NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Draft guidance consultation

Dostarlimab with platinum-containing chemotherapy for treating primary advanced or recurrent endometrial cancer with microsatellite stability or mismatch repair proficiency

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using dostarlimab with platinum-containing chemotherapy in the NHS in England. The evaluation committee has considered the evidence submitted by the company and the views of non-company stakeholders, clinical experts and patient experts.

This document has been prepared for consultation with the stakeholders. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the stakeholders for this evaluation and the public. This document should be read along with the evidence (see the committee papers).

The evaluation committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex or sexual orientation?

Note that this document is not NICE's final guidance on dostarlimab with platinum-containing chemotherapy. The recommendations in section 1 may change after consultation.

After consultation:

- The evaluation committee will meet again to consider the evidence, this evaluation consultation document and comments from the stakeholders.
- At that meeting, the committee will also consider comments made by people who are not stakeholders.
- After considering these comments, the committee will prepare the final draft guidance.
- Subject to any appeal by stakeholders, the final draft guidance may be used as the basis for NICE's guidance on using dostarlimab with platinum-containing chemotherapy in the NHS in England.

For further details, see NICE's manual on health technology evaluation.

The key dates for this evaluation are:

- Closing date for comments: 20 August 2025
- Second evaluation committee meeting: 2 September 2025
- Details of the evaluation committee are given in section 4

1 Recommendations

1.1 Dostarlimab plus platinum-containing chemotherapy should not be used to treat primary advanced or recurrent endometrial cancer with microsatellite stability (MSS) or mismatch repair proficiency (MMRp) in adults when systemic treatment is suitable.

1.2 This recommendation is not intended to affect treatment with dostarlimab plus platinum-containing chemotherapy that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS healthcare professional consider it appropriate to stop.

What this means in practice

Dostarlimab plus platinum-containing chemotherapy is not required to be funded in the NHS in England to treat primary advanced or recurrent endometrial cancer with MSS or MMRp in adults when systemic treatment is suitable. It should not be used routinely in the NHS in England for this indication.

This is because there is not enough evidence to determine whether dostarlimab plus platinum-containing chemotherapy offers value for money in this population.

Why the committee made these recommendations

Usual treatment for primary advanced or recurrent endometrial cancer with MSS or MMRp is platinum-containing chemotherapy (for example, carboplatin and paclitaxel).

Evidence collected up to September 2022 from an ongoing clinical trial suggests that dostarlimab plus carboplatin and paclitaxel may increase the time before a person's cancer gets worse more than placebo plus carboplatin and paclitaxel. But this is uncertain taking into account later evidence collected up to September 2023. It is

also unclear whether adding dostarlimab to usual treatment increases how long people live.

There are also uncertainties in the economic model related to modelling of:

- how long people live before their condition gets worse
- the use of treatments after the condition progresses
- the related impact on how long people live and how long treatment effects may last.

Because of the uncertainties in the clinical-effectiveness evidence and economic model, it is not possible to determine the most likely cost-effectiveness estimates for dostarlimab plus platinum-containing chemotherapy. So, it should not be.

2 Information about dostarlimab

Marketing authorisation indication

2.1 Dostarlimab (Jemperli, GlaxoSmithKline) is indicated 'in combination with platinum-containing chemotherapy for the treatment of adult patients with primary advanced or recurrent endometrial cancer (EC) and who are candidates for systemic therapy'.

Dosage in the marketing authorisation

2.2 The dosage schedule is available in the summary of product characteristics for dostarlimab.

Price

2.3 The list price for dostarlimab is £5,887.33 per 500-mg vial (excluding VAT; BNF online accessed July 2025).

2.4 The company has a commercial arrangement. This makes dostarlimab available to the NHS with a discount and it would have also applied to this indication if dostarlimab had been recommended. The size of the discount is commercial-in-confidence.

Carbon Reduction Plan

2.5 Information on the Carbon Reduction Plan for UK carbon emissions for GlaxoSmithKline will be included here when guidance is published.

3 Committee discussion

The evaluation committee considered evidence submitted by GlaxoSmithKline, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the committee papers for full details of the evidence.

The condition

Impact on quality of life

3.1 Endometrial cancer starts in the lining of the uterus and is the most common type of uterine cancer. At diagnosis, primary advanced endometrial cancer refers to stage 3 or 4 disease that has spread beyond the uterus. Recurrent endometrial cancer refers to cancer that is detected either radiologically or histologically, when there has been remission after initial treatment. Mismatch repair (MMR) status, the functionality of the DNA MMR system in tumours, is routinely tested in endometrial cancer. About 75% of people with endometrial cancer have tumours that are MMR proficient (MMRp) or microsatellite stable (MSS). In MMRp, the DNA repair mechanisms are intact and mutations can be corrected. In MSS, the length of microsatellites remains unchanged. People from Black ethnic backgrounds have a higher incidence of the p53-abnormal (p53abn) subtype of endometrial cancer with MSS or MMRp. This may correlate with TP53-mutated (TP53mut) tumours (see section 3.4). This represents a small proportion of all endometrial cancers, but is often more aggressive and associated with poorer outcomes. The clinical experts explained that endometrial cancer with MSS or MMRp is a molecularly heterogeneous group. They suggested that routinely available molecular testing cannot further identify subgroups of endometrial cancer with MSS or MMRp. They highlighted that the median survival for people with endometrial cancer with MSS or MMRp is usually less than 2 years. The patient experts explained that living with stage 3 or 4 endometrial cancer with MSS or

MMRp has a substantial impact on all aspects of life for both the person and their family. This includes debilitating physical symptoms, psychological distress from the uncertainty of disease progression and financial burden. The committee acknowledged that primary advanced or recurrent endometrial cancer with MSS or MMRp can have a negative impact on people with the condition, as well as on their families and carers.

Clinical management

Treatment options

3.2 Standard care for primary advanced or recurrent endometrial cancer is platinum-containing chemotherapy, typically a combination of carboplatin and paclitaxel, followed by surveillance scans every 12 weeks. People whose cancer progresses after chemotherapy may be offered immunotherapy, further chemotherapy or, for a very small proportion, maintenance hormone treatment. Pembrolizumab plus lenvatinib is available as an option for people who have had treatment for endometrial cancer (see NICE's technology appraisal guidance on pembrolizumab with lenvatinib for previously treated advanced or recurrent endometrial cancer). The clinical experts explained that, once cancer has progressed after chemotherapy, about 35% to 40% of people are unable to tolerate further treatment at second line, including immunotherapy. They highlighted that the side effects are more often related to lenvatinib than to pembrolizumab. The patient experts agreed and emphasised the high unmet need. They highlighted the limited treatment options for endometrial cancer with MSS or MMRp at this stage, which can leave people feeling frustrated, hopeless and abandoned. The committee acknowledged the high unmet need because of limited first-line treatment options for endometrial cancer with MSS or MMRp. It concluded that people with the condition, and their families, would welcome safe and effective treatments that offer durable responses and are well tolerated.

Positioning of dostarlimab plus platinum-containing chemotherapy

3.3 For this evaluation, the company positioned dostarlimab as an add-on treatment to platinum-containing (also referred to as platinum-based) chemotherapy as a first-line option for primary advanced or recurrent endometrial cancer with MSS or MMRp, when systemic treatment is suitable. The company explained that its target population is narrower than the marketing authorisation. The committee noted that dostarlimab is recommended for a different subpopulation in NICE's technology appraisal guidance on dostarlimab with platinum-based chemotherapy for treating primary advanced or recurrent endometrial cancer with high microsatellite instability or mismatch repair deficiency. The company explained that the only relevant comparator is carboplatin plus paclitaxel, which is standard care in the NHS for primary advanced or recurrent endometrial cancer with MSS or MMRp (see section 3.2). It also highlighted that, if recommended, dostarlimab plus platinum-containing chemotherapy would preclude using pembrolizumab-based regimens at second line for this population. This is because immunotherapies are not offered more than once for this condition in the NHS. The clinical experts confirmed that, for the company's target population, the choice of comparator aligns with NHS practice. The committee agreed with the company's positioning of dostarlimab plus platinum-containing chemotherapy and concluded that the relevant comparator is carboplatin plus paclitaxel.

Clinical effectiveness

Key clinical-effectiveness evidence for dostarlimab plus platinum-containing chemotherapy

3.4 The key clinical-effectiveness evidence used in the company's submission and economic model came from RUBY-1, an ongoing phase 3 multinational double-blind randomised trial. It compared 18 weeks of dostarlimab plus carboplatin and paclitaxel (from now, platinum-containing chemotherapy) followed by dostarlimab monotherapy for up to 3 years (from now, the dostarlimab arm) with 18 weeks of placebo plus platinum-containing chemotherapy followed by placebo for up to 3 years (from now,

the placebo arm). Randomisation was stratified by MMR and MSS status, prior external pelvic radiotherapy and disease status. The trial included 494 adults (aged 18 years and over) with primary stage 3 or 4, or recurrent endometrial cancer, and an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. Of these, 76% (376 of 494) had endometrial cancer with MSS or MMRp. Mutational data was available for 400 people, of which 88 people had TP53mut tumours. The primary endpoints were overall survival (OS) and progression-free survival (PFS), assessed by the investigator according to Response Evaluation Criteria in Solid Tumors v1.1. In this evaluation, the company presented results from 2 planned interim data cuts, which were used in the economic model:

- IA1 (28 September 2022) for PFS, health-related quality of life and time to treatment discontinuation
- IA2 (22 September 2023) with a median follow up of 37.5 months for OS and adverse events.

The company considers the median follow up for IA1 to be commercial-in-confidence, so this information cannot be reported here. The company highlighted that only 54.8% of data maturity in OS was reached in the population with MSS or MMRp at IA2. So, the OS data at this interim analysis was still immature. The EAG highlighted that no further interim data cuts were planned before RUBY-1's expected completion in around the third quarter of 2026. The EAG highlighted concerns about the reliability of the OS data from RUBY-1, particularly the data beyond 30 months, because of heavy censoring. The committee took this into account in its consideration.

Generalisability of results from the RUBY-1 population

3.5 The clinical experts noted that people in RUBY-1 were generally younger than the population likely to have dostarlimab in the NHS. But they thought that the RUBY-1 population was broadly representative of NHS clinical practice. This was because people in the NHS would typically

need to have an ECOG performance status of 0 or 1 to be considered fit enough for triplet therapy (chemotherapy and immunotherapy). About 63.6% (239 of 376) of people with endometrial cancer with MSS or MMRp from RUBY-1 had a subsequent treatment after disease progression. These included chemotherapy, immunotherapy (such as pembrolizumab plus lenvatinib and pembrolizumab monotherapy), radiation therapy, hormone treatment and bevacizumab. At the IA2 data cut, more people in the placebo arm (72.8%, 134 of 184) had a subsequent treatment compared with in the dostarlimab arm (54.7%, 105 of 192). About 27.1% (102 of 376) of people with endometrial cancer with MSS or MMRp had subsequent immunotherapies. More people in the placebo arm (37%, 68 of 184) had subsequent immunotherapies compared with people in the dostarlimab arm (17.7%, 34 of 192). The EAG highlighted that the subsequent treatments used in RUBY-1 were not fully generalisable to NHS clinical practice. Specifically, bevacizumab monotherapy is not used for endometrial cancer in the NHS. Also, people whose cancer progresses after first-line immunotherapy would not usually have further immunotherapy in later lines of treatment. The committee recalled its discussion on managing endometrial cancer in the NHS (see section 3.2). It noted that the proportion of people with endometrial cancer with MSS or MMRp in RUBY-1 who went on to have a second-line treatment was likely higher than what would be seen in the NHS. The committee concluded that there was uncertainty on whether the findings of RUBY-1 were generalisable to people who would likely have dostarlimab added onto platinum-containing chemotherapy for endometrial cancer with MSS or MMRp in the NHS in particular. This was because of differences in subsequent treatments.

RUBY-1 results

3.6 The company presented PFS results from the IA1 and IA2 data cuts. At IA1, the median PFS was 9.9 months in the dostarlimab arm compared with 7.9 months in the placebo arm. The difference was statistically significant (hazard ratio [HR] 0.76, 95% confidence interval [CI] 0.59 to 0.98). But the difference was not statistically significant at the IA2 data

cut. The company considers the PFS results at IA2 to be commercial-in-confidence and so they cannot be reported here. The company also presented results for PFS2. This was defined as the time from treatment randomisation to the date of assessment of progression on the first subsequent anticancer treatment after study treatment or death by any cause (whichever is earlier) in people with endometrial cancer with MSS or MMRp at IA2. Median PFS2 was 24.6 months in the dostarlimab arm compared with 15.9 months in the placebo arm (HR 0.74, 95% CI 0.57 to 0.97). The EAG noted that results from this analysis showed a median improvement of 8.7 months in the time to a second progression event for people in the dostarlimab arm compared with people in the placebo arm.

The company did not present OS results at IA1 in its submission. At IA2, the median OS was 34.0 months in the dostarlimab arm compared with 27.0 months in the placebo arm. But the difference was not statistically significant (HR 0.79, 95% CI 0.60 to 1.04).

The committee noted that subgroup analyses in the TP53mut population (see section 3.4) showed better PFS benefit compared with that in the overall population at IA1 (HR 0.55, 95% CI 0.30 to 0.99). But it showed that OS benefit in this subgroup was not statistically significant (HR 0.59, 95% CI 0.33 to 1.03). The committee acknowledged that these subgroup analyses were post hoc and involved a small cohort, so they were not statistically powered to detect differences. But it recalled that endometrial cancer with the p53abn subtype is associated with poorer outcomes (see section 3.1). Having seen the relative clinical-effectiveness evidence from RUBY-1 for the TP53mut subgroup, the committee thought that it would be useful to see exploratory analyses in the p53abn and TP53mut subgroups.

The EAG highlighted that the RUBY-1 OS data was immature (see section 3.4 and section 3.5). The committee questioned the potential impact of subsequent treatments on OS in RUBY-1. The company explained that, in most people in RUBY-1, the cancer had progressed in

the first 12 months. The clinical experts thought that the OS data was relatively mature and thought that it was unlikely that the OS estimates would change substantially at final follow up. They highlighted that there is no data on the effectiveness of second-line immunotherapy after progression on first-line immunotherapy. But they thought it unlikely that this would have a substantial impact on OS in RUBY-1 because they did not expect later lines of immunotherapy to be effective. The committee questioned why 17.7% (34 of 192) of people in the dostarlimab arm of RUBY-1 had subsequent immunotherapy if it is not thought to be clinically effective. The company explained that RUBY-1 was a double-blind trial, so investigators were unaware of treatment group allocations. The committee concluded that there was uncertainty about the clinical effectiveness of adding dostarlimab to platinum-containing chemotherapy compared with platinum-containing chemotherapy alone.

Economic model

Company's modelling approach

3.7 To estimate the cost effectiveness of adding dostarlimab to platinum-containing chemotherapy to treat primary advanced or recurrent endometrial cancer with MSS or MMRp, the company used a partitioned survival model. This had 3 health states (progression-free, progressed disease and death), a 1-week cycle with no half-cycle correction and a 36-year time horizon. Data from the placebo arm of RUBY-1 was used to inform the comparator arm in the model (that is, platinum-containing chemotherapy). In line with the marketing authorisation, a 3-year stopping rule was applied for dostarlimab (see section 2.2). The committee concluded that the company's model was suitable for decision making.

Extrapolating survival over time

3.8 The company extrapolated the long-term effects of dostarlimab plus platinum-containing chemotherapy, and of platinum-containing chemotherapy alone, on PFS and OS in people with primary advanced or recurrent endometrial cancer with MSS or MMRp beyond the trial data. It

assumed non-proportional hazards for PFS and OS. This was because dostarlimab has a different mechanism of action compared with platinum-containing chemotherapy. There was a longer time on treatment with dostarlimab but only 6 cycles of platinum-containing chemotherapy in RUBY-1, and the commonly observed delayed response with immunotherapies. To extrapolate the long-term effects, it fitted independent parametric distributions to model PFS and OS in the 2 treatment arms. The EAG agreed with the company that the proportional hazard assumption did not hold. It also agreed that fitting independent parametric distributions to model PFS and OS in the 2 arms was reasonable.

Extrapolating PFS

3.9 The company used PFS data at IA1 from RUBY-1 to inform the extrapolation of PFS in the model because statistical significance for PFS was reached at IA1 in the trial (see section 3.6). Because standard parametric distributions did not provide plausible extrapolations, the company selected:

- the Odds k=3 flexible spline model for the dostarlimab arm
- the Normal, k=2 flexible spline model for the platinum-containing chemotherapy arm.

The EAG thought that the company's approach to modelling PFS was appropriate. It noted that the Kaplan–Meier curves for PFS at IA2 showed that the tail of the curve (from 32 months onwards) appeared to plateau for both treatment arms. So, the EAG thought that the company's approach of extrapolating PFS in the model based on PFS data at IA1 from RUBY-1 was reasonable. This was because modelling a long-term plateau in PFS would not be appropriate because outcomes for the endometrial cancer with MSS or MMRp population tend to be poor and relapses are likely. The EAG thought that the PFS curves at IA2 were more uncertain because of the censoring in RUBY-1. But the committee noted that censoring existed both at IA1

and IA2 data cuts, even though at different time points. The committee did not think that the PFS curve at IA2 was more uncertain than at IA1. This was because the observed plateau on the PFS Kaplan–Meier curves at IA1 was likely related to censoring. The committee noted that the PFS hazard rate plot was similar in both arms around year 2 in the model but the hazard rate plot for OS diverged. The EAG explained that this was likely because of the impact of subsequent immunotherapies on OS in the platinum-containing chemotherapy arm. It also noted that there was no impact of subsequent immunotherapies on the PFS curves. The committee thought that modelling based on longer follow up would be more informative and reliable. It concluded that it would prefer to see analyses using the more mature and most recent IA2 data cut to extrapolate PFS.

Extrapolating OS

3.10 The company used OS data at IA2 from RUBY-1 to inform the extrapolation of OS. To model OS over time, it selected the log-normal distribution for the dostarlimab arm and the log-logistic distribution for the platinum-containing chemotherapy arm. This was based on statistical and visual fit, and clinical validation of the extrapolated OS curves. The EAG agreed with the company's selection of curves. The EAG explained that the hazard rate plot based on the company's selected OS curves showed that the risk of death in the 2 arms gradually converged around year 15 and became similar after that. The EAG thought that the risk of death as shown in the platinum-containing chemotherapy arm was partly because of the impact of subsequent immunotherapies in both arms. This then led to similar risks of death in the 2 arms over time. The committee recalled its discussion on the uncertainties in the treatment effect of dostarlimab on OS (see section 3.6) and the impact of subsequent treatments on OS seen in RUBY-1. It concluded that there was high uncertainty in the modelling of OS and further explored the uncertainty of subsequent treatments on OS (see section 3.11).

Modelling subsequent treatments

3.11 To model subsequent treatments, the company adjusted data from RUBY-1 on subsequent treatment use. This was based on feedback from UK healthcare professionals about the options available in the relapsed setting for endometrial cancer with MSS or MMRp. At the clarification stage, the EAG highlighted that bevacizumab monotherapy is not used in the NHS to treat endometrial cancer. So, the company redistributed the proportions having bevacizumab monotherapy to other subsequent treatment options and, for the platinum-containing chemotherapy arm only, also to immunotherapy (51.2% to pembrolizumab plus lenvatinib). The EAG thought the company's approach of using adjusted RUBY-1 data to reflect NHS practice to be reasonable. It also agreed with the redistribution of bevacizumab monotherapy use in the dostarlimab arm. But it disagreed with the company's redistribution of bevacizumab monotherapy use to immunotherapy in the platinum-containing chemotherapy arm. The EAG explained that bevacizumab monotherapy is not a very effective treatment for endometrial cancer. So, reallocating its use to immunotherapy increased costs without a corresponding clinical benefit. Instead, it preferred to redistribute bevacizumab monotherapy use across all other non-immunotherapy treatments. In the EAG's base case, the proportion of people in the platinum-containing chemotherapy arm having subsequent pembrolizumab plus lenvatinib was 48.8%. It also noted that this redistribution of subsequent treatment had a small impact on the cost-effectiveness estimate.

The committee noted that the unadjusted subsequent immunotherapy use in RUBY-1 was different between the dostarlimab arm (17.7%, 34 of 192) and the placebo arm (37.0%, 68 of 184), despite the trial's randomised and double-blind design (see section 3.6). The company explained that the dostarlimab arm had fewer progression events, and so lower use of subsequent anticancer treatments. It highlighted that further analysis using data from IA2 showed that 51.2% of people in the platinum-containing chemotherapy arm had subsequent pembrolizumab plus lenvatinib. The company also explained that most progression events

occurred within the first 12 months, with some occurring between 12 and 24 months. So, it suggested that the follow-up data from RUBY-1 may have captured the benefits of subsequent treatment, as shown in the PFS IA2 data.

The clinical experts had differing views on whether the company's or the EAG's subsequent treatment distributions best reflected NHS clinical practice. One clinical expert thought that the company's approach of redistributing bevacizumab monotherapy use to pembrolizumab plus lenvatinib was reasonable. They also noted that bevacizumab and lenvatinib have similar mechanisms of action. The committee recalled its discussion that the subsequent treatment used in RUBY-1 did not reflect NHS practice (see section 3.5). It was aware that more people in the placebo arm had subsequent immunotherapies in RUBY-1 compared with people in the dostarlimab arm. But it noted that people in the dostarlimab arm also had second-line immunotherapies which is unlikely to happen in the NHS, and that the company did not adjust the OS hazard ratios for second-line treatments. This meant that the impact of subsequent treatment, particularly the impact of second-line immunotherapies on OS, was unclear. It was also unclear whether the estimates for treatment effect on OS from RUBY-1 was over- or under-estimated. This could also have had an impact on the assumptions about treatment waning in the longer term (see section 3.12).

Given the uncertainties in the treatment effect seen in RUBY-1, the committee would have preferred to see analyses for OS adjusting for benefits and costs of subsequent treatments, particularly subsequent immunotherapies. It thought that further understanding of the impact of these subsequent treatments on both PFS and OS Kaplan–Meier and extrapolated curves in the dostarlimab and placebo arms, using data from the latest data cut at IA2, would be helpful. It requested that the company provide analyses exploring the impact of subsequent immunotherapies on

dostarlimab's treatment effect on both PFS and OS, using data from IA2. For example, this could include:

- using PFS2 (see section 3.6) to address pre- and post-progression survival
- presenting Kaplan–Meier curves for PFS and OS with and without subsequent immunotherapies to assess the potential impact of subsequent immunotherapies on the treatment effect
- presenting Kaplan–Meier curves for PFS and OS that account for the potential differences in the timing of subsequent immunotherapy started across the 2 treatment arms (for example, using treatment switching methods) because people in the 2 arms may have started subsequent immunotherapies at different time points in RUBY-1, which may have an impact on the treatment effect of dostarlimab.

Treatment-effect waning

3.12 In its base case, the company assumed that treatment waning was captured in the modelled OS. This assumption was based on RUBY-1, which the company suggested had shown a sustained OS benefit in the dostarlimab arm compared with the placebo arm. The company also highlighted that its independent modelling of OS curves should have implicitly captured any waning of the treatment effect. The EAG thought that the company's modelling of OS was generally appropriate, and agreed with the company that treatment waning was likely captured in the OS extrapolations. This was because the PFS plots showed that the risk of progression was similar for both arms after about 2 years. But the EAG noted that, at IA2, the Kaplan–Meier curve for OS in the 2 treatment arms appeared to converge from month 30 then diverge again from month 36 onwards. So, it thought that a scenario of gradual treatment-effect waning may be informative. The company also provided 2 treatment-effect waning scenarios: one with a 2-year stopping rule and another with a 3-year stopping rule. This was in line with dostarlimab's marketing authorisation (see section 2.2). The committee did not think that treatment-effect waning was implicitly captured in the model. This was because the

company's extrapolated OS curves with and without incorporated treatment waning were different. The committee recalled the uncertainties associated with the evidence on OS. These included data immaturity, heavy censoring, the potential impact of subsequent treatments on OS and the lack of adjustment of subsequent treatments on OS (see section 3.11). It thought that there was high uncertainty related to the treatment-effect waning assumptions. It concluded that it would like to have seen evidence and analyses in which:

- including or excluding treatment-effect waning in the model was sufficiently justified
- the impact of second-line treatment effect on OS was adjusted for
- the potential interplay between the impact of subsequent treatments on OS and treatment-effect waning is explored.

Time on treatment

3.13 To model time on treatment in its base case, the company used weighted completion rates for platinum-containing chemotherapy from RUBY-1 across both treatment arms during the first 6 cycles. For dostarlimab, it used completion rates for the first 6 cycles, followed by time to treatment discontinuation Kaplan–Meier data adjusted for relative dose intensity up to 3 years. The EAG thought that using completion rates did not fully capture the cost of starting treatment in either arm. This was because the intention-to-treat population included people who were randomised but did not start treatment. So, the completion rate for the first treatment cycle in the model was less than 100%. To capture the full treatment costs in its base case, the EAG preferred to use time to treatment discontinuation Kaplan–Meier data for both arms. In addition, for dostarlimab, it used the relative dose intensity from cycle 1 up to 3 years. The committee concluded that the EAG's approach to modelling time on treatment was appropriate.

Resource use

Health-state resource use for dostarlimab arm

3.14 In its base case, the company modelled health-state resource use for the dostarlimab arm based on advice from 6 UK healthcare professionals. It assumed that, after the first 18 weeks of treatment, people having dostarlimab who were progression-free would have specific resource use that differed from that in the platinum-containing chemotherapy arm. The EAG disagreed and thought that, after 3 years of dostarlimab monotherapy, people who were progression-free would incur the same resource use as that in the platinum-containing chemotherapy arm after the first 18 weeks of treatment. The clinical experts thought that the level of surveillance would be similar for people who are progression-free after treatment, regardless of whether they have had dostarlimab or platinum-containing chemotherapy. At the committee meeting, the company explained that it agreed with the EAG's modelling. The committee concluded that it preferred the EAG's approach to modelling health-state resource use for the dostarlimab arm.

Costs

Oral administration cost for lenvatinib

3.15 In its base case, the company included an oral administration cost for lenvatinib to account for specialist oversight related to procurement, prescribing, dispensing and administration. The EAG disagreed and excluded this cost from its base case. It noted that, based on published advice, people are likely to take lenvatinib at home, so there would likely be no administration cost to the NHS. It highlighted that these administration costs only affect the platinum-containing chemotherapy arm because pembrolizumab plus lenvatinib is not used after dostarlimab treatment. The clinical experts agreed that there is likely no cost associated with administering lenvatinib. But they noted that there would be costs related to managing its side effects. The EAG confirmed that these were accounted for in the monitoring costs already included in the model. The committee concluded that the oral administration cost of lenvatinib should be excluded from the model.

Severity

3.16 NICE's methods on conditions with a high degree of severity did not apply.

Cost-effectiveness estimates

Committee's preferred assumptions

3.17 The committee's preferred assumptions were to:

- use the EAG's approach to model time on treatment (see section 3.13)
- use the EAG's approach to model health-state resource use for the dostarlimab arm (see section 3.14)
- exclude the cost of oral administration for lenvatinib (see section 3.15).

Acceptable ICER

3.18 NICE's manual on health technology evaluations notes that, above a most plausible incremental cost-effectiveness ratio (ICER) of £20,000 per quality-adjusted life year (QALY) gained, judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. But it will also take into account other aspects including uncaptured health benefits. The committee noted the high level of uncertainty in the evidence and company's modelling, specifically that:

- longer data cut of PFS was not statistically significant and OS data was immature (see section 3.6)
- subsequent treatments from RUBY-1 may not be generalisable to NHS clinical practice and its impact on OS estimates (see section 3.5 and section 3.11)
- the extrapolation of PFS (see section 3.9).
- the extrapolation of OS (see section 3.103.12).
- modelling of subsequent treatment (see section 3.113.12).

- whether treatment-effect waning has been implicitly included in the model (see section 3.12).

The committee thought that the further analyses requested (see section 3.19) would likely affect these uncertainties. So, the committee concluded that it did not have an acceptable ICER level.

Areas needing clarification and further analyses

3.19 The committee decided that there were several areas of uncertainty (see section 3.18). It would like clarification, further evidence and analyses:

- using the more mature and most recent IA2 data cut to extrapolate PFS (see section 3.9)
- for OS adjusting for benefits and costs of the second-line treatments that reflect NHS clinical practice and using PFS data at IA2 (see section 3.10 and section 3.11)
- in which including or excluding treatment-effect waning in the model is sufficiently justified, and the potential interplay between the impact of subsequent treatments on OS and treatment-effect waning is explored (see section 3.12)
- specific for the p53-abnormal or TP53mut subgroups, including cost-effectiveness estimates, that include relevant diagnostic testing costs (see section 3.4, section 3.6 and section 3.20).

Company and EAG cost-effectiveness estimates

3.20 The committee noted that there was little difference between the cost-effectiveness estimates in the company's and the EAG's base cases. The exact figures cannot be reported because of confidential discounts for dostarlimab, pembrolizumab and lenvatinib. But both the company's and the EAG's base case ICERs were higher than what NICE normally considers an acceptable use of NHS resources. The committee thought that there were important uncertainties that need to be addressed to inform decision making (see section 3.18 and section 3.19). So, it was unable to conclude that dostarlimab was a cost-effective option for routine

commissioning to treat primary advanced or recurrent endometrial cancer with MSS or MMRp in adults when systemic treatment is suitable.

Managed access

3.21 Having concluded that dostarlimab plus platinum-containing chemotherapy could not be recommended for routine use in the NHS, the committee then considered whether it could be recommended for use during a managed access period for treating primary advanced or recurrent endometrial cancer with MSS or MMRp. The committee noted that the company had not submitted a managed access proposal. It recalled the clinical experts' views that OS estimates are unlikely to change substantially at final follow up, expected in 2026 (see section 3.6). It also noted that there were no plausible cost-effective ICERs. So, the committee concluded that a recommendation with managed access could not be made for dostarlimab plus platinum-containing chemotherapy to treat primary advanced or recurrent endometrial cancer with MSS or MMRp in adults when systemic treatment is suitable.

Other factors

Equality

3.22 Stakeholders highlighted that people from Black ethnic background have a higher incidence of the more aggressive p53-abn subtype of endometrial cancer with MSS or MMRp, which is associated with poorer outcomes (see section 3.1). The committee requested further analyses for consideration in the p53-abnormal or TP53mut subgroups (see section 3.19).

Uncaptured benefits

3.23 The committee acknowledged that there is a high unmet need for early treatment for people with primary advanced or recurrent endometrial cancer with MSS or MMRp (see section 3.2). It acknowledged that this would be the first immunotherapy available for this condition at first line. It considered whether there were any uncaptured benefits of dostarlimab

plus platinum-containing chemotherapy. It did not identify additional benefits of dostarlimab plus platinum-containing chemotherapy not captured in the economic modelling. So, the committee concluded that all additional benefits of dostarlimab plus platinum-containing chemotherapy had already been taken into account.

Conclusion

Recommendation

3.24 The committee noted that the company's and the EAG's base case ICERs were higher than what NICE normally considers an acceptable use of NHS resources. It recalled that there were important uncertainties that need to be addressed to inform decision making. So, dostarlimab plus platinum-containing chemotherapy could not be recommended to treat primary advanced or recurrent endometrial cancer with MSS or MMRp in adults when systemic treatment is suitable. Also, further evidence and analyses are needed.

4 Evaluation committee members and NICE project team

Evaluation committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by committee A.

Committee members are asked to declare any interests in the technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each evaluation committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Chair

Radha Todd

Chair, technology appraisal committee A

NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser, a project manager and an associate director.

Sharlene Ting

Technical lead

Yelan Guo

Technical adviser

Jennifer Upton and Greg O'Toole

Project managers

Ian Watson

Associate director

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