Canada's Drug and
Health Technology Agency

Updated CADTH Reimbursement Recommendations From a Streamlined Drug Class or Therapeutic Review

Optimal Pharmacotherapy for Transplant-Ineligible Multiple Myeloma

Therapeutic Review
May 6, 2024

Rationale for Updates to CADTH Reimbursement Recommendations

On November 30, 2023, the Formulary Management Expert Committee (FMEC) deliberated on a therapeutic review for optimal pharmacotherapy for transplant-ineligible multiple myeloma.

Based on the overall evidence on efficacy, safety, and costs, FMEC outlined the following reimbursement recommendations:

Recommendation 1

- FMEC supports the use of first-line daratumumab in patients with multiple myeloma who are ineligible for transplant.

Recommendation 2

- FMEC recommends the choice between the use of carfilzomib plus dexamethasone or pomalidomide plus bortezomib plus dexamethasone in the second-line or third-line setting be left at the physician's discretion for patients with relapsed or refractory multiple myeloma who received a daratumumab-containing regimen in the first-line setting.

As described in the Therapeutic Review Framework and Process, FMEC may provide updates to previous CADTH reimbursement recommendations, which can include amendments to the recommendation status, criteria, and/or conditions, as appropriate.

FMEC has updated the previous criteria and/or conditions set out by the pCODR Expert Review Committee (pERC) for therapeutics in multiple myeloma based on the scope of the therapeutic review, specifically multiple myeloma treatments that are in use or being considered for public reimbursement in Canada as of May 2021. Note that only recommendations deemed to be relevant within the scope of the therapeutic review have been updated.

Updates to CADTH Reimbursement Recommendations

The CADTH recommendations in this document now supersede the previously published recommendations for the relevant therapeutics.

Refer to Table 1 (summary of revisions), Table 2 (summary of additions), and Table 3 (summary of affirmations with no changes) for the updated CADTH reimbursement recommendations for these drugs, which includes the previous final recommendations (from pERC) and updates by FMEC.

Table 1: Summary of Revisions to Previous CADTH Reimbursement Recommendations

Generic name (brand name), project number	Indication and date final recommendation (pERC) issued	Final recommendation (pERC)	Revisions to pERC recommendation (by FMEC)
NA	NA	NA	NA

FMEC = Formulary Management Expert Committee; NA = not applicable; pERC = pCODR Expert Review Committee.

Table 2: Summary of Additions to Previous CADTH Reimbursement Recommendations

Generic name (brand name), project number	Indication and date final recommendation (pERC) issued	Final recommendation (pERC)	Addition(s) to pERC recommendation (by FMEC)
Recommendation 1: FMEC supports the use of first-line daratumumab in patients with multiple myeloma who are ineligible for transplant.			
Daratumumab (Darzalex), PC0148	In combination with bortezomib, melphalan, and prednisone for the treatment of patients with newly diagnosed multiple myeloma who are not suitable for autologous stem-cell transplant August 29, 2019	pERC conditionally recommends to reimburse daratumumab in combination with bortezomib, melphalan, and prednisone (DVMP) for patients with newly diagnosed multiple myeloma who are not suitable for autologous stem-cell transplant if the following conditions are met: • cost-effectiveness being improved to an acceptable level	FMEC affirms the pERC recommendation. Eligibility for reimbursement of daratumumab in the first-line setting should not be limited to its use as part of DVMP. The following addition to conditions for reimbursement will now apply. Pricing: • A reduction in the price of daratumumab is required for this treatment to be considered cost-effective at conventional willingness-to-pay thresholds in the first-line setting

Generic name (brand name), project number	Indication and date final recommendation (pERC) issued	Final recommendation (pERC)	Addition(s) to pERC recommendation (by FMEC)
		• feasibility of adoption (budget impact) being addressed. Eligible patients include those with good performance status and treatment with the daratumumab component should continue until unacceptable toxicity or disease progression. Read the Darzalex recommendation.	relative to being used as a treatment in the second-line setting.
Daratumumab (Darzalex), PC0189	In combination with lenalidomide and dexamethasone for the treatment of patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant March 5, 2020	pERC conditionally recommends to reimburse daratumumab in combination with lenalidomide and dexamethasone (DRd) for patients with newly diagnosed multiple myeloma 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. Eligible patients include those with good performance status and treatment with DRd should continue until unacceptable toxicity or disease progression. Read the Darzalex recommendation.	FMEC affirms the pERC recommendation. Eligibility for reimbursement of daratumumab in the first-line setting should not be limited to its use as part of DRd. The following addition to conditions for reimbursement will now apply. Pricing: • A reduction in the price of daratumumab is required for this treatment to be considered cost-effective at conventional willingness-to-pay thresholds in the first-line setting relative to being used as a treatment in the second-line setting.
Recommendation 2: FMC recommends the choice between the use of carfilzomib plus dexamethasone or pomalidomide plus bortezomib plus dexamethasone in the second-line or third-line setting be left at the physician's discretion for patients with relapsed or refractory multiple myeloma who received a daratumumab-containing regimen in the first-line setting.			
Pomalidomide (Pomalyst), PC0165	In combination with dexamethasone and bortezomib for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 1 prior treatment regimen including lenalidomide September 18, 2019	pERC conditionally recommends the reimbursement of pomalidomide (Pomalyst) in combination with dexamethasone and bortezomib (PVd) for the treatment of adult patients with relapsed or refractory multiple myeloma (RRMM) who have received at least one prior treatment regimen including lenalidomide, if the following condition is met: • cost-effectiveness being	FMEC affirms the pERC recommendation. The following addition to conditions for reimbursement will now apply. Initiation: • Patient should have also received a daratumumab-containing regimen in the first-line setting (after the implementation date of daratumumab funding in their local jurisdiction). This may not apply to patients who did not receive daratumumab in the first-line setting when funding for this drug was not available.

Generic name (brand name), project number	Indication and date final recommendation (pERC) issued	Final recommendation (pERC)	Addition(s) to pERC recommendation (by FMEC)
		improved to an acceptable level. Patients should have good performance status and treatment should be continued until disease progression or unacceptable toxicity. Read the Pomalyst recommendation.	
Carfilzomib (Kyprolis), PC0084	In combination with dexamethasone alone in the treatment of patients with relapsed multiple myeloma who have received 1 to 3 prior lines of therapy March 30, 2017	pERC recommends reimbursement of carfilzomib (Kyprolis) in combination with dexamethasone (Dex) for patients with relapsed multiple myeloma 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. Read the Kyprolis recommendation.	FMEC affirms the pERC recommendation. The following addition to conditions for reimbursement will now apply. Initiation: • The patient should have also received a daratumumab-containing regimen in the first-line setting (after the implementation date of daratumumab funding in their local jurisdiction). This may not apply to patients who did not receive daratumumab in the first-line setting when funding for this drug was not available.

DEX = dexamethasone; DRd = daratumumab in combination with lenalidomide and dexamethasone; DVMP = daratumumab in combination with bortezomib, melphalan, and prednisone; FMEC = Formulary Management Expert Committee; pERC = pERC = pCODR Expert Review Committee; PVd = pomalidomide in combination with dexamethasone and bortezomib; RRMM = relapsed or refractory multiple myeloma.

Table 3: Summary of Affirmations With No Changes to Previous CADTH Reimbursement Recommendations

Generic name (brand name), project number	Indication and date final recommendation (pERC) issued	Final recommendation (pERC)	Affirmations with no changes to pERC recommendation (by FMEC)
Recommendation 1: FMEC supports the use of first-line daratumumab in patients with multiple myeloma who are ineligible for transplant.			
Daratumumab (Darzalex), PC0079	For the treatment of patients with multiple myeloma 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 who have failed or are	pERC does not recommend reimbursement of daratumumab for the treatment of patients with multiple myeloma 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 who have failed or are intolerant to an IMiD.	Given the lack of certainty in the clinical evidence of daratumumab for the relapsed or refractory setting from the therapeutic review, FMEC affirms that the current recommendation remains unchanged.

Generic name (brand name), project number	Indication and date final recommendation (pERC) issued	Final recommendation (pERC)	Affirmations with no changes to pERC recommendation (by FMEC)
	intolerant to an IMiD December 1, 2016	Read the Darzalex recommendation.	
Daratumumab (Darzalex) (second-line), PC0104	In combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least 1 prior therapy October 5, 2017	pERC recommends the reimbursement of daratumumab (Darzalex) in combination with lenalidomide and dexamethasone (Len-dex) or bortezomib and dexamethasone (Bor-dex) for the treatment of patients with multiple myeloma 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. Read the Darzalex recommendation.	FMEC affirms the pERC recommendation.

bor-dex = bortezomib and dexamethasone; FMEC = Formulary Management Expert Committee; IMiD = immunomodulatory agent; len-dex = lenalidomide and dexamethasone; pERC = pCODR Expert Review Committee; PI = proteasome inhibitor.

The information in this document is intended to help Canadian health care decision-makers, health care professionals, health The information in this document is intended to help Canadian health care decision-makers, health care professionals, health systems leaders, and policy-makers make well-informed decisions and thereby improve the quality of health care services. While patients and others may access this document, the document is made available for informational purposes only and no representations or warranties are made with respect to its fitness for any particular purpose. The information in this document should not be used as a substitute for professional medical advice or as a substitute for the application of clinical judgment in respect of the care of a particular patient or other professional judgment in any decision-making process. The Canadian Agency for Drugs and Technologies in Health (CADTH) does not endorse any information, drugs, therapies, treatments, products, processes, or services.

While care has been taken to ensure that the information prepared by CADTH in this document is accurate, complete, and up-to-date as at the applicable date the material was first published by CADTH, CADTH does not make any guarantees to that effect. CADTH does not guarantee and is not responsible for the quality, currency, propriety, accuracy, or reasonableness of any statements, information, or conclusions contained in any third-party materials used in preparing this document. The views and opinions of third parties published in this document do not necessarily state or reflect those of CADTH.

CADTH is not responsible for any errors, omissions, injury, loss, or damage arising from or relating to the use (or misuse) of any information, statements, or conclusions contained in or implied by the contents of this document or any of the source materials.

This document may contain links to third-party websites. CADTH does not have control over the content of such sites. Use of third-party sites is governed by the third-party website owners' own terms and conditions set out for such sites. CADTH does not make any guarantee with respect to any information contained on such third-party sites and CADTH is not responsible for any injury, loss, or damage suffered as a result of using such third-party sites. CADTH has no responsibility for the collection, use, and disclosure of personal information by third-party sites.

Subject to the aforementioned limitations, the views expressed herein are those of CADTH and do not necessarily represent the views of Canada's federal, provincial, or territorial governments or any third-party supplier of information.

This document is prepared and intended for use in the context of the Canadian health care system. The use of this document outside of Canada is done so at the user's own risk.

This disclaimer and any questions or matters of any nature arising from or relating to the content or use (or misuse) of this document will be governed by and interpreted in accordance with the laws of the Province of Ontario and the laws of Canada applicable therein, and all proceedings shall be subject to the exclusive jurisdiction of the courts of the Province of Ontario, Canada.

Confidential information in this document may be redacted at the request of the sponsor in accordance with the CADTH Drug Reimbursement Review Confidentiality Guidelines. CADTH was established by Canada's federal, provincial, and territorial governments to be a trusted source of independent information and advice for the country's publicly funded health care systems. Health administrators and policy experts rely on CADTH to help inform their decisions about the life cycle management of drugs, devices, and services used to prevent, diagnose, and treat medical conditions.

Canada's Drug and
Health Technology Agency

CADTH was established by Canada's federal, provincial, and territorial governments to be a trusted source of independent information and advice for the country's publicly funded health care systems. Health administrators and policy experts rely on CADTH to help inform their decisions about the life cycle management of drugs, devices, and services used to prevent, diagnose, and treat medical conditions.

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

cadth.ca

May 2024