CADTH

CADTH Reimbursement Review

Provisional Funding Algorithm

Indication: Metastatic urothelial carcinoma

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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.

Background

Following a request from jurisdictions, CADTH may design or update an algorithm depicting the sequence of funded treatments for a particular tumour type. These algorithms are proposals for the jurisdictions to implement and adapt to the local context. As such, they are termed “provisional.” Publishing of provisional algorithms is meant to improve transparency of the oncology drug funding process and promote consistency across jurisdictions.

Provisional funding algorithms are based on 3 principal sources of information:

- CADTH pCODR Expert Review Committee (pERC) reimbursement recommendations and/or implementation guidance regarding the place of drug in therapy and sequencing
- implementation advice from panels of clinicians convened by CADTH concerning sequencing of drugs in the therapeutic space of interest
- existing oncology drug reimbursement criteria and legacy funding algorithms adopted by jurisdictional drug plans and cancer agencies.

Note that provisional funding algorithms are not treatment algorithms; they are neither meant to detail the full clinical management of each patient nor the provision of each drug regimen. The diagrams may not contain a comprehensive list of all available treatments, and some drugs may not be funded in certain jurisdictions. All drugs are subject to explicit funding criteria, which may also vary between jurisdictions. Readers are invited to refer to the cited sources of information on the CADTH website for more details.

Provisional funding algorithms also delineate treatment sequences available to patients who were never treated for the condition of interest (i.e., incident population). Time-limited funding of new options for previously or currently treated patients (i.e., prevalent population) is not detailed in the algorithm.

Provisional funding algorithms may contain drugs that are under consideration for funding. Algorithms will not be dynamically updated by CADTH following changes to drug funding status. Revisions and updates will occur only upon request by jurisdictions.

Jurisdictional cancer drug programs requested a CADTH provisional funding algorithm on metastatic urothelial carcinoma. However, no outstanding implementation issues were identified, and no additional implementation advice is provided in this report. The algorithm depicted herein is meant to reflect the current and anticipated funding landscape based on the previously mentioned sources of information.

Table 1: Relevant CADTH Recommendations

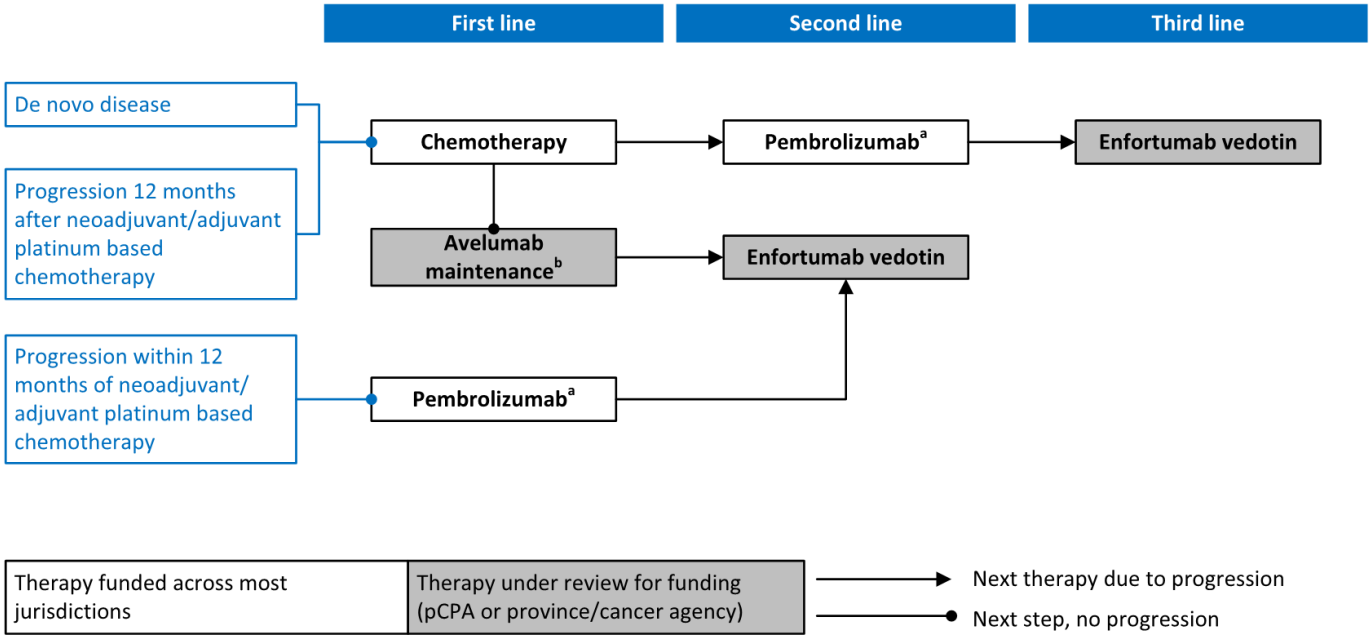
Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
Pembrolizumab (Keytruda)	September 20, 2017	pERC recommends reimbursement of pembrolizumab (Keytruda) conditional on cost-effectiveness being improved to an acceptable level. Reimbursement should be for the treatment of patients with locally advanced or metastatic urothelial carcinoma (MUC) who have disease progression during or following platinum-containing chemotherapy or within 12 months of completing neoadjuvant or adjuvant platinum-containing chemotherapy. Funding should be for patients with a good performance status. Treatment should continue until confirmed disease progression or unacceptable toxicity or after completing two years of pembrolizumab therapy, whichever comes first.
Avelumab (Bavencio)	March 23, 2021	pERC conditionally recommends reimbursement of avelumab (Bavencio) plus best supportive care (BSC) for the first-line maintenance treatment of patients with histologically confirmed, unresectable, locally advanced, or metastatic urothelial carcinoma whose disease has not progressed with first-line platinum-based induction chemotherapy if the following conditions are met: • cost-effectiveness is improved to an acceptable level • feasibility of adoption (budget impact) is addressed. pERC agreed with the CGP that there is currently no evidence to support the use of a second-line immune checkpoint inhibitor following first-line avelumab maintenance given that they work through similar mechanisms of action. There remains a lack of evidence-based therapies for these patients; however, chemotherapy and clinical trials may be appropriate. In terms of whether it would preferable to give avelumab for maintenance or wait and give pembrolizumab to patients who progress, the CGP noted that the JAVELIN Bladder 100 clinical trial investigated whether patients treated with avelumab plus BSC had better outcomes than patients treated with BSC only. Given the results of the trial, pERC agreed with the CGP that it would be preferable to give avelumab for maintenance therapy rather than wait and give pembrolizumab to patients who progress. pERC agreed with the CGP that patients who progressed on avelumab maintenance treatment should not be treated with subsequent anti-PD1 therapy. For patients who stop treatment with avelumab for reasons related to infusion reaction or unrelated to progression after a short duration of exposure (i.e., 6 months) and who then experience disease progression after a progression free interval of 6-months, pERC agreed with the CGP that subsequent treatment with pembrolizumab may be considered. pERC agreed with the CGP that treatment with avelumab should only be continued if the disease is still in remission. If the disease had progressed, then the patient would receive the next line of treatment for their disease. pERC agreed with the CGP that shorter durations of treatment with chemotherapy in the first line (< 4 cycles) may be eligible for treatment with avelumab plus BSC maintenance. However, patients receiving fewer than 4 cycles of chemotherapy due to intolerance should have no evidence of disease progression on or after treatment, and reasons for

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		shortened chemotherapy exposure should be clearly justified so as not to encourage inadequate exposure to chemotherapy treatment
Enfortumab vedotin (Padcev)	January 24, 2022	The CADTH pCODR Expert Review Committee (pERC) recommends that enfortumab vedotin be reimbursed for the treatment of adult patients with unresectable locally advanced or metastatic urothelial cancer (UC) who have previously received: • a PD-1 or PD-L1 inhibitor in the locally advanced or metastatic setting; and • a platinum-containing chemotherapy in the neoadjuvant/adjuvant, locally advanced or metastatic setting pERC considered the sequencing of treatments given the newly recommended listing for avelumab as maintenance therapy following the first-line platinum-based chemotherapy in the locally advanced or metastatic setting. As per the eligibility criteria of Study EV-301, patients are required to fail platinum-containing chemotherapy, and PD-1/PD-L1 inhibitor therapy. pERC noted that unless there is a re-treatment with a PD-1/PD-L1 inhibitor, patients would fulfill the eligibility criteria for treatment with enfortumab vedotin, thus a significant portion of patients would be eligible to receive enfortumab vedotin as second-line therapy. Conversely, it was also noted that if the treatment-free interval is of sufficient length following treatment with avelumab maintenance therapy, second-line treatment with a PD-1/PD-L1 inhibitor (i.e., pembrolizumab) would be justified prior to enfortumab vedotin.

BSC = best supportive care; CGP = clinical guidance panel; MUC = metastatic urothelial carcinoma; pERC = CADTH pCODR Expert Review Committee.

Provisional Funding Algorithm

Figure 1: Provisional Funding Algorithm Diagram for Metastatic Urothelial Carcinoma



pCPA = pan-Canadian Pharmaceutical Alliance.

[a] Patients who stopped pembrolizumab treatment after 2 years (35 cycles) for reasons other than disease progression or intolerability are allowed up to 1 additional year of pembrolizumab upon release.

[b] If received 4 cycles to cycles of chemotherapy without disease progression.

Description of the Provisional Funding Algorithm

Patients With De Novo Disease or Disease Progression Greater Than or Equal to 12 Months After Neoadjuvant or Adjuvant Platinum-Based Chemotherapy

Available first-line therapies include chemotherapy with or without subsequent avelumab maintenance treatment. Avelumab maintenance treatment is under consideration for funding in patients who received 4 cycles to 6 cycles of chemotherapy and did not experience disease progression.

Upon progression while on or after chemotherapy without avelumab maintenance, pembrolizumab can be offered until disease progression. In patients who stopped pembrolizumab treatment after 2 years (35 cycles) for reasons other than disease progression or intolerability, up to 1 additional year of pembrolizumab treatment is allowed. Following progression on pembrolizumab or avelumab maintenance therapy, enfortumab vedotin is under consideration for funding.

Patients With Disease Progression Within 12 Months of Neoadjuvant or Adjuvant Platinum-Based Chemotherapy

Pembrolizumab is available in first line. Upon disease progression, enfortumab vedotin may be offered pending a funding decision by jurisdictions.