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CDA-AMC REIMBURSEMENT REVIEW

Provisional Funding Algorithm: Proposed Scope

Indication: Multiple Myeloma

Version: 1.0
Publication Date: TBC
Report Length: 16 Pages

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1. Background

At the request of the drug programs that participate in the CDA-AMC drug reimbursement review processes, CDA-AMC is convening an implementation advice panel to advise the drug programs on a provisional funding algorithm for drugs used in the treatment of multiple myeloma. This advice will be used by the drug programs and the Canadian Association of Provincial Cancer Agencies in the development of their funding criteria. For this project, CDA-AMC will be updating previously completed related work. Appendix 1 lists the past CDA-AMC algorithm implementation advice panels conducted for the indication of interest. Appendix 2 lists all past CDA-AMC recommendations for drugs in the same therapeutic space. This document outlines a draft scope for the panel discussions, including which drugs are under consideration and questions to be addressed by the panel.

2. Consultation Process and Objectives

The implementation advice panel will be comprised of clinical specialists in Canada with expertise in the diagnosis and management of patients with multiple myeloma. The objective of the panel will be to provide advice to the participating drug programs regarding the funding algorithm and any related implementation questions. In addition to the clinical panellists and CDA-AMC staff, representatives from public drug programs, the pan-Canadian Pharmaceutical Alliance, and the Canadian Association of Provincial Cancer Agencies may participate in the discussion and provide input in advance of the meeting on the topics for discussion. For more information on the implementation advice process, please refer to *Procedures for CDA-AMC Drug Reimbursement Reviews*.

The CDA-AMC Provincial Advisory Group raised the following issues pertaining to the development of a provisional funding algorithm. These are to be addressed by the implementation advice panel.

Implementation Issues

1. What is the available evidence to support the downstream treatment options for patients with relapsed/refractory multiple myeloma who have received prior BCMA-directed therapy?

3. Engagement Opportunities

CDA-AMC welcomes input from patient and clinician groups as well as manufacturers whose product(s) may be impacted by changes in the funding algorithm. Community Partners are invited to provide comments and/or complementary information, including published evidence on treatment sequencing, if available, in support of algorithm development. The input will be considered in the finalization of the implementation advice scope.

When ready, a draft provisional funding algorithm report will be posted for feedback. The final provisional funding algorithm report will be posted on the CDA-AMC website.

4. Current Multiple Myeloma Algorithm and Drugs Under Consideration

Please refer to PH0047 Multiple Myeloma final report published on August 1, 2024 for the current CDA-AMC Provisional Funding Algorithm for Multiple Myeloma.

Table 1: List of Drugs Under Consideration

Generic name (brand name)	Manufacturer
Ciltacabtagene autolecel (Carvykti)	Janssen Canada
Elranatamab (Elrexfio)	Pfizer Canada
Teclistamab (Tecvayli)	Janssen Canada

Appendix 1: History of CDA-AMC Algorithm Panels on Multiple Myeloma

Table 2: Previous CDA-AMC Implementation Advice With Funding Algorithms

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).

CDA-AMC = Canada's Drug Agency

Appendix 2: CDA-AMC Recommendations on Drugs for Multiple Myeloma

Table 3: Related 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.
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.
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

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		• 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.
Relapsed or refractory		
Ciltacabtagene autolecel (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

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

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

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

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

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

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		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 one prior therapy if the following conditions are met:
		
		• Adult (≥ 18 years) patients who have all of the following:
		  ○ Histologically confirmed multiple myeloma
		  ○ received at least one 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.

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

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

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

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		• 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. 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.
Idecabtagene vicleucel (Abecma)	November 12, 2021	CADTH recommends that Abecma should not be reimbursed by public drug plans for the treatment of MM.
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.

ASCT = autologous stem cell transplant; CGP = clinical guidance panel; DCyBord = daratumumab-cyclophosphamide-bortezomib-dexamethasone; DRd = daratumumablenalidomide-dexamethasone; DVd = daratumumab-bortezomib-dexamethasone; DVMp = daratumumab-bortezomib-melphalan-prednisone; 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; PVd = pomalidomide-dexamethasone-bortezomib; R = lenalidomide; Rd = lenalidomide-dexamethasone; RVd = lenalidomide-bortezomib-dexamethasone; SVd = Selinexor-bortezomib-dexamethasone; V = bortezomib; Vd = bortezomib-dexamethasone; cilta-cel = ciltacabtagene autoleucel; PI = protease inhibitor; IMiD = immunomodulatory drug.