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

Reimbursement Recommendation

Reimbursement Recommendation

(Draft)

dostarlimab (Jemperli)

Indication: In combination with carboplatin and paclitaxel for the treatment of adult patients with primary advanced or first recurrent endometrial cancer who are candidates for systemic therapy.

Sponsor: GlaxoSmithKline Inc.

Recommendation: Reimburse with Conditions

Version: Draft
Publication Date: May 2025

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Recommendation

The CDA-AMC pCODR Expert Review Committee (pERC) recommends that dostarlimab in combination with carboplatin-paclitaxel be reimbursed for treatment of adults with primary advanced or first recurrent endometrial cancer who are candidates for systemic therapy, only if the conditions listed in Table 1 are met.

Rationale for the Recommendation

One phase III, double-blind, placebo-controlled trial (RUBY Part 1; N = 494) demonstrated that treatment with dostarlimab plus carboplatin-paclitaxel followed by dostarlimab maintenance compared to matching placebo plus carboplatin-paclitaxel resulted in added benefit in overall survival (OS) and progression-free survival (PFS) for adults with primary advanced (stage III or IV) or first recurrent endometrial cancer who are candidates for systemic therapy. At the time of the second interim analysis at a median follow-up time of 37.2 months, the median OS was 44.6 months (95% confidence interval [CI], 32.6 to not estimable [NE]) in the dostarlimab plus carboplatin-paclitaxel group versus 28.2 months (95% CI, 22.1 to 35.6) in the placebo plus carboplatin-paclitaxel group (one sided P value = 0.002), with a between-group hazard ratio (HR) of 0.69 (95% CI, 0.54 to 0.89) in the intention-to-treat (ITT) population. When compared to placebo plus carboplatin-paclitaxel, the Kaplan-Meier (KM)–estimated between-group difference in probabilities of being alive at 24 and 36 months were [redacted]% (95% CI, [redacted] to [redacted]) and [redacted]% (95% CI, [redacted] to [redacted]) in favour of dostarlimab plus carboplatin-paclitaxel, respectively. At the time of the first interim analysis at a median follow-up time of 25.4 months, the median PFS was 11.8 months (95% CI, 9.6 to 17.1) in the dostarlimab plus carboplatin-paclitaxel group versus 7.9 months (95% CI, 7.6 to 9.5) in the placebo plus carboplatin-paclitaxel group (one sided P value < 0.0001), with a between-group HR of 0.64 (95% CI, 0.51 to 0.80) in the ITT population. When compared to placebo plus carboplatin-paclitaxel, the KM–estimated between-group difference in probabilities of PFS at 12 and 24 months in the ITT population were [redacted]% (95% CI, [redacted] to [redacted]) and [redacted]% (95% CI, [redacted] to [redacted]) in favour of dostarlimab plus carboplatin-paclitaxel, respectively. pERC noted that the trial showed a greater PFS benefit in the subgroup of patients with mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) disease (HR, 0.28; 95% CI, 0.16 to 0.50; n = 53 [21.6%] in dostarlimab group and n = 65 [26.1%] in placebo group) compared to those with mismatch repair proficient (pMMR)/microsatellite stable (MSS) disease (HR, 0.76; 95% CI, 0.59 to 0.98; n = 192 [78.4%] dostarlimab group and n = 184 [73.9%] in placebo group). In the dMMR/MSI-H subgroup, the median PFS was not reached in the dostarlimab plus carboplatin-paclitaxel group versus 7.7 months in the placebo plus carboplatin-paclitaxel group. In the pMMR/MSS subgroup, the median PFS was 9.9 months in the dostarlimab plus carboplatin-paclitaxel group versus 7.9 months in the placebo plus carboplatin-paclitaxel group.

Patients identified a need for easily accessible (e.g., oral administration) and effective treatment options that control disease, prolong life, improve quality of life, and have fewer side effects. pERC concluded that dostarlimab plus carboplatin-paclitaxel met some important needs identified by patients, such as prolonged OS and PFS, and represents an additional treatment option for first-line therapy.

Using the sponsor submitted price for dostarlimab and publicly listed prices for all other drug costs, the incremental cost-effectiveness ratio (ICER) for dostarlimab plus carboplatin-paclitaxel was $159,924 per quality-adjusted life-year (QALY) gained compared with carboplatin-paclitaxel. At this ICER, dostarlimab plus carboplatin-paclitaxel is not cost-effective at a $50,000 per QALY gained willingness to pay (WTP) threshold for the first-line treatment of adults with primary advanced or first recurrent endometrial cancer who are candidates for systemic therapy. A price reduction is required for dostarlimab plus carboplatin-paclitaxel to be considered cost-effective at this threshold. In scenario analysis, dostarlimab plus carboplatin-paclitaxel was associated with an ICER of $273,097 per QALY gained among patients with pMMR disease, and $34,971 per QALY gained among patients with dMMR disease, compared to carboplatin-paclitaxel.

Table 1: Reimbursement Conditions and Reasons

Reimbursement condition	Reason	Implementation guidance
Initiation		
1. Treatment with dostarlimab plus carboplatin-paclitaxel should be reimbursed in adult patients with primary advanced or first recurrent endometrial cancer not amenable to curative therapy who meet at least 1 of the following criteria: 1.1. have primary stage III or IV endometrial cancer 1.2. have a first recurrence and have not previously received systemic anticancer therapy in advanced disease 1.3. have received prior neoadjuvant or adjuvant systemic anticancer therapy and a first recurrence at a minimum of 6 months after completion of treatment.	Evidence from the RUBY Part 1 trial demonstrated that treatment with dostarlimab plus carboplatin-paclitaxel resulted in a clinical benefit in patients with these characteristics.	—
2. Patients should have good performance status.	Patients with an ECOG performance status of 0 or 1 were included in the RUBY Part 1 trial.	Treating patients with an ECOG performance status of 2 may be at the discretion of the treating clinician.
3. Patients must not have any of the following: 3.1. first recurrence within 6 months of completing neoadjuvant or adjuvant systemic anticancer therapy 3.2. prior therapy with an anti–PD-1, anti–PD-L1, or anti–PD-L2 drug for advanced disease 3.3. uncontrolled brain metastases.	There is no evidence to support a benefit of dostarlimab plus carboplatin-paclitaxel treatment in patients with these characteristics as they were excluded from the RUBY Part 1 trial.	Patients with treated or stable brain metastases should be eligible for treatment.
Discontinuation		
4. Discontinuation should be based on a combination of clinical and radiological progression and or significant adverse events potentially related to dostarlimab plus carboplatin-paclitaxel.	Consistent with clinical practice, patients from the RUBY Part 1 trial discontinued treatment upon progression or unacceptable toxicity.	—
5. Dostarlimab should be reimbursed for a maximum of 3 years (i.e., 500 mg every 3 weeks [cycles 1 to 6] and 1,000 mg every 6 weeks [cycle 7 and thereafter]).	Patients in the RUBY Part 1 trial were treated with dostarlimab for up to 3 years.	—
Prescribing		
6. Dostarlimab plus carboplatin-paclitaxel should be prescribed by clinicians with expertise in advanced endometrial cancer; treatment should be supervised	This will ensure that treatment is prescribed only for appropriate patients and adverse effects are appropriately managed.	—

Reimbursement condition	Reason	Implementation guidance
and delivered in institutions with expertise in systemic therapy delivery.		
Pricing		
7. A reduction in price	The ICER for dostarlimab plus carboplatin-paclitaxel is $159,924 per QALY gained when compared with carboplatin-paclitaxel alone. A price reduction of at least 56% would be required for dostarlimab plus carboplatin-paclitaxel to achieve an ICER of $50,000 per QALY compared to carboplatin-paclitaxel alone.	In a scenario analysis, a higher price reduction was needed to achieve cost-effectiveness at this threshold for patients with pMMR/MSS disease.
Feasibility of adoption		
8. The economic feasibility of adoption of dostarlimab plus carboplatin-paclitaxel must be addressed	At the submitted price, the incremental budget impact of dostarlimab plus carboplatin-paclitaxel is expected to be greater than $40 million in years 2 and 3.	—

ECOG = Eastern Cooperative Oncology Group; ICER = incremental cost-effectiveness ratio; MSS = microsatellite stable; PD-1 = programmed cell death protein 1; PD-L1 = programmed death-ligand 1; PD-L2 = programmed death-ligand 2; QALY = quality-adjusted life year.

Discussion Points

- **Input from patient group and clinicians**: pERC highlighted the input from the patient group and clinicians that advanced endometrial cancer is an aggressive disease with poor prognosis. pERC acknowledged that there is an unmet need for effective and safe therapy options in the requested patient population, particularly for patients with pMMR disease. pERC noted that the exploratory subgroup analysis by MMR-MSI status for PFS was consistent with the primary analysis, in favour of dostarlimab plus carboplatin-paclitaxel. pERC also noted that patients would be eligible for dostarlimab plus carboplatin-paclitaxel regardless of having pMMR versus dMMR disease, although patients with dMMR disease may experience a greater clinical benefit from this treatment.
- **Side effects:** pERC acknowledged that patients expressed a need for treatments that have fewer side effects. Although a higher proportion of serious treatment-emergent adverse events (TEAEs) and any immune-related TEAEs (a notable harm) were reported in patients taking dostarlimab plus carboplatin-paclitaxel than in those taking placebo plus carboplatin-paclitaxel, pERC considered the side effects to be manageable, given that treatment is expected to be prescribed and overseen by clinicians who are experienced in treating patients with endometrial cancer. pERC agreed with the clinical experts that the safety profile of dostarlimab plus carboplatin-paclitaxel appeared consistent with expectations about immunotherapy treatment and the known safety profiles of dostarlimab and chemotherapy.
- **Health-related quality of life (HRQoL):** pERC noted that patients and clinicians highlighted improvement in health-related quality of life as an important outcome and treatment goal for patients with primary advanced or recurrent endometrial cancer. However, pERC was unable to draw definitive conclusions regarding the effects of dostarlimab plus carboplatin-paclitaxel compared to placebo plus carboplatin-paclitaxel on HRQoL due to concerns about imprecision and missing outcome data in the RUBY Part 1 trial.
- **Dostarlimab maintenance therapy:** pERC discussed that the extended 3-year duration of dostarlimab maintenance therapy will increase the need for treatment administration, monitoring, and toxicity management. Further comparison of a more conventional 2-year duration of immune-checkpoint inhibitor therapy would be of benefit to establish an optimal duration of maintenance therapy.
- **Cost-effectiveness by MMR-MSI status:** The committee considered a set of scenario analyses that explored the cost-effectiveness of dostarlimab plus carboplatin-paclitaxel in dMMR/MSI-H and pMMR/MSS cohorts separately. In patients with dMMR/MSI-H disease, dostarlimab plus carboplatin-paclitaxel was associated with an ICER of $34,971 per QALY gained compared to carboplatin-paclitaxel alone. In patients with pMMR/MSS disease, dostarlimab plus carboplatin-

paclitaxel was associated with an ICER of $273,097 per QALY gained compared to carboplatin-paclitaxel. At these ICERs, no price reduction was needed to achieve cost-effectiveness at a WTP threshold of $50,000 per QALY gained among patients with dMMR/MSI-H disease. Among patients with pMMR/MSS disease, the price of dostarlimab would need to be reduced by 67% to be considered cost-effective at this threshold. These estimates are subject to a high degree of uncertainty due to the exploratory nature of the subgroup analysis for PFS. Additional information about the subgroup analyses is available in Appendix 4 of the CDA-AMC Pharmacoeconomic Report.

- **Confidential pricing for carboplatin-paclitaxel**: The committee noted that the public list price for carboplatin and paclitaxel are likely higher than the negotiated prices paid by drug plans. Consequently, the ICERs associated with the overall indicated population (and MMR subgroups) are likely underestimated. Additional price reduction may be necessary to achieve cost-effectiveness.
- **Presence of additional therapies not reflected within the submission:** the Committee discussed the fact that, per a deviation request accepted by CDA-AMC, several treatment regimens exist for first- and second-line treatment of endometrial cancers that were not included as comparators in this analysis. Furthermore, there are additional approaches that are currently under evaluation by CDA-AMC. The Committee noted that the relative efficacy and cost-effectiveness of these options is unknown, and that this lack of evidence adds a great deal of complexity to decision-making. The cost-effectiveness of dostarlimab plus carboplatin-paclitaxel compared to these excluded treatments is unknown. Consequently, there is insufficient evidence to support a higher price for dostarlimab plus carboplatin-paclitaxel above other treatments that were not included within this analysis.

Background

Endometrial cancer (EC) is the most common gynecologic cancer in high-income countries, with approximately 8,600 new cases estimated in Canada in 2024. Recurrence occurs in 10%-15% of patients, with poor outcomes for advanced or recurrent cases. For patients with primary advanced or recurrent EC, the current standard of care is platinum-based combination regimens, with response rates between 40%-62% in the first line setting. However, for patients whose disease progresses after platinum-based chemotherapy, there is no standard second-line treatment. Current options, such as single-drug chemotherapies or hormonal therapies, have low response rates and limited survival benefits.

Dostarlimab (Jemperli), a PD-1 monoclonal antibody, is currently indicated for treating adults with primary advanced or recurrent endometrial cancer, particularly those with deficient mismatch repair (dMMR) or microsatellite instability-high (MSI-H) tumor status, which is found in approximately 13%-30% of recurrent EC cases. For this review, the approved Health Canada indication involves using dostarlimab in combination with carboplatin-paclitaxel for adult patients with primary advanced or first recurrent endometrial cancer who are candidates for systemic therapy. The recommended dose is 500 mg IV every 3 weeks for 6 cycles in combination with carboplatin-paclitaxel, followed by 1,000 mg monotherapy every 6 weeks for up to 3 years. Dostarlimab has also already been approved by Health Canada for dMMR/MSI-H recurrent or primary advanced EC in combination with carboplatin/paclitaxel, and in 2024, CDA-AMC's pERC recommended reimbursement for its use as part of a combination therapy in this setting.

Sources of Information Used by the Committee

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

- a review of 1 phase III, randomized controlled trial in patients with primary advanced or first recurrent endometrial cancer
- patient perspectives gathered by 1 patient group, Colorectal Cancer Resource & Action Network, regarding the use of dostarlimab for advanced or recurrent endometrial cancer
- input from public drug plans and cancer agencies that participate in the CDA-AMC review process
- 2 clinical specialists with expertise diagnosing and treating patients with endometrial cancer
- input from 2 clinician groups, including the Society of Gynecologic Oncology of Canada (GOC), and Ontario Health (CCO) Gynecology Cancer Drug Advisory Committee
- a review of the pharmacoeconomic model and report submitted by the sponsor.

Perspectives of Patients, Clinicians, and Drug Programs

Patient Input

CDA-AMC received input from 1 patient group, the Colorectal Cancer Resource & Action Network (CCRAN), regarding the use of dostarlimab for advanced or recurrent endometrial cancer. CCRAN collaborated with the Canadian Cancer Survivor Network (CCSN) to collect additional perspectives from endometrial cancer patients. The input was gathered through interviews with four patients and two clinicians, all women residing in Canada. The patients had undergone a variety of treatments, including surgery, chemotherapy, immunotherapy, hormonal therapy, and targeted therapies.

Endometrial cancer had a significant impact on the daily lives of the patients and their families. Patients reported struggling with debilitating side effects, such as neuropathy, fatigue, sexual dysfunction, and digestive issues, all of which diminished their quality of life. In addition to the physical burdens, the patients highlighted the emotional strain of managing the disease, including inadequate mental health support and challenges accessing treatment, particularly for those in rural areas. In addition, patients also noted the debilitating impact of the disease on caregivers.

Key outcomes that were important to patients included better symptom control, improved survival, and reduced treatment-related side effects. There was a strong preference for therapies that would allow patients to maintain their quality of life and engage in day-to-day activities, such as work, hobbies, and family care.

The input from CCRAN highlighted several unmet needs in the current treatment landscape, particularly for patients with recurrent or metastatic disease. Patients expressed a need for new treatments that could strike a balance between effectiveness and tolerable side effects, which is critical for their ability to maintain a normal life while managing the disease. This perspective is essential for interpreting the clinical trial results for dostarlimab and assessing how the treatment may improve patient outcomes in the Canadian health care context.

Clinician Input

Input From Clinical Experts Consulted by CDA-AMC

The clinical experts indicated that the treatment goals for patients with primary advanced or recurrent endometrial cancer is to prolong survival, delay disease progression and improve quality of life. The experts noted that standard of care for majority of patients is chemotherapy, usually with carboplatin and paclitaxel, or immunotherapy, and to a lesser extent hormonal therapy, surgery, or radiation, depending on extent of disease and sites of recurrence. They noted that most patients become refractory to current treatment options and subsequent therapy is limited to chemotherapy (e.g., doxorubicin, topotecan, paclitaxel, oxaliplatin, docetaxel and bevacizumab), which have poor response rates and high toxicity. The experts also indicated that an important unmet need is effective first line treatment for patients with metastatic proficient mismatch repair (pMMR) EC. The clinical experts considered dostarlimab's mechanism of action as distinct from chemotherapy, and thereby causing a significant shift in the current treatment paradigm. The clinical experts noted that dostarlimab would be used in the first line setting in combination with carboplatin and paclitaxel for all patients with primary advanced recurrent endometrial cancer, including those with deficient mismatch repair (dMMR) mutations. The clinical experts agreed that the patients best suited for dostarlimab plus carboplatin-paclitaxel would be those with advanced or recurrent endometrial cancer. In their opinion, patients that would gain the most benefit would be those with a dMMR status, and to a lesser extent, pMMR status. The experts highlighted that patients would be identified based on clinical examination and judgement, and a companion diagnostic would not be needed. The clinical experts indicated that in clinical practice, a combination of radiographic and clinical parameters is used to determine whether a patient is responding or progressing on treatment. The clinical experts indicated that treatment with dostarlimab plus carboplatin-paclitaxel should be discontinued if patients experience disease progression (as defined radiologically or clinically) or treatment is intolerable. They noted that discontinuation should be based on several cycles of treatment since tumor swelling or enlargement could occur with immunochemotherapy. The clinical experts indicated that patients receiving dostarlimab plus carboplatin-paclitaxel should be under the care of a gynecologic oncologist or medical oncologist who can manage toxicity associated with the therapy. They noted that it would be reasonable for patients to receive the therapy in a community setting where day-to-day follow up is with a general practitioner in oncology.

Clinician Group Input

Two clinician groups, the OH (CCO) Gynecologic Cancer Drug Advisory Committee and the Society of Gynecologic Oncology of Canada (GOC), provided input to this review.

There were no significant contrary views between the input from the clinical experts consulted by CDA-AMC and the OH (CCO) groups.

Both clinician groups and CDA-AMC clinical experts agreed on key areas such as the unmet need for durable responses in current treatments, the treatment goals of prolonging life and improving health-related quality of life, and the most appropriate patient population being those with dMMR tumors.

The clinician group highlighted that dostarlimab, in combination with chemotherapy, offers a valuable new option as a first-line treatment in clinical practice, particularly for patients with primary Stage III or IV or recurrent pMMR endometrial cancer who have limited treatment options and poor outcomes with chemotherapy alone.

Drug Program Input

Input was obtained from the drug programs that participate in the reimbursement review process. The following were identified as key factors that could potentially impact the implementation of a recommendation for dostarlimab plus carboplatin-paclitaxel:

- Consideration for initiation of therapy
- Generalizability
- Funding algorithm
- Care provision issues

The clinical experts consulted for the review provided advice on the potential implementation issues raised by the drug programs (refer to Table 2).

Table 2: Responses to Questions from the Drug Programs

Drug program implementation questions	Response
Relevant comparators	
The comparator in the RUBY trial Part 1 was carboplatin in combination with paclitaxel which is an appropriate comparator. Other comparators are hormonal therapies for hormone receptor positive endometrial cancer.	pERC acknowledged input from clinical experts that dostarlimab could be used in combination with alternative taxane and/or platinum drugs also used in endometrial cancer treatment regimens, based on clinical judgment of the treating clinician. However, pERC noted that the committee did not review evidence where dostarlimab was used in combination with other chemotherapy regimens.
Considerations for initiation of therapy	
Testing for dMMR and pMMR status needs to be completed prior to initiation of therapy.	The CDA-AMC review team noted that as per the Health Canada approved indication and reimbursement request, MMR-MSI testing may not be required to initiate therapy since both patients with pMMR and dMMR would be eligible. pERC acknowledged and agreed with the CDA-AMC review team's response. pERC also noted that MMR testing may be done because it may have implications for prognosis and/or subsequent lines of therapy.
Is the recommendation for pMMR the same as dMMR patients (i.e. patients who progress while on or within 6 months of adjuvant therapy would not be eligible for dostarlimab plus paclitaxel plus carboplatin)?	The clinical experts indicated that patients with pMMR and dMMR should be eligible for dostarlimab plus carboplatin-paclitaxel if they had not progressed with 6 months of neoadjuvant or adjuvant chemotherapy pERC acknowledged and agreed with the clinical experts' response.
For the dMMR indication, the Expert Review Committee thought it would be reasonable to allow an additional 1 year of dostarlimab upon disease progression for those who completed 3 years of dostarlimab. Can the same be said for pMMR endometrial cancer indication?	The clinical experts noted that re-treatment with an additional year of dostarlimab would be reasonable in patients with dMMR or pMMR who experience disease progression after completing 3 years of dostarlimab treatment. pERC acknowledged and agreed with the clinical experts' response.
Considerations for prescribing of therapy	
Dostarlimab is administered as 500 mg dose on day 1 with carboplatin and paclitaxel on day 1 every 21 days for 6	*Comment from the drug plans to inform pERC deliberations.*

Drug program implementation questions	Response
cycles followed by dostarlimab single-agent 1000 mg IV every 6 weeks up to a total of 3 years of therapy.	
Dostarlimab is administered as a 30 minute IV infusion.	*Comment from the drug plans to inform pERC deliberations.*
Generalizability	
Patients with ECOG performance status >1 were excluded from the trial. Can they be considered eligible for dostarlimab in combination with paclitaxel and carboplatin followed by dostarlimab maintenance?	The clinical experts indicated that patients with good ECOG performance status or a score of 0 to 2 should be eligible for dostarlimab plus carboplatin-paclitaxel, followed by dostarlimab maintenance, if they are able to tolerate the therapy. They noted that patients with ECOG performance status greater than 2 would likely be unable to tolerate the combination of 2 chemotherapy drugs and immunotherapy. pERC acknowledged and agreed with the clinical experts' response.
For patients who are currently receiving paclitaxel plus carboplatin for 1st line pMMR endometrial cancer: is it recommended to add dostarlimab to carboplatin and paclitaxel? If yes, what would be the maximum number of cycles recommended that patient had received of carboplatin and paclitaxel (i.e. patient should have no more than 3 cycles of carboplatin and paclitaxel if dostarlimab is to be added)?	The clinical experts noted that patients who are already on chemotherapy should be able to add dostarlimab within 3 to 6 cycles. pERC acknowledged that dostarlimab could be added to chemotherapy if patients have not experienced disease progression with chemotherapy, and they have not completed all of their planned chemotherapy cycles.
Funding algorithm (oncology only)	
Durvalumab with paclitaxel and carboplatin followed by durvalumab and olaparib maintenance is currently under review for 1st line pMMR endometrial cancer. Is there a reason why a prescriber would choose dostarlimab plus chemotherapy instead of durvalumab plus chemotherapy followed by durvalumab plus olaparib maintenance or vice versa?	The clinical experts noted that it is unclear who would benefit from the addition of a PARP inhibitor, and the added toxicity of a fourth drug could be burdensome to patients. pERC acknowledged and agreed with the clinical experts' response. pERC does not recommend adding a PARP inhibitor to dostarlimab at this time because pERC has not reviewed evidence supporting this.
Care provision issues	
More pharmacy preparation time to prepare dostarlimab.	*Comment from the drug plans to inform pERC deliberations.*
Dostarlimab is an immune checkpoint inhibitor and monitoring for immune-mediated toxicities will be required.	*Comment from the drug plans to inform pERC deliberations.*
dMMR and pMMR testing is required. When is the best time to test for dMMR and pMMR status?	The clinical experts indicated that while there is variability across cancer centres regarding time frame for MMR-MSI testing (e.g., shortly upon diagnosis, after biopsy, after surgery), the ideal time to test for dMMR and pMMR status is during diagnosis. As noted under Consideration for Initiation of Therapy, the clinical experts indicated that patients with pMMR and dMMR should be eligible for dostarlimab plus carboplatin-paclitaxel. pERC acknowledged and agreed with the clinical experts' response.
System and economic issues	
Large budget impact anticipated if dostarlimab plus chemotherapy is recommended for pMMR endometrial cancer.	*Comment from the drug plans to inform pERC deliberations.*
Generic paclitaxel and carboplatin available with confidential prices.	*Comment from the drug plans to inform pERC deliberations.*

Drug program implementation questions	Response
It will be important to provide the economics for pMMR population and not the ITT population as CDA has already issued their economic report and recommendation for dMMR. It is anticipated based on the results that pMMR will not have as good as cost-effectiveness as the dMMR indication and it is anticipated that pMMR will have a large budget impact as approximately 75% of patients are pMMR.	*Comment from the drug plans to inform pERC deliberations.*

dMMR = deficient mismatch repair; ECOG = Eastern Cooperative Oncology Group; mg = milligrams; IV = intravenous; pERC = The pan-Canadian Oncology Drug Review Expert Review Committee; pMMR = proficient mismatch repair.

Clinical Evidence

Systematic Review

Description of Studies

One trial, RUBY Part 1 (N = 494), met the inclusion criteria for the systematic review conducted by the sponsor. The objective of RUBY Part 1 was to assess the efficacy and safety of dostarlimab intravenous infusion plus carboplatin-paclitaxel followed by dostarlimab monotherapy, compared with placebo plus carboplatin-paclitaxel followed by placebo in adults with primary advanced or first recurrent endometrial cancer. The trial enrolled patients who were at least 18 years of age and had histologically or cytologically confirmed primary advanced or first recurrent endometrial cancer that was not amenable to curative therapy, an Eastern Cooperative Oncology Group (ECOG) performance status score of 0 or 1, and adequate organ function. Patients were excluded if they had received neo-adjuvant or adjuvant chemotherapy without recurrence or with recurrence in the prior 6 months before entering the trial, and prior treatment with an anti-PD[L]-1 antibody. The approved Health Canada indication and reimbursement request aligned with the trial population. The outcomes most relevant to the CDA-AMC review included the dual primary outcomes of overall survival (OS), progression-free survival (PFS) per investigator assessment and secondary outcomes of health-related quality of life (HRQoL) measured via the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire 30 Item (EORTC QLQ-C30) global health status and safety. Efficacy and safety data were evaluated at the data cut-off dates of September 28, 2022 (interim analysis 1) and September 22, 2023 (interim analysis 2). Overall, key baseline characteristics were generally balanced between treatment groups. The trial population was predominately white (approximately 77%) with a mean age of 64 years, with half of patients representing the 19 to 64 years age group. Most patients had an ECOG performance-status of 0 (approximately 63%), indicating good overall performance, endometrioid (adenocarcinoma or adenocarcinoma-variants) histology at diagnosis (approximately 55%), recurrent (48%) or primary stage IV (33%) disease status, Federation of Gynecology and Obstetrics (FIGO) stage III or IV at diagnosis (approximately 60%), mismatch repair-microsatellite instability (MMR–MSI) status of pMMR– microsatellite stability (MSS) (approximately 76%), and received prior surgery for endometrial cancer (approximately 90%), and did not receive prior external pelvic radiotherapy (approximately 83%).

Efficacy Results

Only those efficacy outcomes and analyses of subgroups identified as important to this review are reported. The main findings for the efficacy outcomes for the RUBY trial Part 1 are from the data cut-off dates of September 28, 2022 (interim analysis 1) and September 22, 2023 (interim analysis 2). The boundary for statistical significance for the dual primary outcomes of PFS and OS were met in interim analysis 1 and interim analysis 2, respectively. PFS was not re-evaluated at interim analysis 2. HRQoL results are from interim analysis 1, and safety results are from interim analysis 2.

Overall Survival

By the second interim analysis, the median duration of follow up for all patients was 37.2 months (range: 31.0 to 49.5), and there were 109 (44.5%) deaths in the dostarlimab plus carboplatin-paclitaxel group and 144 (57.8%) deaths in the placebo plus carboplatin-paclitaxel group. The median OS was 44.6 months (95% CI, 32.6 to NE) in the dostarlimab plus carboplatin-paclitaxel group versus 28.2 months (95% CI, 22.1 to 35.6) in the placebo plus carboplatin-paclitaxel group (one sided P value = 0.0020), with a between-group HR of 0.69 (95% CI, 0.54 to 0.89). The result of the sensitivity analysis was consistent with the primary analysis.

The Kaplan–Meier (KM)-estimated probability of being alive at 24 and 36 months was 70.1% (95% CI, [redacted] to [redacted]) versus 54.3% (95% CI, [redacted] to [redacted]; between-group difference: [redacted]% [95% CI, [redacted] to [redacted]), and 54.9% (95% CI, [redacted] to [redacted] versus 42.9% (95% CI, [redacted] to [redacted]; between-group difference: [redacted]% [95% CI, [redacted] to [redacted]) in the dostarlimab plus carboplatin-paclitaxel and placebo plus carboplatin-paclitaxel groups, respectively.

The efficacy results for OS were generally consistent across the subgroup analyses of interest (age and histology), in favour of dostarlimab plus carboplatin-paclitaxel, however, there was inconsistency in effects across the disease status subgroup. The subgroup analyses did not include MMR/MSI status.

Progression-Free Survival by Investigator Assessment

At the time of the first interim analysis, the median duration of follow up for all patients was 25.4 months (range: 19.2 to 37.8), and PFS events had been reported for 135 (55.1%) patients in the dostarlimab plus carboplatin-paclitaxel group and 177 (71.1%) patients in the placebo plus carboplatin-paclitaxel group. The median PFS was 11.8 months (95% CI, 9.6 to 17.1) in the dostarlimab plus carboplatin-paclitaxel group versus 7.9 months (95% CI, 7.6 to 9.5) in the placebo plus carboplatin-paclitaxel group (one sided P value < 0.0001), with a between-group HR of 0.64 (95% CI, 0.51 to 0.80). The results of sensitivity analyses were consistent with the primary analysis. The KM-estimated probability of PFS at 12 and 24 months was 48.2% (95% CI, [redacted] to [redacted]) versus 29.0% (95% CI, [redacted] to [redacted]; between-group difference: [redacted]% [95% CI, [redacted] to [redacted]), and 36.1% (95% CI, [redacted] to [redacted]) versus 18.1% (95% CI, [redacted] to [redacted]; between-group difference: [redacted]% [95% CI, [redacted] to [redacted]) in the dostarlimab plus carboplatin-paclitaxel and placebo plus carboplatin-paclitaxel groups, respectively. The results of the secondary outcome of PFS by blinded independent central review (BICR) assessment were consistent with those from the investigator assessment results (data not shown).

The efficacy results for PFS were generally consistent across the exploratory subgroup analyses by MMR/MSI status at baseline, age, disease status at baseline and histology, in favour of dostarlimab plus carboplatin-paclitaxel. The HRs for the dMMR/MSI-H and MMRp/MSS subgroups were 0.28 (95% CI, 0.16 to 0.50) and 0.76 (95% CI, 0.59 to 0.98), respectively. There were some inconsistent effects across the disease status subgroup, particularly primary stage III.

HRQoL by EORTC QLQ-C30

At baseline and at cycles 7 and 13, the EORTC QLQ-C30 global health status mean scores for the ITT population were similar between treatment groups, and there were no clinically meaningful changes observed (defined by the sponsor as change in the score from baseline of ≥ 10 points) in either group at cycles 7 or 13. The between-group LS mean difference in change from baseline at cycles 7 and 13 was [redacted] (95% CI, [redacted] to [redacted]) and [redacted] (95% CI, [redacted] to [redacted]), respectively.

Harms Results

Harms data reported in this section are from the second interim analysis (data cut-off date of September 22, 2023). There were no significant changes in the incidence of TEAEs from the time of the first interim analysis to the time of the second interim analysis. All patients in both treatment groups reported at least one TEAE. The most frequently reported TEAEs in the dostarlimab plus carboplatin-paclitaxel and placebo plus carboplatin-paclitaxel groups were fatigue (52.3% versus 54.9%), alopecia (53.9% versus 50.0%), nausea (54.4% versus 46.3%), neuropathy peripheral (44.0% versus 41.9%), and anemia (37.8% versus 42.7%). Of these TEAEs, a higher proportion of nausea was reported in patients taking dostarlimab plus carboplatin-paclitaxel. A higher proportion of patients in the dostarlimab plus carboplatin-paclitaxel group experienced at least one grade 3 or higher TEAE (72.2%) versus placebo plus carboplatin-paclitaxel (60.2%). The most common grade 3 or higher TEAEs in both groups were anemia (14.9% versus 16.7%), neutropenia (9.5% versus 9.3%), and neutrophil count decreased (8.3% versus 13.8%). The incidence of serious TEAEs was higher in the dostarlimab plus carboplatin-paclitaxel group (39.8%) versus placebo plus carboplatin-paclitaxel (28.0%). The most frequently reported serious TEAEs in the dostarlimab plus carboplatin-paclitaxel group were pulmonary embolism (3.3% versus 2.0%) and sepsis (3.3% versus 0.4%), and the most common in the placebo plus carboplatin-paclitaxel group were anemia (2.4% versus 1.2%) and pulmonary embolism. A higher proportion of TEAEs that led to study treatment discontinuation were reported in patients treated with dostarlimab plus carboplatin-paclitaxel (24.9%) versus placebo plus carboplatin-paclitaxel (16.3%). The most common TEAEs leading to discontinuation in both groups were peripheral neuropathy (2.1% versus 2.8%), peripheral sensory neuropathy (2.9% versus 0.4%), and infusion related reaction (2.1% versus 3.3%). A lower proportion of deaths were reported in the dostarlimab plus carboplatin-paclitaxel group ([redacted]%) versus placebo plus carboplatin-paclitaxel ([redacted]%), with the

primary reason for death in both groups being disease progression ([redacted]% versus [redacted]%). For notable harms, a higher proportion of any immune-related TEAEs were reported in patients taking dostarlimab plus carboplatin-paclitaxel (58.5%) versus placebo plus carboplatin-paclitaxel (37.0%). The incidence of infusion-related reactions was similar between groups ([redacted]% versus [redacted]%).

Critical Appraisal

The RUBY trial Part 1 was a randomized, double-blind, placebo-controlled, phase III trial. Randomization procedures, including stratification by MMR–MSI status, previous external pelvic radiotherapy and disease status, were appropriate and conducted by interactive response system. In general, key baseline characteristics of patients appeared balanced between groups. Sample size and power calculations were based on the dual primary outcome of PFS, and the trial was powered to detect significant differences for PFS and OS. The interim analyses were preplanned with adequately justified stopping boundaries, which provides confidence that the statistical significance of PFS and OS are not a result of type I error. The pre-specified analyses of PFS and OS were appropriately controlled for multiple comparisons. All other analyses were descriptive, including the HRQoL outcome EORTC QLQ-C30 global health status, which were deemed a clinically important outcome for the disease. The sample size for the exploratory subgroup analyses of PFS and OS, including by MMR status, were small. Aside from PFS in the dMMR population, the trial was not powered to detect subgroup differences. To minimize the risk of bias in the measurement of PFS, the trial performed tumour assessments using response evaluation criteria in solid tumors (RECIST) v1.1 criteria per investigator assessment and radiographic scans were assessed by BICR as a secondary outcome. The PFS per BICR assessment results were similar to the investigator-assessed results. In addition, the findings of the sensitivity analyses for the dual primary outcomes of PFS and OS were consistent with the primary analysis. Patients were permitted to receive post-treatment anti-cancer medications after study treatment had been discontinued, which may influence the assessment of OS. Since no sensitivity analyses were performed to test the treatment policy strategy for OS (e.g., exclude the effect of subsequent therapies), the estimated effect would be a combination of treatment with dostarlimab plus carboplatin-paclitaxel versus placebo plus carboplatin-paclitaxel, plus subsequent treatments. Therefore, survival results might be partially attributable to treatments administered after disease progression rather than the study treatment itself. This is a relevant comparison, however, as it is reflective of how the intervention and comparator would be used in practice. The trial authors stated that the proportional hazards assumption was assessed by visual inspection of a survival curve fit to KM data, inspection of log-cumulative hazard plots over time, and statistical goodness of fit based on relative Akaike and Bayesian information criterion values, however the assessment results were not reported. Despite the absence of these results, visual inspection of the K-M curves for PFS and OS appear to indicate a clear separation (at approximately 5 and 7 months, respectively), after which there appeared to be sustained proportionality throughout study treatment. The EORTC QLQ-C30 questionnaire has been validated in patients with cancer, with evidence of reliability, and MID ranges. Based on the MID ranges identified in the literature, the sponsor suggested a 10-point change from baseline score as a clinically meaningful change, which was considered reasonable by the review team. Additionally, the result of the EORTC QLQ-C30 global health status outcome was subject to bias potentially due to missing data, although the direction and extent of bias is unclear.

The population requested for reimbursement aligns with the approved Health Canada indication and overall trial population. The dosing and administration of dostarlimab was consistent with the approved product monograph. According to the clinical experts consulted by CDA-AMC, the eligibility criteria and baseline characteristics of the RUBY trial part 1 were generalizable to adults with primary advanced or first recurrent endometrial cancer in the Canadian setting. Although, the trial did not include patients with an ECOG performance status of greater than 1. The clinical experts indicated that patients with good ECOG performance status or a score of 0 to 2 should be eligible for dostarlimab plus carboplatin-paclitaxel, followed by dostarlimab maintenance, if they are able to tolerate the therapy. The timing of administering dostarlimab or placebo in combination with carboplatin-paclitaxel appears to be aligned with the chemotherapy regimens in the current standard of care, according to the clinical experts consulted by CDA-AMC. In the RUBY Part 1 trial, treatment duration was up to 3 years if patients did not experience disease progression, unacceptable toxicity, or death. The trial included outcomes that were important to patients and clinicians. The patient group indicated that stopping disease progression, prolonging life, improving HRQoL and reducing treatment side effects are important to them.

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.

Following the GRADE approach, evidence from RCTs started as high-certainty evidence and could be rated down for concerns related to study limitations (which refers to internal validity or risk of bias), inconsistency across studies, indirectness, imprecision of effects, and publication bias.

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 reference points for the certainty of evidence assessment for OS, PFS, any immune-related TEAEs and any infusion-related reactions were set according to the presence or absence of an important effect based on thresholds informed by the clinical experts consulted for this review. The reference point for the certainty of the evidence assessment for EORTC QLQ-C30 global health status score were set according to the presence or absence of an important effect based on a threshold suggested by the sponsor that was informed by the literature.

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:

- Survival outcomes (OS and PFS)
- HRQoL outcome (EORTC QLQ-C30 global health status)
- Notable harms (any immune-related TEAEs and any infusion-related reactions)

Results of GRADE Assessments

Table 3 presents the GRADE summary of findings for dostarlimab plus carboplatin-paclitaxel versus placebo plus carboplatin-paclitaxel.

Table 3: Summary of Findings for Dostarlimab Plus Carboplatin-Paclitaxel Versus Placebo Plus Carboplatin-Paclitaxel for Patients with Primary Advanced or First Recurrent Endometrial Cancer – RUBY Trial Part 1

Outcome and follow-up	Patients (studies), N	Relative effect (95% CI)	Absolute effects (95% CI)			Certainty	What happens
			Placebo plus carboplatin-paclitaxel	Dostarlimab plus carboplatin-paclitaxel	Difference		
OS – ITT population, second interim analysis data-cutoff date of September 22, 2023							
Probability of survival at 24 months Median follow-up for all patients: 37.2 months	494 (1 RCT)	NA	543 per 1,000	701 per 1,000 ([redacted] to [redacted])	[redacted] fewer per 1,000 ([redacted] fewer to [redacted] fewer)	High [a]	Dostarlimab plus carboplatin-paclitaxel results in a clinically important increase in the probability of survival at 24 months when compared with placebo plus carboplatin-paclitaxel.
Probability of survival at 36 months Median follow-up for all patients: 37.2 months	494 (1 RCT)	NA	429 per 1,000	549 per 1,000 ([redacted] to [redacted])	[redacted] fewer per 1,000 ([redacted] fewer to [redacted] fewer)	High [a]	Dostarlimab plus carboplatin-paclitaxel results in a clinically important increase in the probability of survival at 36 months when compared with placebo plus carboplatin-paclitaxel.
PFS – ITT population, first interim analysis data-cutoff date of September 28, 2022							
Probability of PFS at 12 months Median follow-up for all patients: 25.4 months	494 (1 RCT)	NA	290 per 1,000	482 per 1,000 ([redacted] to [redacted])	[redacted] more per 1,000 ([redacted] more to [redacted] more)	High [b]	Dostarlimab plus carboplatin-paclitaxel results in a clinically important increase in the probability of PFS at 12 months when compared with placebo plus carboplatin-paclitaxel.
Probability of PFS at 24 months Median follow-up for all patients: 25.4 months	494 (1 RCT)	NA	181 per 1,000	361 per 1,000 ([redacted] to [redacted])	[redacted] more per 1,000 ([redacted] more to [redacted] more)	High [b]	Dostarlimab plus carboplatin-paclitaxel results in a clinically important increase in the probability of PFS at 24 months when compared with placebo plus carboplatin-paclitaxel.
EORTC QLQ-C30 global health status – ITT population, first interim analysis data-cutoff date of September 28, 2022							
LS mean change from baseline in global health status; scores range from 0 to 100, with higher scores indicating better health status	[redacted] (1 RCT)	NA	-2.3	-1.8 (SD = 22.79)	[redacted] ([redacted] to [redacted])	Low [c]	Dostarlimab plus carboplatin-paclitaxel may result in little to no clinically important difference in global health status at cycle 7 when compared with placebo plus carboplatin-paclitaxel.

Outcome and follow-up	Patients (studies), N	Relative effect (95% CI)	Absolute effects (95% CI)			Certainty	What happens
			Placebo plus carboplatin-paclitaxel	Dostarlimab plus carboplatin-paclitaxel	Difference		
Time point: cycle 7							
LS mean change from baseline in global health status; scores range from 0 to 100, with higher scores indicating better health status Time point: cycle 13	[redacted] (1 RCT)	NA	-0.9	3.3 (SD = 23.5)	[redacted] ([redacted] to [redacted])	Very low [d]	The evidence is very uncertain about the effect of dostarlimab plus carboplatin-paclitaxel on global health status at cycle 13 when compared with placebo plus carboplatin-paclitaxel.
Harms – Safety population, second interim analysis data-cutoff date of September 22, 2023							
Any immune-related TEAEs Median follow-up for all patients: 37.2 months	487 (1 RCT)	NA	370 per 1,000	585 per 1,000 (NA)	[redacted] more per 1,000 ([redacted] more to [redacted] more)	High [e]	Dostarlimab plus carboplatin-paclitaxel results in a clinically important increase in any immune-related TEAEs when compared to placebo plus carboplatin-paclitaxel.
Any infusion-related reactions Median follow-up for all patients: 37.2 months	487 (1 RCT)	NA	[redacted] per 1,000	[redacted] per 1,000 (NA)	[redacted] fewer per 1,000 ([redacted] fewer to [redacted] more)	Low [f]	Dostarlimab plus carboplatin-paclitaxel may result in little to no difference in any infusion-related reactions when compared to placebo plus carboplatin-paclitaxel.

CI = confidence interval; EORTC QLQ-C30 = European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire 30 item; ITT = intention to treat; LS = least squares; MID = minimum important difference; NA = not applicable; OS = overall survival; PFS = progression-free survival; RCT = randomized controlled trial; SD = standard deviation; TEAEs = treatment-emergent adverse events.

Note: Study limitations (which refer to internal validity or risk of bias), inconsistency across studies, indirectness, imprecision of effects, and publication bias were considered when assessing the certainty of the evidence. All serious concerns in these domains that led to the rating down of the level of certainty are documented in the table footnotes.

[a] A between-group absolute risk difference of 5% (50 fewer or more events per 1,000 patients) at 24 and 36 months was clinically important according to the clinical experts. The point estimate and entire confidence interval exceeded the threshold.

[b] A between-group absolute risk difference of 10% (100 fewer or more events per 1,000 patients) at 12 and 24 months was clinically important according to the clinical experts. The point estimate and entire confidence interval exceeded the threshold.

[c] Rated down 2 levels for risk of bias due to missing outcome data. There is no imprecision in the estimate (the point estimate and entire 95% CI for the between-group difference shows little to no difference) Based on the ranges identified in the literature and suggested by the sponsor, a 10-point change from baseline in EORTC QLQ-C30 scale score was considered clinically important.

[d] Rated down 1 level for serious imprecision due to the 95% CI for the between-group difference including the possibility of both harm and little to no difference when compared with placebo plus carboplatin-paclitaxel; based on the ranges identified in the literature and suggested by the sponsor, a 10-point change from baseline in EORTC QLQ-C30 scale score was considered clinically important. Rated down 2 levels for risk of bias due to missing outcome data.

[e] A between-group absolute risk difference of 5% (50 fewer or more events per 1,000 patients) was clinically important according to the clinical experts. The point estimate and entire confidence interval exceeded the threshold (i.e., more TEAEs).

[f] Rated down 2 levels for very serious imprecision due to the 95% CI for the between-group absolute risk difference including the possibility of both important benefit and important harm; a between-group absolute risk difference of 5% (50 fewer or more events per 1,000 patients) was clinically important according to the clinical experts.

Source: Source: RUBY Part 1 Clinical Study Report. Details included in the table are from the sponsor's Summary of Clinical Evidence and additional information provided in the submission.

Long-Term Extension Studies

No long-term extension studies were submitted by the sponsor.

Indirect Comparisons

No indirect treatment comparisons were submitted by the sponsor.

Studies Addressing Gaps in the Evidence From the Systematic Review

No studies addressing gaps were submitted by the sponsor.

Conclusions

Evidence from 1 phase III, randomized, double-blind trial (RUBY Part 1) reported on outcomes that were important to both patients and clinicians. The trial showed high certainty of evidence that treatment with dostarlimab plus carboplatin-paclitaxel results in a clinically important increase in OS at 24 and 36 months and PFS at 12 and 24 months, compared to placebo plus carboplatin-paclitaxel in adults with primary advanced or first recurrent endometrial cancer. At cycle 7 of treatment, there was low certainty of evidence in little to no clinically important between-group difference in HRQoL, and no definitive conclusions can be drawn on HRQoL at cycle 13 due to concerns of imprecision and missing outcome data. There were no new safety signals identified and the safety of dostarlimab plus carboplatin-paclitaxel was consistent with the known safety profiles of the individual drugs, although the trial showed high certainty of evidence for a clinically important increase in the proportion of patients who experience any immune-related TEAEs when compared with placebo plus carboplatin-paclitaxel.

Economic Evidence

Cost and Cost-Effectiveness

Component	Description
Type of economic evaluation	Cost-utility analysis Partitioned Survival Model (PSM)
Target population	Adult patients with primary advanced or first recurrent endometrial cancer who are candidates for systemic therapy
Treatments	Dostarlimab plus carboplatin-paclitaxel
Dose regimen	500 mg administered as an intravenous infusion over 30 minutes every 3 weeks for 6 doses (in combination with carboplatin dosed at AUC 5 mg/ml and paclitaxel 175 mg/m^2), followed by 1,000 mg every 6 weeks until progression of disease, unacceptable toxicity, or up to 3 years
Submitted price	Dostarlimab, 50 mg/mL, solution for infusion, $10,031.08 per 500 mg vial
Submitted treatment cost	Cycles 1-6: $14,515 per 3-week cycle (dostarlimab plus carboplatin-paclitaxel); Cycles 7+: $20,062 per 6-week cycle (dostarlimab alone)
Comparator	Carboplatin-paclitaxel
Perspective	Canadian publicly funded health care payer
Outcomes	QALYs, LYs
Time horizon	Lifetime (36.10 years)
Key data sources	RUBY Part 1 trial IA1 and IA2
Key limitations	• The long-term extrapolation of OS data was likely overestimated, leading to clinically implausible estimates of the proportion of patients surviving at various time points. • The sponsor's use of a PSM introduces a post-progression survival bias in favor of dostarlimab plus carboplatin-paclitaxel, with the extent of this bias being uncertain.

Component	Description
	• The distribution of subsequent treatments in the submitted model does not accurately reflect Canadian clinical practice, and the proportions used did not match those reported in the submitted clinical study report. • Additional issues identified with the sponsor's model include the health state utility values, which lacked transparency and likely overestimated the quality-of-life in favor of dostarlimab. Moreover, incorrect drug price for carboplatin-paclitaxel likely led to an underestimation of the drug costs associated with dostarlimab plus carboplatin-paclitaxel.
CDA-AMC reanalysis results	• To address the identified limitations, CDA-AMC made the following revisions to the sponsor's pharmacoeconomic model: corrected unit prices for carboplatin and paclitaxel; applied observed values for time on treatment; used the Weibull distribution to predict OS for both treatments; and, adjusted the distribution of patients receiving no treatment to align with Canadian clinical practice. • In the CDA-AMC base case, compared with carboplatin-paclitaxel alone, dostarlimab plus carboplatin-paclitaxel is associated with an ICER of $159,924 per QALY gained (incremental costs: 163,962; incremental QALYs: 1.03). • A price reduction of at least 56% would be needed for dostarlimab plus carboplatin-paclitaxel to be cost-effective at a WTP threshold of $50,000 per QALY gained.

Budget Impact

CDA-AMC identified the following key limitations with the sponsor's analysis: the distribution of subsequent treatments may not reflect clinical practice in Canada, and the market share for dostarlimab may have been underestimated.

CDA-AMC performed a reanalysis in which the distribution of subsequent treatment matched the values used in the cost-utility analysis. In the CDA-AMC base case, the budget impact of reimbursing dostarlimab is expected to be $28,806,630 in year 1, $64,428,453 in year 2, and $90,091,568 in year 3, with a three-year total of $183,326,651.

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 Villeneuve, and Danica Wasney.

Meeting date: January 8, 2025

Regrets:

None

Conflicts of interest:

None