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CADTH DRUG REIMBURSEMENT REVIEW

Pharmacoeconomic Report

Avelumab (BAVENCIO)

(EMD Serono - Pfizer Alliance)

Indication: for the first-line maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma whose disease has not progressed with first-line platinum-based induction chemotherapy

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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.

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Abbreviations

1L	first-line
AE	adverse vent
AIC	akaike information criterion
BIA	budget impact analysis
BIC	Bayesian information criterion
BSC	best supportive care
ICER	incremental cost-effectiveness ratio
KM	Kaplan-Meier
LY	life years
NOC	notice of compliance
NR	not reported
PSM	partitioned survival model
QALY	quality adjusted life year

Executive Summary

The executive summary is comprised of two tables (Table 1: Background and Table 2: Economic Evaluation) and a conclusion.

Table 1: Submitted for Review

Item	Description
Drug product	Avelumab (Bavencio). Solution for Intravenous Infusion 20 mg/mL single-use vial
Submitted price	Avelumab, 10 mL (20 mg/mL), solution, $1,325.00
Indication	For the first-line maintenance treatment of patients with locally advanced or metastatic urinary cancer whose disease has not progressed with first-line platinum-based induction chemotherapy.
Health Canada approval status	NOC
Health Canada review pathway	Priority review
NOC date	Dec 10, 2020
Reimbursement request	As per indication
Sponsor	EMD Serono - Pfizer Alliance
Submission history	Previously reviewed: Yes Indication: For the treatment of metastatic Merkel cell carcinoma in previously treated adults Recommendation date: March 21, 2018 Recommendation: Recommended pending cost-effectiveness improved to an acceptable level

NOC = Notice of Compliance

Table 2: Summary of Economic Evaluation

Component	Description
Type of economic evaluation	Cost-utility analysis Partitioned survival analysis
Target population	Patients with locally advanced or metastatic urinary cancer that has not progressed with first-line platinum-containing chemotherapy, meeting the JAVELIN Bladder 100 eligibility criteria.
Treatment	Avelumab (Bavencio) with best supportive care
Comparator	Best supportive care (BSC): antibiotics, nutritional support, correction of metabolic disorders, optimal symptom control and pain management such as palliative radiotherapy
Perspective	Canadian publicly funded health care payer
Outcome	Quality-adjusted life years (QALYs) and life years (LY)
Time horizon	10 years
Key data source	JAVELIN Bladder 100 study
Submitted results for base case	Incremental cost-effectiveness ratio (ICER) for avelumab with BSC versus BSC: $281,149 per QALY gained (incremental QALYs: 0.58; incremental cost: $162,149)
Key limitations	• Long term survival for both BSC and avelumab with BSC was deemed optimistic by the clinical experts consulted by CADTH given the lack of long-term data outcomes beyond the trial duration. • After treatment discontinuation, due to disease progression or treatment intolerance, a proportion of patients receive a second line therapy. This proportion was different for BSC and avelumab with BSC. The proportions used in the model were not in line with data taken from the trial. • Disutility associated with adverse events (AEs) was omitted including immune-mediated pneumonitis, hyperthyroidism, and immune-mediated diabetes. Costs incurred from moderate adverse events were omitted. • Costs for BSC were omitted. Although BSC costs would appear in both treatment arms as patients on avelumab with BSC live for longer these costs are excluded in the additional period for which they live. • The time horizon used was not reflective of a lifetime time horizon.
CADTH reanalysis results	• The CADTH reanalysis included: changing the distribution of the extrapolated survival curves both BSC and avelumab with BSC to align with expectations from clinical experts consulted by CADTH; adjusting the percentage of patients who receive subsequent therapy to align with the JAVELIN Bladder 100 trial; and, extending the time horizon to 15 years. • CADTH reanalysis could not address omitted costs for BSC, omitted disutility for AEs, and the exclusion of costs incurred from moderate AEs • Avelumab with BSC was found to have higher costs and higher QALYs than BSC alone. The ICER was $278,373 per QALY gained (incremental costs $181,617; incremental QALYs 0.64). A price reduction of 83% for avelumab is necessary to achieve an ICER below $50,000 per QALY gained.

ICER = incremental cost-effectiveness ratio; QALY= quality-adjusted life-year; BSC = best supportive care; AEs; Adverse Events

Conclusions

CADTH undertook reanalyses to address limitations with the sponsor's submission, including: updating the choice of distribution for survival curves to align with expectations of clinical experts; adjusting the percentage of patients receiving pembrolizumab as subsequent therapy to align with the JAVELIN bladder 100 trial; and, extending the time horizon to 15 years.

The CADTH reanalysis found avelumab with BSC to have higher costs (incremental: $181,617) and higher QALYs (incremental: 0.65), for an ICER of $278,373 per QALY gained compared to BSC alone. CADTH's findings remained aligned with the sponsor's in that avelumab with BSC has a 0% probability of being cost-effective option at a willingness-to-pay threshold of $50,000 per QALY. A price reduction of at least 83% is necessary for avelumab with BSC to be considered cost-effective at a $50,000 per QALY threshold.

There remains some outstanding uncertainty within the model regarding potential cost and health consequences associated with adverse events, subsequent treatment costs and utility post disease progression. This means the CADTH reanalysis may overestimate the cost effectiveness of avelumab and further price reductions may be required.

Based on the sponsor's submitted budget impact analysis (BIA), the total incremental cost for reimbursement of avelumab for patients with locally advanced or metastatic urinary cancer that have not progressed with first-line platinum-containing chemotherapy is estimated to be [redacted] over three years. CADTH found that the sponsor significantly underestimated the budget impact of introducing avelumab to the market. Due to unclear calculations regarding subsequent therapy costs, CADTH could only conduct a reanalysis and not a base case estimate. The CADTH reanalysis estimated that avelumab could add $312,553,246 to budgets over the first three years, although acknowledged this to be an overestimation as cost savings due to lower subsequent therapy use could not be reliably estimated.

Stakeholder Input Relevant to the Economic Review

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Economic Review

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Appendix 1: Cost Comparison Table

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Appendix 2: Submission Quality

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Appendix 3: Additional Information on the Submitted Economic Evaluation

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Appendix 4: Additional Details on the CADTH Reanalyses and Sensitivity Analyses of the Economic Evaluation

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

Appendix 5: Submitted BIA and CADTH Appraisal

This section outlines the technical details of the pCODR Economic Guidance Panel's evaluation of the economic evidence that is summarized in the executive summary. In accordance with the *Disclosure of Information Guidelines for the CADTH Pan-Canadian Oncology Drug Review*, this section is not eligible for disclosure. It was provided to the pCODR Expert Review Committee (pERC) for their deliberations and the participating drug programs for their information.

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