NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Draft guidance consultation

Mirvetuximab soravtansine for treating folate receptor-alpha-positive platinum-resistant advanced epithelial ovarian, fallopian tube or primary peritoneal cancer [ID6442]

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using mirvetuximab soravtansine 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?

Issue date: November 2025

Note that this document is not NICE's final guidance on mirvetuximab soravtansine. 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- After considering these comments, the committee will prepare the final draft guidance.
- Subject to any appeal by stakeholders, the final draft guidance may be used as the basis for NICE's guidance on using mirvetuximab soravtansine in the NHS in England.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: 17 December 2025
- Second evaluation committee meeting: TBC
- Details of the evaluation committee are given in section 4

1 Recommendations

1.1 Mirvetuximab soravtansine should not be used to treat folate receptor-alpha (FR-alpha)-positive, platinum-resistant, high-grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer in adults after 1 to 3 lines of systemic treatment.

1.2 This recommendation is not intended to affect treatment with mirvetuximab soravtansine 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

Mirvetuximab soravtansine is not required to be funded and should not be used routinely in the NHS in England for the condition and population in the recommendations.

This is because the available evidence does not suggest that mirvetuximab soravtansine is value for money in this population.

Why the committee made these recommendations

Usual treatment for FR-alpha-positive, platinum-resistant, high-grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer after 1 to 3 lines of systemic treatment is chemotherapy.

Clinical trial evidence shows that mirvetuximab soravtansine increases how long people have before their condition gets worse and how long they live compared with chemotherapy.

But there are uncertainties in the economic model, including:

- how health-related quality of life differs for people having mirvetuximab soravtansine and people having chemotherapy
- how long people live after having mirvetuximab soravtansine and after having chemotherapy
- the average age of people starting treatment.

Even when considering the condition's severity, and its effect on quality and length of life, the most likely cost-effectiveness estimates are above the range that NICE considers an acceptable use of NHS resources. So, mirvetuximab soravtansine should not be used.

2 Information about mirvetuximab soravtansine

Marketing authorisation indication

2.1 Mirvetuximab soravtansine (Elahere, AbbVie) is indicated for 'the treatment of adult patients with folate receptor-alpha (FRα) positive, platinum-resistant high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received one to three prior systemic treatment regimens'.

Dosage in the marketing authorisation

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

Price

2.3 The list price of mirvetuximab soravtansine is £4,950 per 100-mg vial.

2.4 The company has a commercial arrangement, which would have applied if mirvetuximab soravtansine had been recommended.

Carbon Reduction Plan

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

3 Committee discussion

The evaluation committee considered evidence submitted by AbbVie, 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

Details of condition

3.1 There are no known specific causes of epithelial ovarian, fallopian tube or primary peritoneal cancer (from now, ovarian cancer). Risk increases with age, a family history of ovarian cancer and inherited gene mutations. Early-stage ovarian cancer is underdiagnosed because it usually causes vague or no symptoms. This means that most people have advanced cancer at diagnosis. The 5-year survival rate for people diagnosed with advanced cancer is estimated to be between 14% and 26%. Symptoms at diagnosis include gastrointestinal issues, ascites, pleural effusion and venous thromboembolism. Symptoms worsen as the condition progresses. While the condition initially responds to treatment for many people, most go on to develop resistance to chemotherapy. Platinum resistance is defined as disease progression within 6 months after a platinum-based chemotherapy regimen. This can occur after 1 or more, and up to several courses of, platinum-based chemotherapy. The clinical experts explained that there is a lack of effective treatment options for people with platinum-resistant ovarian cancer. The committee concluded that there is a need for new treatments for people with platinum-resistant ovarian cancer.

Effects of condition and treatment on quality of life

3.2 Ovarian cancer has a substantial impact on quality of life for people with the condition and their families. Statements submitted by the patient experts explained that many people who are diagnosed are in their 50s and 60s, and lead active lives that include work and family responsibilities. A patient expert said that they often worked full time, so had to call in sick

and take time off work because of symptoms or side effects from treatment. Physical symptoms caused by the condition included ascites and gastrointestinal issues. A patient expert explained that chemotherapy treatment can have long-lasting effects and that these had a severe negative impact on their quality of life. They lost their sense of taste and smell, and had a poor appetite as a result. They said that chemotherapy treatment made them feel very low and tired. The patient experts also said that knowing there is a lack of effective treatment options for platinum-resistant ovarian cancer can have a severe psychological and emotional impact. They said that a new treatment option that could improve survival and quality of life in a population with limited options would offer hope. The committee concluded that there is a high disease burden for people with ovarian cancer, and the availability of a new treatment would be beneficial to people with the condition.

Clinical management

Treatment options and comparators

3.3 NICE has recommended pegylated liposomal doxorubicin (PLD) and paclitaxel for treating recurrent ovarian cancer (see NICE's technology appraisal guidance on topotecan, pegylated liposomal doxorubicin hydrochloride, paclitaxel, trabectedin and gemcitabine for treating recurrent ovarian cancer, from here TA389). The company used pooled chemotherapy (PLD, paclitaxel and topotecan) as the comparator in its analysis of mirvetuximab soravtansine (from now, mirvetuximab). The EAG noted that topotecan is not recommended within its marketing authorisation for treating recurrent platinum-resistant or platinum-refractory ovarian cancer in TA389. The clinical experts said that topotecan is rarely used in clinical practice. The committee concluded that the relevant comparator was pooled chemotherapy, including PLD and paclitaxel.

Clinical effectiveness

MIRASOL trial

3.4 The company presented clinical evidence for mirvetuximab from 3 clinical trials: MIRASOL, FORWARD-1 and SORAYA. MIRASOL and FORWARD-1 were phase 3, randomised, open-label studies, and SORAYA was a phase 2, single-arm study. The comparator in MIRASOL and FORWARD-1 was investigator's choice of chemotherapy, including paclitaxel, PLD or topotecan (from now, pooled chemotherapy). The key clinical evidence for mirvetuximab came from MIRASOL (n=453). This was because the population in FORWARD-1 included a broader range of FR-alpha expression than specified in the marketing authorisation for mirvetuximab. Also, SORAYA did not have a comparator arm. MIRASOL was done at 136 sites across multiple countries including the UK. The company presented evidence from the September 2024 data cut of MIRASOL. The primary outcome of MIRASOL was investigator-assessed progression-free survival (PFS). Other key outcomes included overall survival (OS), objective response rate and EQ-5D-5L.

Generalisability of MIRASOL

3.5 The EAG highlighted uncertainties with the generalisability of MIRASOL to UK clinical practice. It noted that the median age of people in MIRASOL was lower than the expected population in NHS clinical practice. The median age at baseline in MIRASOL was 64 years in the mirvetuximab arm and 62 years in the pooled chemotherapy arm. This compared with a median age at diagnosis of 68 years in a study by Pickwell-Smith et al. (2025). This was a retrospective cohort study of people diagnosed with ovarian cancer in England between 2016 and 2017. The NHS England Cancer Drugs Fund clinical lead (from here, Cancer Drugs Fund lead) said that, over the previous 12 months, the average age of people starting first-line maintenance treatment with poly-ADP polymerase (PARP) inhibitors for ovarian cancer in England was 69 years. The clinical experts said that, in clinical practice, the mean age at diagnosis of people with

ovarian cancer was 66 years. This was based on the National Ovarian Cancer Audit State of the Nation Report published in 2025. They said that age of diagnosis is unlikely to affect outcomes in ovarian cancer and that it is common for clinical trials to have younger people than in clinical practice.

The EAG also noted that the proportion of people who had had treatment with a PARP inhibitor was likely to be lower in MIRASOL than in clinical practice. In MIRASOL, 54.6% of people in the mirvetuximab arm and 57.0% of people in the pooled chemotherapy arm had had a PARP inhibitor. The EAG explained that the results of MIRASOL could have overestimated the benefits of chemotherapy. This was because prior treatment with PARP inhibitors can reduce sensitivity to subsequent chemotherapy after disease progression. The clinical experts thought that the proportion of people previously treated with a PARP inhibitor in MIRASOL was representative of clinical practice. They also said that they did not expect prior PARP inhibitor use to affect outcomes. The EAG also highlighted that 23.5% of people in the comparator arm of MIRASOL had topotecan, but clinical advice indicated that topotecan is rarely used in clinical practice. The EAG said that topotecan has similar effectiveness to other chemotherapy regimens, so this was not expected to affect the generalisability of MIRASOL. The clinical experts confirmed that topotecan has similar clinical effectiveness to PLD and paclitaxel. The committee noted that there may be some differences between the MIRASOL population and the expected population in NHS clinical practice. But it concluded that these were unlikely to affect the generalisability of MIRASOL. So, it concluded that MIRASOL was acceptable for decision making.

PFS and OS

3.6 In MIRASOL, mirvetuximab showed a statistically significant improvement in PFS and OS compared with pooled chemotherapy. The hazard ratio for PFS was 0.63 (95% confidence interval [CI], 0.51 to 0.79) and for OS was

0.68 (95% CI 0.54 to 0.84). The company also provided a post-hoc analysis of FORWARD-1 that included only people who met the marketing-authorisation requirement for FR-alpha expression. The hazard ratio for PFS in the FORWARD-1 post-hoc analysis was 0.65 (95% CI 0.41 to 1.03) and for OS was 0.68 (95% CI 0.41 to 1.12). It also provided a meta-analysis that pooled the results of MIRASOL and the FORWARD-1 post-hoc analysis. The EAG noted that the results of the meta-analysis were statistically significant and consistent with the results of MIRASOL and FORWARD-1. The committee concluded that mirvetuximab improved OS and PFS compared with pooled chemotherapy for treating FR-alpha-positive platinum-resistant ovarian cancer.

Subgroup analysis

3.7 The company said that the subgroup analyses in MIRASOL were exploratory only and were not appropriate for decision making. But the EAG noted that there may be clinical rationale for a different prognosis in subgroups based on length of primary platinum-free interval. The primary platinum-free interval is the period after the first course of platinum-based chemotherapy treatment for ovarian cancer. During this time people do not need a further course of chemotherapy. A primary platinum-free interval of 6 months or less suggests that the ovarian cancer had had responded poorly to first-line treatment. The EAG's clinical experts said it was plausible that a longer primary platinum-free interval would lead to a better response to mirvetuximab treatment. The OS hazard ratio for the subgroup of people with a primary platinum-free interval of more than 6 months was 0.54 (95% CI 0.42 to 0.71). It was 1.07 (95% CI 0.74 to 1.57) for the subgroup of people with a primary platinum-free interval of 6 months or less. The EAG said that the subgroup analyses should be interpreted with caution because the PFS results were not consistent with the OS results. The PFS hazard ratio for the subgroup of people with a primary platinum-free interval of more than 6 months was 0.62 (95% CI, 0.48 to 0.80). It was 0.68 (95% CI, 0.47 to 0.98) for the subgroup of people with a primary platinum-free interval of 6 months of less.

The committee noted that the OS hazard ratio for the subgroup with a primary platinum-free interval of more than 6 months was more favourable for mirvetuximab than the OS hazard ratio for the whole MIRASOL population. It also thought that this subgroup group was identifiable in clinical practice. But the committee thought that it would be helpful to have more information about the characteristics of this subgroup in clinical practice. It concluded that mirvetuximab may be more clinically effective in people with a primary platinum-free interval of more than 6 months.

Cost effectiveness

Company's modelling approach

3.8 The company presented a partitioned survival model with 3 health states: pre-progression, post-progression and death. The model used clinical data from MIRASOL, had a 1-week cycle length, and included a half-cycle correction for PFS and OS. The EAG thought the model structure was appropriate given the high level of maturity of the observed data from MIRASOL. The committee concluded that the model structure was appropriate.

The committee recalled its conclusion that the relevant comparator was pooled chemotherapy, including PLD and paclitaxel (section 3.3). It also recalled that the clinical experts thought that topotecan had similar efficacy to other chemotherapy regimens (section 3.5). It recalled its conclusion that the inclusion of topotecan in the comparator arm of MIRASOL was unlikely to affect the generalisability of the trial. The committee concluded that it was acceptable to use data from MIRASOL in the model. But, given that it preferred to exclude topotecan as a comparator, the committee concluded to exclude the cost of topotecan.

Modelling OS

3.9 The company's model used a time horizon of 40.8 years, which exceeded the length of the trials. So, to extrapolate beyond the end of the trials, the company fitted independent parametric models to the mirvetuximab and pooled chemotherapy OS data from MIRASOL. The company adjusted the OS curves so that survival did not exceed the survival of the general population. In its base case, the company chose the log-logistic distribution for mirvetuximab OS and the Weibull distribution for pooled chemotherapy OS. The company consulted clinical experts, who expected survival rate in the mirvetuximab arm to be between 8% and 12% at 5 years. But they were uncertain about the survival rate at 10 years. They also expected survival in the pooled chemotherapy arm to be between 0% and 5% at 5 years and 0% at 10 years. For mirvetuximab, the company said that the log-logistic distribution implied a hazard function that was consistent with the observed hazard in the mirvetuximab arm (initially increasing then decreasing). The log-logistic distribution predicted a 5-year survival rate of 10%, which the company noted was in the range that its clinical experts had predicted. The 10-year survival rate predicted using the log-logistic distribution was 3%, which the company said was plausible given mirvetuximab's mechanism of action. For pooled chemotherapy, the company said that the Weibull distribution had the best statistical fit. It was also considered plausible by its clinical experts because it aligned with their prediction of 0% to 5% survival at 5 years.

The EAG preferred to use the gamma distribution for both mirvetuximab and pooled chemotherapy OS in its base case. For the mirvetuximab arm, the EAG thought that using the log-logistic distribution for mirvetuximab was implausible. This was because its clinical experts expected survival at 10 years to be 0% in both treatment arms. It said that the gamma distribution provided a better statistical and visual fit, and noted that the company's clinical experts considered it to be plausible. Five-year survival in the mirvetuximab arm with the gamma distribution was predicted to be

4% and 10-year survival was predicted to be 0%. The EAG also said that the Kaplan–Meier curve for mirvetuximab should be interpreted with caution after month 24 because of increased censoring. For pooled chemotherapy, the EAG said the gamma distribution had a good fit to the observed hazard. It was also consistent with survival predictions from both the company and EAG's clinical experts.

During the committee meeting, the clinical experts said that survival for people having chemotherapy is very poor. They said that it was difficult to predict the long-term survival of people having mirvetuximab, but it was plausible that about 10% could live beyond 5 years. This was because of mirvetuximab's novel mechanism of action. The committee noted the uncertainty associated with the long-term survival of people having mirvetuximab. It agreed with the EAG that the later part of the Kaplan–Meier curve should be interpreted with caution because of heavy censoring. It thought that the log-logistic distribution had a poor visual fit towards the end of the mirvetuximab Kaplan–Meier curve. The committee noted that the model included an adjustment for general population mortality. But it thought that the hazard function implied by the log-logistic distribution (initially increasing then decreasing) was implausible in an older population. This was because the hazards would be expected to increase over time as more people die of old age. The committee noted that the log-logistic hazards appeared to be inconsistent with observed hazards because the observed hazard increased again after having initially increased then decreased. It thought that the gamma distribution was a better fit and recalled that the clinical experts thought the gamma distribution to be a plausible extrapolation in both treatment arms. It thought that there was not a strong justification for using different distributions in each arm. So, the committee concluded that the EAG's approach to modelling OS was more appropriate than the company's, but that there was uncertainty associated with both approaches. The committee thought that it would be useful for the company to provide a

more recent data cut from MIRASOL if available. It also thought that it would be useful to have alternative data sources for pooled chemotherapy to help validate the pooled chemotherapy OS extrapolations.

Health-state utilities

3.10 The company included treatment-dependent utility values for the pre- and post-progression health states. It preferred to use health-state utility values from MIRASOL in the mirvetuximab arm and from Havrilesky et al. (2009) in the pooled chemotherapy arm. The company said that the utility values from MIRASOL may have overestimated the health-related quality of life (HRQoL) of people having chemotherapy. This was because the EQ-5D questionnaire was only administered at the start of each chemotherapy cycle. So, it may not have captured the impact of the side effects of chemotherapy. In the pre-progression state, the utility value from MIRASOL was 0.737 for mirvetuximab and 0.706 for pooled chemotherapy. The company preferred to use a pre-progression health-state utility value for pooled chemotherapy of 0.500. It said that utilities were expected to differ substantially between the mirvetuximab and pooled chemotherapy arms in the pre-progression health state because they had differing adverse-event profiles. Mirvetuximab showed a lower frequency of grade 3 and above treatment-emergent adverse events and serious adverse events. The company also said that mirvetuximab was associated with higher response rates and reduced time to response compared with pooled chemotherapy, which could have led to improved HRQoL. It noted that mirvetuximab showed statistically significant improvements compared with pooled chemotherapy in the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-OV30 (EORTC QLQ-OV30). In the post-progression state, the utility values from MIRASOL were 0.655 for mirvetuximab and 0.625 for pooled chemotherapy. The company preferred to use a post-progression health-state utility value for pooled chemotherapy of 0.400. It argued that utilities were also expected to differ substantially in the post-progression state. This was because, at the point of progression, people

who had mirvetuximab were expected to have a better HRQoL than people having chemotherapy because of reduced tumour volume and disease burden. The company also noted that mirvetuximab was associated with a statistically significant improvement in time to second disease progression compared with pooled chemotherapy (HR 0.59, 95% CI 0.48 to 0.73).

The company's preferred utilities for pooled chemotherapy from Havrilesky et al. were based on a time trade-off exercise using vignettes. The vignettes had been valued by a mixed sample of 13 people with the condition and 37 female members of the public. So, the EAG said that the company's approach was not consistent with the NICE reference case. Section 4.3.4 in NICE's health technology evaluations manual states that the valuation of HRQoL measured by people with the condition should be based on a valuation of public preferences from a representative sample of the UK population. The EAG also noted some inconsistencies in the results from Havrilesky et al. These included a higher utility for people having grade 3 to 4 adverse events than for people having grade 1 to 2 adverse events. The EAG thought that the company's approach was implausible and lacked face validity. This was because the company's mirvetuximab post-progression utility value (0.655) was higher than its pooled chemotherapy pre-progression utility value (0.500). The EAG also highlighted that the large difference in post-progression utilities between mirvetuximab (0.655) and pooled chemotherapy (0.400) was not supported by clinical logic. It thought that the size of the difference was unlikely to be plausible because people would be expected to have similar subsequent treatments after progression in both arms. The EAG thought that the timing of the EQ-5D measurement in MIRASOL was not a meaningful source of bias. It compared the utilities from MIRASOL with those from the OVA-301 clinical trial (considered in TA389), in which the EQ-5D was measured at the start and the end of each treatment cycle. The pooled chemotherapy utilities in OVA-301 (0.718 in the pre-

progression state and 0.649 in the post-progression state) were similar to those in MIRASOL (0.706 in the pre-progression state and 0.625 in the post-progression state). The EAG concluded that the health-state utility values from MIRASOL showed a difference in HRQoL between the mirvetuximab and chemotherapy arms that was more likely to be plausible than the values in the company's approach. So, the EAG preferred to use the utility values from MIRASOL in its base case. It also noted that the company did not include disutilities associated with adverse events in its base case. The EAG preferred to incorporate these. It acknowledged the risk of double counting but said that this was likely mitigated by the missing EQ-5D data in MIRASOL.

The patient experts emphasised that people having mirvetuximab have a substantially better quality of life compared with people having chemotherapy. One patient expert said that, when they had chemotherapy, they felt tired and low because of the side effects and had to take time off work. But they said that with mirvetuximab they were able to live a relatively normal live and felt significantly less anxious and depressed. The patient experts also said that people have fewer and less-serious side effects with mirvetuximab than with chemotherapy. The clinical experts noted that any ocular side effects of mirvetuximab tended to be resolved quickly. They highlighted that the proportion of people who stopped treatment because of these was small.

The committee agreed with the EAG that the company's preferred source for the utility values in the pooled chemotherapy arm was not consistent with the NICE reference case. It also agreed that the company's approach lacked face validity because of the large difference in the mirvetuximab post-progression utility and the pooled chemotherapy pre-progression utility. The committee noted that there was uncertainty in the difference in HRQoL between people having mirvetuximab and people having chemotherapy. It highlighted that the MIRASOL utility values were

consistent with the utility values used in previous NICE technology appraisals. The EAG provided a scenario analysis that used the pre- and post-progression utility values from TA389 for both treatment arms. The committee noted that the cost-effectiveness results of this scenario were higher than the results of the EAG base case using the MIRASOL utility values. It noted that the MIRASOL utility values suggested a small difference in HRQoL between people having mirvetuximab and people having chemotherapy. But, based on the patient and clinical expert feedback, the committee thought it was possible that the MIRASOL utilities did not fully capture the improvement in HRQoL potentially offered by mirvetuximab compared with pooled chemotherapy. But it thought that the MIRASOL utilities were more methodologically robust than the utilities from Havrilesky et al. for pooled chemotherapy preferred by the company. So, the committee concluded that it was more appropriate to use the MIRASOL health-state utility values in both treatment arms. It also preferred to include the disutilities associated with adverse events to capture the impact of side effects on HRQoL.

Adverse events

3.11 The company and EAG had differing approaches to modelling adverse events for the following assumptions:

- The company assumed the duration of grade 2 or higher ocular adverse events to be 4 weeks in its base case, but the EAG preferred to assume 8 weeks. The EAG thought ocular adverse events were unlikely to resolve in 4 weeks.
- The company assumed the frequency of ophthalmology visits for grade 2 or higher ocular adverse events to be once every 6 weeks, but the EAG preferred to assume once every 3 weeks.
- For the costs of managing anaemia and neutropenia, the company preferred to use a weighted average of day case, non-elective inpatient long stay and non-elective inpatient short stay. This was because some people develop sepsis that needs to be managed in hospital. The EAG

preferred to assume that anaemia and neutropenia were managed as day cases only.

- The company preferred to assume that parenteral nutrition was needed to manage fatigue, but the EAG preferred to exclude this cost and assume that fatigue is self-managed.

The clinical experts said that grade 2 or higher ocular adverse events resolve relatively quickly. So, it would be more reasonable to assume people have an ophthalmology visit every 6 weeks instead of every 3 weeks. They also said that, while some people with neutropenia develop sepsis that needs managing in hospital, this happens rarely. The clinical experts also said that fatigue is managed with parenteral nutrition only in highly severe cases. Based on feedback from the clinical experts, the committee concluded that it preferred to assume:

- a duration of grade 2 or higher ocular adverse events of 4 weeks
- a frequency of ophthalmology visits of every 6 weeks
- that anaemia and neutropenia is managed as a day case
- that fatigue is self-managed.

Relative dose intensity

3.12 The company used a single average relative dose intensity (RDI) value for each treatment used in the model. The EAG preferred to use a cycle-specific RDI that separately accounted for the proportion of people having treatment in each cycle and the average RDI among people treated. The EAG said that this approach allowed for a more accurate estimate of drug use and wastage by explicitly incorporating missed doses, reduced dosing and time dependency. The committee noted that it is common to use a single average RDI value when cycle-specific RDI data is not usually available. Because cycle-specific RDI data was available for this appraisal, the committee concluded that the EAG's cycle-specific RDI approach more accurately reflected drug use and wastage in the model.

Vial sharing

3.13 The company assumed 50% vial sharing for mirvetuximab and pooled chemotherapy. It noted that, in NICE's technology appraisal guidance on trastuzumab deruxtecan for treating HER2-positive unresectable or metastatic breast cancer after 1 or more anti-HER2 treatments, the committee concluded that vial sharing should be assumed in 50% of cases for trastuzumab deruxtecan. This was because the Cancer Drugs Fund lead had said that NHS England encourages vial sharing. The company thought that a similar degree of vial sharing may be expected for mirvetuximab. It also noted that its clinical experts said that vial sharing was common for PLD and paclitaxel. But the EAG preferred to assume no vial sharing for mirvetuximab and 50% vial sharing for pooled chemotherapy. This was because its clinical experts were uncertain about the plausibility of vial sharing for mirvetuximab because it would not be reasonable to delay treatment so that vials could be shared. The Cancer Drugs Fund lead said that vial sharing for mirvetuximab was unlikely to be feasible because the anticipated eligible population for mirvetuximab was substantially lower than for trastuzumab deruxtecan. This suggests it is unlikely that multiple people in each hospital will need treatment at the same time. Based on the Cancer Drugs Fund lead's opinion, the committee concluded that the model should include not include vial sharing for mirvetuximab and should assume 50% vial sharing for pooled chemotherapy.

Clinical management costs

3.14 The company sourced its resource-use frequencies from NICE's technology appraisal guidance on bevacizumab in combination with gemcitabine and carboplatin for treating the first recurrence of platinum-sensitive advanced ovarian cancer. It assumed that people in the pre-progression state had a gynaecological oncology consultation once monthly. In the post-progression state, it assumed that people had a gynaecological oncology consultation once every 3 months. The EAG's

clinical experts said that visit frequency depended on whether a person was having treatment or not. They explained that a gynaecological oncology consultation took place once monthly while a person was on treatment and once every 3 months while they were off treatment. The EAG thought that the company's resource-use frequencies in the pre-progression state were broadly consistent with its clinical expectation. But, in the post-progression state, it preferred to assume that people had a gynaecological oncology consultation once monthly for the average duration of post-progression chemotherapy and then once every 3 months. During the committee meeting, the clinical experts explained that they tend to see people with the condition around once every 6 weeks. This is regardless of whether they are on or off treatment, or whether their cancer has progressed. Based on the advice from the clinical experts, the committee concluded that the model should include gynaecological oncology consultations once every 6 weeks in both the pre-progression and post-progression health states.

Mirvetuximab duration of treatment

3.15 The company modelled duration of treatment for mirvetuximab by fitting an exponential distribution to the duration-of-treatment curve from MIRASOL because it had the best statistical fit. The EAG thought that the company's approach underestimated mirvetuximab duration of treatment, especially in the early part of the Kaplan–Meier curve. It preferred to use the observed Kaplan–Meier data up to 120 weeks, followed by the exponential extrapolation. The committee noted that this issue had a small impact on the incremental cost-effectiveness ratio (ICER). It agreed that the company's approach may have slightly underestimated mirvetuximab duration of treatment and concluded it preferred the EAG's approach.

Subsequent treatment

3.16 In its base case, the company included mirvetuximab as a subsequent treatment for the 9% of people in the chemotherapy arm who had a subsequent treatment. This was based on the treatment crossover in

MIRASOL. It also provided a scenario analysis that used a rank-preserving structural-failure time model to adjust for the treatment crossover and removed the mirvetuximab costs post-progression in the pooled chemotherapy arm. The EAG thought that the inclusion of mirvetuximab as a subsequent treatment in the chemotherapy arm was inappropriate because mirvetuximab is not available in the NHS. It preferred to incorporate the company's scenario analysis in its base case and removed the cost of mirvetuximab post-progression from both arms. The committee concluded that the EAG's approach was more appropriate.

Severity

3.17 The committee considered the severity of the condition (the future health lost by people living with the condition and having standard care in the NHS). The committee may apply a greater weight to quality-adjusted life years (QALYs; a severity modifier) if technologies are indicated for conditions with a high degree of severity. The company and EAG provided absolute and proportional QALY shortfall estimates in line with NICE's health technology evaluations manual. The committee noted that 3 main factors influenced the absolute and proportional QALY shortfall estimates. These were the:

- choice of utility values for the pooled chemotherapy arm
- choice of OS extrapolation for pooled chemotherapy
- average age of people starting treatment.

The committee recalled its preference to use the utility values from MIRASOL for chemotherapy (see section 3.10) and the gamma distribution for chemotherapy OS (see section 3.9). For the starting age of the population, the company preferred to use 59.2 years, based on a publication by Parikh et al. (2018). The EAG preferred to use 62.8 years, which was the mean baseline age in MIRASOL. The committee recalled that the clinical experts and the Cancer Drugs Fund lead had said that the average age of people starting treatment was likely to be

higher than in MIRASOL (see section 3.5). But to ensure consistency with the clinical data used in the model, the committee preferred to assume the starting age was the mean baseline age in MIRASOL (62.8 years). Using the committee's preferred assumptions, the absolute QALY shortfall was 10.8 and the proportional QALY shortfall was 0.93. So, the committee concluded that applying a severity weight of 1.2 to the QALYs was appropriate.

Cost-effectiveness estimates

Committee's preferred assumptions

3.18 Given the available evidence, the committee concluded that its preferred assumptions for the cost-effectiveness modelling were:

- using pooled chemotherapy, including PLD and paclitaxel, as the relevant comparator (see section 3.3)
- excluding the costs of topotecan (see section 3.8)
- using the gamma distribution for modelling mirvetuximab and pooled chemotherapy OS (see section 3.9)
- applying the treatment-dependent health-state utility values from MIRASOL for both the mirvetuximab and pooled chemotherapy arms (see section 3.10)
- including disutilities associated with adverse events (see section 3.10)
- assuming the duration of grade 2 or higher ocular adverse events is 4 weeks (see section 3.11)
- assuming that the frequency of ophthalmology visits is every 6 weeks (see section 3.11)
- assuming that anaemia and neutropenia are managed as day cases (see section 3.11)
- assuming that fatigue is self-managed (see section 3.11)
- using the cycle-specific approach for modelling RDI (see section 3.12)
- assuming no vial sharing for mirvetuximab and 50% vial sharing for pooled chemotherapy (see section 3.13)

- having gynaecological oncology consultations once every 6 weeks in both the pre-progression and post-progression health states (see section 3.14)
- using the observed Kaplan–Meier data up to 120 weeks, followed by the exponential extrapolation for modelling mirvetuximab duration of treatment (see section 3.15)
- adjusting for the treatment crossover and removing the cost of mirvetuximab in the post-progression state (see section 3.16)
- using the mean baseline age in MIRASOL (62.8 years) for the starting age in the model (see section 3.17)
- applying a severity weight of 1.2 to the QALYs (see section 3.17).

Acceptable ICER

3.19 NICE's manual on health technology evaluations notes that, above a most plausible ICER of £20,000 per 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 uncertainty, specifically around the:

- the utility values for people having mirvetuximab and people having chemotherapy
- long-term survival estimates for people having mirvetuximab and people having chemotherapy
- average age of people starting treatment.

So, the committee concluded that it preferred to give stakeholders the opportunity to provide any further analyses or data. It said that this should help the committee to understand the extent of the uncertainty and determine its preferred ICER threshold for decision making.

Other factors

Equality

3.20 The committee noted that ovarian cancer affects women, trans men and non-binary people registered female at birth. Sex is a protected characteristic under the Equality Act 2010. But because the recommendation does not restrict access to treatment for some people over others, the committee agreed that this was not a potential equality issue.

Conclusion

Recommendation

3.21 The committee concluded that mirvetuximab increases PFS and OS compared with chemotherapy. It thought that mirvetuximab may also improve the HRQoL of people with platinum-resistant ovarian cancer compared with chemotherapy. But, when considering the condition's severity, and its effect on quality and length of life, the most likely cost-effectiveness estimates are above the range that NICE considers an acceptable use of NHS resources. So, the committee concluded that mirvetuximab should not be used.

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 or principal technical adviser.

Chris Shah

Technical lead

Emily Leckenby

Technical adviser

Jennifer Upton

Project manager

Lizzie Walker

Principal technical adviser

ISBN: [to be added at publication]