Economic Considerations:** pERC identified substantial remaining uncertainty in the economic analysis, particularly with respect to the relative efficacy of IsaVRd versus DRd. This uncertainty stems from the lack of head-to-head comparative evidence and limitations in the sponsor's indirect treatment comparisons. pERC also noted that most of the QALY benefit for IsaVRd was derived from extrapolation in the post-trial period, reflecting model-based outcomes rather than direct trial evidence. pERC highlighted differences in the mode of administration between IsaVRd and DRd. Isatuximab is administered

intravenously, requiring chair time, patient time at treatment centres, travel time to treatment centres for both patients and caregivers, and sterile compounding. In contrast, daratumumab is delivered as a subcutaneous injection, which is expected to place less demand on health system resources. The CDA-AMC base case incorporated administration-related costs, including infusion chair time, nursing and pharmacist wages to account for observation and preparation time, respectively, and a physician specialist fee to reflect supervision of the infusion. In this analysis, IsaVRd was associated with $11,712 higher administration costs compared with DRd ($25,886 vs. $14,174). pERC noted that administration costs in real-world clinical practice may be higher than those estimated in the model — due to more pronounced differences in chair time, administration frequency, or care setting for isatuximab relative to daratumumab. In addition, pERC observed that while the incremental differences in total treatment costs between IsaVRd and DRd are small, the use of weight-based dosing for isatuximab — compared to flat dosing for daratumumab — could result in higher real-world treatment costs for IsaVRd. These considerations further underscore the need for IsaVRd to be priced such that its total treatment cost does not exceed that of DRd.

- **Budget Impact Considerations:** pERC noted that the estimated budget impact — suggesting cost savings with the reimbursement of IsaVRd — is subject to uncertainty due to limitations in the sponsor-submitted model, most notably the exclusion of subsequent therapy costs from the analysis. pERC emphasized that the exclusion of subsequent therapy costs prevents a complete estimation of the budgetary impact associated with IsaVRd's adoption in clinical practice, as differences in progression rates and treatment sequences may lead to downstream cost implications. Finally, at pERC's request, an additional analysis was conducted from the broader Canadian health care payer perspective to incorporate administration costs associated with intravenous and subcutaneous treatments. When administration costs were included, the reimbursement of IsaVRd for this indication was associated with reduced cumulative cost savings of $15,216,695 over 3 years compared with $23,184,144 in the CDA-AMC base case.

Background

Multiple myeloma (MM) is an incurable, malignant plasma cell disease that originates from multipotent hematopoietic cells in the bone marrow. It is characterized by clonal proliferation of plasma cells in the bone marrow and excess production of a monoclonal immunoglobulin (Ig). As the malignant plasma or myeloma cells accumulate in the bone marrow, they may form localized tumours or plasmacytomas. They also may interfere with normal blood cell production. When multiple plasmacytomas form either inside or outside bone, the condition is called MM. MM is the second most common hematologic cancer worldwide and the 15th most diagnosed cancer in Canada. There is limited information on the prevalence of MM in Canada; however, in 2024, it was estimated that 4,100 Canadians were diagnosed and 1,750 would die from it.[1] According to GLOBOCAN 2022 data, the 5-year prevalence for both sexes in North America was 117,011 cases or 21.7% of all prevalent cases worldwide. In Canada, the 1-year prevalence (2022 data for both sexes) was reported to be 4,044 cases or 10.5 per 100,000 population, whereas the 5-year prevalence was 14,553 cases or 37.9 cases per 100,000 population.

In eligible patients, previously untreated, newly diagnosed MM is usually treated with autologous stem cell transplant (ASCT) following induction therapy (i.e., typically with high-dose chemotherapy). Albeit the number of patients who may not be eligible for ASCT is estimated to be as high as 81%. Further, not all patients who are eligible for ASCT are willing to undergo therapy. Despite treatment advances over the past 2 decades, MM remains an incurable disease with the treatment options currently available.

Isatuximab is currently under review in combination with bortezomib, lenalidomide, and dexamethasone (IsaVRd), for the treatment of adult patients with transplant-ineligible, newly diagnosed MM, and the NOC was received on April 17, 2025. Isatuximab has been approved by Health Canada in combination with pomalidomide and dexamethasone, for the treatment of patients with relapsed and refractory MM who have received at least two prior therapies including lenalidomide and a proteasome inhibitor; in combination with carfilzomib and dexamethasone, for the treatment of adult patients with relapsed or refractory MM who have received 1 to 3 prior lines of therapy.
Isatuximab is a monoclonal antibody that binds to a specific extracellular epitope of CD38, triggering mechanisms that result in the death of CD38-expressing tumour cells. It is available as an IV infusion and the dosage recommended in the product monograph is 10 mg/kg.

Sources of Information Used by the Committee

To make its recommendation, the committee considered the following information:

- a review of 1 ongoing, randomized, open-label, phase III trial in patients with newly diagnosed MM who are not eligible for ASCT; and 2 indirect treatment comparisons (1 matching-adjusted indirect treatment comparison 1 and non-randomized, observational comparison).
- patients' perspectives gathered by 1 patient group, Myeloma Canada
- input from public drug plans and cancer agencies that participate in the reimbursement review process
- 2 clinical specialists with expertise diagnosing and treating patients with MM
- input from 2 clinician groups, the Canadian Myeloma Research Group and the Ontario Health Cancer Care Ontario Hematology Cancer Drug Advisory Committee
- a review of the pharmacoeconomic model and report submitted by the sponsor

Perspectives of Patients, Clinicians, and Drug Programs

Patient Input

Myeloma Canada, an advocacy group supporting individuals with MM, provided input for CDA-AMC's review of isatuximab. Information for this submission was gathered through an online survey of patients and caregivers conducted by Myeloma Canada from October 11 to November 10, 2024. The survey was distributed via email and social media by Myeloma Canada and the Leukemia and Lymphoma Society of Canada.

Of 43 survey responses, 24 were complete and eligible and divided into 2 subsets: 22 respondents ineligible for or not receiving ASCT as first-line therapy (Subset C) and 2 patients who received IsaVRd as first-line therapy (Subset T).

Respondents rated the most important myeloma symptoms to control as bone issues such as fractures or pain (extremely important), followed by infections, mobility, and neuropathy. Myeloma symptoms were reported to have a significant impact on daily activities and quality of life (QoL), with respondents indicating an extreme effect on their ability to travel, work, and carry out household chores. The factors that patients considered most important to myeloma treatment consisted of effectiveness and remission, overall QoL, manageable side effects, minimizing hospital visits, and ease of access.

The 2 respondents with IsaVRd experience reported having received the treatment for 1 to 2 years. They found supportive care very effective, with treatment side effects and hospital visits having a slight to moderate negative impact on QoL. Both respondents rated IsaVRd as effective in controlling myeloma and manageable in terms of side effects. Despite side effects like diarrhea, infections, and neuropathy, they reported overall improved QoL, with 1 respondent noting significant health improvements.

Clinician Input

Input from Clinical Experts Consulted by CDA-AMC

According to the clinical experts consulted by CDA-AMC, newer, more cost-effective treatments are welcomed as the currently available options are limited.

Unmet Needs

In absence of a cure for MM, the goal is to prevent disease progression and prolong QoL. Even so, a significant number of patients on the current standard of care in Canada (daratumumab/lenalidomide/dexamethasone) progress after 8 months of treatment, therefore never reaching the landmark 5-year PFS average. Prognosis is even worse for patients with early relapses, as no other therapy offers this duration of response. With the average age of individuals with MM being in the transplant-ineligible category, there is an unmet need for treatments that effectively delay first relapse, lessen frailty from progressive disease, and to minimize health care utilization from the symptoms of progressive disease.

Place in Therapy

According to the clinical experts, IsaVRd would be an alternative to the currently funded first-line therapy for transplant-ineligible myeloma patients, (e.g., DRd). It is expected that combinations using isatuximab would be equally considered for first-line treatment in this patient population. Subsequently, bortezomib, lenalidomide, and dexamethasone (VRd) may be used more frequently because of starting patients on IsaVRd as some patients may not tolerate the side-effects of isatuximab and remain on VRd only.

Patient Population

All patients requiring first-line therapy for transplant-ineligible MM would be eligible for treatment with IsaVRd.

Assessing the Response Treatment

Together with traditional measures of response as per IMWG response criteria, reduction in the frequency and/or severity of symptoms such as bone pain and renal failure would be documented monthly with lab investigations. Improvement in QoL and function would be expected with better and faster response to therapy.

Discontinuing Treatment

The clinical experts noted that treatment discontinuation is guided by IWMG response criteria, or clinically determined, progressive disease and intolerable side effects (e.g., infusion reactions and infection.

Prescribing Considerations

IsaVRd would be considered as a first-line treatment option for individuals with transplant-ineligible MM. The clinical experts noted that a myeloma therapy expert would be needed to facilitate therapy.

Clinician Group Input

Two clinician groups comprising 19 clinicians provided input for this review: the Canadian Myeloma Research Group (CMRG) (13 clinicians contributed to the input) and the Ontario Health (Cancer Care Ontario) (OH [CCO]) Hematology Cancer Drug Advisory Committee (6 clinicians contributed to the input). Overall, the input was aligned with the input from the clinical experts consulted by CDA-AMC.

The OH (CCO) Hematology Cancer Drug Advisory Committee highlighted the lack of comparative data with DRd and noted that isatuximab's IV administration may be less appealing than daratumumab's subcutaneous option. The clinical experts consulted by CDA-AMC noted that this may be a less-relevant issue once isatuximab subcutaneous administration become approved.

The CMRG pointed out that the key shift in treatment would involve adding bortezomib to the anti-CD38 monoclonal antibody, lenalidomide, and steroid backbone, supporting IsaVRd as the new first-line standard of care for newly diagnosed, transplant-ineligible multiple myeloma due to its potential for greater efficacy than VRd alone. They also remarked that while isatuximab requires longer infusion times, shorter durations are feasible. Furthermore, bortezomib-refractory patients in the frontline setting could still benefit from carfilzomib-based regimens, making IsaVRd unlikely to alter the relapsed treatment landscape significantly.

Drug Program Input

The clinical experts consulted for the review provided advice on the potential implementation issues raised by the drug programs.

Table 2: Responses to Questions from the Drug Programs

Implementation issues	Response
Relevant comparators	
Funded treatment options for newly diagnosed transplant-ineligible myeloma patients include VRd, DRd, and DCyborD, DVMP. The trial compared IsaVRd against VRd, with 4 induction cycles of VRd +/- isatuximab, followed by continuous Rd +/- isatuximab until disease progression or unacceptable toxicity. *How does IsaVRd compare to DRd, DCyBorD, or DVMP?*	The clinical experts theorized that IsaVRd would have better, if not similar, efficacy to DRd but that head-to-head trials would be needed to confirm this. The experts also noted that DCyBorD and DVMP are not commonly used due to their safety profiles and clinical inferiority compared with DRd. Additionally, the MRD response rates are higher with the combinations containing bortezomib. pERC agreed with the clinical experts but noted that the comparisons between DCyBorD and DVMP relative to DRd were not evaluated.
Considerations for initiation of therapy	
Should the following patients be considered for IsaVRd: • *Age > 80 years* • *ECOG PS > 2* • *Amyloidosis, or monoclonal gammopathy of undetermined significance, smoldering multiple myeloma* • *Concomitant plasma cell leukemia* • *High risk cytogenetics*	The clinical experts confirmed that these patient populations should be considered for IsaVRd on a case-by-case basis, and delivery of treatment would vary depending on the situation (e.g., may start oral treatments only in patients >80 years, and add on other treatments if tolerated). It should also be noted that frailty assessment would be better than age itself. Age does contribute to frailty, but it is not unto itself the only definition of frailty. PERC agreed with the clinical experts that amyloidosis is a different disease from myeloma, and no treatments are given in patients with monoclonal gammopathy of undetermined significance or smoldering myeloma, thus, treatment with IsaVRd is not warranted in these populations.
Considerations for continuation or renewal of therapy	
Should cyclophosphamide be added to IsaVRd upon biochemical progression, given the clinical practice of adding cyclophosphamide to other myeloma regimens to prolong the response.	pERC agreed with the clinical experts that adding cyclophosphamide is not recommended as it is generally used as a bridging therapy and only adds more toxicity without an expectation of real benefit.

Implementation issues	Response
Should treatments be resumed if prolonged treatment breaks occur.	The clinical experts confirmed that treatment should be resumed if progression has not occurred prior to the prolonged treatment break. pERC agreed with the clinical experts.
If 1 of the drugs is discontinued can the other drugs in the regimen be continued until disease progression or unacceptable toxicity.	The clinical experts confirmed that if 1 of the drugs in the regimen is discontinued, then the treatment can continue with the other drugs in the regimen until disease progression or unacceptable toxicity. pERC agreed with the clinical experts.
Considerations for prescribing of therapy	
The dosing schedule for VRd in the IMROZ trial appears different from that used in jurisdictions in Canada (weekly at a dose of 1.3 to 1.5 mg/m^2). Are there alternative dosing schedules for bortezomib or VRd that can be used?	pERC and the clinical experts noted that bortezomib should be dosed at the Canadian and International standard of once weekly.
Rapid infusion for isatuximab has been adopted by some jurisdictions to save on chair time.	This is a comment from the drug plans to inform pERC deliberations, though pERC and the clinical experts highlighted that this should be conducted when possible.
Generalizability	
On a time-limited basis, should isatuximab be added to patients receiving VRd?	The clinical experts confirmed that this should be considered for this patient population.
Funding algorithm	
Under what clinical circumstances would IsaVRd be preferred over daratumumab-based regimens and vice-versa? *Note: If the patient's disease progresses on an anti-CD38 biologic, then the patient would not be eligible for any downstream anti-CD38 biologic.*	The clinical experts noted that IsaVRd would be a substitute for daratumumab-based regimens and the choice would come down to patient and clinician preference on a case-by-case basis. pERC also noted that efficacy and safety of IsaVRd has not been demonstrated in patients older than 80 years, though agrees that use in this population according to clinician judgement on a case-by-case basis is acceptable.
Care provision issues	
Isatuximab interferes with blood compatibility testing; hence, the product monograph recommends that patients undergo phenotyping prior to the first isatuximab infusion.	This is a comment from the drug plans to inform pERC deliberations.
System and economic issues	
In the trial, prophylactic administration of G-CSF was given at the investigator's discretion if there was recurrent neutropenia or if there were serious neutropenic complications.	This is a comment from the drug plans to inform pERC deliberations.
Confidential prices exist for daratumumab	This is a comment from the drug plans to inform pERC deliberations.

DRd = daratumumab; DCyBord = daratumumab, bortezomib, cyclophosphamide, and dexamethasone; DVMP = daratumumab, bortezomib, melphalan, and prednisone; ECOG PS = Eastern Cooperative Oncology Group Performance Status; IsaVRd = isatuximab, bortezomib, lenalidomide, and dexamethasone; Rd = lenalidomide and dexamethasone; VRd = bortezomib, lenalidomide, and dexamethasone.

Clinical Evidence

Systematic Review

Description of Studies

The systematic review included 3 reports of 1 pivotal trial (IMROZ). IMROZ is an ongoing, prospective, international (no Canadian sites), multicentre, open-label, parallel-group phase III randomized controlled trial (RCT) to assess the clinical benefit of IsaVRd

compared to VRd alone in patients with newly diagnosed MM who are not eligible for ASCT. A total of 446 patients were randomized in a 3:2 ratio to IsaVRd (N = 265) or VRd (N = 181). Randomization was stratified by country (China versus other countries), age (under 70 versus 70 years of age or older), and Revised International Staging System (R-ISS) stage I to II versus III versus not classified (i.e., inconclusive fluorescence in situ hybridization [FISH] unless the randomization stratum could be determined based on lactate dehydrogenase [LDH], albumin, and beta-2 microglobulin only). Patients in the IsaVRd group received isatuximab 10 mg/kg IV in 42-day cycles (cycles 1 to 4) or 28-day cycles (after 4 cycles) in combination with VRd. Patients were treated until they died, experienced disease progression, unacceptable toxicity or they decided to discontinue study treatment. The primary outcome was progression free survival (PFS), and the key secondary outcomes included minimal residual disease (MRD) and overall survival (OS). During the continuous treatment period, patients randomized to the VRd group who had confirmed progressive disease (PD) during the VRd portion of the continuous treatment period (as assessed by the Investigator) could crossover to the IsaVRd group. Harms including treatment-emergent adverse events (TEAEs), serious adverse events (SAEs), and adverse events (AEs) of special interest, were also measured and reported. Patient-reported outcomes (e.g., health-related quality of life [HRQoL]) were also measured.

Patients were an average of 71.5 years of age (standard deviation [SD] 4.8 years), 53.1% were male, and 46.9% were female. Most patients (89.0%) had an Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0 or 1. The most common international staging system (ISS) stage at study entry was stage I (53.0%), followed by stage II (31.1%), and stage III (15.2%). The MM subtype at baseline was most frequently IgG (64.1%) and the R-ISS stage at study entry was most frequently stage II (n = 286; 64.1%). The median time from initial diagnosis to randomization was 1.18 months. The main reason for transplant ineligibility was age 65 years or older (95.7%).

Unless otherwise specified, all data reported are from the second interim analysis for the IMROZ trial corresponding with a data cut-off of September 26, 2023, and reported for the intention-to-treat (ITT) population. This data cut-off corresponds with the planned second PFS interim analysis cut-off date (i.e., date when 167 PFS events [75% information fraction] from the global population were expected to be observed). At the September 26, 2023, data cut-off, a total of 162 PFS events were observed, as determined by an independent review committee (IRC). The median follow-up at this data cut-off was 59.73 months (range: 0.17 to 68.99).

Efficacy Results

At the time of the September 26, 2023 data cut-off, 78 (43.1%) patients in the VRd group and 84 (31.7%) patients in the IsaVRd group experienced PFS events. The median PFS was 54.34 months (95% CI, 45.207 to NC) in the VRd group and not reached in the IsaVRd group. The HR was 0.596 (98.5% CI, 0.406 to 0.876) in favour of IsaVRd group compared to VRd. At 60 months, the PFS probability was 45.2% in the VRd group and 63.2% in the IsaVRd group. The risk difference at 60 months was 18.0% (95% CI, 6.5% to 29.5%). The results for sensitivity analyses (e.g., without censoring for further antimyeloma treatment, using investigator assessment of response, without censoring of progression or death occurring at least 13 weeks after the last valid disease assessment, etc.), and planned subgroup analyses (e.g., by age, sex, race, geographic location, etc.) were consistent with the primary analysis.

At the interim analysis, 128 deaths had occurred (VRd = 59; IsaVRd = 69) representing an OS information fraction of 63%. The median OS was not calculable at the data cut-off for IsaVRd or VRd groups (HR = 0.776; 99.97% CI, 0.407 to 1.48). OS was not formally analyzed due to earlier failure of the statistical hierarchy (the final OS analysis will be conducted at the time that there have been 202 deaths). The OS event-free probability at 60-months was 66.3% in the VRd group and 72.3% in the IsaVRd group, representing an absolute risk difference of 5.9% (95% CI, –3.3 to 15.2%).

The overall response rate (ORR) was similar in the VRd and IsaVRd groups (92.3% vs. 91.3%; OR, 0.888 [95% CI, 0.439 to 1.794]). The complete response (CR) rate (consisting of patients with stringent CR and CR) was statistically significant in favour of IsaVRd (odds ratio [OR] = 1.656, 95% CI, 1.097 to 2.500) with a CR or better in 74.7% of patients in the IsaVRd compared with 64.1% in the VRd group. The MRD negativity rate for patients with a CR was statistically lower in the VRd group (40.9%) compared with the IsaVRd group (55.5%) (OR = 1.803, 95% CI, 1.229 to 2.646). The rate of very good partial response (VGPR) or better based on IRC assessment was 82.9% in the VRd group and 89.1% in the IsaVRd group (OR = 1.729, 95% CI, 0.994 to 3.008). The p-value did not cross the multiplicity-adjusted efficacy boundary of 0.025. Most (> 90%) of patients in both treatment groups achieved a tumour response.

HRQoL was assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30). Completion rates were over 90% of patients to cycle 14, and over 80% at each cycle among patients remaining in follow-up, however, the total number of patients declined over time. Global health status remained stable throughout the treatment period, with no apparent differences between groups with regards to change from baseline.

Harms Results

Most patients had a TEAE (IsaVRd = 99.6%; VRd = 98.3%), with the most frequently reported TEAEs (≥ 10% of patients) in the IsaVRd and VRd treatment group being peripheral sensory neuropathy (54.4% vs. 60.8%), diarrhea (54.8% vs. 48.6%), constipation (35.7% vs. 40.9%), upper respiratory tract infection (34.2% vs. 33.7%), peripheral edema (32.7% vs. 32.6%), fatigue (34.6% vs. 26.5%), and cataract (38.0% vs. 25.4%).

More individuals in the IsaVRd group had a Grade 3 or greater TEAE compared to VRd (91.6% vs. 84.0%). Similarly, more patients in the IsaVRd group had treatment-emergent SAEs (70.7% vs. 67.4%). The most frequently reported SAE (≥ 10% of patients in either treatment group was pneumonia (29.7% vs. 21.0%).

TEAEs leading to definitive treatment discontinuation were reported in 22.8% of patients receiving IsaVRd and 26.0% of patients receiving VRd. The most frequent reason for definitive treatment discontinuation was due to COVID-19 pneumonia (3.0% vs. 0.6%).

There were 128 deaths reported (IsaVRd = 26.2%; VRd = 32.6%). AEs accounted for 11.0% in the IsaVRd group and 6.1% in the VRd group.

Infusion reactions and infections were notable harms of interest to this review. Infusion reactions were more frequent with IsaVRd compared to VRd (23.6% vs. 1.1%). The rate of infections was similar across groups, occurring in 91.3% patients in the IsaVRd group and 86.7% patients in the VRd group, consisting primarily of pneumonia, upper respiratory tract infections, and COVID-19 infections.

Critical Appraisal

The randomization method, and allocation concealment of the IMROZ trial were considered adequate. However, IMROZ was an open-label trial, and lack of blinding may have biased results, particularly for subjective, patient-reported outcomes (e.g., HRQoL), harms reporting, or willingness to remain in the trial. Objective outcomes like death and assessment of outcomes like PFS were conducted by a blinded IRC, and therefore were unlikely to have been influenced by lack of blinding. Even so, there was an exploratory component to this trial in which patients in the VRd control arm were allowed to crossover to the IsaVRd arm after disease progression was confirmed. Multiplicity was controlled in the key secondary outcomes with the use of a hierarchical testing procedure; however, early failure of the hierarchy meant that statistical testing was not conducted for OS, one of the key secondary outcomes, and no inferences could be drawn about differences between groups for this outcome. HRQoL was not included in the hierarchy, and differences between groups were not tested statistically; therefore, no conclusions could be drawn about this outcome. While the IMROZ trial is still ongoing, the available results were based on a planned interim analysis, with an information fraction of 75% for PFS; therefore, there is a risk of overestimation of the primary effect for PFS. However, given the statistically significant difference observed between the groups, and the calculation of the 98.5% CIs, the potential for overestimation is unlikely to alter the conclusions. In the analysis of PFS, 18.8% of patients in the VRd group and 23.8% in the IsaVRd group were censored due to not having a valid disease assessment in the 13 weeks prior to the data cut-off (i.e., missed 2 or more scheduled disease assessments). Because the reason for missed assessments is not known, there is a potential for risk of bias due to informative censoring. There was no sensitivity analysis addressing this issue and the direction of potential bias cannot be ascertained. At the data cut-off date, the OS information fraction was 63%. This is important because while PFS can be viewed as a surrogate for OS, death is not an immediate consequence of treatment failure as further lines of treatment can prolong life. Furthermore, the OS analysis is confounded by crossovers (the risk of bias may be toward the null). As the trial progressed, more patients discontinued treatment or died. This may have led to attrition bias for outcomes analyzed based on change scores like HRQoL or incidence of AEs which were only documented for patients still being followed. For the latter, results were additionally reported after adjustment for the duration of exposure.

The IMROZ trial excluded patients over the age of 80 years and those with ECOG PS greater than 2, however, some patients with ECOG PS of 2 or more were enrolled. The clinical experts noted that the efficacy of VRd in the trial was higher than would normally be expected, which could be the result of a learning curve in jurisdictions that use VRd regularly. Further, in the IMROZ trial, bortezomib was not dosed at the Canadian and international standard of once weekly. Lastly, while the study was a conducted in 96 sites (21 countries), none of the sites were in Canada.

GRADE Summary of Findings and Certainty of the Evidence

The selection of outcomes for GRADE assessment was based on the sponsor's Summary of Clinical Evidence, consultation with clinical experts, and input received from patient and clinician groups and public drug plans. The following list of outcomes was finalized in consultation with expert committee members:

- PFS: median, 18-, 36-, 60-months
- OS: median, 60 months
- HRQoL using the EORTC QLQ-C30: change from baseline
- Individuals with SAEs: up to the data cut-off.

Table 3: Summary of Findings for IsaVRd Versus VRd for Patients with Multiple Myeloma

Outcome and follow-up	Patients (studies), N	Relative effect (95% CI)	Absolute effects (95% CI)			Certainty	Interpretation
			IsaVRd	VRd	Difference		
Survival outcomes (median follow-up 59.7 months [range: 0.17 to 68.99])							
Probability of PFS by IRC at 18 months	446 (1 RCT)	[redacted]	882 per 1,000 (835 to 916 per 1,000)	796 per 1,000 (726 to 850 per 1,000)	86 more per 1,000 (13 to 159 more per 1,000)	Moderate[a]	IsaVRd likely results in an improvement in PFS compared to VRd.
Probability of PFS by IRC at 36 months	446 (1 RCT)	[redacted]	761 per 1,000 (702 to 809 per 1,000)	664 per 1,000 (583 to 732 per 1,000)	97 more per 1,000 (5 to 189 more per 1,000)	Moderate[a]	IsaVRd likely results in an improvement in PFS compared to VRd.
Probability of PFS by IRC at 60 months	446 (1 RCT)	[redacted]	632 per 1,000 (562 to 694 per 1,000)	452 per 1,000 (356 to 542 per 1,000)	180 more per 1,000 (65 to 295 more per 1,000)	Moderate[a]	IsaVRd likely results in an improvement in PFS compared to VRd.
Probability of OS by IRC at 60 months	446 (1 RCT)	[redacted]	723 per 1,000 (661 to 775 per 1,000)	663 per 1,000 (585 to 731 per 1,000)	59 more per 1,000 (33 fewer to 152 more per 1,000)	Low[b]	IsaVRd may result in an improvement in OS compared to VRd.
Patient-reported outcomes (HRQoL)							
EORTC QLQ-C30 global health status Follow-up: up to 90 days after the last study treatment	446 (1 RCT)	NA	NA	The mean difference between groups in change from baseline in assessments using the EORTC QLQ-C30 was not tested statistically. The mean global health status appeared relatively stable over time in both groups with wide overlapping CIs.		Low[c]	IsaVRd may result in little-to-no difference in global health status compared to VRd

Outcome and follow-up	Patients (studies), N	Relative effect (95% CI)	Absolute effects (95% CI)			Certainty	Interpretation
			IsaVRd	VRd	Difference		
Safety outcomes (treatment-emergent SAEs)							
SAEs Follow-up: up to 20 days after the last dose of study treatment[d]	444 (1 RCT)	RR, 1.05 (0.92 to 1.19)	707 per 1,000 (648 to 762 per 1,000)	674 per 1,000 (601 to 742 per 1,000)	33 more per 1,000 (54 fewer to 121 more per 1,000)	Moderate[e]	IsaVRd likely results in an increase in SAEs compared to VRd

CI = confidence interval; EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Quality of Life Core 30; HRQoL = health-related quality of life; IsaVRd = isatuximab, bortezomib, lenalidomide, and dexamethasone; NA = not applicable; OS = overall survival; PFS = progression-free survival; RCT = randomized controlled trial; RR = risk ratio; SAE = serious adverse event; VRd = bortezomib, lenalidomide, and dexamethasone.

Note: Study limitations (which refer to internal validity or risk of bias), inconsistency across studies, indirectness, imprecision of effects, and publication bias were considered when assessing the certainty of the evidence. All serious concerns in these domains that led to the rating down of the level of certainty are documented in the table footnotes.

[a] No threshold of clinical importance could be established; effects were appraised using the null. Rated down 1 level for study limitations; 18.8% of patients in the VRd group and 23.8% in the IsaVRd group were censored due to not having a valid disease assessment in the 13 weeks prior to the data cut-off (i.e., missed 2 or more scheduled disease assessments). Because the reason for missed assessments is not known, there is a potential for risk of bias due to informative censoring.

[b] Rated down 1 level for study limitations; results are from an interim analysis where OS was not formally tested, there is a risk of bias due to confounding as a result of crossover of patients from the VRd to the IsaVRd group post-progression, and there is a potential for risk of bias due to informative censoring. No threshold of clinical importance could be established; effects were appraised using the null. Rated down 1 level for imprecision; the point estimate suggests benefit and the CI includes no difference and potential harm.

[c] Rated down 2 levels for study limitations; there is risk of bias due to (a) lack of blinding and a subjective outcome, (b) substantial missing outcome data.

[d] For patients in the VRd group who crossed over, the follow-up was to the crossover date minus 1 day.

[e] No threshold of clinical importance could be established; effects were appraised using the null. Rated down 1 level for imprecision; the point estimate suggests harm and the CI includes no difference and potential benefit (i.e., lesser harm than VRd).

Long-Term Extension Studies

There is no long-term extension phase planned for the IMROZ trial. The IMROZ trial remains ongoing with an anticipated completion date of June 30, 2027. No other long-term extension studies were included in the submission.

Indirect Comparisons

Description of Studies

Unanchored matching-adjusted indirect comparisons (MAICs) were used as the source of indirect treatment comparison (ITC) to compare individual patient data for IsaVRd from IMROZ to aggregate data from studies of DRd, lenalidomide and dexamethasone (Rd), DVMP, and DCyBord. For the comparison to CyBord (Flatiron data source), a nonrandomized comparison using inverse probability weighting (IPW) methods was used because individual patient data were available for each arm.

Efficacy Results

Progression-Free Survival

The MAIC of IsaVRd versus DRd resulted in HRs of [redacted] at 1 year and [redacted] at 5 years.

The MAIC of IsaVRd versus DVMP resulted in HRs of [redacted] at 1 year and [redacted] at 5 years.

The MAIC of IsaVRd versus DCyBord resulted in HRs of [redacted] at 1 year and [redacted] at 5 years.

The MAIC of IsaVRd versus Rd using data from MAIA resulted in HRs of [redacted] at 1 year and [redacted] at 5 years. Using data from FIRST, the HR was [redacted] at 1 year and [redacted] at 5 years.

The observational comparison of IsaVRd versus CyBord resulted in HRs of [redacted] at 1 year and [redacted] at 5 years.

Overall Survival

The MAIC of IsaVRd versus DRd resulted in HRs of [redacted] at 1 year and [redacted] at 5 years.

The MAIC of IsaVRd versus DVMP resulted in HRs of [redacted] at 1 year and [redacted] at 5 years.

There were no data available to compare OS for IsaVRd versus DCyBord.

The MAIC of IsaVRd versus Rd using data from MAIA resulted in HRs of [redacted] at 1 year and [redacted] at 5 years. Using data from FIRST, the HR was [redacted] at 1 year and [redacted] at 5 years.

The observational comparison of IsaVRd versus CyBord resulted in HRs of [redacted] at 1 year and [redacted] at 5 years.

Harms Results

Harms were not evaluated in the submitted ITCs.

Critical Appraisal

The ITC analyses were preceded by a feasibility appraisal, and the decision to use MAICs and IPW as the ITC method of choice (instead of NMA) was adequately justified. However, the unanchored nature of the comparisons imposes an unrealistic assumption that all prognostic factors and effect modifiers are adequately adjusted for. The choice of the adjustment factors was based on internal expert opinion and availability and completeness of data in the trials. An assessment of the potential magnitude of residual confounding was not presented for any comparison, therefore the extent of potential bias is unknown. The adjustment methods used cannot overcome methodological or design differences across the comparators which can introduce bias (e.g., region or setting, length of follow-up, outcome definitions [event and censoring rules, schedule and method of assessments], co-interventions, subsequent treatments). Important outcomes for decision-making like HRQoL and AEs were not included in the analyses, even though the MAIC included real-world evidence (RWE) which could have provided important insights and generation of hypotheses for future confirmation. The OS data from the IMROZ trial is still immature and final data will not be available until 2027, so any MAIC based on this is premature. Generalizability may be an issue due to the small sample size remaining after the exclusions and matching in some of the analyses.

Studies Addressing Gaps in the Evidence from the Systematic Review

No studies addressing gaps were submitted.

Economic Evidence

Cost and Cost-Effectiveness

Table 4: Summary of Economic Evaluation

Component	Description
Type of economic evaluation	Cost-utility analysis PSM
Target population	Adult patients with NDMM who are not eligible for ASCT.
Treatment	Isatuximab in combination with bortezomib, lenalidomide and dexamethasone (henceforth, referred to as IsaVRd).
Dose regimen	Cycle 1 (42-day cycle), isatuximab (10 mg/kg) is dosed weekly on Days 1, 8, 15, 22 and 29. Cycles 2 to 4 (42-day cycles), isatuximab (10 mg/kg) is dosed every 2 weeks on Days 1, 15, and 29. Cycles 5 to 17 (28-day cycles), isatuximab (10 mg/kg) is dosed every 2 weeks on Days 1 and 15. Cycles 18 and beyond (28-day cycles), isatuximab (10 mg/kg) is dosed every 4 weeks on Day 1.

Component	Description
Submitted price	Isatuximab: $757.90 per 100 mg/5 mL Isatuximab: $3,789.49 per 500 mg/25 mL
Submitted treatment cost	$33,695 in cycle 1, $20,217 in cycles 2 to 4, $11,669 in cycles 5 to 17, $5,835 in cycles 18 and beyond.
Comparators	• CyBord • DCyBord • DRd • DVMP • Rd • VRd
Perspective	Canadian publicly funded health care payer
Outcomes	QALYs, LYs
Time horizon	Lifetime (29 years)
Key data sources	• Efficacy inputs for IsaVRd and VRd were informed by the IMROZ trial (data cut-off date: September 26, 2023). • Efficacy inputs for CyBord, DCyBord, DRd, DVMP, and Rd were derived from sponsor-submitted ITCs.
Key limitations	• The comparative clinical efficacy of IsaVRd, CyBord, DCyBord, DRd, DVMP, and Rd therapies is uncertain due to the lack of head-to-head evidence and limitations with the sponsor's ITCs. Factors such as unaddressed prognostic and effect-modifying variables, study design differences, reductions in effective sample size, and imprecision in estimates contribute to uncertainty in the modeled OS and PFS for these comparators. The CADTH base case focused on comparing IsaVRd and DRd, as clinical experts identified DRd as the most relevant comparator and ITC limitations restricted other comparisons. • The long-term OS benefit of IsaVRd is highly uncertain due to immature data from the IMROZ trial and reliance on extrapolated survival projections. These projections suggest a curative effect among patients receiving IsaVRd that is not supported by evidence, with the majority of predicted OS benefits (82%) occurring beyond the observed trial period. • Subsequent therapy costs are highly uncertain due to the sponsor's use of a single one-time cost for all patients transitioning to the post-progression health state. This approach likely overestimates costs by not accounting for treatment duration and prior therapy exposure. Clinical experts noted that treatment selection is typically influenced by previous therapies, rendering the sponsor's assumption unrealistic. • The sponsor used median DoT as a proxy for median TTD, assuming a time-invariant relationship between median PFS and DoT. This approach may not accurately represent the true TTD distribution and does not account for censoring, potentially leading to an overestimation of treatment persistence. For DRd, the sponsor applied the HR of TTD versus PFS from the MAIA trial to the IMROZ population, despite differences in trial populations, methodologies, and treatment regimens. This adds to the uncertainty in the TTD estimates. • The submitted model had transparency challenges due to the use of formulas to manage errors generated in the model, which made it difficult to track how key values were calculated. This limited CADTH's ability to thoroughly validate the model, introducing some uncertainty around the reliability of the results.
CADTH reanalysis results	• The CADTH base case was derived by assuming equal OS efficacy, excluding subsequent therapy costs, and aligning TTD with PFS, focusing on DRd as the primary comparator. • In the CADTH base case, IsaVRd is associated with an ICER of $311,681 per QALY gained relative to DRd (incremental costs = $22,340; incremental QALYs = 0.07). A price reduction of

Component	Description
	2.5% for isatuximab would be required for IsaVRd to be cost-effective compared with DRd at a WTP threshold of $50,000 per QALY gained.

ASCT = autologous stem cell transplant; CyBord = cyclophosphamide in combination with bortezomib and dexamethasone; DCyBord = daratumumab in combination with cyclophosphamide, bortezomib and dexamethasone; DoT = duration of treatment; DRd = daratumumab in combination with lenalidomide and dexamethasone; DVMP = daratumumab in combination with melphalan, prednisone and bortezomib; HR = hazard ratio; ICER = incremental cost-effectiveness ratio; IsaVRd = isatuximab in combination with bortezomib, lenalidomide and dexamethasone; ITC = indirect treatment comparison; LY = life-year; NDMM = newly diagnosed multiple myeloma; OS = overall survival; PFS = progression-free survival; PSM = partitioned survival model; QALY = quality-adjusted life-year; Rd = lenalidomide in combination with dexamethasone; TTD = time to treatment discontinuation; VRd = lenalidomide in combination with dexamethasone and bortezomib.

Budget Impact

CDA-AMC identified the following key limitations with the sponsor's analysis: inappropriate use of RDI to calculate drug acquisition costs; potential overestimation of market uptake for IsaVRd; and exclusion of subsequent therapy costs.

The CDA-AMC BIA base case increased RDI for all comparators to be 100%. The analysis indicates that funding IsaVRd for the treatment of adult patients with NDMM who are not eligible for ASCT resulted in cost savings of $3,304,157 in year 1, $2,016,456 in year 2, and $17,863,532 in year 3. This results in cumulative cost savings of $23,184,144 over 3 years.

pERC Information

Members of the Committee:

Dr. Catherine Moltzan (Chair), Dr. Philip Blanchette, Dr. Kelvin Chan, Dr. Matthew Cheung, Dr. Michael Crump, Annette Cyr, Dr. Jennifer Fishman, Dr. Jason Hart, Terry Hawrysh, Dr. Yoo-Joung Ko, Dr. Aly-Khan Lalani, Amy Peasgood, Dr. Anca Prica, Dr. Adam Raymakers, Dr. Patricia Tang, Dr. Pierre Villeneuve, and Danica Wasney.

Meeting date: April 9, 2025

Regrets:

1 expert committee member did not attend.

Conflicts of interest:

None