CADTH Reimbursement Review

Provisional Funding Algorithm

Indication: Multiple myeloma

This report supersedes the CADTH Provisional Funding Algorithm report for multiple myeloma dated November 14, 2022.

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

Background

Following a request from jurisdictions, CADTH may 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.

Provisional funding algorithms are based on 3 principal sources of information:

- CADTH pCODR Expert Review Committee (pERC) reimbursement recommendations and/or implementation guidance regarding drug place in therapy and sequencing
- implementation advice from panels of clinicians convened by CADTH concerning sequencing of drugs in the therapeutic space of interest
- existing oncology drug reimbursement criteria and legacy funding algorithms adopted by jurisdictional drug plans and cancer agencies.

Note that 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 CADTH website for more details.

Provisional funding algorithms also 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.

Provisional funding algorithms may contain drugs that are under consideration for funding. Algorithms will not be dynamically updated by CADTH following changes to drug funding status. Revisions and updates will occur only upon request by jurisdictions.

Jurisdictional cancer drug programs requested a CADTH provisional funding algorithm on multiple myeloma. However, no outstanding implementation issues were identified, and no additional implementation advice is provided in this report. The algorithm depicted herein is meant to reflect the current and anticipated funding landscape based on the previously mentioned sources of information.

History and Development of the Provisional Funding Algorithm

To date, CADTH has published 2 provisional funding algorithm reports for multiple myeloma. 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.

In May 2023, jurisdictional cancer drug programs requested another rapid algorithm to update and incorporate the CADTH recommendation for ciltacabtagene autoleucel (Carvykti), the first CAR T-cell therapy approved for the treatment of adult patients with multiple myeloma.

Table 1: Relevant CADTH 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 • treatment with daratumumab should continue until unacceptable toxicity or disease progression. *Optimal sequencing of available therapies after progression on*

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		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 a 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 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 1-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.

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

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		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.
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 are met: • measurable disease • received at least 1 prior line of therapy • good performance status

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		• must not:
		  ◦ have prior treatment with anti-CD38 mab
		  ◦ be refractory to carfilzomib
		  ◦ have a LVEF < 40%.
		Treatment should be discontinued if:
		• there is evidence of disease progression (IMWG)
		• there is 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.

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

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

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		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; 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; IsaKd = isatuximab-carfilzomib-dexamethasone; IsaPd = isatuximab-pomalidomide-dexamethasone; KRd = carfilzomib-lenalidomide-dexamethasone; LVEF = left ventricular ejection fraction; MM = multiple myeloma; Pd = pomalidomide-dexamethasone; PI = protease inhibitor; PVd = pomalidomide-dexamethasone-bortezomib; R = lenalidomide; Rd = lenalidomide-dexamethasone; RVd = lenalidomide-bortezomib-dexamethasone; SVd = Selinexor-bortezomib-dexamethasone; V = bortezomib; Vd = bortezomib-dexamethasone.

Table 2: CADTH Implementation Advice Panel on Multiple Myeloma

Date of publication	Implementation advice
May 2022	The panel advises that 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 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 Pd and Kd backbones should be available as sequential treatment options after failure of an anti-CD38–containing regimen. The panel advises that Pd or PCd are valid options after failure of first-line RVd.

Kd = carfilzomib-dexamethasone; KRd = carfilzomib-lenalidomide-dexamethasone; PCd = pomalidomide-cyclophosphamide-dexamethasone; Pd = pomalidomide-dexamethasone; RVd = lenalidomide-bortezomib-dexamethasone.

Provisional Funding Algorithm

Description of the Provisional Funding Algorithm

Figure 1 depicts the provisional funding algorithm proposed. Note that this diagram is a summary representation of the drug funding options for the condition of interest. It is not a treatment algorithm; it is neither meant to detail the full clinical management of each patient nor the provision of each drug regimen. The diagram may not contain a comprehensive list of all available treatments, and some drugs may not be funded in certain provinces. All drugs are subject to explicit funding criteria, which may also vary between provinces. Readers are invited to refer to the individual drug entries on the CADTH website for more details.

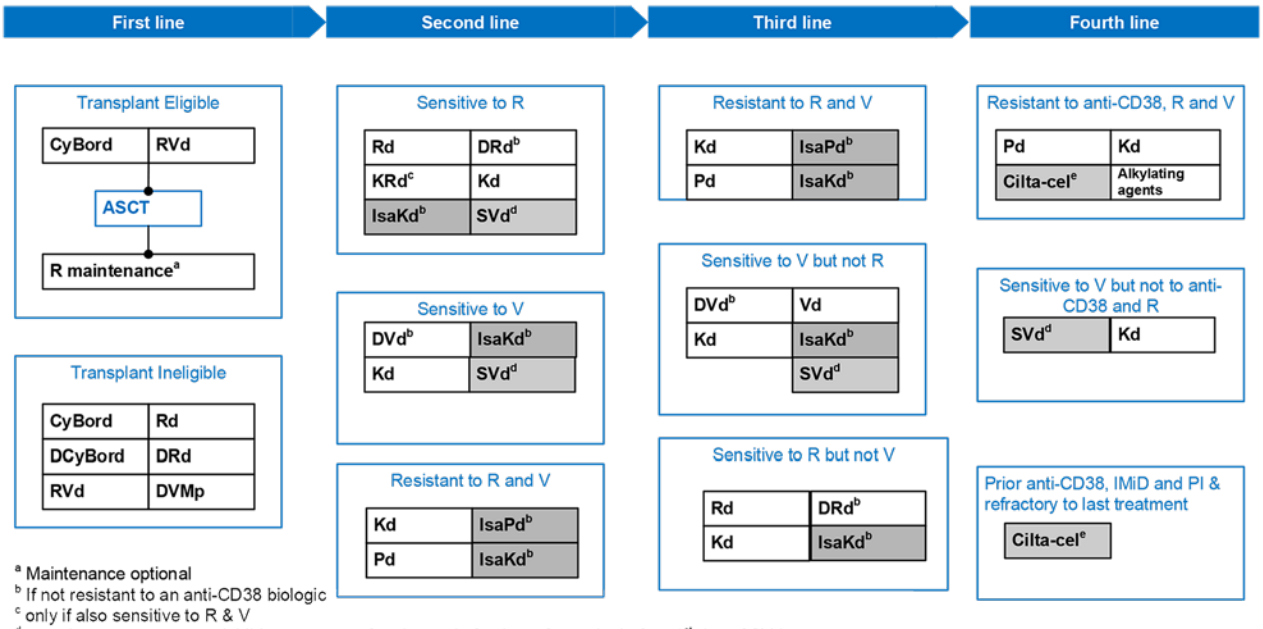
First-Line Setting

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 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

Figure 1: Provisional Funding Algorithm Diagram for Multiple Myeloma



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

Notes:
1) Patients with drug resistance cannot be re-treated with same drug(s)
2) Cyclophosphamide may be added to Kd, Pd and Rd
3) PVd is not represented in the algorithm as it is not commonly used or a standard of care; PVd has been recommended by pCODR for relapsed or refractory multiple myeloma in patients who have received at least 1 prior treatment regimen including R

Legend

Therapy funded across most jurisdictions	Therapy funding under review for funding (pCPA or province/cancer agency)

ASCT = autologous stem cell transplant; 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; IsaKd = isatuximab-carfilzomib-dexamethasone; IsaPd = isatuximab-pomalidomide-dexamethasone; KRd = carfilzomib-lenalidomide-dexamethasone; LVEF = left ventricular ejection fraction; MM = multiple myeloma; Pd = pomalidomide-dexamethasone; PI = protease inhibitor; PVd = pomalidomide-dexamethasone-bortezomib; R = lenalidomide; Rd = lenalidomide-dexamethasone; RVd = lenalidomide-bortezomib-dexamethasone; SVd = Selinexor-bortezomib-dexamethasone; V = bortezomib; Vd = bortezomib-dexamethasone.

in all regimens. Cyclophosphamide may be added to some regimens such as pomalidomide-dexamethasone (Pd), carfilzomib-dexamethasone (Kd), and Rd.

Second-Line Setting

In patients who are sensitive to lenalidomide, 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; Rd; carfilzomib-lenalidomide-dexamethasone (KRd), only if the patient is also sensitive to bortezomib; Kd; or selinexor-bortezomib-dexamethasone (SVd).

For patients to receive SVd, they must have a proteasome inhibitor (PI) treatment-free interval of at least 6 months before the first day of treatment.

In patients who are sensitive to bortezomib, their options include the following: daratumumab-bortezomib-dexamethasone (DVd) or IsaKd, if the patient is not resistant to an anti-CD38 biologic; Kd; or SVd.

For patients to receive SVd, they must have a PI treatment-free interval of at least 6 months before the first day of treatment.

In patients who are resistant to lenalidomide and bortezomib, their options include the following: isatuximab-pomalidomide-dexamethasone (IsaPd) or IsaKd, if not resistant to an anti-CD38 biologic; Kd; or Pd.

Third-Line Setting

In patients who are resistant to lenalidomide and bortezomib, their options include the following: IsaPd or IsaKd, if not resistant to an anti-CD38 biologic; Kd; or Pd.

In patients who are sensitive to bortezomib but not lenalidomide, their options include the following: DVd or IsaKd, if the patient is not resistant to an anti-CD38 biologic; Kd; bortezomib-dexamethasone (Vd); or SVd.

For patients to receive SVd, they must have a PI treatment-free interval of at least 6 months before the first day of treatment.

In patients who are sensitive to lenalidomide but not bortezomib, their options include the following: DRd or IsaKd, if the patient is not resistant to an anti-CD38 biologic; Rd; or Kd.

Fourth-Line Setting:

In patients who are resistant to an anti-CD38 biologic, lenalidomide, and bortezomib, their options include: Pd, Kd, ciltacabtagene autoleucel, or other alkylating agents.

In patients who are sensitive to bortezomib but not to an anti-CD38 biologic or lenalidomide, the options include: SVd or Kd. For patients to receive SVd, they must have a PI treatment-free interval of at least 6 months before the first day of treatment.

In patients who have received anti-CD38, immunomodulatory drugs (IMiDs), and PIs, and were refractory to the last treatment, they have the option of ciltacabtagene autoleucel. For patients to receive this therapy,

they must not have prior treatment with any therapy to target b-cell maturation antigen (BCMA) or any CAR T-cell therapy.

Note that PVd is not represented in the algorithm, as it is not commonly used or a standard of care; however, PVd has been recommended by pCODR for relapsed or refractory multiple myeloma in patients who have received at least 1 prior treatment regimen including lenalidomide.

The following options are also under review for funding: IsaKd, IsaPd, SVd, and ciltacabtagene autoleucel.

About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.