Optimal Pharmacotherapy for Transplant-Ineligible Multiple Myeloma

Myeloma Canada Stakeholder Feedback Submission - Draft Recommendation -TR0014

1. **Are the draft recommendations presented in a clear manner (i.e., wording)? If not, how can the wording of the recommendations be improved for clarity?**

Yes. In general, the wording of the draft recommendations is clear.
We recommend the following clarifications be made:

a. Recommendation 2:
    i. Proposed change: "For patients with relapsed or refractory multiple myeloma who received a daratumumab-containing regimen as part of first-line therapy, the FMEC recommends the choice between the use of carfilzomib/dexamethasone or pomalidomide/bortezomib/dexamethasone in the second- or third-line setting be left at the physician's discretion."
        - Rationale: communication is clearer if situating first that the recommendation is made for patients with relapsed/refractory MM who have received daratumumab in the first-line setting.
b. Table 2
    i. Bullets should be consistent in all columns of table. See row 2 column 3 vs. row 2 column 4: "cost effectiveness…" should have a minimal indent, "A reduction in…" should be lowercase (i.e., "a reduction in...")
    ii. Capitalization should be consistent in all columns of table. See row 2 column 3 vs. row 2 column 4: "cost effectiveness…" is lowercase, so, "A reduction in…" should be lowercase (i.e., "a reduction in...) or vice versa.
    iii. Some cells have punctuation whereas others do not. Recommended to be consistent.

2. **Will the draft recommendations be helpful to those making policy or clinical practice decisions?**
    a. For the draft recommendations to provide value to policy/clinical decisionmakers, the authors must provide a rationale or some data supporting why the recommendations were made. Presuming this data is included in the previous clinical and pharmacoeconomic reports, at minimum, references should

be clearly made, and the appropriate documents linked. Similarly, the updated recommendation documents should include the analysis and rationale for the updates made. This will aid decisionmakers in easily accessing the evidence considered by FMEC supporting the recommendations.

3. **Has all the relevant evidence in the science report been taken into account in regard to these recommendations? If not, please explain why, citing evidence to support your position.**
   Yes, considering the publication date cutoff for the evidence gathered for review, the majority of relevant evidence has been taken into account.
   We would like to note:

   a. Lenalidomide-based regimens are a standard-of-care, yet they are not included as a potential second line treatment. The FMEC should recommend the use of RD/RVD as a potential second line if lenalidomide was not used in conjunction with daratumumab as first-line treatment.
   b. There is evidence that Dara-CyBorD is highly effective in NDMM / RRMM, regardless of transplant status (e.g., the LYRA study; https://pubmed.ncbi.nlm.nih.gov/30828799/). This should also be considered for reimbursement as first-line therapy.

4. **Please provide any additional comments you may have about this report.**

   a. There were no references provided in the report to justify the FMEC's recommendations. It is also unclear if clinicians and decision-makers were surveyed for this report. Supporting information on efficacy, safety, and costs should be publicly accessible, and either included with, or clearly referenced in this report.
   b. We hope that in practice, these recommendations succeed in balancing the principles of improving patient access to treatments, and providing enough flexibility in treatment options to ensure clinicians can use their professional discretion to choose the best treatment option for each individual patient. If the recommendations serve to curtail patient access to treatments, they will have failed to achieve their goal.

c. In Table 2 Recommendation 1, the additional reimbursement condition for the daratumumab recommendations states: "*A reduction in the price of daratumumab is required for this treatment to be considered costeffective at conventional willingness to pay thresholds, in the first line setting relative to being used as a treatment in the second-line setting*." First, the proposed price reduction to achieve cost-effectiveness should be stated in the recommendation. Second, if the reduction referred to is the 90% price reduction indicated in previous reports, we would reiterate our earlier feedback, that this steep of a price reduction is unfeasible.

d. In Table 2 Recommendation 2, the additional reimbursement condition applied to pomalidomide and carfilzomib states: "*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) …"*
It is unclear why this restriction is recommended and why patients who received daratumumab in the first-line setting before it was funded should be excluded from reimbursement for pomalidomide/carfilzomib containing regimens in the second-line setting. Considering this indication has just been recommended for reimbursement, there are likely very few transplant-ineligible MM patients who *have* received provincial/territorial funding for daratumumab as a first line treatment. Similarly, between the provinces and territories there are significant differences in terms of how long funding for daratumumab has been available, meaning this recommendation will have an outsized impact on Canadians in the Atlantic provinces, and the territories.

March 21st, 2024

Optimal Pharmacotherapy for Transplant-Ineligible Multiple Myeloma

Janssen Inc. Stakeholder Feedback Submission – Reimbursement Recommendation

In the interest of relevance, we respectfully request that the pricing condition "*A reduction in the price of daratumumab is required for this treatment to be considered cost-effective at conventional willingness to pay thresholds*" be removed for the following reasons:

- it is not meaningfully different than the existing condition of "cost-effectiveness being improved to an acceptable level"
- Daratumumab was listed on public drug formularies following a price negotiation agreement with the provinces. Therefore, further price reduction recommendations are not relevant and can be misleading.

If CADTH is not in agreement with removal of this condition, Janssen has the following requests:

- Please make it clear in the updated recommendation that the following condition: *"A reduction in the price of daratumumab is required for this treatment to be considered cost-effective at conventional willingness to pay thresholds*" will supersede the original cost-effectiveness condition: '*cost-effectiveness being improved to an acceptable level'*
- Additionally, please add the following sentence to the updated pricing recommendation to improve transparency :

  "Please note the price negotiation process for Daratumumab concluded with an LOI on March of 2022. Daratumumab was subsequently listed on public drug formularies after reaching a price negotiation agreement."

Please note the last request is in line with previously submitted feedback on the Draft recommendation, in which Janssen requested the paragraph to be added throughout the document.

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1. Are the draft recommendations presented in a clear manner (i.e., wording)" if not how can they wording of the recommendations be improved for clarity?

FORUS Therapeutics Inc is the marketing authorization holder for [Pr] XPOVIO® (Selinexor). XPOVIO in combination with bortezomib and dexamethasone (XVd) is indicated for the treatment of adult patients with multiple myeloma who have received at least one prior therapy. ([Pr] XPOVIO® Canadian Product Monograph May 31, 2022).

The Therapeutic Review for Optimal Pharmacotherapy for Transplant Ineligible Multiple Myeloma (MM) has reported on recommended updates to CADTH reimbursement recommendations for selected drugs within the scope of the review. FORUS respectfully provides comments on aspects of the draft recommendation issued for transplant-ineligible relapse refractory multiple myeloma (TI rrMM), as follows:

(1) The therapeutic review did not consider drugs with a CADTH review completed after May 2021. This includes XVd, for the treatment of rrMM recommended for use by CADTH on July 29th, 2022. The actual cut off date of May 2021 should be added to TR0014 Reimbursement Recommendation since it is the primary reason for exclusion of consideration of more recent drug regimens.

Suggested Revision (highlighted in yellow):

Please consider updating **Rationale for Updates to CADTH Reimbursement Recommendations** to "FMEC have updated the previous criteria/conditions set out by 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.". (page 2, last paragraph)

2. Will the draft recommendation be helpful to those making policy or clinical practise decisions?

(1) The reference to Selinexor should be added back to the recommendation, as outlined in the January 2024 Reimbursement Recommendation. As XVd is currently funded by provinces across Canada, it should be referenced as not being considered by FMEC since its omission may suggest it was not recommended.

Suggested Revision (highlighted in yellow):

Please consider updating **Rationale for Updates to CADTH Reimbursement Recommendations** and **Updates to CADTH Reimbursement Recommendations**, as follows:

- "FMEC have updated the previous criteria/conditions set out by 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. Of note, selinexor was not considered by FMEC in the second-line setting as it was not available at the time of the review nor included at the time of the initiation of the review". (page 2, last paragraph)
- FMEC recommends the choice between the use of carfilzomib/dexamethasone or pomalidomide/bortezomib/dexamethasone in the second- 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. Of note, selinexor was not considered by FMEC in the second-line setting as it was not available at the time of the review nor included at the time of the initiation of the review." (page 4-5, Table 2, Recommendation 2)

FORUS is very pleased to have achieved a positive recommendation for XVd from CADTH and provincial funding across Canada. Publishing the TR0014 final recommendation without the additional information as suggested above, will likely unfairly remove SVd from consideration as a treatment option for rrMM in this important setting.

Friday March 15, 2024

Canadian Agency for Drugs and Technologies in Health (CADTH)
865 Carling Ave, Suite 600
Ottawa, ON Canada K1S 5S8

Dear CADTH Review Team,

Re: Call for Feedback: Optimal Pharmacotherapy for Transplant-Ineligible Multiple Myeloma (TI MM), Project Number: TR00014-000- OP0547-000, posted 07-Mar-2024

In response to CADTH's Call for Feedback on the Therapeutic Review "Optimal Pharmacotherapy for TI MM" (Project Number TR00014-000), please find below Amgen Canada's feedback and comments on CADTH's Updated Reimbursement Recommendations:

1. **Are the draft recommendations presented in a clear manner (i.e., wording)? If not, how can the wording of the recommendations be improved for clarity?**

The draft recommendations are presented in a clear manner. Amgen Canada agrees with the draft reimbursement recommendations in particular for carfilzomib (Kyprolis PC0084- March 30, 2017) with the addition to conditions for reimbursement.

2. **Will the draft recommendations be helpful to those making policy or clinical practice decisions?**

Amgen Canada agrees with the FMEC recommendation that the sequencing choice between the use of carfilzomib/dexamethasone and pomalidomide/bortezomib/dexamethasone in the second- and third-line settings 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.

However, we strongly suggest FMEC to explicitly describe the caveat that many current and emerging regimens (e.g. Selinexor, BCMA CAR-T's) were not included in the treatment sequencing analyses and therefore limits the applicability of this draft recommendation to inform policy making or clinical practice decisions.

3. **Has all the relevant evidence in the science report been taken into account in regard to these recommendations? If not, please explain why, citing evidence to support your position.**

Relevant evidence in the science report has been taken into account in regard to these recommendations.

4. **Please provide any additional comments you may have about this report.**

Amgen Canada applauds FMEC's recognition that the choice of the optimal sequence will depend on what therapies were used in the first line as well patient characteristics and patient/clinician preferences. Multiple myeloma treatment should be individualized to ensure optimal care is

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delivered for each and every MM patient. Due to inter- and intra-patient heterogeneity within MM, it is insufficient and impractical to have a linear or “one-size-fits-all” algorithm that can be applied across all patients while achieving the target treatment goals; this multi-faceted disease should not be treated as “one disease”, and tailoring treatment to each individual patient is important to achieving the best overall outcome(s).

We appreciate the opportunities to provide multiple feedback on the Optimal Pharmacotherapy for Transplant- Ineligible Multiple Myeloma Therapeutic Review. Should you have any questions regarding our comments please contact either Diana Mak, Health Economics and Market Access Senior Manager (dmak@amgen.com) or Ben Peacock, Director, Health Economics and Market Access (bpeacock@amgen.com).

Sincerely,

DocuSigned by:
John Snowden
Signer Name: John Snowden
Signing Reason: I approve this document
Signing Time: 3/14/2024 | 12:57:35 PM GMT
F896054FB42F4D6B8D0DBA9901B6BE62

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