

## 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

<b>1L</b>	first-line
<b>AE</b>	adverse vent
<b>AIC</b>	akaike information criterion
<b>BIA</b>	budget impact analysis
<b>BIC</b>	Bayesian information criterion
<b>BSC</b>	best supportive care
<b>ICER</b>	incremental cost-effectiveness ratio
<b>KM</b>	Kaplan-Meier
<b>LY</b>	life years
<b>NOC</b>	notice of compliance
<b>NR</b>	not reported
<b>PSM</b>	partitioned survival model
<b>QALY</b>	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
<b>Type of economic evaluation</b>	Cost-utility analysis Partitioned survival analysis
<b>Target population</b>	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.
<b>Treatment</b>	Avelumab (Bavencio) with best supportive care
<b>Comparator</b>	Best supportive care (BSC): antibiotics, nutritional support, correction of metabolic disorders, optimal symptom control and pain management such as palliative radiotherapy
<b>Perspective</b>	Canadian publicly funded health care payer
<b>Outcome</b>	Quality-adjusted life years (QALYs) and life years (LY)
<b>Time horizon</b>	10 years
<b>Key data source</b>	JAVELIN Bladder 100 study
<b>Submitted results for base case</b>	Incremental cost-effectiveness ratio (ICER) for avelumab with BSC versus BSC: \$281,149 per QALY gained (incremental QALYs: 0.58; incremental cost: \$162,149)
<b>Key limitations</b>	<ul style="list-style-type: none"> <li>• 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.</li> <li>• 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.</li> <li>• 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.</li> <li>• 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.</li> <li>• The time horizon used was not reflective of a lifetime time horizon.</li> </ul>
<b>CADTH reanalysis results</b>	<ul style="list-style-type: none"> <li>• 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.</li> <li>• CADTH reanalysis could not address omitted costs for BSC, omitted disutility for AEs, and the exclusion of costs incurred from moderate AEs</li> <li>• 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.</li> </ul>

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.

## References

1. Pharmacoeconomic evaluation. In: pan Canadian Oncology Drug Review sponsor submission: Bavencio (avelumab), 20 mg/mL single-use vial. EMD Serono - Pfizer Alliance. Kirkland (ON): EMD Serono - Pfizer Alliance; 2020 Sep 18.
2. Akaza H, Naito S, Usami M, et al. Efficacy and safety of gemcitabine monotherapy in patients with transitional cell carcinoma after cisplatin-containing therapy: a Japanese experience. *Jpn J Clin Oncol*. 2007;37(3):201-206.
3. Furubayashi N, Negishi T, Yamashita T, et al. The combination of paclitaxel and carboplatin as second-line chemotherapy can be a preferred regimen for patients with urothelial carcinoma after the failure of gemcitabine and cisplatin chemotherapy. *Mol Clin Oncol*. 2017;7(6):1112-1118.
4. Han KS, Joung JY, Kim TS, et al. Methotrexate, vinblastine, doxorubicin and cisplatin combination regimen as salvage chemotherapy for patients with advanced or metastatic transitional cell carcinoma after failure of gemcitabine and cisplatin chemotherapy. *Br J Cancer*. 2008;98(1):86-90.
5. Schedule of benefits for physician services under the Health Insurance Act: effective April 1, 2020. Toronto (ON): Ontario Ministry of Health; 2020: [http://www.health.gov.on.ca/en/pro/programs/ohip/sob/physserv/sob\\_master20200306.pdf](http://www.health.gov.on.ca/en/pro/programs/ohip/sob/physserv/sob_master20200306.pdf). Accessed 2021 Feb 4.
6. Canadian Institute for Health Information. Patient cost estimator. 2021; <https://www.cihi.ca/en/patient-cost-estimator>. Accessed 2021 Feb 4.
7. pan-Canadian Oncology Drug Review sponsor submission: Bavencio (avelumab), 20 mg/mL single-use vial. EMD Serono - Pfizer Alliance. Kirkland (QC): EMD Serono - Pfizer Alliance; 2020 Sep 18.
8. Medicine USNLo. A Study to Evaluate Enfortumab Vedotin Versus (vs) Chemotherapy in Subjects With Previously Treated Locally Advanced or Metastatic Urothelial Cancer (EV-301) - Full Text View - ClinicalTrials.gov. 2021; <https://clinicaltrials.gov/ct2/show/NCT03474107>.
9. Bavencio (avelumab): 20 mg/mL single-use vial, solution for intravenous infusion [product monograph]. Mississauga (ON): EMD Serono, a division of EMD Inc; 2020 Dec 10.
10. Bednova O, Leyton JV. Targeted molecular therapeutics for bladder cancer-a new option beyond the mixed fortunes of immune checkpoint inhibitors? *Int J Mol Sci*. 2020;21(19).
11. Kim H, Liew D, Goodall S. Cost-effectiveness and financial risks associated with immune checkpoint inhibitor therapy. *Br J Clin Pharmacol*. 2020;86(9):1703-1710.
12. Ma E, Bilir S, Munakata J, Ogale S. Cost of immunotherapy to treat locally advanced or metastatic urothelial cancer. *J Manag Spec Pharm*. 2018;24 (10 A):S28.
13. Statistics Canada. Life expectancy and other elements of the life table, Canada, all provinces except Prince Edward Island. Table: 13-10-0114-01. 2019; <https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1310011401>. Accessed 2021 Feb 4.
14. Guidelines for the economic evaluation of health technologies: Canada. 4th ed. Ottawa (ON): CADTH; 2017: <https://www.cadth.ca/dv/guidelines-economic-evaluation-health-technologies-canada-4th-edition>. Accessed 2021 Feb 4.