Panel Provisional Funding Algorithm

Indication: Multiple myeloma

This report supersedes the CDA-AMC Provisional Funding Algorithm report for multiple myeloma dated August 1, 2024.

Please always check Provisional Funding Algorithms | CDA-AMC to ensure you are reading the most recent algorithm report.

Background

Following a request from jurisdictions, Canada's Drug Agency (CDA-AMC) will design or update an algorithm depicting the sequence of funded treatments for a particular tumour type. These algorithms are proposals for the jurisdictions to implement and adapt to the local context. As such, they are termed "provisional." Publishing of provisional algorithms is meant to improve transparency of the oncology drug funding process and promote consistency across jurisdictions. Please refer to Provisional Funding Algorithm Procedures.

Provisional funding algorithms delineate treatment sequences available to patients who were never treated for the condition of interest (i.e., incident population). Time-limited funding of new options for previously or currently treated patients (i.e., prevalent population) is not detailed in the algorithm.

Further, provisional funding algorithms may contain drugs that are under consideration for funding. Algorithms will not be dynamically updated by CDA-AMC following changes to drug funding status. Revisions and updates will occur only upon request by jurisdictions. Note that as per process, implementation advice from panellists and the resulting algorithms cannot contradict prior expert committee (e.g., the pan-Canadian Oncology Drug Review Expert Review Committee [pERC] or the Formulary Management Expert Committee [FMEC]) recommendations or expand target populations beyond what was recommended.

Jurisdictional cancer drug programs requested a panel provisional funding algorithm for multiple myeloma (MM).

History and Development of the Provisional Funding Algorithm

To date, CDA-AMC has published 4 provisional funding algorithms for MM. The first report was published in May 2022 which was a panel algorithm. The second report was a rapid algorithm published in November 2022 to update and incorporate the CADTH recommendation for selinexor.

The third report was a rapid algorithm published in July 2023 to incorporate the CDA-AMC recommendation for ciltacabtagene autoleucel (Carvykti), the first chimeric antigen receptor (CAR) T-cell therapy approved for the treatment of adult patients with MM who have received at least 3 prior lines of therapy, including a proteasome inhibitor (PI), an immunomodulatory drug (IMiD), and an anti-CD38 antibody, and who are refractory to their last treatment. The fourth update was a rapid algorithm published in August 2024 to incorporate CDA-AMC recommendations for teclistamab (Tecvayli) and elranatamab (Elrexfio).

This purpose of this latest update to the provisional algorithm report is two-fold:

- to incorporate the latest reimbursement recommendation for ciltacabtagene autoleucel (Carvykti) for the treatment of adult patients with MM, who have received 1 to 3 prior lines of therapy, including a PI and an IMiD, and whose disease is refractory to lenalidomide — this is a rapid algorithm update based solely on the pERC recommendation
- to convene a panel to address the outstanding implementation issue related to reimbursement recommendations for elranatamab (Elrexfio) and teclistamab (Tecvayli), focusing on the downstream treatment options for patients with relapsed or refractory MM who have received prior B-cell maturation antigen (BCMA)–directed therapy.

The panel did not discuss the latest ciltacabtagene autoleucel recommendation nor its place in therapy; rather, the jurisdictional cancer programs used this update as an opportunity to resolve the outstanding implementation issue between elranatamab and teclistamab.

Details of the relevant CDA-AMC recommendations are outlined in Table 3, and Table 1 summarizes conclusions from the previous implementation advice panel.

Table 1: CDA-AMC Implementation Advice From Previous Panel Provisional Funding Algorithms for Multiple Myeloma

Date of publication	Implementation advice
May 2022	The panel advises that lenalidomide-bortezomib-dexamethasone (RVd) should be considered as an option for induction therapy in patients with multiple myeloma who are eligible for a transplant. The panel advises that carfilzomib-lenalidomide-dexamethasone (KRd) can be sequenced before or after an anti-CD38-based regimen. The panel advises that isatuximab-containing regimens would be important second-line options, particularly for patients who are eligible for transplant, contingent on them being funded by public payers. The panel advises that both pomalidomide-dexamethasone (Pd) and carfilzomib-dexamethasone (Kd) backbones should be available as sequential treatment options after failure of an anti-CD38-containing regimen. The panel advises that Pd or pomalidomide-cyclophosphamide-dexamethasone (PCd) are valid options after failure of first-line lenalidomide-bortezomib-dexamethasone (RVd).

Implementation Issue

At the request of the participating drug programs, CDA-AMC convened a panel of clinical experts in Canada to provide advice for addressing the outstanding implementation issues as follows:

What is the available evidence to support the downstream treatment options for patients with relapsed or refractory MM who have received prior BCMA-directed therapy?

Consultation Process and Objectives

A panel algorithm is undertaken when the advice of clinical specialists is required to adapt an existing provisional funding algorithm or establish a completely new provisional funding algorithm. The implementation advice panel comprised 4 specialists practising in Canada with expertise in the diagnosis and management of patients with MM, 2 representatives from the public drug programs, and a panel chair.

The panel's objective was to provide advice to the participating drug programs regarding the implementation issues noted in the Background section. Following the identification of implementation issues, discussion guide questions were developed to provide guidance on the panel discussion. Refer to Appendix 2: Discussion Guide Questions. A consensus-based approach was used to develop advice from the panel. In

addition, discussion on whether the panel advice was supported by the participating drug programs (or our Provincial Advisory Group [PAG]) is detailed in this report.

Eligible patient groups, clinician groups, and industry contributors were invited to provide input and feedback at 2 key stages of the project. First, input was gathered on the proposed scope of the report, posted before project initiation, to help shape the direction and scope of the funding algorithm. Second, feedback was collected on the draft algorithm report, publicly posted near project completion, to support its refinement. The panel aimed to incorporate external input on the proposed scope and external feedback on the draft report as was relevant and applicable. Input and feedback falling within the scope of this panel's algorithm are summarized in this report and have also been posted in full on the report's landing page for transparency.

Summary of Input on the Proposed Scope

Input was provided by 1 patient group, Myeloma Canada, and by 1 clinician group, Ontario Health – Cancer Care Ontario Hematology Cancer Drug Advisory Committee. Additionally, 2 manufacturers, Janssen Inc. and GlaxoSmithKline Inc., submitted input for this panel algorithm.

The patient group highlighted that many patients with MM living in Canada have received BCMA-directed treatments through clinical trials in earlier lines of therapy. They noted that some preliminary studies have demonstrated efficacy with BCMA-directed therapies using different mechanisms of action in the same patients. In particular, they pointed out that patients who have received ciltacabtagene autoleucel in earlier lines of treatment may be suitable candidates for subsequent treatment with teclistamab or elranatamab in later lines. The clinician group raised questions regarding the selection criteria for BCMA-targeted bispecific T-cell engagers. Industry input included questions about downstream treatment options for patients with relapsed or refractory MM who have previously received BCMA-directed therapy.

Input that was submitted but fell outside the scope of this panel included discussions on CAR T-cell therapy eligibility for patients who have previously received BCMA-directed treatments, prioritization and accessibility considerations for CAR T-cell therapies, challenges related to sequencing treatments as more patients receive triplet and quadruplet therapies in earlier lines as well as unmet needs following BCMA-directed therapy in the fourth-line setting. The full input from interested parties for this report can be found on the report's landing page.

Clinician Panellists' Advice on Funding Algorithm

Summary of Implementation Advice

Implementation advice regarding the optimal sequencing of treatments is summarized in Table 2. For each implementation issue, a summary of the relevant panel discussion is provided for additional context.

Table 2: Summary of Advice for Addressing Implementation Issues

Issue	Advice	Rationale
Use of BCMA-targeted bispecific T-cell engagers in patients with relapsed/refractory multiple myeloma who have previously received BCMA-directed therapy	The panel advises that BCMA-directed bispecific T-cell engagers be considered as treatment options for patients previously exposed to BCMA-directed therapy. The panel advises against their use in patients whose disease is refractory to BCMA-directed therapy.	Based on the 2025 IMWG immunotherapy sequencing guidelines and limited retrospective data,[1-3] BCMA-targeted bispecific T-cell engagers are safe and effective in patients who have previously received BCMA-directed therapy. These results are discussed in the Panel Discussion section. In the context of patients whose disease is refractory to BCMA-directed therapy, the lack of response to prior BCMA-targeted treatments suggests that these therapies may not be as effective, and alternative therapeutic approaches should be considered. The panel agreed with the IMWG definition of refractory multiple myeloma, which is defined as disease that is nonresponsive to therapy or progresses within 60 days of the last line of therapy.[4]
Selection of elranatamab or teclistamab in patients who have previously received BCMA-directed therapy	The panel advises that both elranatamab and teclistamab should be available as treatment options for patients who have previously received BCMA-directed therapy.	No clinical trial data suggest a preference for 1 agent over the other in this setting. Given the similar mechanisms of action, both should be available in patients who have prior BCMA therapy.

BCMA = B-cell maturation antigen; IMWG = International Myeloma Working Group.

In addition to the previously outlined advice, an improvement in cost-effectiveness was a condition for reimbursement in each of the recommendations related to the drugs in scope. Implementation of any advice herein should be contingent upon ensuring that the relevant treatments are affordable to public payers.

Sources of Evidence

To address the implementation issues, the panel considered the following sources of information:

- pERC recommendation reports for elranatamab (Elrexfio) and teclistamab (Tecvayli)
- input from public drug plans that participate in the provisional funding algorithm process
- four clinical specialists with expertise in diagnosing and treating patients with MM
- patients' perspectives gathered by 1 patient group, Myeloma Canada
- input from 1 clinician group, Ontario Health – Cancer Care Ontario Hematology Cancer Drug Advisory Committee
- input from 2 industry groups, Janssen Inc. and GlaxoSmithKline Inc.
- the following references or publications cited by panel members during the discussion:

- a review of 1 ongoing phase II, noncomparative, open-label trial (MagnetisMM-3) in adult patients with relapsed or refractory MM who have received at least 3 prior lines of therapy, including a PI, an IMiD, and an anti-CD38 monoclonal antibody (mAb)
- a review of 1 ongoing, phase I and II, single-arm open-label trial (MajesTEC-1) in adult patients with relapsed or refractory MM who have received at least 3 prior lines of therapy, including a PI, an IMiD, and an anti-CD38 mAb
- a review of 3 retrospective studies
- a review of a guideline on sequencing immunotherapy for treatment of MM from the international myeloma working group (IMWG) immunotherapy committee.

Panel Discussion

BCMA-Targeted Bispecific T-Cell Engagers in Patients With Relapsed or Refractory MM Who Have Previously Received BCMA-Directed Therapy

The panel discussed the evidence supporting the use of BCMA-targeted bispecific T-cell engagers in patients with relapsed or refractory MM who have previously received BCMA-directed therapy. According to the 2025 IMWG immunotherapy sequencing guidelines,[5] BCMA-targeted bispecific T-cell engagers have been administered following BCMA-directed CAR T-cell therapy. In a dedicated cohort of the MajesTEC-1 trial, teclistamab demonstrated an objective response rate of 53% in 15 patients previously treated with BCMA-targeted CAR T-cell therapy, although the median progression-free survival was only 4.4 months.[6] A pooled analysis of elranatamab in a similar patient population (n = 86) reported a 53% objective response rate, with a longer median progression-free survival of 10.0 months.[7] Real-world data[8,9] indicate that patients with a longer interval since their last BCMA-directed therapy (> 6 months) may experience better responses. However, as with other therapies in this setting, outcomes may be influenced by disease aggressiveness and T-cell fitness.

Two panel members highlighted that in 3 multicentre retrospective observational studies,[1-3] BCMA-targeted bispecific T-cell engagers have shown some favourable efficacy and safety outcomes when used as salvage therapy following BCMA-directed therapy.

There was consensus among panel members that BCMA-targeted bispecific T-cell engagers remain a viable option in patients previously exposed to BCMA-directed therapy.

The panel advised against their use in patients whose disease was refractory to BCMA-directed therapy. The lack of response to BCMA-directed therapy suggests that these agents may not be effective, and alternative therapeutic approaches should be considered. The panel acknowledged that treatment options for patients who progress on BCMA-directed therapy remain limited outside of clinical trials, and both economic considerations and clinician judgment play a role in determining the most appropriate course of action.

The panel agreed with the IMWG definition of refractory MM, which is defined as disease that is nonresponsive to therapy or progresses within 60 days of the last line of therapy.[4]

Selection of Elranatamab or Teclistamab in Patients Who Have Previously Received BCMA-Directed Therapy

The panel discussed the selection of BCMA-targeted bispecific T-cell engagers, specifically elranatamab and teclistamab, in patients who have previously received BCMA-directed therapy. The panel noted that pERC did not impose restrictions on the use of teclistamab in this setting but recommended against the use of elranatamab in patients with prior BCMA exposure. However, the panel saw no clinical rationale for differentiating between the 2 agents because both share a similar mechanism of action and target the same antigens. Given the absence of clinical trial data to suggest favouring 1 drug over the other, the panel indicated that treatment selection may be guided by practical considerations, including site-specific preferences, logistical factors, and supply chain stability. Given these considerations, the panel voiced the importance of maintaining access to both agents as treatment options for patients previously exposed to BCMA-directed therapy.

Other Discussion

The following discussion points were outside the scope of this panel algorithm but were raised by the panellists and have been included here for transparency.

Eligibility Criteria for Elranatamab and Teclistamab

The panel discussed the challenges associated with restricting teclistamab and elranatamab to patients who have received at least 3 prior lines of therapy. Clinicians noted that as treatment paradigms evolve, an increasing number of patients — including both those who are eligible and those ineligible for transplant — are receiving quadruplet therapy during induction. This shift is reshaping treatment sequencing, potentially leading to earlier exposure to key drug classes, which could limit access to BCMA-targeted bispecific T-cell engagers if reimbursement criteria remain strictly tied to the number of prior lines of therapy. This was noted to be out of scope for this review.

CAR T-Cell Therapy Eligibility and Sequencing Considerations

The panel also briefly discussed the sequencing of BCMA-directed therapies in patients eligible for both CAR T-cell therapy and bispecific T-cell engagers. According to the IMWG's 2025 recommendations on immunotherapy sequencing for MM,[5] CAR T-cell therapy should be prioritized. This recommendation is supported by emerging evidence demonstrating that responses to CAR T-cell therapy following disease progression on BCMA-targeted bispecific T-cell engagers are less frequent and durable. However, the panel acknowledged that logistical constraints, including treatment availability and access, may impact treatment selection in clinical practice.

Final Advice Supported by Participating Drug Programs

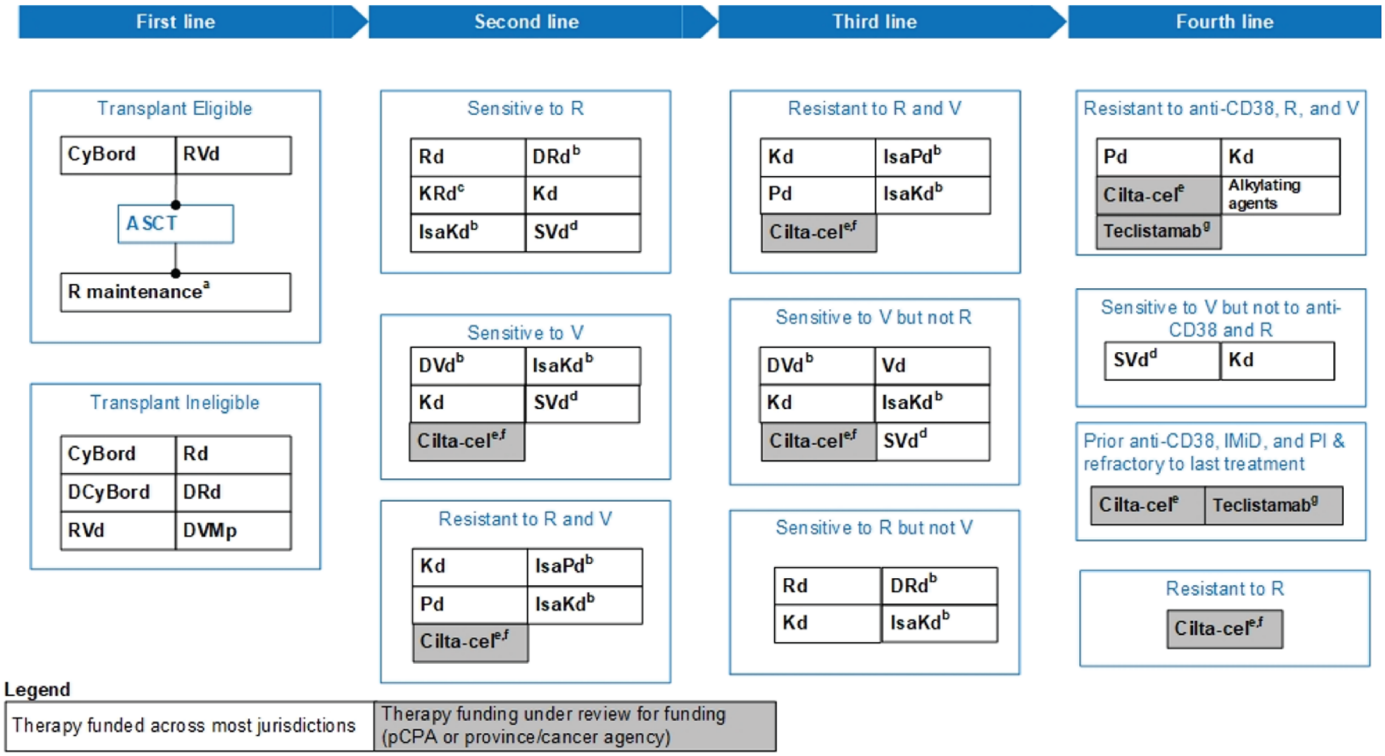
Participating drug programs (or PAG) have reviewed the implementation advice as recommended by the clinician panellists. Efforts are made to incorporate the advice while balancing the need for system affordability and sustainability. In the spirit of consistency with treatment implementation across jurisdictions, advice without evidence or based on insufficient or evolving evidence may not be endorsed, or it may be recommended to be revisited at a later time when more high-quality evidence is available.

PAG endorses the panel advice as described in Table 2.

Finally, PAG has a mandate to support recommendations issued by expert committees (e.g., pERC, FMEC) for implementation across the various jurisdictions. However, the final decisions for how these therapies are to be implemented reside with the individual jurisdictions, where they may adapt the advice locally based on regional differences and needs.

Provisional Funding Algorithm

Figure 1: Provisional Funding Algorithm Diagram for Multiple Myeloma



ASCT = autologous stem cell transplant; cilta-cel = ciltacabtagene autoleucel; CyBord = cyclophosphamide-bortezomib-dexamethasone; DCyBord = daratumumab-cyclophosphamide-bortezomib-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone; DVd = daratumumab-bortezomib-dexamethasone; DVMp = daratumumab-bortezomib-melphalan-prednisone; IMiD = immunomodulatory drug; IsaKd = isatuximab-carfilzomib-dexamethasone; IsaPd = isatuximab-pomalidomide-dexamethasone; Kd = carfilzomib-dexamethasone; KRd = carfilzomib-lenalidomide-dexamethasone; pCPA = pan-Canadian Pharmaceutical Alliance; Pd = pomalidomide-dexamethasone; PI = proteasome inhibitor; R = lenalidomide; Rd = lenalidomide-dexamethasone; RVd = lenalidomide-bortezomib-dexamethasone; SVd = selinexor-bortezomib-dexamethasone; V = bortezomib; Vd = bortezomib-dexamethasone.

Notes:
- Patients with drug resistance cannot be re-treated with same drug(s).
- Cyclophosphamide may be added to Kd, Pd, and Rd.
- Pomalidomide-dexamethasone-bortezomib (PVd) is not represented in the algorithm as it is not commonly used or a standard of care; PVd had been recommended by pERC (previously pCODR) for relapsed or refractory multiple myeloma in patients who have received at least 1 prior treatment regimen including R.
- Elranatamab is not funded at the time of publication of this report as pCPA negotiations concluded without an agreement. Should this status change, the algorithm will be updated.

[a]Maintenance optional.
[b]If not resistant to an anti-CD38 biologic.
[c]Only if also sensitive to R and V.
[d]Must have a PI treatment–free interval of at least 6 months before first day of SVd.
[e]If no prior treatment with any therapy that targets BCMA or any anti-BCMA CAR T-cell therapy.
[f]Must have received 1 to 3 prior lines of therapy, including a PI and an IMiD.
[g]If not refractory to BCMA-directed therapy.

Source: This provisional funding algorithm is the most recent as of May 2025. It was updated following the panel consultation meeting and subsequently endorsed by the panellists. Users are permitted to make copies of this figure for noncommercial purposes only, provided it is not modified when reproduced and appropriate credit is given to CDA-AMC and its licensors.

Provisional funding algorithms are not treatment algorithms; they are neither meant to detail the full clinical management of each patient nor the provision of each drug regimen. The diagrams may not contain a comprehensive list of all available treatments, and some drugs may not be funded in certain jurisdictions. All drugs are subject to explicit funding criteria, which may also vary between jurisdictions. Readers are invited to refer to the cited sources of information on the CDA-AMC website for more details.

Description of the Provisional Funding Algorithm

First-Line Setting

Patients who are eligible for an autologous stem cell transplant can receive induction therapy with either cyclophosphamide-bortezomib-dexamethasone (CyBord) or lenalidomide-bortezomib-dexamethasone (RVd), if funded by the jurisdictions. After transplant, maintenance with lenalidomide is available. Patients who are ineligible for transplant can be given cyclophosphamide-bortezomib-dexamethasone (CyBord) or lenalidomide-dexamethasone (Rd) (with or without daratumumab), RVd or daratumumab-bortezomib-melphalan-prednisone (DVMp).

Relapsed or Refractory

Treatment in the relapsed or refractory setting depends on response to prior therapies. As a rule, patients with drug resistance cannot be treated again with the same drug, except for dexamethasone, which is found in all regimens. Cyclophosphamide may be added to some regimens, such as pomalidomide-dexamethasone (Pd), carfilzomib-dexamethasone (Kd), and lenalidomide-dexamethasone (Rd).

Second-Line Setting

In patients who are sensitive to lenalidomide (R), their options include the following: Daratumumab-lenalidomide-dexamethasone (DRd) or isatuximab-carfilzomib-dexamethasone (IsaKd) if the patient is not resistant to an anti-CD38 biologic, lenalidomide-dexamethasone (Rd), carfilzomib-lenalidomide-dexamethasone (KRd) only if the patient is also sensitive to bortezomib (V), carfilzomib-dexamethasone (Kd), or selinexor-bortezomib-dexamethasone (SVd). For patients to receive selinexor-bortezomib-dexamethasone (SVd), they must have a proteasome inhibitor treatment–free interval of at least 6 months before the first day.

In patients who are sensitive to bortezomib (V), their options include the following: Daratumumab-bortezomib-dexamethasone (DVd) or isatuximab-carfilzomib-dexamethasone (IsaKd) if the patient is not resistant to an anti-CD38 biologic, carfilzomib-dexamethasone (Kd), selinexor-bortezomib-dexamethasone (SVd), or ciltacabtagene autoleucel (cilta-cel). For patients to receive SVd, they must have a proteasome inhibitor treatment–free interval of at least 6 months before the first day. For patients to receive ciltacabtagene autoleucel (cilta-cel), they must have received 1 to 3 prior lines of therapy, including a PI and an IMiD, their disease is refractory to lenalidomide, and they must not have received prior treatment with any therapy that is targeted to BCMA or prior anti-BCMA CAR T-cell therapy.

In patients who are resistant to lenalidomide (R) and bortezomib (V), their options include the following: Isatuximab-pomalidomide-dexamethasone (IsaPd) or isatuximab-carfilzomib-dexamethasone (IsaKd) if not resistant to an anti-CD38 biologic, carfilzomib-dexamethasone (Kd), pomalidomide-dexamethasone (Pd), or ciltacabtagene autoleucel (cilta-cel). For patients to receive ciltacabtagene autoleucel (cilta-cel), they must have received 1 to 3 prior lines of therapy, including a proteasome inhibitor and an IMiD, their disease is refractory to lenalidomide, and they must not have received prior treatment with any therapy that is targeted to BCMA or prior anti-BCMA CAR T-cell therapy.

Third-Line Setting

In patients who are resistant to lenalidomide (R) and bortezomib (V), their options include the following: Isatuximab-pomalidomide-dexamethasone (IsaPd) or isatuximab-carfilzomib-dexamethasone (IsaKd) if not resistant to an anti-CD38 biologic, carfilzomib-dexamethasone (Kd), pomalidomide-dexamethasone (Pd), or ciltacabtagene autoleucel (cilta-cel). For patients to receive ciltacabtagene autoleucel (cilta-cel), they must have received 1 to 3 prior lines of therapy, including a proteasome inhibitor and an IMiD, their disease is refractory to lenalidomide, and they must not have received prior treatment with any therapy that is targeted to BCMA or prior anti-BCMA CAR T-cell therapy.

In patients who are sensitive to bortezomib (V) but not lenalidomide (R), their options include the following: daratumumab-bortezomib-dexamethasone (DVd) or isatuximab-carfilzomib-dexamethasone (IsaKd) if the patient is not resistant to an anti-CD38 biologic, carfilzomib-dexamethasone (Kd), bortezomib-dexamethasone (Vd), selinexor-bortezomib-dexamethasone (SVd), or ciltacabtagene autoleucel (cilta-cel). For patients to receive SVd, they must have a proteasome inhibitor treatment–free interval of at least 6 months before the first day. For patients to receive ciltacabtagene autoleucel (cilta-cel), they must have received 1 to 3 prior lines of therapy, including a proteasome inhibitor and an IMiD, their disease is refractory to lenalidomide, and they must not have received prior treatment with any therapy that is targeted to BCMA or prior anti-BCMA CAR T-cell therapy.

In patients who are sensitive to lenalidomide (R) but not bortezomib (V), their options include the following: daratumumab-lenalidomide-dexamethasone (DRd) or isatuximab-carfilzomib-dexamethasone (IsaKd) if the patient is not resistant to an anti-CD38 biologic, lenalidomide-dexamethasone (Rd), or carfilzomib-dexamethasone (Kd).

Fourth-Line Setting

In patients who are resistant to anti-CD38 biologic, lenalidomide (R) and bortezomib (V), the options include: Pomalidomide-dexamethasone (Pd), carfilzomib-dexamethasone (Kd), teclistamab, ciltacabtagene autoleucel, or other alkylating drugs. For patients to receive ciltacabtagene autoleucel therapy, they must not have prior treatment with any therapy that targets BCMA or any CAR-T-cellular therapy.

In patients who are sensitive to bortezomib (V) but not to anti-CD38 biologic or lenalidomide (R), their options include the following: Selinexor-bortezomib-dexamethasone (SVd) or carfilzomib-dexamethasone (Kd). For patients to receive SVd, they must have a proteasome inhibitor treatment–free interval of at least 6 months before the first day.

In patients who have received anti-CD38, IMiD and proteasome inhibitor (PI) and refractory to last treatment, their options include the following: teclistamab or ciltacabtagene autoleucel (cilta-cel). For patients to receive ciltacabtagene autoleucel therapy, they must not have prior treatment with any therapy that targets BCMA or any CAR-T-cellular therapy.

In patients who are resistant to lenalidomide (R), their options include: ciltacabtagene autoleucel (cilta-cel). For patients to receive ciltacabtagene autoleucel (cilta-cel), they must have received 1 to 3 prior lines of therapy, including a proteasome inhibitor and an IMiD, their disease is refractory to lenalidomide, and

they must not have received prior treatment with any therapy that is targeted to BCMA or prior anti-BCMA CAR T-cell therapy.

Additional Remarks

Note that pomalidomide-dexamethasone-bortezomib (PVd) is not represented in the algorithm because it is not commonly used or considered a standard of care. However, PVd recommended by pan-Canadian Oncology Drug Review (pCODR) for relapsed or refractory MM in patients who have received at least 1 prior treatment regimen, including lenalidomide (R).

Although CADTH had issued a reimbursement recommendation for elranatamab for the treatment of patients with relapsed or refractory MM who have received at least 3 prior lines of therapy, including a PI, an IMiD, and an anti-CD38 mAb, and who have demonstrated disease progression on the last therapy, it is not funded because pan-Canadian Pharmaceutical Alliance (pCPA) negotiations concluded without an agreement at the time of publication of this algorithm. Should this status change, the algorithm may be updated at the next request by the public drug programs.

Summary of Feedback on the Draft Report

A patient group, Myeloma Canada; 2 clinician groups, CMRG and Ontario Health – Cancer Care Ontario Hematology Cancer Drug Advisory Committee; 2 industry groups, Amgen Canada and Janssen Inc.; and the public drug programs provided feedback on the draft algorithm report. The patient group indicated support and agreement with the draft report. The clinician groups were largely in support and agreement with the draft report but provided some feedback that was out of scope for this algorithm update. The industry groups were also largely in agreement with the draft report and provided some feedback that was out of scope for this algorithm update. One industry group indicated that pCPA negotiations for elranatamab had concluded without agreement at the time of publication of this algorithm. The public drug programs discussed and provided suggestions that have been incorporated. Other editorial suggestions were provided and addressed where feasible. All feedback is posted on the landing page for this project.

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Appendix 1: Relevant CDA-AMC Recommendations

Table 3: Relevant CDA-AMC Recommendations

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
Newly diagnosed		
Daratumumab (Darzalex) + lenalidomide (Revlimid) + dexamethasone	March 5, 2020	pERC conditionally recommends to reimburse daratumumab in combination with lenalidomide and dexamethasone (DRd) for patients with newly diagnosed MM who are not suitable for autologous stem cell transplant if the following conditions are met: • cost-effectiveness being improved to an acceptable level • feasibility of adoption (budget impact) being addressed. pERC concluded that the optimal sequencing of therapies for patients with newly diagnosed MM who are not suitable for autologous stem cell transplant is unknown. Therefore, pERC was unable to make an evidence-informed recommendation on sequencing of treatments. pERC recognized that provinces will need to address this issue upon implementation of a reimbursement recommendation for DRd and noted that collaboration among provinces to develop a national, uniform approach to optimal sequencing would be of great value.
Daratumumab (Darzalex) + bortezomib (Velcade) + melphalan + prednisone	August 29, 2019	pERC conditionally recommends to reimburse daratumumab in combination with bortezomib, melphalan, and prednisone (DVMp) for patients with newly diagnosed MM who are not suitable for ASCT if the following conditions are met: • cost-effectiveness being improved to an acceptable level • feasibility of adoption (budget impact) being addressed • treatment with daratumumab should continue until unacceptable toxicity or disease progression **Optimal sequencing of available therapies after progression on daratumumab in combination with bortezomib, melphalan, and prednisone:** pERC concluded that the optimal sequencing of therapies for patients with newly diagnosed MM who are not suitable for ASCT is unknown. Therefore, pERC was unable to make an evidence-based recommendation on sequencing of treatments. pERC recognizes that provinces will need to address this issue upon implementation of a reimbursement recommendation for daratumumab and noted that collaboration among provinces to develop and national, uniform approach to optimal sequencing would be of great value. **Daratumumab in combination with cyclophosphamide, bortezomib, and dexamethasone:** At the time of implementing a reimbursement recommendation for DVMp, jurisdictions may consider extending the reimbursement to daratumumab in combination with cyclophosphamide, bortezomib, and dexamethasone (DCyBord) because pERC agreed with the registered clinician input and the CGP that DCyBord would likely be equally as effective as DVMp and possibly less toxic.

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
Lenalidomide (Revlimid) + bortezomib (Velcade) + dexamethasone	June 19, 2019	pERC conditionally recommends to reimburse lenalidomide in combination with bortezomib and low-dose dexamethasone in patients with newly diagnosed MM in whom stem cell transplantation is not intended if the following condition is met: • feasibility of adoption is addressed (budget impact). Reimbursement should be in patients with good performance status and treatment (with lenalidomide or low-dose dexamethasone for the maintenance phase) should continue until unacceptable toxicity or disease progression. pERC concluded that the optimal sequencing of therapies for patients with newly diagnosed MM in whom stem cell transplantation is not intended is unknown. Therefore, pERC was unable to make an evidence-based recommendation on sequencing of treatments. pERC recognizes that provinces will need to address this issue upon implementation of a reimbursement recommendation for VLd, and noted that collaboration among provinces to develop a national, uniform approach to optimal sequencing would be of great value.
Relapsed or refractory		
Ciltacabtagene autoleucel (Carvykti)	November 20, 2024	pERC recommends that ciltacabtagene autoleucel (cilta-cel) be reimbursed for the treatment of adult patients with MM, who have received 1 to 3 prior lines of therapy, including a proteasome inhibitor and an immunomodulatory drug, and whose disease is refractory to lenalidomide, only if the following conditions are met: **Initiation** 1. Cilta-cel should be reimbursed in adult patients aged 18 years or older who meet all of the following criteria: 1.1. documented diagnosis of MM 1.2. have received 1 to 3 prior lines of therapy, including a proteasome inhibitor and an immunomodulatory drug 1.3. refractory to lenalidomide 1.4. have good performance status. 2. Cilta-cel should not be initiated in patients with active CNS involvement or exhibiting signs of meningeal involvement of MM. 3. Cilta-cel should not be reimbursed in patients who have received prior treatment with any therapy that is targeted to BCMA, or prior anti-BCMA CAR T-cell therapy. **Prescribing** 4. Treatment with cilta-cel is a one-time therapy. 5. Cilta-cel should only be prescribed by clinicians with expertise in the treatment of MM. Cilta-cel should be administered in specialized centres with adequate infrastructure, resources, and expertise to facilitate treatment with CAR T-cell therapy. **Pricing** 6. A reduction in price. **Feasibility of adoption** 7. The economic feasibility of the adoption of cilta-cel must be addressed

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		8. Organizational feasibility 8.1. The administration of cilta-cel requires expertise, infrastructure, and human resources to ensure that the treatment and adverse events are managed in an optimized and timely manner for patients. 8.2. Prioritization considerations may include patient prognosis, prior therapy, and/or geographic location if cilta-cel exceeds manufacturing or delivery capacity. **Guidance on sequencing or treatment considerations:** pERC agreed with the clinical experts that patients with an ECOG Performance Status of more than 1 may be treated at the discretion of the treating physician. pERC noted it would be appropriate to consider patients with controlled CNS metastases for eligibility. pERC acknowledges that the current limited availability of specialized centres with adequate infrastructure and resources to administer CAR T-cell therapy in Canada is a barrier that needs to be addressed. The clinical experts anticipated prioritizing patients with suitable prognostic factors who are likely to respond to the treatment and better able to tolerate side effects. The clinical experts noted that if difficult prioritization decisions need to be made, consideration could be given to patients for whom BCMA-directed therapies such as bispecific T-cell engagers would not be a suitable choice. The clinical experts would also prioritize those who live in remote communities, often requiring frequent long-distance journeys to receive continuous systemic treatment. pERC agreed with the clinical experts that local provincial governments should increase their ability to provide CAR T-cell therapies to patients. However, pERC noted that it is not the committee's mandate to decide the allocation of resources or prioritization of patients to receive treatment. pERC noted that the current review did not include any evidence to support the efficacy of cilta-cel in patients who had prior BCMA therapy. Therefore, the committee was unable to comment on the eligibility of these patients to receive cilta-cel.
Elranatamab (Elrexfio)	June 18, 2024	pERC recommends that elranatamab be reimbursed for the treatment of adult patients with relapsed or refractory (r/r) multiple myeloma (MM) who have received at least 3 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy and without prior exposure to B-cell maturation antigen (BCMA)–directed therapy only if the following conditions are met: **Initiation** 1. Elranatamab should be reimbursed in adult patients aged 18 years or older who meet all the following criteria: 1.1. documented diagnosis of MM 1.2. documented evidence of progressive disease within the

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		previous 6 months 1.3. received at least 3 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody 1.4. no prior exposure to BCMA-directed therapy 1.5. refractory to their last treatment 1.6. good performance status 2. Elranatamab should not be initiated in patients with active CNS involvement or exhibiting signs of meningeal involvement of MM, amyloidosis, POEMS syndrome, or plasma cell leukemia. **Discontinuation** 3. Treatment with elranatamab should be discontinued upon the occurrence of any of the following, whichever occurs first: 3.1. disease progression 3.2. unacceptable toxicity **Prescribing** 4. Elranatamab should be administered by health professionals at treatment centres with adequate medical resources and personnel to manage severe reactions, including cytokine release syndrome and neurologic toxicities. **Pricing** 5. A reduction in price. **Feasibility of adoption** 6. The feasibility of adoption of elranatamab must be addressed. 7. The organizational feasibility of jurisdictions having specialized treatment centres with the infrastructure and resources required to administer elranatamab and manage adverse events must be addressed. **Guidance on sequencing or treatment considerations:** pERC acknowledged that clinicians may consider using elranatamab for patients with an ECOG performance status ≥ 2 at their discretion. pERC recognized that tocilizumab must be readily available for the treatment of CRS. The product monograph recommends monitoring patients for CRS and neurologic toxicity, including ICANS, and states that elranatamab should be administered by a health care professional with appropriate medical support to manage these severe reactions. Although pERC acknowledged that clinical experts thought it would be reasonable to consider patients previously treated with BCMA-targeted therapy (e.g., CAR T-cell therapy) eligible for elranatamab, pERC also noted that there is limited evidence to support this. pERC additionally noted that there was no evidence included in this review to support the appropriateness of CAR T-cell therapy in patients previously treated with elranatamab. pERC noted that there is no evidence reviewed to inform the use of elranatamab in earlier lines of therapy. Aligned with the Health Canada–approved indication, the reimbursement request for

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		elranatamab is for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 3 prior lines of therapy, including PI, IMiD, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy. pERC acknowledged the clinical experts' opinion that patients who are resistant to PIs, an immunomodulatory agent, and an anti-CD38 antibody (i.e., all 3), or intolerant to any of them and resistant to the others should be eligible to receive elranatamab, regardless of what line of therapy it is in; however, this would be outside of the Health Canada indication and therefore pERC could not recommend this. The clinical experts noted that the toxicity profile and likelihood of CRS could be a consideration. They indicated that elranatamab is given subcutaneously which could be an advantage over the other therapies where infusion access is limited, although elranatamab still needs to be given in a trained infusion or chemotherapy unit. They also noted that using a bispecific over CAR T-cell therapy may be necessary when geographic access or capacity is an issue and where immediate treatment is required. pERC agreed that treatment selection would rely on patient and logistical factors.
Teclistamab (Tecvayli)	April 24, 2024	pERC recommends that teclistamab be reimbursed by public drug plans for the treatment of adults with relapsed or refractory (r/r) multiple myeloma (MM) who have received at least 3 prior lines of therapy, including a proteasome inhibitor (PI), an immunomodulatory drug (IMiD), and an anti-CD38 monoclonal antibody (mAb), and who have demonstrated disease progression on the last therapy if the following conditions are met: **Initiation** 1. Teclistamab should be reimbursed in adults aged 18 years or older who meet all the following criteria: 1.1. documented diagnosis of MM 1.2. documented evidence of progressive disease within the previous 6 months 1.3. received at least 3 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory drug, and an anti-CD38 antibody 1.4. refractory to their last treatment 1.5. must have good performance status. 2. Teclistamab should not be initiated in patients with active CNS involvement or those who are exhibiting signs of meningeal involvement of MM, primary amyloidosis, or plasma cell leukemia. **Discontinuation** 3. Treatment with teclistamab should be discontinued upon any of the following, whichever occurs first: 3.1. disease progression 3.2. unacceptable toxicity. **Prescribing**

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		4. Teclistamab should be administered by health professionals at treatment centres with adequate medical resources and personnel to manage severe reactions, including cytokine release syndrome and neurologic toxicities. **Pricing** 5. A reduction in price **Feasibility of adoption** 6. Feasibility of adoption of teclistamab must be addressed. **Guidance on sequencing or treatment considerations:** pERC acknowledged that clinicians may consider using teclistamab for patients with an ECOG PS ≥ 2 at their discretion. pERC recognized that access to tocilizumab for the treatment of cytokine release syndrome is necessary. While pERC agreed with the clinical experts that it would be reasonable to consider patients previously treated with a BCMA-targeted therapy (e.g., CAR T-cell therapy) eligible for teclistamab, pERC noted that there is limited evidence to support this. pERC additionally noted that there was no evidence included in this CDA-AMC review to support the appropriateness of CAR T-cell therapy in patients previously treated with teclistamab. There is no evidence reviewed to inform the use of teclistamab in early lines of therapy. Aligned with the Health Canada–approved indication, the reimbursement request for teclistamab is for the treatment of adults with r/r MM who have received at least 3 prior lines of therapy, including a PI, an IMiD, and an anti-CD38 mAb, and who have demonstrated disease progression on the last therapy. pERC acknowledged the clinical experts' opinion that patients who are resistant to PIs, an IMiD, and an anti-CD38 mAb (i.e., all 3), or are intolerant to any of them and resistant to the others should be eligible to receive teclistamab, regardless of what line of therapy it is in.
Ciltacabtagene autoleucel (Carvykti)	May 17, 2023	pERC recommends that ciltacabtagene autoleucel be reimbursed for the treatment of adult patients with MM, who have received at least 3 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 antibody, and who are refractory to their last treatment only if the following conditions are met: **Initiation** 1. Ciltacabtagene autoleucel should be reimbursed in adult patients aged 18 years or older who meet all the following criteria: 1.1. Documented diagnosis of MM. 1.2. Received at least 3 prior lines of therapy including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 antibody. 1.3. Refractory to their last treatment. 1.4. Have good performance status. 2. Ciltacabtagene autoleucel should not be initiated in patients with active CNS involvement or exhibiting signs of meningeal involvement of MM.

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		3. Ciltacabtagene autoleucel should not be reimbursed in patients who have received prior treatment with any therapy that is targeted to BCMA or any CAR-T-cell therapy. **Prescribing** 4. Treatment with ciltacabtagene autoleucel is a one-time therapy. 5. Ciltacabtagene autoleucel should only be prescribed by clinicians with expertise in the treatment of MM. Ciltacabtagene autoleucel should be administered in specialized centres with adequate infrastructure, resources, and expertise to facilitate treatment with CAR T-cell therapy. **Pricing** 6. A reduction in price. **Feasibility of adoption** 7. The feasibility of adoption of ciltacabtagene autoleucel must be addressed. **Guidance on Sequencing** **If capacity limitations exist, how would you prioritize which patients should be offered ciltacabtagene autoleucel?** pERC could not comment on how to prioritize which patients should be offered ciltacabtagene autoleucel as it was outside of the scope of this review. **Is there a time-limited need to consider patients who were not able to access anti-CD38 (e.g., patients previously treated with the RVd regimen whose disease ended up being refractory to both lenalidomide and bortezomib)?** The clinical experts indicated that it is important to include those patients who have not had the 3 classes of treatment due to lack of funded access to anti-CD38 antibodies. The clinical experts noted they would not expect the outcome of treatment with **ciltacabtagene autoleucel** to be inferior in these patients compared to patients who met the CARTITUDE-1 eligibility criteria. pERC noted that patients should have generally received an anti-CD38 antibody to be eligible for ciltacabtagene autoleucel, but agreed with the clinical experts that there is a time-limited need to consider patients who were not able to access an anti-CD38 antibody. **The CARTITUDE-1 trial excluded patients who had received an allogeneic stem cell transplant within 6 months before apheresis or an *autologous stem cell transplant ≤ 12 weeks before apheresis*.** pERC indicated that patients who have previously received an allogeneic stem cell transplant > 6 months before apheresis or an autologous stem cell transplant > 12 weeks before apheresis could be eligible to receive ciltacabtagene autoleucel.
Selinexor (Xpovio) + bortezomib (Velcade) + dexamethasone	August 17, 2022	pERC recommends that selinexor in combination with bortezomib and dexamethasone (SVd) be reimbursed for the treatment of adult patients with multiple myeloma who have received at least 1 prior therapy if the following conditions are met: • Adult (≥ 18 years) patients who have all of the following:

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		◦ Histologically confirmed multiple myeloma ◦ received at least 1 prior therapy • SVd should only be prescribed by clinicians with expertise and experience in all of the following: ◦ the management of patients with multiple myeloma ◦ the adverse effects associated with selinexor • Selinexor should only be prescribed and reimbursed in combination with bortezomib and dexamethasone. As per the BOSTON trial, prior treatment with bortezomib or other proteasome inhibitor (PI) should be permitted, provided all of the following criteria are met: • Best response achieved with prior bortezomib at any time was ≥ partial response (PR) and the last PI therapy (alone or in combination) was ≥ PR • Patient did not discontinue bortezomib due to grade ≥ 3 related toxicity • Must have had a PI treatment-free interval of at least 6 months before the first day of SVd. Based on clinical expert opinion, patients with plasma cell leukemia and systemic light chain amyloidosis should be permitted to receive SVd as these patients would be treated in clinical practice and could receive benefit from therapy with SVd. **Guidance on sequencing:** • pERC does not anticipate SVd will displace previous and subsequent lines of therapies that are reimbursed; rather, pERC agreed with the clinical experts that daratumumab-containing regimens will likely shift to first line for transplant-ineligible patients. pERC noted that bortezomib-refractory would likely preclude reimbursement of other bortezomib-containing regimen options. • pERC agreed with the clinical experts that SVd could be administered to patients in the second line or later, but that other treatment options may be preferred. pERC highlighted if DRd was used in frontline transplant-ineligible patients, SVd is a potential second-line option for these patients. Other funded options are Pd, CyBord, and Kd. • pERC agreed with the clinical experts that patients who are refractory to bortezomib would be unlikely to respond to therapy with SVd. pERC felt that, as per the BOSTON trial, prior treatment with bortezomib or other PI should be permitted, provided all of the following criteria are met: ◦ best response achieved with prior bortezomib at any time was at least a partial response, and with the last PI therapy (alone or in combination) was at least a partial response ◦ the patient did not discontinue bortezomib due to grade 3 or higher related toxicity must have had a PI treatment-free interval of at least 6 months before the first day of SVd.

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing

Isatuximab (Sarclisa) + carfilzomib (Kyprolis) + dexamethasone	February 15, 2022	pERC recommends that isatuximab combined with carfilzomib and dexamethasone (IsaKd) be reimbursed for the treatment of adult patients with relapsed or refractory MM who have received 1 to 3 prior lines of therapy, and the following conditions met:
		• measurable disease
		• received at least 1 prior line of therapy
		• good performance status
		• must not:
		  ◦ have prior treatment with antiCD38 mab
		  ◦ be refractory to carfilzomib
		  ◦ have a LVEF < 40%.
		Treatment should be discontinued if:
		• evidence of disease progression (IMWG)
		• unacceptable toxicity despite dose modification
		• pERC also called for a reduction in price.
		• pERC agreed with the clinical experts that the preferred regimen depends on what the patient has received previously. If a patient experienced disease progression on a lenalidomide-based regimen in the first-line setting, then IsaKd and DVd are available options.
		• pERC agreed with the clinical experts that it is preferential to give an anti-CD38 as soon as possible, and therefore second-line IsaKd is preferred over third-line IsaPd for those who have not had a CD38 mAb.
		• pERC agreed with the clinical experts that there is currently no evidence to support sequencing of isatuximab and daratumumab.
		• pERC agreed with the clinical experts that there is currently no evidence in support of sequencing IsaKd and IsaPd.

Idecabtagene vicleucel (Abecma)	November 12, 2021	CDA-AMC recommends that Abecma should not be reimbursed by public drug plans for the treatment of MM.
Isatuximab (Sarclisa) + pomalidomide (Pomalyst) + dexamethasone	April 1, 2021	pERC conditionally recommends the reimbursement of isatuximab in combination with pomalidomide and dexamethasone (IsaPd) in patients with relapsed or refractory MM who have received at least 2 prior lines of therapy including lenalidomide and a PI, if the following conditions are met: • cost-effectiveness improved to an acceptable level • feasibility of adoption (budget impact) being assessed. Eligible patients include adults with RRMM who have failed treatment on lenalidomide and a PI, administered either alone or in combination in any prior line of treatment, have disease that was refractory to the last line of treatment received, and good performance status. Treatment should be continued until acceptable toxicity or disease progression. **Optimal sequencing of IsaPd with other therapies for RRMM including daratumumab:** pERC noted that the eligibility criteria in the ICARIA-MM trial included patients who had previous treatment with but were not refractory to an anti-CD38 mAb, but that only 1 patient in the IsaPd treatment group of the trial had prior exposure to an anti-CD38

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		mAb (i.e., daratumumab). In the absence of evidence, pERC concluded that the efficacy of IsaPd in eligible patients who have received at least 2 prior lines of therapy that includes daratumumab is unknown. pERC also concluded that due to the absence of evidence on sequencing of IsaPd and currently available treatments for RRMM, no informed recommendation on optimal sequencing could be made. pERC recognized that jurisdictions would need to address this issue upon implementation of IsaPd reimbursement and noted that collaboration among jurisdictions to develop a common approach to sequencing would be of value.
Pomalidomide (Pomalyst) + bortezomib (Velcade) + dexamethasone	September 18, 2019	pERC conditionally recommends the reimbursement of pomalidomide in combination with dexamethasone and bortezomib (PVd) for the treatment of adults with relapsed or refractory MM who have had at least 1 prior regimen including lenalidomide, if the following condition, cost-effectiveness being improved to an acceptable level, is met. Patients should have good performance status and treatment should be continued until disease progression or unacceptable toxicity. pERC concluded that the optimal sequencing of PVd and other treatments now available for the treatment of MM is currently unknown. pERC was therefore unable to make an evidence-informed recommendation on sequencing. However, pERC recognized that provinces would need to address this issue upon implementation of pomalidomide reimbursement and noted that collaboration among provinces to develop a common approach would be of value.
Daratumumab (Darzalex) + lenalidomide (Revlimid) or bortezomib (Velcade) + dexamethasone	October 5, 2017	pERC recommends the reimbursement of daratumumab in combination with lenalidomide and dexamethasone (DRd) or bortezomib and dexamethasone (DVd) for treatment of patients with MM with good performance status who have received at least 1 prior therapy, conditional on the cost-effectiveness being substantially improved and adoption feasibility being addressed. pERC noted that daratumumab should be continued until disease progression or unacceptable toxicity. pERC concluded that the optimal sequencing of daratumumab plus lenalidomide-dexamethasone or bortezomib-dexamethasone and other treatments now available for the treatment of MM is currently unknown. pERC noted the opinion of the pCODR CGP that daratumumab in combination with lenalidomide-dexamethasone or bortezomib-dexamethasone may be a favourable second-line option over triplet therapy with carfilzomib; however, the committee acknowledged that there is no appropriate treatment sequence for daratumumab and carfilzomib for the treatment of MM after failure of 1 prior therapy. Therefore, pERC was unable to make an evidence-informed recommendation on sequencing of treatments for RRMM. However, pERC recognized that provinces would need to address this issue upon implementation of daratumumab reimbursement and noted that collaboration among provinces to develop a common approach would be of value.

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
Carfilzomib (Kyprolis) + dexamethasone	March 30, 2017	pERC recommends reimbursement of carfilzomib in combination with dexamethasone for patients with relapsed MM with a good performance status who have received 1 to 3 prior treatments, on the condition that the cost-effectiveness be improved to an acceptable level. pERC concluded that optimal sequencing of carfilzomib plus dexamethasone and other treatments now available for the treatment of MM is currently unknown. pERC was therefore unable to make an evidence-informed recommendation on sequencing. However, pERC recognized that provinces would need to address this issue upon implementation of carfilzomib reimbursement and noted that collaboration among provinces to develop a common approach would be of value. pERC acknowledged that carfilzomib plus dexamethasone would be an alternative therapy for patients who are ineligible to receive triplet therapy and not an add-on to the existing sequence of treatments.
Daratumumab (Darzalex)	December 1, 2016	pERC does not recommend daratumumab for the treatment of patients with MM who 1) have received at least 3 prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent (IMiD), or 2) have failed or are intolerant to a PI and have failed or are intolerant to an IMiD.
Carfilzomib (Kyprolis) + lenalidomide (Revlimid) + dexamethasone	November 11, 2016	pERC recommends reimbursement of carfilzomib in combination with lenalidomide and dexamethasone for patients with MM who have received at least 1 prior treatment, on condition that the cost-effectiveness be improved to an acceptable level. Patients must not have had disease progression during treatment with bortezomib or if previously treated with lenalidomide and dexamethasone patients must not have: • discontinued therapy because of adverse effects • disease progression during the first 3 months of treatment, or • progression at any time during treatment if lenalidomide plus dexamethasone was their most recent treatment. Treatment should be in patients who have good performance status and are deemed to have adequate renal function. Treatment with carfilzomib should continue until disease progression or unacceptable toxicity, up to a maximum of 18 cycles. pERC concluded that the optimal sequencing of carfilzomib plus lenalidomide-dexamethasone and other treatments now available for the treatment of MM is currently unknown. pERC was therefore unable to make an evidence-informed recommendation on sequencing. However, pERC recognized that provinces would need to address this issue upon implementation of carfilzomib reimbursement and noted that collaboration among provinces to develop a common approach would be of value.
Pomalidomide (Pomalyst) + dexamethasone	July 31, 2014	pERC recommends funding pomalidomide (Pomalyst) in patients with relapsed and/or refractory MM who have previously failed at least 2 treatments, including both bortezomib and lenalidomide, and demonstrated disease progression on the last treatment, conditional on the cost-effectiveness being improved to an acceptable level.

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		Pomalidomide should also be an option in rare instances where bortezomib is contraindicated, or when patients are intolerant to it but, in all cases, patients should have failed lenalidomide. pERC made this recommendation because it was satisfied that there is a net clinical benefit of pomalidomide in this setting. However, at the submitted price and based on the Economic Panel's range of best estimates of the incremental cost-effectiveness ratio, pomalidomide could not be considered cost-effective compared with best supportive care.

ASCT = autologous stem cell transplant; CDA-AMC = Canada's Drug Agency; CGP = clinical guidance panel; cilta-cel = ciltacabtagene autoleucel; DCyBord = daratumumab-cyclophosphamide-bortezomib-dexamethasone; DRd = daratumumab-lenalidomide-dexamethasone; DVd = daratumumab-bortezomib-dexamethasone; DVMp = daratumumab-bortezomib-melphalan-prednisone; IMiD = immunomodulatory drug; IMWG = International Myeloma Working Group; IsaKd = isatuximab-carfilzomib-dexamethasone; IsaPd = isatuximab-pomalidomide-dexamethasone; KRd = carfilzomib-lenalidomide-dexamethasone; LVEF = left ventricular ejection fraction; MM = multiple myeloma; Pd = pomalidomide-dexamethasone; PI = proteasome inhibitor; PVd = pomalidomide-dexamethasone-bortezomib; R = lenalidomide; Rd = lenalidomide-dexamethasone; RVd = lenalidomide-bortezomib-dexamethasone; SVd = Selinexor-bortezomib-dexamethasone; V = bortezomib; Vd = bortezomib-dexamethasone.

Appendix 2: Discussion Guide Questions

Figure 2: Discussion Guide Questions for the Clinical Panel

Implementation Issues Raised by Jurisdictions

Implementation Issue: Downstream treatment options for relapsed/refractory multiple myeloma (r/rMM) in patients who have received prior BCMA-directed therapy?

Clinical Panel Discussion Questions

1. Downstream Treatment Options

1.1	**What is the evidence available to support the use of BCMA-targeted bispecific T-cell engagers in r/rMM patients previously treated with BCMA-directed therapy?** a) What is the evidence available to support the use of elranatamab or teclistamab in patients who have received prior BCMA-directed therapy? **Background:** • pERC recommends that elranatamab be reimbursed for the treatment of adult patients with r/rMM who have received at least 3 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody, who have demonstrated disease progression on the last therapy and without prior exposure to BCMA-directed therapy. ○ Although pERC acknowledged that clinical experts thought it would be reasonable to consider patients previously treated with BCMA-targeted therapy eligible for elranatamab, pERC also noted that there is limited evidence to support this. pERC additionally noted that there was no evidence included in this review to support the appropriateness of CAR T-cell therapy in patients previously treated with elranatamab. • pERC recommends that teclistamab be reimbursed for the treatment of adult patients with r/rMM who have received at least 3 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody, who have demonstrated disease progression on the last therapy. ○ While pERC agreed with the clinical experts that it would be reasonable to consider patients previously treated with a BCMA-targeted therapy eligible for teclistamab, pERC noted that there is limited evidence to support this. pERC additionally noted that there was no evidence included in this CADTH review to support the appropriateness of CAR T-cell therapy in patients previously treated with teclistamab.
Response:	

1.2	**Do clinicians have a preference between teclistamab or elranatamab in patients who received prior BCMA-targeted therapy?** **Background:** • In the MagnetisMM-3 trial, treatment with elranatamab in patients with prior BCMA-directed therapy (cohort B) did not demonstrate there was a meaningful clinical benefit. A reimbursement condition for elranatamab is that patients should have 1.4 no prior exposure to BCMA-directed therapy. This is not a reimbursement condition for teclistamab.
Response:	

2. Additional Information

2.1	**Is there any additional information you feel is pertinent to the panel discussion?**
Response:	

BCMA = B-cell maturation antigen; pERC = pan-Canadian Oncology Drug Review Expert Review Committee; r/rMM = relapsed or refractory multiple myeloma.

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Questions or requests for information about this report can be directed to Requests@CDA-AMC.ca.