Canada's Drug Agency
L'Agence des médicaments du Canada

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Drugs Health Technologies Health Systems

Provisional Funding Algorithm

Indication: Metastatic urothelial carcinoma

This report supersedes the Provisional Funding Algorithm report for metastatic urothelial carcinoma dated January 11, 2023. Please always check Provisional Funding Algorithms to ensure you are reading the most recent algorithm report.

Background

Following a request from jurisdictions, Canada's Drug Agency (CDA-AMC) 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:

- pan-Canadian Oncology Drug Review Expert Review Committee (pERC) reimbursement recommendations and/or implementation guidance regarding drug place in therapy and sequencing
- implementation advice from panels of clinicians convened by CDA-AMC 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 CDA-AMC 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 CDA-AMC following changes to drug funding statuses. Revisions and updates will occur only upon request by jurisdictions.

Jurisdictional cancer drug programs requested a CDA-AMC Provisional Funding Algorithm on metastatic urothelial carcinoma (mUC). 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.

History and Development of the Provisional Funding Algorithm

CDA-AMC first published a provisional funding algorithm for urothelial carcinoma in March 2022. This was a rapid algorithm with the aim to incorporate the CDA-AMC recommendation for enfortumab vedotin (Padcev) for the treatment of adult patients with unresectable, locally advanced or mUC who have previously received a platinum-containing chemotherapy and programmed death receptor-1 or programmed death-ligand 1 inhibitor therapy.

A second provisional funding algorithm report was later released on January 11, 2023, to incorporate the recommendation for nivolumab (Opdivo) as a monotherapy for the adjuvant treatment of adult patients with urothelial carcinoma (UC) at high risk for recurrence after undergoing radical resection.

Jurisdictional cancer drug programs have recently requested to update this rapid algorithm to incorporate the CDA-AMC recommendation for erdafitinib (Balversa) for the treatment of adult patients with locally advanced unresectable or mUC harbouring susceptible *FGFR3* genetic alterations who have disease progression during at least 1 line of prior therapy as well as the CDA-AMC recommendation for enfortumab vedotin (Padcev) in combination with pembrolizumab for the treatment of adult patients with locally advanced UC or mUC with no prior systemic therapy for mUC.

Table 1: Relevant Previous Recommendations

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
Erdafitinib (Balversa)	January 28, 2025	pERC recommends that erdafitinib be reimbursed for the treatment of patients with locally advanced unresectable or metastatic urothelial carcinoma (UC) harbouring susceptible *FGFR3* genetic alterations, who have disease progression during or following at least 1 line of prior therapy, including within 12 months of neoadjuvant or adjuvant therapy, only if the following conditions are met: **Initiation** 1. Erdafitinib should be reimbursed in patients with a diagnosis of locally advanced or metastatic UC harbouring susceptible *FGFR3* genetic alterations who have disease progression during or following at least 1 line of prior therapy, including within 12 months of neoadjuvant or adjuvant therapy. 2. Erdafitinib should not be reimbursed in patients who are eligible for but have not received prior PD-1 or PD-L1 inhibitor therapy. 3. Treatment with erdafitinib should be initiated following confirmation of a susceptible *FGFR3* genetic alteration using a validated test. **Discontinuation** 4. Reimbursement of erdafitinib should be discontinued upon evidence of: 4.1. clinically significant disease progression as assessed by imaging and clinical criteria 4.2. intolerable or unmanageable drug toxicity. **Prescribing** 5. Erdafitinib should be prescribed by clinicians with expertise in treating patients with UC. **Pricing** 6. A reduction in price. **Feasibility of adoption** 7. The feasibility of adoption of erdafitinib must be addressed. The organizational feasibility of conducting *FGFR3* testing must be addressed.
Enfortumab vedotin (Padcev)	December 17, 2024	pERC recommends that enfortumab vedotin in combination with pembrolizumab be reimbursed for the treatment of adult patients with locally advanced urothelial cancer (UC) or metastatic urothelial cancer (mUC) with no prior systemic therapy for mUC only if the following conditions are met: **Initiation**

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		1. Enfortumab vedotin in combination with pembrolizumab should be reimbursed for the treatment of adult patients with unresectable locally advanced urothelial cancer or metastatic urothelial cancer with no prior systemic therapy. 2. For additional clarity, the following patients who have received the following are also eligible: 2.1. neoadjuvant chemotherapy, but experienced recurrence more than 12 months after neoadjuvant chemotherapy was completed 2.2. adjuvant chemotherapy following cystectomy, but experienced recurrence more than 12 months after adjuvant chemotherapy was completed 2.3. adjuvant nivolumab, but experienced recurrence more than 6 months after nivolumab treatment was completed. 3. Patients should have a good performance status. 4. Treatment with enfortumab vedotin in combination with pembrolizumab should not be initiated in patients with: 4.1. active CNS metastases 4.2. uncontrolled diabetes 4.3. prior enfortumab vedotin or other MMAE-based ADC. **Renewal** 5. Patients should be assessed by the treating clinician before each treatment cycle with diagnostic imaging conducted every 2 to 3 months. **Discontinuation** 6. Treatment should be discontinued in patients with any of the following: 6.1. documented disease progression 6.2. unacceptable toxicity 6.3. note that pembrolizumab may be used up to 24 months in patients without disease progression, according to the pembrolizumab product monograph. **Prescribing** 7. Treatment with enfortumab vedotin in combination with pembrolizumab should only be initiated by a medical oncologist with experience treating incurable urothelial cancer. 7.1. Given the known complications associated with enfortumab vedotin in combination with pembrolizumab, initial treatment must be administered in centres where there is experience using a drug at risk for extravasation. 8. Enfortumab vedotin in combination with pembrolizumab should not be used in combination with other anti-cancer drugs in routine clinical practice for locally advanced urothelial cancer or metastatic urothelial cancer. **Pricing** 9. A reduction in price. 10. The feasibility of adoption of enfortumab vedotin must be addressed. **Guidance on sequencing (adapted from Table 1: Reimbursement Conditions and Reasons and the Discussion Points section and other relevant sections, and Table 2: Responses to Questions From the Drug Programs of the recommendations and reason report)** **Implementation guidance for initiation from Table 1** • The clinical expert stated that as per standard clinical practice with other regimens after immunotherapy, patients with adjuvant and/or neoadjuvant immune checkpoint

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		inhibitors who experienced relapse at least 6 months after treatment completion should be eligible to be treated with enfortumab vedotin in combination with pembrolizumab. pERC agreed with the clinical expert. • pERC determined that patients with CNS metastases may be eligible for treatment with enfortumab vedotin in combination with pembrolizumab if they have stable brain metastases on baseline scans before treatment. However, patients with leptomeningeal disease should not be treated with enfortumab vedotin. **Implementation guidance for discontinuation from Table 1** • pERC agreed with the clinical expert that as per Study EV0392, patients who experience unacceptable AEs attributable only to enfortumab vedotin may continue pembrolizumab monotherapy for a maximum of 24 months, and patients who experienced an unacceptable AE attributable only to pembrolizumab may continue enfortumab vedotin monotherapy. • pERC noted that the decisions to discontinue treatment should be made in consultation with the patient. **Discussion points** • pERC deliberated whether patients currently receiving alternate first-line therapy for locally advanced UC or mUC could be switched to enfortumab. The committee decided that patients who have not started or have not completed platinum-based first-line chemotherapy may be eligible candidates to receive enfortumab vedotin plus pembrolizumab. pERC noted that based on the inclusion criteria of Study EV-302, enfortumab vedotin in combination with pembrolizumab should not be offered to patients who have completed or progressed on first-line chemotherapy. The committee agreed with the clinical expert that patients who are receiving avelumab for maintenance therapy are, by definition, either in remission or have stable disease, and those who progress on avelumab will be eligible for enfortumab vedotin as third-line single drug therapy, which is already approved and funded.
Nivolumab (Opdivo)	October 17, 2022	pERC recommends that nivolumab be reimbursed as a monotherapy for the adjuvant treatment of adult patients with UC who are at high risk of recurrence after undergoing radical resection of UC. Conditions included a reduction in price and the feasibility of adoption being addressed. **Initiation** 1. Treatment with nivolumab should only be reimbursed when initiated in patients who have all of the following: 1.1. Pathologic evidence of urothelial carcinoma at high risk of recurrence based on pathologic staging of radical surgery tissue in patients who have either: 1.1.1. received cisplatin-based neoadjuvant chemotherapy (ypT2-pT4a or ypN+) 1.1.2. not received neoadjuvant cisplatin chemotherapy (pT3-pT4a or pN+) and are ineligible for adjuvant therapy with cisplatin chemotherapy (based on Galsky ineligibility criteria, 2011), or 1.1.3. not received neoadjuvant cisplatin chemotherapy (pT3-pT4a or pN+) and are eligible for adjuvant cisplatin-based chemotherapy but decline to take it. 1.2. Evidence of no recurrence should be confirmed before initiating therapy. 1.3. Muscle-invasive UC (MIUC) at disease diagnosis.

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		2. Patient must not have any of the following: 2.1. metastatic disease 2.2. active autoimmune disease 3. Patients should have good performance status. 4. Treatment with nivolumab should be initiated in patients within 120 days after completion of local therapy **Discontinuation** 5. Nivolumab should be discontinued upon the occurrence of either of the following: 5.1. disease recurrence 5.2. unacceptable toxicity. 6. Patients should be assessed for disease recurrence every 3 to 6 months. 7. Nivolumab should be reimbursed for a maximum of 1 year (240 mg IV every 2 weeks or 480 mg IV every 4 weeks). **Prescribing** 8. Treatment should be prescribed by clinicians with expertise and experience in treating urothelial cancer. The treatment should be supervised and delivered in hospital outpatient clinics with expertise in systemic therapy delivery and management of immunotherapy-related side effects. 9. Nivolumab should only be reimbursed when administered as monotherapy. **Pricing** 10. A reduction in price **Feasibility of adoption** 11. The feasibility of adoption of nivolumab must be addressed. **Guidance on sequencing:** • The CheckMate-274 trial did not assess the comparative efficacy of adjuvant nivolumab compared with adjuvant chemotherapy. pERC agreed that given the absence of robust direct or indirect comparison, there is insufficient evidence to ascertain which of the agents (i.e., adjuvant nivolumab or adjuvant chemotherapy) has superior efficacy. • pERC noted that pERC noted that patients whose disease recurs more than 6 months after receiving adjuvant treatment with nivolumab would be treated according to the established treatment algorithm (i.e., eligibility for downstream enfortumab vedotin).
Enfortumab (Padcev)	January 24, 2022	pERC recommends that enfortumab vedotin be reimbursed for the treatment of adult patients with unresectable locally advanced or MUC who have previously received a platinum-containing chemotherapy and PD-1 or PD-L1 inhibitor only if the following conditions are met: **Initiation** 1. Enfortumab vedotin should be reimbursed for adult patients (age ≥ 18 years) with locally advanced or metastatic UC who have previously received both of the following treatments: 1.1. a PD-1 or PD-L1 inhibitor in the locally advanced or metastatic setting 1.2. a platinum-containing chemotherapy in the neoadjuvant or adjuvant, locally advanced or metastatic setting. 2. Patients should have a good performance status.

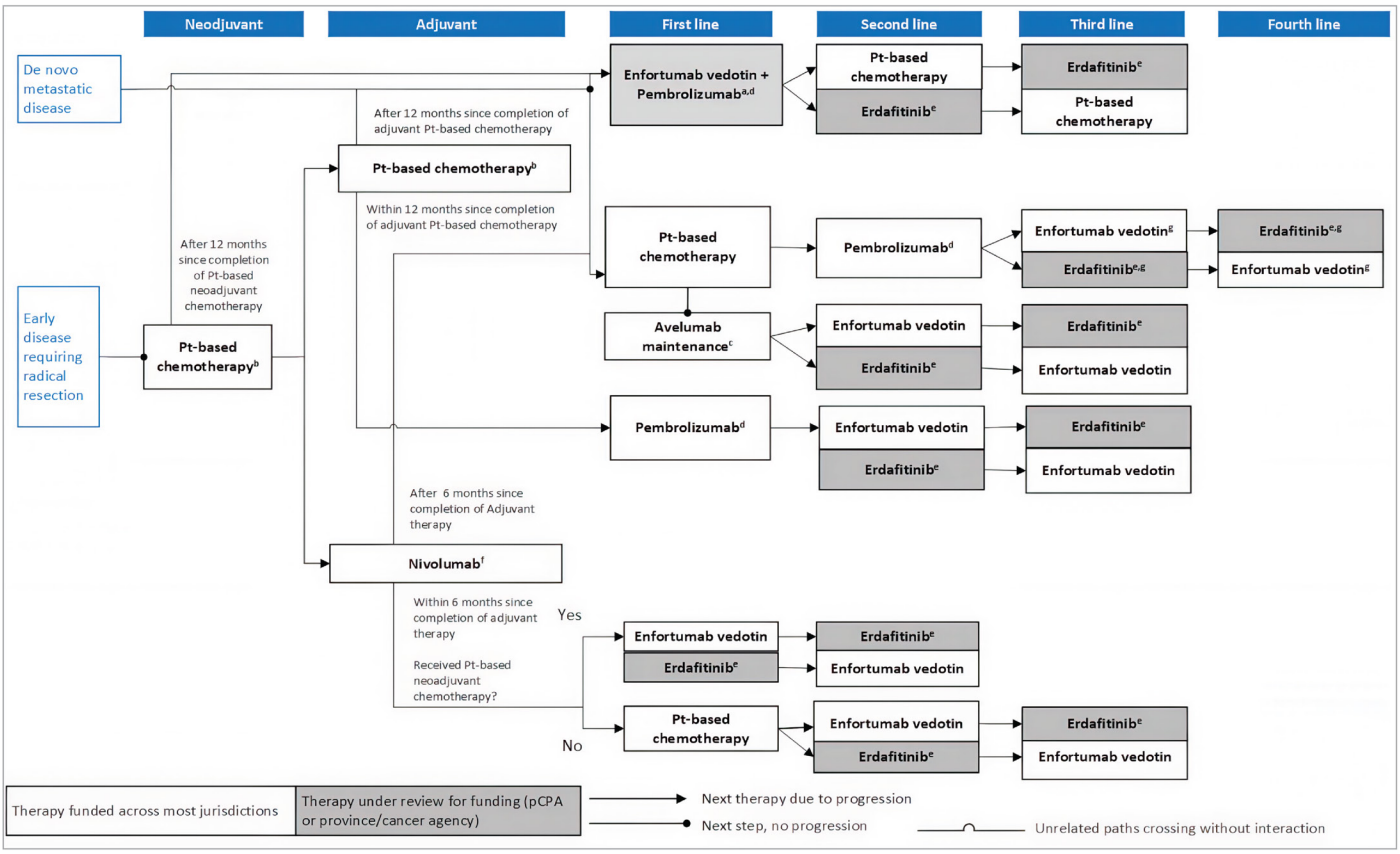
Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		3. Treatment with enfortumab vedotin should not be initiated in patients with: 3.1. preexisting grade 2 or higher sensory or motor neuropathy or ongoing clinically significant toxic effects associated with previous treatment 3.2. active CNS metastases, uncontrolled diabetes, or active keratitis or corneal ulcerations. **Renewal** 4. Patients should be assessed by the treating physician before each treatment cycle with diagnostic imaging conducted every 2 months to 3 months. **Discontinuation** 5. Enfortumab vedotin should be discontinued in patients with either of the following: 5.1. documented disease progression 5.2. unacceptable toxicity. **Prescribing** 6. Enfortumab vedotin should only be prescribed by clinicians with experience and expertise in treating advanced UC in centres with expertise in the administration of IV drugs with the potential for extravasation, and pharmacy resources to monitor drug interactions. 7. Enfortumab vedotin should not be used in combination with other drugs. **Pricing** 8. A reduction in price. **Feasibility of adoption** 9. The feasibility of adoption of enfortumab vedotin must be addressed. **Guidance on sequencing:** 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 before enfortumab vedotin.
Avelumab (Bavencio)	March 23, 2021	pERC conditionally recommends reimbursement of avelumab (Bavencio) plus 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

Generic name (brand name)	Date of recommendation	Recommendation and guidance on treatment sequencing
		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 shortened chemotherapy exposure should be clearly justified so as not to encourage inadequate exposure to chemotherapy treatment.
Pembrolizumab (Keytruda)	March 2, 2018	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 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 2 years of pembrolizumab therapy, whichever comes first.

ADC = antibody drug conjugate; AE = adverse event; BSC = best supportive care; CGP = Clinical Guidance Panel; CNS = central nervous system; MMAE = monomethyl auristatin E; mUC = metastatic urothelial carcinoma; PD-1 = programmed death receptor-1; PD-L1 = programmed death-ligand 1; pERC = pan-Canadian Oncology Drug Review Expert Review Committee; UC = urothelial carcinoma.

Provisional Funding Algorithm

Figure 1: Provisional Funding Algorithm Diagram for Metastatic Urothelial Carcinoma



pCPA = pan-Canadian Pharmaceutical Alliance; pt = platinum.

[a]Patients who experience unacceptable adverse events attributable only to enfortumab vedotin may continue pembrolizumab monotherapy for a maximum of 24 months; patients who experience unacceptable adverse events attributable only to pembrolizumab may continue enfortumab vedotin monotherapy.

[b]In usual practice, individuals would not receive platinum-based chemotherapy in both the neoadjuvant and adjuvant settings sequentially.

[c]If patients received 4 to 6 cycles of chemotherapy without disease progression.

[d]Patients who stopped pembrolizumab treatment after 2 years for reasons other than disease progression or intolerability are eligible for up to 1 additional year of pembrolizumab upon disease relapse.

[e]Treatment with erdafitinib should be initiated following confirmation of a susceptible *FGFR3* genetic alteration using a validated test.

[f]For patients with muscle-invasive urothelial carcinoma who are at high risk of recurrence after undergoing radical resection. Treatment with nivolumab should be initiated within 120 days after completion of therapy.

[g]Patients who progress on enfortumab vedotin in the third line may now receive erdafitinib in the fourth line, and those who progress on erdafitinib in the third line may now receive enfortumab vedotin in the subsequent treatment line.

Description of the Provisional Funding Algorithm

Patients With de Novo Metastatic Disease

For patients with de novo metastatic disease, several first-line therapy options are available. One option is enfortumab vedotin in combination with pembrolizumab, which has been recommended for use in the

advanced setting and is currently under review for funding. Upon disease progression on or after this combination therapy, platinum-based chemotherapy or erdafitinib, currently under review for funding, are available as second-line options. For patients who have completed second-line platinum-based chemotherapy, the third-line option is erdafitinib, which is under review for funding. Those patients whose disease progresses on erdafitinib in the second line may receive platinum-based chemotherapy in the subsequent treatment.

Note that treatment with erdafitinib should be initiated following confirmation of a susceptible *FGFR3* genetic alteration using a validated test.

Another option for first-line therapy is platinum-based chemotherapy, which may be administered with or without subsequent avelumab maintenance therapy. Upon progression on or after chemotherapy without avelumab maintenance, pembrolizumab is available until disease progression. Patients who discontinue pembrolizumab treatment after 2 years for reasons other than disease progression or intolerability may receive up to 1 additional year of pembrolizumab treatment. After progression on pembrolizumab, enfortumab vedotin or erdafitinib, which is under review for funding, become available. Patients whose disease progresses on enfortumab vedotin in the third line may receive erdafitinib in the fourth line, while those patients whose disease progresses on erdafitinib in the third line may receive enfortumab vedotin in the subsequent treatment line.

For patients who have completed first-line platinum-based chemotherapy with subsequent avelumab maintenance treatment, the second-line options are enfortumab vedotin or erdafitinib which is under review for funding. Patients whose disease progresses on enfortumab vedotin in the second line may receive erdafitinib in the third line, while those patients whose disease progresses on erdafitinib in the second line may receive enfortumab vedotin in the subsequent treatment line.

Patients With Early Disease Requiring Radical Resection and Neoadjuvant or Adjuvant Treatment

For patients with early disease, platinum-based chemotherapy is an option in the neoadjuvant setting before surgical resection, with cisplatin-based chemotherapy being the preferred choice in most jurisdictions. In the adjuvant setting, therapy options following surgery include platinum-based chemotherapy and nivolumab.

Patients Who Have Received Neoadjuvant Chemotherapy

In the neoadjuvant setting, patients may receive platinum-based chemotherapy before surgical resection. It is acknowledged that most jurisdictions would start with cisplatin-based chemotherapy in this setting.

After surgery, patients may receive adjuvant treatment, which includes platinum-based chemotherapy. More recently, nivolumab has been recommended for use in the adjuvant setting.

For patients who have received neoadjuvant chemotherapy and experienced disease recurrence more than 12 months after completing treatment, an option is enfortumab vedotin in combination with pembrolizumab, which has been recommended for use in the advanced setting and is currently under review for funding. Upon disease progression on or after this combination therapy, platinum-based chemotherapy or erdafitinib,

currently under review for funding, are available as second-line options. Note that treatment with erdafitinib should be initiated following confirmation of a susceptible *FGFR3* genetic alteration using a validated test. For patients who have completed second-line platinum-based chemotherapy, the third-line option is erdafitinib, which is under review for funding. Those patients whose disease progresses on erdafitinib in the second line may receive platinum-based chemotherapy in subsequent treatment.

Another option for first-line therapy in the metastatic setting is platinum-based chemotherapy, which may be administered with or without subsequent avelumab maintenance therapy. For patients who have completed first-line platinum-based chemotherapy without subsequent avelumab maintenance treatment, pembrolizumab is available until disease progression. Patients who discontinue pembrolizumab treatment after 2 years for reasons other than disease progression or intolerability may receive up to 1 additional year of pembrolizumab treatment. After progression on pembrolizumab, enfortumab vedotin or erdafitinib, which is under review for funding, become available. Note that treatment with erdafitinib should be initiated following confirmation of a susceptible *FGFR3* genetic alteration using a validated test. Patients whose disease progresses on enfortumab vedotin in the third line may now receive erdafitinib in the fourth line, while those patients whose disease progresses on erdafitinib in the third line may now receive enfortumab vedotin in the subsequent treatment line.

For patients who have completed first-line platinum-based chemotherapy with subsequent avelumab maintenance treatment, the second-line options are enfortumab vedotin or erdafitinib. Note that treatment with erdafitinib should be initiated following confirmation of a susceptible *FGFR3* genetic alteration using a validated test.

Patients whose disease progresses on enfortumab vedotin in the second line may now receive erdafitinib as a third-line treatment, while those patients whose disease progresses on erdafitinib in the second line may now receive enfortumab vedotin in the subsequent treatment line.

Patients Who Have Received Adjuvant Chemotherapy

For patients who have received adjuvant chemotherapy and have experienced disease recurrence more than 12 months after completing treatment, the treatment sequence is similar to that of de novo metastatic disease.

For patients whose disease progresses within 12 months of receiving adjuvant platinum-based chemotherapy, the subsequent first-line option is pembrolizumab. In patients who stop pembrolizumab treatment after 2 years for reasons other than disease progression or intolerability, up to an additional year of pembrolizumab treatment is available. Second-line options include enfortumab vedotin or erdafitinib, which is under review for funding. Note that treatment with erdafitinib should be initiated following confirmation of a susceptible *FGFR3* genetic alteration using a validated test. Patients whose disease progresses on enfortumab vedotin in the second line may now receive erdafitinib as a third-line treatment, and those patients whose disease progresses on erdafitinib in the second line may now receive enfortumab vedotin in the subsequent treatment line.

Patients Who Have Received Adjuvant Nivolumab

For patients who have received adjuvant nivolumab, which is used for those with a high risk of recurrence after surgical resection, therapy options depend on the timing of progression. For patients whose disease progresses to mUC after more than 6 months, the treatment approach is similar to that of de novo metastatic disease.

For patients whose disease progresses to mUC within 6 months of receiving adjuvant nivolumab, the first-line therapy depends on whether they have previously received platinum-based neoadjuvant chemotherapy. For those who have received platinum-based neoadjuvant chemotherapy, the first-line options are enfortumab vedotin or erdafitinib. Note that treatment with erdafitinib should be initiated following confirmation of a susceptible *FGFR3* genetic alteration using a validated test. Patients whose disease progresses on enfortumab vedotin in the first line may now receive erdafitinib as a second-line treatment, while those patients whose disease progresses on erdafitinib in the first line may now receive enfortumab vedotin in the subsequent treatment line.

For those patients who have not received platinum-based neoadjuvant chemotherapy, platinum-based chemotherapy is the first-line therapy, followed by enfortumab vedotin or erdafitinib as second-line options. Note that treatment with erdafitinib should be initiated following confirmation of a susceptible *FGFR3* genetic alteration using a validated test. Patients whose disease progress on enfortumab vedotin in the second line may now receive erdafitinib as a third-line treatment, while those patients whose disease progresses on erdafitinib in the second line may now receive enfortumab vedotin in the subsequent treatment line.

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Questions or requests for information about this report can be directed to Requests@CDA-AMC.ca.