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

Reimbursement Recommendation

Reimbursement Recommendation

(Draft)

erdafitinib (Balversa)

Indication: for the treatment of adult patients with locally advanced unresectable or metastatic urothelial carcinoma (UC) harboring susceptible FGFR3 genetic alterations who have disease progression during at least one line of prior therapy.

Sponsor: Janssen Inc.

Recommendation: Reimburse with Conditions

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Recommendation

The CDA-AMC pCODR Expert Review Committee (pERC) recommends that erdafitinib be reimbursed for the treatment of patients with locally advanced unresectable or metastatic urothelial carcinoma (UC), harboring susceptible fibroblast growth factor receptor 3 (FGFR3) genetic alterations, who have disease progression during or following at least one line of prior therapy, including within 12 months of neoadjuvant or adjuvant therapy, only if the conditions listed in **Error! Reference source not found.** are met.

Rationale for the Recommendation

Evidence from one randomized, open label, phase 3 trial (THOR, Cohort 1, N = 266) demonstrated that, in patients with locally advanced or metastatic urothelial carcinoma (la/mUC) harboring FGFR3 alterations, erdafitinib provides clinically meaningful benefits compared to chemotherapy (docetaxel or vinflunine). Specifically, the primary analysis of the THOR trial showed that the median overall survival (OS) was 12.06 months in the erdafitinib arm compared with 7.79 months in the chemotherapy arm (hazard ratio [HR] of 0.64; 95% CI: 0.47 to 0.88). Similarly, the OS rate at 6 months was better with erdafitinib than chemotherapy (85% vs 66%), with a risk difference of [redacted] in favour of erdafitinib. These OS benefits were statistically significant and clinically meaningful. Erdafitinib also showed a statistically significant improvement in objective response rate (ORR, defined as complete and partial responses), with a difference of [redacted] more patients achieving response with erdafitinib than chemotherapy. pERC noted that although the THOR trial permitted patients in the chemotherapy group to crossover to receive treatment with erdafitinib, the crossing over occurred after erdafitinib had demonstrated superiority over chemotherapy and did not influence the results from the interim efficacy and safety analyses used in the CDA-AMC review (data cut-off date: January 15, 2023). The observed adverse events in the THOR trial were previously known and clinically manageable.

pERC recognized that erdafitinib treatment addresses several unmet needs identified by clinicians and patients. These include expanding treatment options to improve overall survival, quality of life, and slow disease progression for patients with la/mUC who have progressed after immune checkpoint therapy, while also maintaining a generally acceptable and manageable safety profile.

Using the sponsor-submitted price for erdafitinib and publicly listed prices for all other drug costs, the incremental cost-effectiveness ratio (ICER) for erdafitinib was $305,091 per quality-adjusted life-year (QALY) gained compared with physician's choice chemotherapy (comprising docetaxel and paclitaxel). At this ICER, erdafitinib is not cost-effective at a willingness to pay (WTP) threshold of $50,000 per QALY gained in the Health Canada indicated population. A price reduction is required for erdafitinib to be considered cost-effective at a $50,000 per QALY gained threshold.

Table 1: Reimbursement Conditions and Reasons

Reimbursement condition	Reason	Implementation guidance
Initiation		
1. Erdafitinib should be reimbursed in patients with a diagnosis of la/mUC harboring susceptible FGFR3 genetic alterations who have disease progression during or following at least one line of prior therapy, including within 12 months of neoadjuvant or adjuvant therapy.	This aligns with the inclusion criteria of the THOR study and the HC indication. Also, the clinical experts consulted by CDA-AMC indicated that it is consistent with current clinical practice in Canada.	—
2. Treatment with erdafitinib should be initiated following confirmation of a susceptible FGFR3 genetic alteration using a validated test.	The HC indication requires a confirmation of at least one of the FGFR3 genetic alterations, and is consistent with the inclusion criteria of the THOR study.	This will require consideration of the availability of testing sites across provinces and territories of Canada; for instance, currently, 1 testing site in Ontario and 1 in Quebec provide FGFR3 testing to all other provinces. No information was identified regarding testing availability in Yukon, Northwest Territories, or Nunavut.
3. Erdafitinib should not be reimbursed in patients who are eligible for but have not received prior programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor therapy.	Based on the HC indication and reflecting the inclusion criteria from the THOR study in alignment with clinical expert input.	—
Discontinuation		
4. Reimbursement of erdafitinib should be discontinued upon evidence of • clinically significant disease progression as assessed by imaging and clinical criteria. • Intolerable or unmanageable drug toxicity.	This is consistent with the criteria used in the THOR trial and input from the clinical experts consulted by CDA-AMC.	—
Prescribing		
5. Erdafitinib should be prescribed by clinicians with expertise in treating patients with urothelial cancer.	This is meant to ensure that erdafitinib is prescribed for appropriate patients and that adverse effects are managed optimally and in a timely manner.	—
Pricing		
6. A reduction in price	The ICER for erdafitinib is $305,091 per QALY gained when compared with physician's choice chemotherapy (comprising docetaxel and paclitaxel). A price reduction of 76% would be required for erdafitinib to achieve an ICER	—

Reimbursement condition	Reason	Implementation guidance
	of $50,000 per QALY gained compared to physician's choice chemotherapy.	
Feasibility of adoption		
7. The feasibility of adoption of erdafitinib must be addressed	At the submitted price, the magnitude of uncertainty in the budget impact must be addressed to ensure the feasibility of adoption, given the difference between the sponsor's estimate and the CDA-AMC estimate(s).	—
8. The organizational feasibility of conducting FGFR3 testing must be addressed.	FGFR3 testing is required to determine eligibility for erdafitinib. The clinical experts consulted by CDA-AMC indicated that implementing routine FGFR3 testing may have impacts on health systems.	—

Discussion Points

- In addition to overall survival and ORR estimates, pERC deliberated other reported efficacy outcomes such as PFS and health-related quality of life following treatment with erdafitinib. The committee noted that the estimates from the THOR study for these outcomes were uncertain due to wide confidence intervals (i.e., indicating imprecision). However, pERC agreed with the clinical experts that the estimated effects were likely clinically meaningful in patients with la/mUC who have disease progression during or following at least one line of prior therapy.
- pERC noted that hyperphosphatemia and central serous retinopathy are adverse effects associated with erdafitinib and acknowledged their importance to patients. Based on input from the clinical experts, pERC considered that these are known and clinically manageable adverse events that do not negate the clinical benefit of erdafitinib in the population for which it is indicated. Other adverse events and the overall safety profile were comparable between erdafitinib and chemotherapy.
- pERC discussed the comparative evidence for erdafitinib and enfortumab vedotin, based on an indirect treatment comparison using an anchored matching-adjusted indirect comparison (MAIC). They noted that limitations in this evidence introduced uncertainty, with imprecise results (indicated by wide credible intervals) and a potential risk of bias, making it challenging to draw strong conclusions.
- pERC noted that enfortumab vedotin recently received a recommendation to reimburse with conditions in combination with pembrolizumab for patients with unresectable locally advanced unresectable or metastatic UC with no prior systemic therapy. Therefore, pERC discussed whether enfortumab vedotin is a relevant comparator in those patients who have disease progression during or following at least one line of prior therapy. pERC determined that since the reimbursement request is for erdafitinib in patients requiring treatment beyond the first-line therapy (who are likely to have previously received a PD-1 inhibitor such as pembrolizumab), if enfortumab vedotin with pembrolizumab is incorporated into the initial steps of the current provisional funding algorithm for la/mUC, platinum-based chemotherapy would become a more appropriate comparator for erdafitinib. If erdafitinib were to displace chemotherapy instead of enfortumab vedotin, the budget impact of reimbursing erdafitinib is underestimated. pERC was informed that at the time of discussion, negotiations with the pan-Canadian Pharmaceutical Alliance (pCPA) for the use of enfortumab vedotin in combination with pembrolizumab in the first line population have not yet begun.
- If enfortumab vedotin remains an appropriate second-line treatment, pERC noted there is no robust evidence to support a price premium for erdafitinib compared with enfortumab vedotin in previously treated patients with la/mUC.
- pERC discussed that FGFR3 genetic alteration testing using a validated DNA- or RNA-based assay test is required to determine eligibility for erdafitinib; however, routine and reflex FGFR3 testing may not be available across all jurisdictions within Canada. Currently, 1 of the 10 testing sites across Ontario and 1 testing site in Quebec provide FGFR3 testing to all other provinces; no information was identified regarding testing availability in the territories. pERC and the clinical experts consulted by CDA-AMC noted the importance of testing for FGFR3 early, especially for patients under investigation for advanced or metastatic UC, to minimize treatment delay at time of potential treatment eligibility for erdafitinib.

Background

Urothelial carcinoma (UC) is a malignant transformation of urothelial cells, primarily affecting the bladder, and accounts for 90% to 95% of bladder cancer cases. In 2023, Canada saw an estimated 13,400 new bladder cancer cases, with 2,600 deaths expected annually. The most common symptom of bladder cancer is hematuria, though other symptoms such as pain during urination, abdominal pain, and fatigue may also occur. The cancer predominantly affects individuals over 50, with a higher incidence in males and those with risk factors like smoking, chemical exposure, or a family history of bladder cancer. Diagnosis is typically made through cystoscopy and biopsy, with most patients diagnosed with non-muscle invasive bladder cancer (NMIBC), though a significant portion may progress to muscle-invasive bladder cancer (MIBC) or metastatic disease. Fibroblast growth factor receptors (FGFRs) play a crucial role in UC, with abnormalities in FGFR3 linked to up to 42% of UC cases.

Treatment for locally advanced or metastatic urothelial carcinoma (la/mUC) focuses on slowing disease progression, extending life, and improving quality of life. The standard first-line treatment is cisplatin-based chemotherapy, though platinum-based chemotherapy is generally preferred. For patients who are ineligible for platinum-based chemotherapy, immune checkpoint inhibitors (ICIs) like pembrolizumab or avelumab are offered as an alternative first-line option and are commonly used as second-line treatment following progression on chemotherapy. Newer therapies, such as enfortumab vedotin and erdafitinib, are also part of the treatment landscape, particularly for cases with specific genetic alterations. Despite these therapies, la/mUC remains largely incurable, with a poor prognosis.

Erdafitinib, a targeted therapy, inhibits FGFRs and is used in cases of locally advanced or metastatic UC with FGFR3 alterations. It has been approved by Health Canada for the for the treatment of adult patients with locally advanced unresectable or metastatic UC, harboring susceptible FGFR3 genetic alterations, who have disease progression during or following at least one line of prior therapy, including within 12 months of neoadjuvant or adjuvant therapy. Erdafitinib should not be used for the treatment of patients who are eligible for and have not received prior PD-1 or PD-L1 inhibitor therapy. Treatment with erdafitinib should be initiated following confirmation of a susceptible FGFR genetic alteration using a validated test.

Erdafitinib is available as tablets 3 mg, 4 mg, and 5 mg, oral, and the dosage recommended in the product monograph is of 8 mg once daily with a dose increase to 9 mg once daily.

Sources of Information Used by the Committee

To make its recommendation, the committee considered the following information:

- a review of one randomized placebo-controlled trial in patients with locally advanced or metastatic urothelial carcinoma (la/mUC) harboring FGFR3/2 alterations; one indirect treatment comparison consisting of a matched-adjusted indirect comparison (MAIC) contrasting the effects of erdafitinib and enfortumab-vedotin in patients with la/mUC and FGFR genetic alterations.
- patients' perspectives gathered by one patient group: Bladder Cancer Canada.
- input from public drug plans that participate in the reimbursement review process.
- Two clinical specialists with expertise diagnosing and treating patients with la/mUC.
- input from one clinician group: the Ontario Health (Cancer Care Ontario) Genitourinary Cancer Drug Advisory Committee (GU DAC).
- a review of testing procedure considerations for detecting FGFR3 genetic alterations related to erdafitinib.
- a review of the pharmacoeconomic model and report submitted by the sponsor.

Perspectives of Patients, Clinicians, and Drug Programs

Patient Input

One patient group, Bladder Cancer Canada (BCC), provided input for this CDA-AMC review. BCC is a registered national charity that serves those facing a bladder cancer diagnosis. The information provided by BCC was collected via an online survey, which asked questions about the impact of FGFR3 metastatic UC on the lives of patients, the effect of current treatments, and patient experience with erdafitinib. The online survey was completed by four people (identified by BCC as Patients A, B, C, and D), all of whom were from Canada and had locally advanced unresectable or metastatic UC with an FGFR3 mutation. Two respondents (Patients A and B) had treatment experience with erdafitinib, one of whom agreed to participate in a telephone interview to elaborate on their survey responses.

The most common cancer symptoms reported by respondents were fatigue, insomnia, neuropathy, and decreased mobility. Responses from survey participants suggested that their cancer symptoms were not adequately managed by current therapies. Fatigue, neuropathy, and hair loss were the most commonly reported side effects of their treatments. One patient reported difficulty in accessing treatment due to travel time. Regarding respondent willingness to tolerate new side effects from drugs that can control disease progression or improve overall survival, the average score was 6.25, with scores ranging from 4 to 10 on a scale of 1 (will not tolerate side effects) to 10 (will tolerate significant side effects).

Of the respondents who were treated with erdafitinib, Patient A had completed their full course of treatment and Patient B had been receiving erdafitinib for 6 weeks. When these patients were asked to rate how their lives had changed on erdafitinib compared to other therapies they had received in terms of certain categories (metastatic cancer symptoms, drug side effects, maintaining quality of life, controlling disease progression, and preventing recurrence), scores generally suggested that neither respondent experienced a major difference with erdafitinib. Reported side effects from erdafitinib were dysgeusia (Patient A) and dry mouth, nausea, and leg pain (Patient B). Tolerability of side effects of erdafitinib on a scale of 1 (completely tolerable) to 10 (completely intolerable) was rated as 9 by Patient A and 3 by Patient B. Both patients reported that taking erdafitinib orally made their treatment easier and both indicated that they would recommend erdafitinib to other patients with bladder cancer.

Clinician Input

Input From Clinical Experts Consulted by CDA-AMC

Clinical experts consulted by CDA-AMC for the review of erdafitinib in the treatment of la/mUC identified several key considerations. For unmet needs, one of the most significant challenges is determining the optimal sequencing of erdafitinib and enfortumab vedotin (EV) for patients with FGFR alterations. While EV is currently the standard treatment after progression on platinum-based chemotherapy and immune checkpoint inhibitors (ICI), its associated toxicities may not be suitable for all patients. Additionally, the anticipated approval of EV combined with pembrolizumab as a first-line therapy raises concerns about the lack of treatment options following this combination, highlighting another area of unmet need.

Erdafitinib is expected to be used as monotherapy following platinum-based chemotherapy and ICI therapy, particularly in patients with FGFR alterations, as supported by the pivotal THOR trial. However, clinical experts noted that the ideal sequencing of EV and erdafitinib remains uncertain, which could impact treatment decisions.

The target population for erdafitinib includes patients with tumors harboring FGFR alterations, necessitating genetic testing to identify these alterations. Experts agreed that la/mUC is not a rare disease and that the patient population studied in clinical trials is consistent with the intended target population for this therapy.

In terms of treatment assessment, experts recommended monitoring clinical symptoms and using imaging studies to evaluate disease progression. Treatment discontinuation should be considered in cases of disease progression, significant toxicity, or intolerability, with decisions made on a case-by-case basis, following the criteria used in clinical trials. The experts also emphasized that the management of diagnosis, treatment, and ongoing patient monitoring should be handled by oncology specialists, including those in outpatient settings, to ensure the best possible care for patients.

Clinician Group Input

Seven clinicians from the Ontario Health (Cancer Care Ontario) Genitourinary Cancer Drug Advisory Committee (GU DAC) provided input for this review. Ontario Health (Cancer Care Ontario) Drug Advisory Committees provide timely evidence-based clinical and

health system guidance on drug-related issues in support of Cancer Care Ontario's mandate, including the Provincial Drug Reimbursement Programs and the Systemic Treatment Program.

In communicating current treatments for la/mUC, the GU DAC noted that patients who have previously received an ICI, chemotherapy, or the combination of both are eligible for treatment with EV, with the goal of treatment being to improve overall survival. The GU DAC expressed an unmet need for a treatment for patients with genomic alterations, noting that erdafitinib is effective for the FGFR genetic alteration and would be the first targeted therapy identified for this patient population based on molecular testing. Regarding place in therapy, the GU DAC indicated that patients who would be eligible and best suited for treatment with erdafitinib are those with FGFR mutations/alterations who have previously received, or have a contraindication to, ICI therapy. The GU DAC stated that treatment with erdafitinib would occur in the outpatient setting under the advisement of a medical oncologist. Patient response to treatment is assessed in clinical practice using conventional imaging (CT scan of the chest/abdomen/pelvis) as per physician discretion. Discontinuation of treatment with erdafitinib would be considered upon unacceptable toxicity or clinically significant disease progression.

Drug Program Input

The clinical experts consulted for the review provided advice on the potential implementation issues raised by the drug programs.

Table 2: Responses to Questions from the Drug Programs

Drug program implementation questions	Clinical expert response
Relevant comparators	
In cohort 1 of the phase III THOR clinical trial, erdafitinib was used for patients with FGFR3 alterations post-PD-(L)1 treatment. There are no targeted treatments currently funded for FGFR3 alterations. Current publicly funded standard of care following disease progression on PD-(L)1 treatment in the advanced setting includes enfortumab vedotin as a single agent or chemotherapy (usually docetaxel or paclitaxel). If a patient experienced disease relapse >6 months from completion of adjuvant nivolumab (after complete resection in high-risk patients), platinum-based chemotherapy would usually be the next line of therapy followed by PD-(L)1 treatment as either maintenance or as a second-line therapy. Note: at the time of this input, enfortumab vedotin in combination with pembrolizumab as first-line treatment for la/mUC is under pCODR review. If recommended and funded, single agent chemotherapy with docetaxel or paclitaxel would likely be the next line of therapy in patients that experience disease progression on first-line enfortumab vedotin with pembrolizumab. *If patients are fit, platinum-doublet chemotherapy may also be an option.*	The clinical experts agreed that a platinum-doublet chemotherapy would be a reasonable second line option after treatment with EV + pembrolizumab.
Considerations for initiation of therapy	
Are all histologic subtypes of urothelial carcinoma eligible provided they harbor a FGFR3 genetic alteration?	Clinical experts advised that the different histological subtypes would need at least some component of urothelial carcinoma (i.e., not purely squamous or adenocarcinoma or small cell carcinoma).
In patients who have been previously treated with PD-(L)1 therapies and remain sensitive despite disease progression (e.g., disease relapse occurs >6 to 12 months after stopping), should erdafitinib be used at any time? or only if a patient is re-treated with PD-(L)1 therapy again and is subsequently considered resistant to PD-(L)1 therapy?	According to clinical experts, erdafitinib should be an option post-ICI regardless of when the progression happened. A re-treatment with ICI can be done at the clinician's discretion and on a case-by-case basis.

Drug program implementation questions	Clinical expert response
Considerations for continuation or renewal of therapy	
The trial allowed erdafitinib to be continued beyond disease progression at the discretion of the investigator. What are the discontinuation criteria for erdafitinib?	The clinical experts acknowledged that erdafitinib would no longer be funded after disease progression. Discontinuation should be based upon evidence of significant disease progression as assessed by imaging and clinical criteria -- signs of toxicity and tolerability would be considered part of such criteria.
Generalizability	
Should patients with a FGFR3 genetic alteration receiving alternate therapies after prior PD-(L)1 treatment be switched to erdafitinib, or could erdafitinib be used as the next line of therapy?	According to the clinical experts, erdafitinib can be used as the next line in this situation.
Funding algorithm (oncology only)	
Drug may change place in therapy of comparator drugs	*This is a comment from the drug programs to inform pERC deliberations.*
Care provision issues	
The recommended starting dose of erdafitinib is 8 mg orally once daily, with a dose increase to 9 mg once daily based on serum phosphate levels and tolerability, as assessed between 14 and 21 days after initiating treatment. *Erdafitinib is available as a 3 mg, 4 mg and 5 mg tablet; some drug wastage may be expected due to dose adjustments, depending on what strength and quantity was previously dispensed.*	*This is a comment from the drug programs to inform pERC deliberations.*
Frequent monitoring is required for toxicities, including palmar-plantar erythrodysesthesia, stomatitis, onycholysis, hyperphosphatemia, diarrhea, central serous retinopathy, and other eye disorders.	*This is a comment from the drug programs to inform pERC deliberations*.
FGFR alteration testing may not be available or routinely tested for la/mUC in some jurisdictions. What is the optimal timing for FGFR biomarker testing? What percentage of la/mUC patients are expected to harbor a FGFR3 genetic alteration?	Approximately 20% of patients with la/mUC harbor the FGFR3 alteration. Ideally, testing should happen early using the initial trans-urethral resection of bladder tumor (TURBT) or cystectomy specimen.
System and economic issues	
A confidential pCPA price exists for enfortumab vedotin. Generic versions of docetaxel and paclitaxel exist.	*This is a comment from the drug programs to inform pERC deliberations.*

FGFR = fibroblast growth factor receptor; ICI = immune check point inhibitor; la/mUC = locally advanced or metastatic urothelial carcinoma; pCODR = pan-Canadian Oncology Drug Review; pCPA = Pan Canadian Pharmaceutical Association; PD-1 = programmed death-1; PDL-1 = programmed death ligand - 1

Clinical Evidence

Systematic Review

Description of Studies

One pivotal study was included in this submission. The THOR study (cohort 1) was a global, phase 3 randomized controlled trial designed to evaluate the efficacy and safety of erdafitinib compared to standard chemotherapy in patients with la/mUC who had specific FGFR3/2 genetic alterations and had progressed after treatment with anti-PD-1 or anti-PD-L1 checkpoint inhibitors. The trial enrolled 266 patients, who were randomly assigned in a 1:1 ratio to receive either erdafitinib (n=136) or the investigator's choice of chemotherapy (docetaxel or vinflunine; n=130). The primary endpoint of the study was OS, with PFS as key secondary outcome and including other endpoints such as objective response rate (ORR) and safety profiles. The pivotal trial had two cohorts of study (1

and 2); the population of interest for this submission is specifically Cohort 1 of the study, i.e., those with prior treatment with an anti-PD-(L)1 agent.

The baseline characteristics of the study population were well balanced between the two treatment arms. The median age of patients was approximately 67 years, with a majority being male. Most patients had an ECOG performance status of 0 or 1, and all had previously received at least one line of therapy, including anti-PD-1 or anti-PD-L1 agents. The genetic profile of the patients, defined by FGFR3/2 alterations, was consistent across both groups, ensuring comparability for evaluating the treatment effects of erdafitinib versus chemotherapy.

Of note, Cohort 1 was stopped early as the IDMC recommended that Cohort 1 be stopped due to superiority of erdafitinib treatment over chemotherapy.

Efficacy Results

Overall Survival (OS)

The primary endpoint of the THOR trial was overall survival (OS), which was deemed critical for decision-making by clinical experts consulted by CDA-AMC. The median OS was 12.06 months (95% CI: 10.28, 16.36) in the erdafitinib group compared to 7.79 months (95% CI: 6.54, 11.07) months in the chemotherapy group. The estimated 6-month survival rates were 85% for erdafitinib and 66% for chemotherapy, a difference of [redacted], while the 24-month rates were 26% and 20%, respectively with a difference of [redacted]. The OS analysis demonstrated that erdafitinib significantly reduced the time to death compared to chemotherapy (hazard ratio [HR]=0.64; p=0.005). Subgroup analyses were not designed to establish treatment effects within specific subgroups.

Progression-Free Survival (PFS)

Progression-free survival (PFS) was a secondary endpoint in the THOR study, showing a median PFS of 5.55 months (95% CI: 4.40, 5.65) for erdafitinib versus 2.73 months (95% CI: 1.81, 3.68) for chemotherapy. The estimated 6-month PFS rates were higher in the erdafitinib group (37%) than in the chemotherapy group (27%), a difference (absolute effect) of [redacted], with both groups showing low PFS rates by 24 months. These absolute effects in PFS at 6- and 24-months presented imprecise confidence intervals (i.e., no evidence of meaningful difference when comparing erdafitinib vs chemotherapy). However, the overall relative effects as measured with the Cox PH regression (hazard ratio) model analysis showed an improvement in PFS for erdafitinib against chemotherapy, with a HR of 0.58 (95% CI 0.44, 0.78; p=0.0002).

Objective Response Rate (ORR)

Objective response rate (ORR), defined as the proportion of patients achieving a complete or partial response, was significantly higher in the erdafitinib group, with 45.6% of patients responding, compared to 11.5% in the chemotherapy group. An absolute difference of [redacted]. The relative risk of achieving an objective response was almost 4 times higher with erdafitinib (RR=3.94; 95% CI: 2.37, 6.57) as compared with chemotherapy.

Duration of Response (DoR)

The median duration of response (DoR) was 4.86 months (95% CI: 3.84, 7.46) for erdafitinib and 5.55 months (95% CI: 2.14, 6.01) for chemotherapy. The results suggest that while erdafitinib is more effective in inducing responses, the duration of these responses may be comparable to that of chemotherapy. For instance, the 6-month probability of remaining in response was 42% (95% CI: 29, 55) in the erdafitinib group vs 32% (95% CI: 10, 57) in the chemotherapy group, a difference of [redacted]. The overall HR was 0.85 (95% CI: 0.43, 1.66) for erdafitinib compared to chemotherapy. The DoR analysis was based on a small number of patients, especially in the chemotherapy group, leading to imprecision in the estimates.

Patient-Reported Outcomes (HRQoL)

Patient-reported outcomes (PROs) were assessed to evaluate the impact of treatments on HRQoL. Baseline HRQoL scores were similar between the treatment groups, and compliance with HRQoL assessments remained high through early treatment cycles but declined in later cycles due to disease progression and death. Across all PRO measures—including the FACT-BI, EQ-5D-5L, and PGIS—there was no significant difference in HRQoL between erdafitinib and chemotherapy. Both treatment groups maintained

general HRQoL and overall health status throughout the study, suggesting that while erdafitinib improves survival outcomes, it does not lead to a substantial difference in PROs compared to chemotherapy.

Harms Results

The THOR study revealed that both erdafitinib and chemotherapy were associated with a high incidence of adverse events (AEs), with nearly all patients experiencing at least one AE. For instance, at least one AE was reported in 133 patients (98.5%) in the erdafitinib group and 109 (97.3%) in the chemotherapy group. The most common AEs (i.e., reported by 10% or more patients) included hyperphosphatemia (80%), diarrhea (62.2%), and stomatitis (48.1%) in the erdafitinib group, and anemia (32.1%), constipation (27.7%), and asthenia (25.0%). in the chemotherapy group

In terms of serious adverse events (SAEs) at least one was reported in 56 (41.5%) patients in the erdafitinib treatment group and 47 (42%) patients in the chemotherapy group. The most frequently reported SAE (>2%) were urinary tract infection (4.4%) and hematuria (3.7%) in the erdafitinib group, and febrile neutropenia (6.3%) and febrile bone marrow aplasia (3.6%) in the chemotherapy group.

Among AEs of special interest, central serous retinopathy (CSR) was a notable adverse event specific to erdafitinib, occurring in 23 (17.0%) of patients (as compared to none in the chemotherapy group), which necessitated regular ophthalmologic monitoring due to the potential for vision impairment. Hyperphosphatemia was another event of interest which occurred in 108 (80%) of 135 patients in the erdafitinib group and 0 in the chemotherapy group presented an event of hyperphosphatemia. Lastly, nail and skin disorders were also deemed worthy of attention, with nail disorders reported in 90 (66.7%) patients in the erdafitinib group and in 6 (5.4%) in the chemotherapy group. Similarly, skin disorders were reported in 74 (54.8%) and 14 (12.5%) patients respectively.

The rates of treatment discontinuation due to adverse events were slightly lower in the erdafitinib group (14.1%) compared to the chemotherapy group (17.9%).

Critical Appraisal

The THOR study was a well-designed randomized controlled trial comparing erdafitinib to chemotherapy in patients with la/mUC harboring FGFR alterations, who have previously been treated with anti-PD-1 or anti-PD-L1 therapies. The randomization process was properly conducted, although some imbalances, such as the difference in numbers of patients declining chemotherapy, were noted. Despite these minor issues, most baseline characteristics were balanced. The open-label design could potentially introduce bias, particularly in subjective measures. The exploratory subgroup analyses were not pre-defined, raising concerns about potential type I errors, although these analyses were not the primary focus of the study and there was no evidence of imbalance among subgroups (i.e., evidence suggesting subgroup effects).

In terms of external validity, the THOR study was conducted 23 countries, which enhances its generalizability, although the underrepresentation of certain demographic groups, particularly Black patients, could limit its applicability in multicultural settings like Canada. According to the clinical experts consulted for this review, the median participant age aligns with the typical age range for urothelial carcinoma patients in Canada, supporting the relevance of the findings. The focus on patients with FGFR alterations highlights the importance of molecular testing availability for the generalizability of the results. The chemotherapy options used in the study are consistent with those available in Canada, further supporting its external validity. Overall, the clinical experts believe that the study's findings are applicable to most la/mUC patients in Canada within the specified criteria.

GRADE Summary of Findings and Certainty of the Evidence

For pivotal studies and RCTs identified in the sponsor's systematic review, GRADE was used to assess the certainty of the evidence for outcomes considered most relevant to inform CDA-AMC's expert committee deliberations, and a final certainty rating was determined as outlined by the GRADE Working Group.

When possible, certainty was rated in the context of the presence of an important (nontrivial) treatment effect; if this was not possible, certainty was rated in the context of the presence of any treatment effect (i.e., the clinical importance is unclear). In all cases, the target of the certainty of evidence assessment was based on the point estimate and where it was located relative to the threshold for a clinically important effect (when a threshold was available) or to the null.

The GRADE assessments are presented in the Summary of Findings table in the executive summary (Table 3). The selection of outcomes for GRADE assessment was based on the sponsor's Summary of Clinical Evidence, consultation with clinical experts, and input received from patient and clinician groups and public drug plans. The following list of outcomes was finalized in consultation with expert committee members: OS, PFS, ORR, DOR, HRQoL, and Harms.

Table 3: Summary of Findings for Erdafitinib versus Chemotherapy for patients with la/mUC harboring a FGFR alteration

Outcome and follow-up	Patients (studies), N	Relative effect (95% CI)	Absolute effects			Certainty	What happens
			Chemotherapy	Erdafitinib	Difference (95% CI)		
Survival							
Overall Survival at 6 months	266 (1 RCT)	-	[redacted] patients per 1000	[redacted] **patients per 1000**	[redacted]	Moderate[a]	Erdafitinib likely results in a clinically important increase in overall Survival at 6 months when compared with chemotherapy.
Overall Survival at 24 months	266 (1 RCT)	-	[redacted] patients per 1000	[redacted] **patients per 1000**	[redacted]	Low[b]	Erdafitinib may result in a clinically important increase in overall Survival at 24 months when compared with chemotherapy.
Progression Free Survival at 6 months	266 (1 RCT)	-	[redacted] per 1000	[redacted] **per 1000**	[redacted]	Low[b]	Erdafitinib may result in a clinically important increase in progression Free Survival at 6 months when compared with chemotherapy.
Progression Free Survival at 24 months	266 (1 RCT)	-	[redacted] per 1000	[redacted] **per 1000**	[redacted]	Low[b]	Erdafitinib may result in little-to-no difference in progression Free Survival at 24 months when compared with chemotherapy.
Clinical Response							
Objective Response Rate, CR + PR	266 (1 RCT)	**RR = 3.94** (2.37 to 6.57)	115 per 1,000	**456 per 1,000**	[redacted]	Moderate[a]	Erdafitinib likely results in a clinically important increase in objective Response Rate when compared with chemotherapy.
Duration of Response at 6 months	77 (1 RCT)	-	[redacted] patients per 1000	[redacted] **patients per 1000**	[redacted]	Low[b]	Erdafitinib may result in a clinically important increase in duration of Response at 6 months when compared with chemotherapy.
HRQoL							
Health Related Quality of Life, FACT-BI, PGIS, and EQ-5D-5L	112 (1 RCT)	Assessment of the FACT-BI, PGIS, and EQ-5D-5L health utility index and VAS for all domains and total scores showed that effects on HRQoL measures were similar between erdafitinib and chemotherapy groups with no evidence of a difference between them at the end of treatment.				Low[c]	Erdafitinib may result in little-to-no difference in HRQoL when compared with chemotherapy.

Outcome and follow-up	Patients (studies), N	Relative effect (95% CI)	Absolute effects			Certainty	What happens
			Chemotherapy	Erdafitinib	Difference (95% CI)		
Harms							
Adverse events	247 (1 RCT)	At least one AE was reported in 133 patients (98.5%) in the erdafitinib group and 109 (97.3%) in the chemotherapy group. AEs reported by 10% or more patients in the erdafitinib group were hyperphosphatemia (80%), diarrhea (62.2%), and stomatitis (48.1%) , while in the chemotherapy group were anemia (32.1%), constipation (27.7%), and asthenia (25.0%).				Moderate[d]	Erdafitinib likely results in little-to-no difference in the total number of AEs when compared with chemotherapy. The types of AEs differ between the groups.
Serious Adverse Events	247 (1 RCT)	At least one SAE was reported in 56 (41.5%) patients in the erdafitinib treatment group and 47 (42%) patients in the chemotherapy group. The most frequently reported SAE (>2%) in the erdafitinib group were urinary tract infection (4.4%) and hematuria (3.7%), while in the chemotherapy group were febrile neutropenia (6.3%) and febrile bone marrow aplasia (3.6%).				Moderate[d]	Erdafitinib likely results in little-to-no difference in the total number of SAEs when compared with chemotherapy. The types of SAEs differ between the groups.
Adverse Events of Special Interest	247 (1 RCT)	*Central serous retinopathy (CSR):* was reported in 23 (17.0%) patients in the erdafitinib treatment group and none in the chemotherapy group. *Hyperphosphatemia*: 108 (80%) of 135 patients in the erdafitinib group and 0 in the chemotherapy group presented an event of hyperphosphatemia. *Nail and skin disorders*: nail disorders were reported in 90 (66.7%) patients in the erdafitinib group and in 6 (5.4%) in the chemotherapy group. Similarly, skin disorders were reported in 74 (54.8%) and 14 (12.5%) patients respectively.				High[d]	Erdafitinib results in higher incidence of these specific AESI when compared with chemotherapy. The clinical significance of each effect is uncertain and varies by AESI.

a. The 95%CI excludes the null and a conservative threshold of 20 patients per 1000 treated, the sample size or optimal information size (in the THOR study calculated for OS) was not reached (N=280) with the study stopped early for benefit. Therefore, the estimate was rated down one level for imprecision.

b. The 95% CI includes the null but also a conservative threshold of 20 patients per 1000 treated (for benefit or harm). Furthermore, the sample size was considered small for a conservative estimate of an optimal information size of 280. Therefore, the imprecision domain was rated down two levels.

c. No statistical tests were performed. However, the number of patients in these analyses tend to decrease over time of assessment hence decreasing the sample size. No evidence of difference was detected, with wide CIs in the estimates at the end of treatment for both arms. Therefore, two levels were rated down for imprecision.

d. No statistical tests were performed. The difference in effects between groups was considered very large and certain based on input from clinical experts, hence we did not rate down for imprecision.

AE = adverse events; AESI = adverse events of special interest; CI = confidence interval; CR = complete response; EQ-5D-5L = European Quality of Life – 5 Dimensions-5 Levels; FACT-BI = Functional Assessment of Cancer Therapy – Bladder; HRQoL = health-related quality of life; PGIS = patient global impression of severity; PR = partial response; RCT = randomized controlled trial; SAE = serious adverse events

Details included in the table are from the sponsor's Summary of Clinical Evidence.

Long-Term Extension Studies

No long-term extension studies were available for this submission.

Indirect Comparisons

Description of Studies

The sponsor submitted an indirect treatment comparison (ITC) aimed to assess the efficacy and safety of erdafitinib relative to EV in patients with urothelial carcinoma who had progressed after one or two prior treatments, including at least one anti-PD-(L)1 agent. Due to the lack of direct head-to-head evidence between erdafitinib and EV, an anchored matching-adjusted indirect comparison (MAIC) was performed. This approach allowed for indirect comparisons while adjusting for differences in measured baseline characteristics between the trials. To estimate the relative efficacy and safety of these treatments, authors used individual patient data (IPD) from one pivotal study (THOR) assessing erdafitinib and aggregate data from one available study (EV-301 trial) evaluating EV. A Bayesian approach was used, with a butcher completed as a sensitivity analysis.

The MAIC produced estimates comparing erdafitinib to enfortumab vedotin within the EV-301 trial population, incorporating additional eligibility criteria that excluded patients with no prior exposure to platinum-based chemotherapy, an ECOG performance status of 2, and those who had received more than one prior chemotherapy. The population matching process reduced the effective sample size (ESS) from 197 to 126, a 36% reduction, which was deemed adequate to support comparisons across all efficacy and safety outcomes.

Efficacy Results

In the base-case analyses, the effect estimates for OS, PFS, ORR, and CR showed wide credible intervals, reflecting an inability to determine whether one treatment is superior to the other for any of these endpoints.

In terms of survival endpoints, the post-adjustment HR for OS of erdafitinib was 0.92 (95% CrI: 0.54, 1.57) compared to EV. Although the credible intervals (CrIs) widened following the adjustment, this was consistent with the observed reduction in ESS.

Similar effects were observed for PFS, where the post-adjustment HR for erdafitinib was 0.93 (95% CrI: 0.55, 1.56).

Regarding the ORR, the relative risk (RR) was 1.49 (95% CrI: 0.56, 3.90), and for CR, it was 2.89 (95% CrI: 0.27, 30.33). Despite these increases, the wide CrIs reflect substantial uncertainty, particularly for CR. Sensitivity analyses, adjusting for each covariate cumulatively, confirmed the consistency of the Bayesian and Bucher estimates across all efficacy outcomes.

When comparing the matched THOR patients to the intent-to-treat (ITT) population and those receiving 1-2 prior lines of therapy in EV-301, similar results were observed for OS and PFS.

Harms Results

For harms, any AE, an RR of 1.02 (95% Crl: 0.98, 1.06) was observed. For the remaining AEs, erdafitinib demonstrated a safety profile comparable to that of enfortumab vedotin, with an RR close to one in most cases.

Critical Appraisal

Overall, the results from the ITC suggest substantial uncertainty regarding whether erdafitinib and EV differ meaningfully in terms of survival, response outcomes, or harms. This uncertainty is primarily attributed to the imprecision observed in the credible intervals of the effect estimates.

Testing Procedure Considerations

FGFRs are transmembrane tyrosine kinade receptors that are involved in cell development, differentiation, survival, and migration, and are associated with carcinogenesis related to UC. There are 4 FGFRs (FGFR1-4) that are typical kinase receptors; however, FGFR3 genetic alterations are most closely associated with the inception and recurrence of UC. Additionally, FGFR1 and FGFR3

amplifications, activating somatic mutations in FGFR3, and gene fusions involving FGFR1, FGFR2, or FGFR3 have all been identified in UC. As per the intended indication of erdafitinib and in line with local and international guidelines, it is recommended that FGFR3 mutation status be determined before treatment decisions are finalized to inform the use of targeted therapy.

FGFR3 genetic alterations are identified using DNA- or RNA-based assay testing from samples primarily taken from tumour tissue at the time of diagnosis. This may include RNA-based reverse transcriptase-PCR (RT-PCR) testing to detect single-gene mutations and fusion mutations, or DNA- or RNA-based next generation sequencing (NGS) panel testing to detect sequencing changes, rearrangements, and fusion mutations. Circulating tumour DNA from plasma samples has shown potential use in NGS testing as a non-invasive alternative to tissue-based samples, but tissue-based samples still remain the gold standard for FGFR3 genetic alteration identification.

Key considerations and relevant information available from materials submitted by the sponsor, input from the clinical experts, and sources from the literature were validated by the review team when possible and summarized in Table 4.

Table 4: Considerations for RT-PCR or RNA/DNA-based NGS testing for FGFR3 genetic alterations for establishing treatment eligibility for erdafitinib in patients with locally advanced unresectable or metastatic urothelial carcinoma

Consideration	Criterion	Available Information
Health System	Availability of the testing procedure in jurisdictions across Canada	Both DNA- and RNA-based NGS testing for FGFR3 genetic alterations on newly diangosed tumours in patients with la/mUC is currently available at 10 testing sites across Ontario and 1 testing site in Quebec. One of the testing sites in Ontario is responsible for testing patients from Ontario, Alberta, Manitoba, and Newfoundland and Labrador, while the 1 testing site in Quebec is responsible for testing patients from Quebec, British Columbia, Saskatchewan, New Brunswick, Nova Scotia, and Prince Edward Island. No other testing availability information could be obtained for the Yukon, Northwest Territioes, or Nunavut. For people living in Ontario, all testing indications are publicly funded through the Comprehensive Cancer Biomarker Testing Program. Funding information for the other jurisdictions was not found.
	Number of individuals in Canada expected to require the test (e.g., per year)	Approximately 13,400 people were diagnosed with UC in 2023, and approximately 12,300 people are expected to be diagnosed with UC in 2024. According to sponsor-submitted information, approximately 50% of patients with UC receive testing for FGFR3 genetic alterations per year; however, 1 clinical expert estimated that it is likely closer to 40% of patients and that FGFR3 genetic alteration testing will increase annually if erdafitinib becomes funded.
	Testing procedure as part of routine care	The clinical experts indicated that FGFR3 is typically done as a reflex test based on the initiation of first-line therapy in Ontario or at the time of diagnosis for patients with suspected metastatic UC in Ontario and Manitoba. Additionally, 1 clinical expert indicated that testing may also be carried out during the proression from first-line therapy in Manitoba. No additional information for other provinces or territiores was found.
	Repeat testing requirements	One clinical expert indicated that repeat FGFR3 testing is not needed once FGFR3 genetic alteration status is determined.
	Impact on human and other health care resources by provision of the testing procedure	Implementation of routine FGFR3 testing for people with UC may have impacts on health system infrastructure and patient-related treatment decision-making such as upscaling personnel, lab equipment, and genetic counselling services for clinical decision making.
Patient-oriented	Accessibility of the testing procedure in jurisdictions across Canada	According to sponsor-submitted information, all essential diagnostic testing for UC is available to people living in Canada in the inpatient or outpatient settings. Currently, testing sites in Ontario and Quebec are

Consideration	Criterion	Available Information
		responsible for processing FGFR3 genetic alteration testing for patients living in other provinces. Information on accessibility to testing for patients living in the Yukon, Northwest Territitories, or Nunavut was not found.
	Expected turnaround times for the testing procedure	One clinical expert indicated that the expected turnaround time for NGS testing is approximately 2 to 4 weeks. RT-PCR testing is reported to take around 12 hours to process and show results, although the total turnaround time might be longer.
	Burden associated with the testing procedure for patients, families, and/or caregivers	Undergoing FGFR3 genetic alteration testing for patients with la/mUC may be physically and psychologically burdensome. Patient, family, and/or caregiver related considerations when undergoing genetic testing should include informed decision-making, possible psychological impacts, adequate communication of procedures and possible outcomes, timing considerations, and access and additional support, all related to testing.
Clinical	Clinical utility of the testing procedure	DNA- or RNA-based assay testing using RT-PCR or NGS testing procedures can identify patients with FGFR3 genetic alterations who are likely eligible for FGFR inhibitor therapy, such as erdafitinib. One clinical expert indicated that testing may also determine eligibility for future clinical trials.
	Risks of harm associated with the testing procedure	FGFR3 genetic alteration testing currently uses tumour or tissue-based sampling, which can involve invasive and non-patients friendly procedures. Harms associated with sampling may be reduced by minimizing the need for repetitive tissue biopsies or by using less invasive, emerging sampling techniques such as ctDNA samples.
Cost	Projected cost of the testing procedure	According to sponsor-submitted information, the cost of the validated tests for FGFR3 genetic alteration testing is estimated to be below $200 for RT-PCR testing and approximately $1000 for NGS testing. For reference, the QIAGEN therascreen® FGFR rotor-gene Q real-time RT-PCR testing kit costs CA$5821 (for 24 tests).

ctDNA = circulating tumour DNA; FGFR3 = fibroblast growth factor receptor 3; la/mUC = locally advanced unresectable or metastatic urothelial carcinoma; NGS = next generation sequencing; RT-PCR = reverse transcriptase polymerase chain reaction; UC = urothelial carcinoma.

Economic Evidence

Cost and Cost-Effectiveness

Component	Description
Type of economic evaluation	Cost-utility analysis PSM
Target population	Adult patients with locally advanced unresectable or metastatic UC, harboring susceptible FGFR3 genetic alterations, with disease progression during or following at least one line of a PD-1 or PD-L1 inhibitor therapy including within 12 months of neoadjuvant or adjuvant therapy
Treatment	Erdafitinib
Dose regimen	The recommended starting dose is 8 mg once daily. Patients can receive a dose increase to 9 mg once daily based on serum phosphate level and tolerability assessed between 14 and 21 days after initiating.
Submitted price	Erdafitinib 3mg tablet: $158.31 4mg tablet: $211.08 5mg tablet: $263.85
Submitted treatment cost	Using dosage information from the THOR trial, the sponsor estimated the cost per 21-day treatment cycle of erdafitinib to be $6,705.87.
Comparators	• Physician's choice chemotherapy (assumed to comprise docetaxel and paclitaxel)[a]

Component	Description
	• Enfortumab vedotin
Perspective	Canadian publicly funded health care payer
Outcomes	QALYs, LYs
Time horizon	Lifetime (10 years)
Key data sources	THOR trial: erdafitinib and physician's choice chemotherapy (comprising docetaxel and vinflunine)[a] EV-301 trial: enfortumab vedotin
Key limitations	• The comparison between erdafitinib and enfortumab vedotin was informed by a naïve indirect comparison as there are no head-to-head trials. This introduced considerable uncertainty in the comparison, as at present enfortumab vedotin is the most relevant comparator. Therefore, any interpretations on the assessment of cost-effectiveness for erdafitinib compared with enfortumab vedotin should consider this uncertainty. • The sponsor used a PSM to estimate costs and clinical outcomes associated with erdafitinib. As the PSM does not explicitly model the transition of progression and the impact of receiving subsequent treatments specifically as health states, the structure of the sponsor's model likely contributed to an overestimation of post-progression survival benefit for patients receiving erdafitinib, for which there is no robust evidence. This is aligned with clinical-expert feedback received by CADTH. • The sponsor's choice of parametric distribution for the OS curve for erdafitinib is not statistically or clinically justified, which resulted in post-progression treatment benefits that did not align with clinical expert input obtained by CADTH. • The sponsor assumed that erdafitinib would have a much lower RDI (69%) than comparator treatments, resulting in lower relative treatment acquisition costs for erdafitinib. This is unlikely to be observed in practice and underestimates the drug acquisition costs associated with erdafitinib. • The sponsor assumed that FGFR testing would have already been performed in all patients within the modelled population as part of eligibility to previous lines of therapy or routine care, regardless of treatment. Clinical experts consulted by CADTH clarified that this is not necessarily the case in a Canadian context, especially as no other treatments have FGFR testing as a pre-requirement to assess eligibility for treatment. As a result, the costs associated with erdafitinib are underestimated. • The sponsor assumed that patients cannot receive erdafitinib once they experienced progression (i.e., were no longer progression-free). This was not aligned to the design of the THOR trial, in which erdafitinib could be continued beyond disease progression at the discretion of the investigator. Clinical expert input noted that clinically significant disease progression was one factor in determining continuation of treatment with erdafitinib.

CADTH reanalysis results	• CADTH undertook reanalyses to address some of the identified limitations. Specifically, CADTH assumed a log-logistic (best fitting) distribution for the OS of erdafitinib and incorporated an RDI of 100% for erdafitinib. The key driver is the assumption regarding RDI.
	• In the CADTH base case:
	  ○ Erdafitinib continued to be associated with higher costs (incremental costs = $104,738) and higher QALYs (incremental QALYs = 0.34) compared with physician's choice of chemotherapy, resulting in an ICER of $305,091 per QALY gained.
	  ○ Erdafitinib remained dominant over enfortumab vedotin.
	• These estimates should be interpreted with caution, as CADTH was unable to remove the long-term post progression benefit associated with erdafitinib that was predicted by the economic model, which was responsible for the incremental QALYs for erdafitinib compared with enfortumab vedotin. The results do not consider the confidential price of enfortumab vedotin.

FGFR: Fibroblast growth factor receptor; ICER = incremental cost-effectiveness ratio; LY = life-year; OS = overall survival; PSM = partitioned survival model; QALY= quality-adjusted life-year, RDI: relative dose intensity

[a] Vinflunine is not approved for use in Canada. As such, the sponsor assumed the proportion of patients that received vinflunine in the THOR trial would be assigned to the paclitaxel in the economic evaluation, based on consultations with Canadian clinical experts who deemed it appropriate to assume similar efficacy between the treatments.

Budget Impact

CADTH identified the following key limitations with the sponsor's analysis: the exclusion of subsequent therapies was inappropriate and underestimates the budget impact of reimbursing erdafitinib, as it is likely to be used in sequence with its comparators for some patients rather than as a replacement; the pan-Canadian and NIHB populations were inappropriately calculated; the proportion of prevalent patients with each stage of UC is uncertain; the number of patients progressing to la/m UC per year was overestimated; the proportion of patients receiving additional therapy after a PD-(L)1 inhibitor is likely underestimated due to the availability of newer treatments; and the proportion of otherwise-eligible patients that undergo genetic testing is uncertain.

In the CADTH combined reanalysis, the proportion of patients diagnosed with each stage of UC, the proportion of patients progressing to la/m UC annually, the proportion of patients who will receive additional therapy after a PD-(L1) inhibitor, and the proportion of potentially eligible patients undergoing testing in the reference case were adjusted, and 100% of genetic testing was assumed to be publicly funded. In this reanalysis, the eligible patient population was lower than estimated by the sponsor, and the budget impact of reimbursing erdafitinib is expected to be $1,657,002 (year 1: $435,584, year 2: $545,317, year 3: $676,101).

Due to the structure of the model, CADTH was unable to adjust for the sponsor's assumption that erdafitinib will replace its comparators rather than be used in sequence with them. As such, it is likely that both the sponsor's and CADTH's analyses substantially underestimate the budgetary impact of funding erdafitinib. Uncertainty also remains in the prices paid by public plans for the comparators as confidential prices exist.

The indication was revised during the review. As noted by the sponsor, the updated indication is slightly broader than the original proposed indication population. As a result, the BIA may slightly underestimate the population size and budget impact.

All feedback received in response to the draft recommendation is available on the CDA-AMC website.

pERC Information

Members of the Committee:

Dr. Catherine Moltzan (Chair), Dr. Philip Blanchette, Dr. Kelvin Chan, Dr. Matthew Cheung, Dr. Michael Crump, Annette Cyr, Dr. Jennifer Fishman, Dr. Jason Hart, Terry Hawrysh, Dr. Yoo-Joung Ko, Dr. Aly-Khan Lalani, Amy Peasgood, Dr. Anca Prica, Dr. Adam Raymakers, Dr. Patricia Tang, Dr. Pierre Villneuve, and Danica Wasney.

Meeting date: November 13, 2024

Regrets:

One expert committee member did not attend

Conflicts of interest:

None