CADTH

pan-Canadian Oncology Drug Review
Stakeholder Feedback on a pCODR Expert Review Committee Initial Recommendation
(Sponsor)

Daratumumab (Darzalex) + Rd for Newly Diagnosed Multiple Myeloma

March 5, 2020

3 Feedback on pERC Initial Recommendation

Name of the Drug and Indication(s):	DARZALEX® (daratumumab) in combination with lenalidomide and dexamethasone for multiple myeloma (newly diagnosed)
Eligible Stakeholder Role in Review (Submitter and/or Manufacturer, Patient Group, Clinical Organization Providing Feedback	Submitter and Manufacturer Janssen Inc.

**The pCODR program may contact this person if comments require clarification. Contact information will not be included in any public posting of this document by the pCODR program.*

3.1 Comments on the Initial Recommendation

a) Please indicate if the eligible stakeholder agrees, agrees in part, or disagrees with the Initial Recommendation:

☐ agrees ☒ agrees in part ☐ disagree

Please explain why the Stakeholder *agrees, agrees in part or disagrees with the Initial Recommendation. If the Stakeholder agrees in part or disagrees with the Initial Recommendation, please provide specific text from the recommendation and rational. Please also highlight the applicable pERC deliberative quadrants for each point of disagreement. The points are to be numbered in order of significance.*

Cost-Effectiveness Analysis Feedback:

Janssen Inc. (Janssen) strongly agrees with the committee's decision that there is a significant net clinical benefit of DRd, based on statistically and clinically meaningful improvements in progression-free survival, a manageable toxicity profile and no detriment to patients' quality of life. Janssen also strongly agrees with the committee's decision that DRd aligns with patient values of providing disease control, having additional treatment options, a manageable side effect profile and no detriment to overall quality of life.

With respect to the economic evaluation, Janssen agrees that uncertainty exists in the economic model due to extrapolation of MAIA trial's current data to estimate long-term outcomes. However, Janssen disagrees with the cost-effectiveness results highlighted in the pERC Initial Recommendation as we have been unable to replicate, within a reasonable range, results presented in the Initial Economic Guidance Report (EGR).

Janssen has been unable to replicate the results of the best-case estimate assessment of the impact of the use of the Gompertz distribution to model time to treatment discontinuation (TTTD – Gompertz) for the comparisons of DRd vs. Rd and CyBorD. The results reported in the Initial EGR are captured in Table 1. Janssen attempted to replicate the best-case reanalysis results by changing the TTTD extrapolations for both DRd and Rd to the Gompertz distribution on the "Treatment Duration" tab. The subsequent results after running the probabilistic model over 2,500 replications differed significantly from those reported in the Initial EGR and are captured in Table 2.

Table 1: pCODR Initial Economic Guidance Report Results from the TTTD - Gompertz Best Case Estimate Parameter Change

	DRd vs. CyBorD	DRd vs. Rd
∆C	$1,026,267	$896,900
∆E QALYs	4.50	4.11
∆E LYs	6.68	6.11
ICER (QALYs)	$376,846	$519,558
∆ From Baseline Submitted ICER	$149,275	$298,970

Table 2: Janssen Results from the TTTD - Gompertz Best Case Estimate Parameter Change

	DRd vs. CyBorD	DRd vs. Rd
∆C	$1,204,494	$1,064,341
∆E QALYs	4.50	4.11
∆E LYs	6.68	6.11
ICER (QALYs)	$267,376	$259,163
∆ From Baseline Submitted ICER	$46,788	$38,575

Janssen was also unable to replicate the results of Initial EGR's overall best-case estimates for the comparisons of DRd vs. Rd, VMP and CyBorD. The results reported in the Initial EGR are highlighted in Table 3. Janssen attempted to validate the EGP best case estimates of the four parameters adjusted by the Economic Guidance Panel by increasing the pooled annual mortality rate by 49% in the "Life Table" tab, changing the DRd OS extrapolation to exponential in the "Overall Survival" tab, changing the DRd PFS extrapolation to Weibull in the "Progression-Free Survival" tab, and changing the TTTD extrapolations to Gompertz as outlined above. Here again the subsequent model results after running the probabilistic base case with 2,500 replications significantly differed from those reported in the Initial EGR. The results from Janssen's attempt at validating the best-case estimates are captured in Table 4.

Table 3: pCODR Initial Economic Guidance Report Results from the Best-Case Estimates of the Four Parameters

	DRd vs. CyBorD	DRd vs. Rd	DRd vs. VMP
∆C	$1,220,947	$896,900	$1,242,785
∆E QALYs	2.45	4.11	2.45
∆E LYs	3.33	6.11	3.33
ICER (QALYs)	$498,339	$519,558	$503,170
∆ from baseline submitted ICER	$270,768	$298,970	$272,960

Table 4: Janssen Results from the Best-Case Estimates of the Four Parameters

	DRd vs. CyBorD	DRd vs. Rd	DRd vs. VMP
∆C	$1,380,687	$1,240,500	$1,392,574
∆E QALYs	3.55	3.15	3.55
∆E LYs	5.04	4.48	5.04
ICER (QALYs)	$389,470	$394,021	$392,823
∆ from baseline submitted ICER	$161,899	$173,433	$162,613

Price Reduction Analysis Feedback:

Janssen does not agree with the scope of the price reduction analysis conducted in this review, specifically the examination and reporting of the daratumumab price reduction required to achieve an ICER of $100,000/QALY for the DRd regimen. Rather, a price reduction analysis evaluating the required reduction of the overall DRd *regimen* price would better align with the mandate of the conducted health economic analysis, which evaluates the cost-effectiveness of DRd compared to other currently reimbursed standard of care regimens for patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplantation.

The cost of the DRd regimen is driven by both the cost of daratumumab and of lenalidomide. In fact, over the median duration of therapy extrapolated for DRd in the Initial EGR reanalysis, the cost of lenalidomide exceeds that of daratumumab. As such, determining a price reduction on only one drug in the combination does not adequately capture how the potential cost-effectiveness of the *regimen* can be improved. Furthermore, given the variance between the best-case estimates between the Initial EGR and Janssen's analyses shown above, Janssen also does not agree with the magnitude of the price reduction required to achieve an ICER of $100,000/QALY.

b) Please indicate if the eligible stakeholder agrees, agrees in part, or disagrees with the provisional algorithm:

☐ agrees ☐ agrees in part ☐ disagree

Please explain why the Stakeholder *agrees, agrees in part or disagrees with the provisional algorithm. Please note that comments should relate* ***only to the proposed place in therapy of the drug under review*** *in the provisional algorithm. If feedback includes New Information or about other therapies that are included in the provisional algorithm, the information will not be considered and will be redacted from the posted feedback. Substantive comments on the provisional algorithm will preclude early conversion of the initial recommendation to a final recommendation.*

Not applicable to this feedback since no provisional algorithm was included as part of the initial recommendation.

c) Please provide editorial feedback on the Initial Recommendation to aid in clarity. Is the Initial Recommendation or are the components of the recommendation (e.g., clinical and economic evidence or provisional algorithm) clearly worded? Is the intent clear? Are the reasons clear?

Page Number	Section Title	Paragraph, Line Number	Comments and Suggested Changes to Improve Clarity
11	Cost-effectiveness estimates: Not cost-effective compared with lenalidomide and dexamethasone; bortezomib, melphalan, and prednisone; or cyclophosphamide, bortezomib, and dexamethasone	1, 12	Given challenges in the scope of the pricing analysis highlighted above, Janssen would recommend that the following statement be removed from the pERC Initial Recommendation: "From these analyses, it was concluded that an ICER around $100,000 QALY could not be achieved even with a price reduction of 95%."

3.2 Comments Related to Eligible Stakeholder Provided Information

Notwithstanding the feedback provided in part a) above, please indicate if the Stakeholder would support this Initial Recommendation proceeding to Final pERC Recommendation ("early conversion"), which would occur two (2) Business Days after the end of the feedback deadline date.

☒ Support conversion to Final Recommendation. Recommendation does not require reconsideration by pERC.	☐ Do not support conversion to Final Recommendation. Recommendation should be reconsidered by pERC.

If the eligible stakeholder does not support conversion to a Final Recommendation, please provide feedback on any issues not adequately addressed in the Initial Recommendation based on any information provided by the Stakeholder in the submission or as additional information during the review.

Please note that new evidence will be not considered at this part of the review process, however, it may be eligible for a Resubmission. If you are unclear as to whether the information you are providing is eligible for a Resubmission, please contact the pCODR program.

Additionally, if the eligible stakeholder supports early conversion to a Final Recommendation; however, the stakeholder has included substantive comments that requires further interpretation of the evidence, including the provisional algorithm, the criteria for early conversion will be deemed to have not been met and the Initial Recommendation will be returned to pERC for further deliberation and reconsideration at the next possible pERC meeting.

Page Number	Section Title	Paragraph, Line Number	Comments related to Stakeholder Information