



mirvetuximab soravtansine concentrate for solution for infusion (Elahere®)

AbbVie Ltd

4 September 2026

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission assessed under the end of life and orphan equivalent medicine process

mirvetuximab soravtansine (Elahere®) is accepted for use within NHSScotland.

Indication under review: as monotherapy for the treatment of adult patients with folate receptor-alpha (FR α) positive, platinum-resistant high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received one to three prior systemic treatment regimens.

In an open-label, phase III study, treatment with mirvetuximab soravtansine was associated with significant improvements in progression free survival and overall survival compared with chemotherapy. An indirect treatment comparison versus bevacizumab plus chemotherapy did not identify any difference in efficacy, safety outcomes may favour mirvetuximab soravtansine.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Mirvetuximab soravtansine is an IgG1 antibody-drug conjugate which binds to folate receptor- α (FR α) expressed on the surface of ovarian cancer cells. DM4 is a microtubule inhibitor attached to the antibody by a linker that is cleaved inside the cancer cell. The released DM4 disrupts the microtubule network, resulting in cell cycle arrest and apoptotic cell death.¹

Eligible patients should have FR α tumour status defined as $\geq 75\%$ viable tumour cells demonstrating moderate (2+) and/or strong (3+) membrane staining by immunohistochemistry (IHC), assessed by a validated test.¹

The recommended dose of mirvetuximab soravtansine is 6 mg/kg per adjusted ideal body weight (AIBW) administered once every 3 weeks (21-day cycle) as an intravenous infusion until disease progression or unacceptable toxicity. See the summary of product characteristics (SPC) for further details including the formula to calculate AIBW, details of pre-medications, recommended concomitant eye drops and dose modifications in the event of adverse reactions.¹

1.2. Disease background

Ovarian cancer is the sixth most common cancer in females in Scotland, with around 611 new cases each year.^{2, 3} Epithelial ovarian, primary peritoneal, and fallopian tube cancers represent a spectrum of diagnoses that originate in the Mullerian tissue and are collectively referred to as epithelial ovarian cancer (EOC). High grade serous carcinoma is the most common subtype and represents 70% of EOC cases. FR α has limited expression in normal tissue but is overexpressed in various epithelial tumours, particularly serous and endometrioid ovarian and endometrial cancers.^{4, 5} Ovarian cancer is often asymptomatic in the early stages and is, therefore, often first detected in advanced stages, when prognosis is poor.

Disease recurring within 6 months of platinum-based chemotherapy is defined as platinum-resistant. Once patients develop platinum-resistant ovarian cancer, their prognosis is very poor, with low response rates to further chemotherapy (<15%), progression free survival (PFS) of 3 to 4 months, and median overall survival (OS) of less than 12 months.^{6, 7}

1.3. Treatment pathway and relevant comparators

Patients with platinum-resistant epithelial ovarian cancer face limited treatment options, with treatment choice dependent on patient fitness, choice and comorbidities. Bevacizumab is accepted for restricted use within NHSScotland in combination with paclitaxel for the treatment of adult patients with platinum-resistant recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who received no more than two prior chemotherapy regimens and who have not received prior therapy with bevacizumab or other vascular endothelial growth factor (VEGF) inhibitors or VEGF receptor-targeted agents (SMC1063/15). Patients may be unsuitable for bevacizumab due to prior use in the first line, if they have received more than two lines of therapy, comorbidities and disease characteristics that present a high risk for bevacizumab infusion. Other treatment options may include single-agent non-platinum chemotherapy such as paclitaxel, topotecan or pegylated liposomal doxorubicin (PLD).^{4, 8}

There is no Cancer Medicines Outcomes Programme Public Health Scotland (CMOP-PHS) real-world evidence report for this submission.

1.4. Category for decision-making process

Eligibility for a PACE meeting

Mirvetuximab soravtansine meets SMC end of life and orphan equivalent criteria for this indication.

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence to support the efficacy or safety of mirvetuximab soravtansine is from the MIRASOL study. Details are presented in Table 2.1.

Table 2.1. Overview of the relevant study

Criteria	MIRASOL ⁹⁻¹¹
Study design	International, multicentre, randomised, open-label, parallel group, phase III study.
Eligible patients	- Female patients ≥ 18 years of age. - Confirmed diagnosis of high grade serous EOC, primary peritoneal cancer, or fallopian tube cancer. - Platinum-resistant disease: - Patients who only had one line of platinum-based therapy must have received at least four cycles of platinum, must have had a response (CR or PR) and then progressed between >3 months and ≤ 6 months after the date of the last dose of platinum. - Patients who had received two or three lines of platinum therapy must have progressed on or within 6 months after the date of the last dose of platinum. - Progressed radiographically on or after their most recent line of therapy. - Positive for FRα expression^A as defined by the Ventana[®] FOLR1 assay. - At least one but no more than three prior systemic lines of anticancer therapy, and an appropriate next line of treatment is single-agent therapy. - ECOG PS of 0 or 1.
Treatments	Patients were randomised to receive mirvetuximab soravtansine 6 mg/kg AIBW IV on day 1 of a 3-week cycle, or investigator's choice of chemotherapy (paclitaxel [80 mg/m² IV once weekly], PLD [40 mg/m² IV every 4 weeks] or topotecan [4 mg/m² IV on day 1, 5 and 15 of 4-week cycle or 1.25 mg/m² IV on days 1 to 5 of 3-week cycle]). Treatment was to continue until disease progression, unacceptable toxicity, withdrawal of consent, death, or until the sponsor terminated the study (whichever came first). Patients in the mirvetuximab soravtansine group received paracetamol, dexamethasone and diphenhydramine premedication approximately 30 minutes before each infusion. An antiemetic was also recommended before each infusion. Patients in the mirvetuximab soravtansine group were required to use corticosteroid eye drops on days 1 to 8 of each cycle and preservative-free lubricating eye drops daily.
Randomisation	Patients were randomised equally. Randomisation was stratified according to number of prior lines of therapy (one, two or three) and investigator's choice of chemotherapy (paclitaxel, PLD or topotecan).

Primary outcome	PFS, defined as the time between date of randomisation to the date of first progression (investigator assessed using RECIST v1.1 criteria) or death due to any cause, whichever occurred first.
Key secondary outcomes	- Investigator assessed ORR (CR or PR) per RECIST v1.1. - OS, defined as time between date of randomisation to the date of death. ≥15-point improvement in abdominal/gastrointestinal symptom subscale of EORTC QLQ-OV28 at week 8 or 9.
Statistical analysis	Efficacy analyses were performed in the ITT population, which included all patients who underwent randomisation. If the primary outcome was statistically significant, a hierarchical statistical testing strategy was applied for the key secondary outcomes in the order detailed above. An interim analysis of OS was undertaken at the primary analysis of PFS with the stopping boundary based on number of deaths.

Abbreviations: AIBW = adjusted ideal body weight; CR = complete response; ECOG PS = Eastern Cooperative Oncology Group performance status; EOC = epithelial ovarian cancer; EORTC QLQ-OV28 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire–Ovarian Cancer Module; FRα = folate receptor-alpha; ITT = intention-to-treat; IV = intravenous; ORR = objective response rate; OS = overall survival; PFS = progression free survival; PLD = pegylated liposomal doxorubicin; PR = partial response; RECIST = Response Evaluation Criteria in Solid Tumours. A = at least 75% of viable tumour cells exhibit level two and/or three membrane staining intensity.

At the primary analysis (06 March 2023), mirvetuximab soravtansine demonstrated statistically significant improvements in the primary outcome, investigator assessed PFS, and key secondary outcomes (objective response rate [ORR] and OS) compared with investigator's choice of chemotherapy.¹¹ See Table 2.2 for further details. There were similar results in an additional analysis at data cut-off 26 September 2024.⁹

Table 2.2: Primary and key secondary outcomes from MIRASOL at the primary analysis (06 March 2023) (ITT population).^{5, 11, 12}

	Mirvetuximab soravtansine (n=227)	Chemotherapy (n=226)
Primary outcome: Investigator assessed PFS per RECIST v1.1 criteria (median follow-up 11.2 months)		
Events, n	176	166
Median PFS, months	5.6	4.0
Hazard ratio (95% CI), p-value	0.65 (0.52 to 0.81), p<0.001	
Key secondary outcome: Investigator assessed ORR per RECIST v1.1 criteria		
ORR, %	42%	16%
CR, %	5.3%	0
PR, %	37%	16%
Odds ratio (95% CI), p-value	3.81 (2.44 to 5.94), p<0.001	
Key secondary outcome: OS (median follow-up 13.1 months)		
Deaths, n	90	114
Median OS, months	16.5	12.8
Hazard ratio (95% CI), p-value	0.67 (0.50 to 0.89), p=0.005 ^A	
Estimated OS rate at 12 months	65%	54%
Key secondary outcome: Achievement of ≥15-point improvement in abdominal/gastrointestinal symptom subscale of EORTC QLQ-OV28 at week 8 or 9		
Evaluable patients, n	162	150
Patients who achieved ≥15-point improvement, n	34	23
Odds ratio (95% CI), p-value	1.5 (0.8 to 2.6), p=0.26	

Abbreviations: CI = confidence interval; CR = complete response; EORTC QLQ-OV28 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire–Ovarian Cancer Module; ITT = intention-to-treat; ORR

= objective response rate; OS = overall survival; PFS = progression free survival; PR = partial response; RECIST = Response Evaluation Criteria in Solid Tumours.

A = this exceeded the p-value boundary for interim analysis of OS of 0.01313.

Sensitivity analyses of PFS and ORR by blinded independent central review (BICR) were generally consistent with the investigator. Median PFS was 5.9 months in the mirvetuximab soravtansine group versus 4.3 months in the chemotherapy group (hazard ratio [HR]: 0.72, 95% CI: 0.56 to 0.92). ORR was 36% in the mirvetuximab soravtansine group versus 15% in the chemotherapy group (OR: 3.22, 95% CI: 2.04 to 5.09).¹¹

2.2. Health-related quality of life outcomes

Health-Related Quality of Life (HRQoL) was assessed using three questionnaires: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire–Ovarian Cancer Module (EORTC QLQ-OV28), Quality of Life Questionnaire-Core 30 (QLQ-C30) and EQ-5D-5L. These questionnaires were used at screening and day 1 of each treatment cycle. After 24 weeks, these were assessed every 12 weeks and every 3 months for patients after the end of treatment.

Results for the primary patient-reported outcome, proportion of patients who reported an improvement of at least 15 points in QLQ-OV28 abdominal and gastrointestinal symptom scores at weeks 8 or 9 are presented in Table 2.2. Results did not reach statistical significance; however, exploratory analyses suggested that HRQoL was generally maintained through 24 weeks of treatment with mirvetuximab soravtansine.¹²

2.3. Supportive studies

The submitting company provided supporting data from a rescored population of the FORWARD-1 study. FORWARD-1 was a phase III, open-label, randomised study. Patients were randomised in a 2:1 ratio to mirvetuximab soravtansine 6 mg/kg AIBW IV every 3 weeks or investigator's choice of chemotherapy (paclitaxel, PLD, or topotecan). Patients were required to have medium or high FR α expression as defined by the VENTANA[®] FOLR1 assay ($\geq 50\%$ tumour staining at $\geq 2+$ intensity), which is a different scoring method to the MIRASOL study.¹³ An exploratory rescoring analysis was therefore undertaken to determine FR α positive tumour cells using the PS2+ scoring method, as per the MIRASOL study, resulting in 116 patients (mirvetuximab soravtansine n=82 and chemotherapy n=34). The primary outcome was PFS as assessed by BICR, with key secondary outcomes being ORR per Response Evaluation Criteria in Solid Tumours (RECIST) v1.1 assessed by BICR, OS and EORTC QLQ-OV28.¹⁴

In the rescored analysis, results were generally consistent with the MIRASOL study. Median PFS by BICR was 5.7 months in the mirvetuximab soravtansine group versus 3.2 months in the chemotherapy group (HR: 0.59; 95% CI: 0.37 to 0.94). The median OS was 16.4 months in the mirvetuximab soravtansine group versus 11.4 months in the chemotherapy group (HR: 0.66; 95% CI: 0.40 to 1.08).¹⁴

2.4. Indirect evidence to support clinical and cost-effectiveness comparisons

In the absence of direct evidence comparing mirvetuximab soravtansine with bevacizumab plus investigator's choice of chemotherapy, the submitting company presented an anchored matching adjusted indirect treatment comparison (MAIC). This has been used to inform the economic base case. Details are presented in Table 2.3.

Table 2.3: Summary of indirect treatment comparison

Criteria	Overview																					
Design	Anchored MAIC																					
Population	Patients with platinum-resistant or refractory epithelial ovarian, primary peritoneal, or fallopian tube cancers who received at least one prior systemic anticancer regimen																					
Comparators	Bevacizumab and investigator choice of chemotherapy																					
Studies included	MIRASOL ⁹⁻¹¹ and AURELIA ¹⁵																					
Outcomes	PFS, OS, ORR, Safety																					
Results	After matching, hazard ratios for PFS favoured bevacizumab plus chemotherapy, while point estimates for OS and ORR favoured mirvetuximab soravtansine. However, the 95% CI crossed 1 for the HR of PFS, OS and the OR of ORR, suggesting no evidence of a difference between treatments. Grade ≥3 TEAEs numerically favoured mirvetuximab soravtansine after matching, although the 95% CI of the OR crossed 1. Discontinuation due to TEAEs favoured mirvetuximab soravtansine compared with bevacizumab plus chemotherapy. Table 2.4: Summary of the indirect treatment comparison results. <table><tr><th></th><th colspan="2">Mirvetuximab soravtansine vs bevacizumab plus chemotherapy</th></tr><tr><th></th><th>Before matching</th><th>After matching</th></tr><tr><td>PFS HR (95% CI)</td><td>1.35 (0.99 to 1.85)</td><td>1.12 (0.66 to 1.89)</td></tr><tr><td>OS HR (95% CI)</td><td>0.80 (0.58 to 1.11)</td><td>0.73 (0.45 to 1.19)</td></tr><tr><td>ORR OR (95% CI)</td><td>1.30 (0.68 to 2.47)</td><td>1.89 (0.75 to 4.76)</td></tr><tr><td>Grade ≥3 TEAE OR (95% CI)</td><td>0.54 (0.36 to 0.81)</td><td>0.61 (0.33 to 1.15)</td></tr><tr><td>Discontinuation due to TEAE OR (95% CI)</td><td>0.13 (0.06 to 0.28)</td><td>0.15 (0.05 to 0.46)</td></tr></table>		Mirvetuximab soravtansine vs bevacizumab plus chemotherapy			Before matching	After matching	PFS HR (95% CI)	1.35 (0.99 to 1.85)	1.12 (0.66 to 1.89)	OS HR (95% CI)	0.80 (0.58 to 1.11)	0.73 (0.45 to 1.19)	ORR OR (95% CI)	1.30 (0.68 to 2.47)	1.89 (0.75 to 4.76)	Grade ≥3 TEAE OR (95% CI)	0.54 (0.36 to 0.81)	0.61 (0.33 to 1.15)	Discontinuation due to TEAE OR (95% CI)	0.13 (0.06 to 0.28)	0.15 (0.05 to 0.46)
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Abbreviations: PFS = progression free survival; HR = hazard ratio; CI = confidence interval; MAIC = matching adjusted indirect comparison; OS = overall survival; ORR = objective response rate; OR = odds ratio; TEAE = treatment-emergent adverse event.

3. Summary of Safety Evidence

Evidence from MIRASOL supports the relative safety of mirvetuximab soravtansine compared with chemotherapy, a relevant comparator, for the indication under review. Safety data from 26 September 2024 data cut-off with a median follow-up of 28.4 months were provided for this submission.

Grade ≥3 treatment-emergent adverse events (TEAEs) were reported in 44% (97/218) of the mirvetuximab soravtansine group versus 55% (113/207) of the chemotherapy group. Any grade serious TEAEs were reported in 25% versus 33%. Treatment was discontinued due to any TEAEs in 11% versus 15%. The most commonly reported grade ≥3 TEAEs in the mirvetuximab soravtansine group versus the chemotherapy group were keratopathy (10% versus 0), blurred vision (8.3% versus 0), abdominal pain (2.8% versus 1.4%), fatigue (2.3% versus 5.3%) and diarrhoea (1.4% versus <1%).^{9, 16}

Overall, the safety profile of mirvetuximab soravtansine was considered acceptable in the context of the poor prognosis of the target population. Adverse events (AEs) could be managed with dose modifications, pre-medications and monitoring. Ocular AEs were more common for mirvetuximab soravtansine but most were mild, manageable and reversible, while myelosuppression was more

common with chemotherapy.⁶ Patients should be monitored for pulmonary signs and symptoms of pneumonitis, ocular toxicity, and peripheral neuropathy. See the SPC for further details on monitoring, dose adjustments, interruptions and discontinuations due to AEs.¹

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- At the primary analysis of the phase III study MIRASOL (06 March 2023), in the ITT population with a median follow-up of 11.2 months, mirvetuximab soravtansine was associated with a statistically significant improvement in PFS compared with investigator's choice of chemotherapy. Although the PFS benefit was only 1.6 months, the result was considered clinically relevant by regulators in an aggressive disease with limited effective treatment options.⁶
- This was supported by statistically significant results for key secondary outcomes, ORR (42% versus 16%) and OS (OS benefit of 3.7 months).¹¹ Data from an additional later analysis with a median PFS follow-up of 28.4 months were consistent with the primary analysis.⁹
- Mirvetuximab soravtansine is a first in class antibody-drug conjugate targeting FR α .

4.2. Key uncertainties

- In the absence of direct evidence versus bevacizumab plus chemotherapy, the submitting company conducted an anchored MAIC. The submitting company concluded that mirvetuximab soravtansine was associated with numerically longer OS but shorter PFS, with improved safety outcomes including fewer grade ≥ 3 TEAEs and discontinuations. While generally well conducted, there were some limitations that make the results difficult to interpret. The population was not fully aligned with the licensed indication (FR α status not specified in AURELIA), and matching could not account for prior bevacizumab use. The effective sample size was substantially reduced after matching (from 227 to 48 and 224 to 58 in the mirvetuximab soravtansine and chemotherapy groups, respectively) and risk of bias was assessed as high for the AURELIA study. The analysis excluded HRQoL outcomes. Due to these limitations, the company's conclusions are uncertain.
- Early dropouts in the chemotherapy group, together with a higher proportion of patients randomised to chemotherapy who did not receive treatment, may have contributed to informative censoring potentially impacting study results.⁵ Sensitivity analyses provided by the submitting company to account for early dropouts suggested consistent results with the primary analysis.^{6, 16}
- MIRASOL was an open-label study, meaning there is a risk of bias in the assessment of efficacy, safety, and patient-reported outcomes. Sensitivity analyses of PFS and ORR by BICR were generally consistent.
- The study included a younger and fitter population (ECOG PS 0 or 1) than may be expected of patients who have received up to three prior treatments. In a subgroup analysis of patients ≥ 65 years, there was no indication of reduced efficacy however it is uncertain if this age group represents frailer, elderly and those with worse performance score. Additionally, the study

excluded patients who may have a poorer treatment response or increased risk of side effects (ocular and lung disorders). MIRASOL included only patients for whom single-agent therapy was appropriate, the direct evidence may be less generalisable to patients within the licensed population who would be eligible for bevacizumab plus chemotherapy in routine practice. This may affect the generalisability of the study results to the Scottish population.⁶

4.3. Clinical expert input

Clinical experts consulted by SMC considered that mirvetuximab soravtansine is a therapeutic advancement due to improvements in efficacy outcomes compared with chemotherapy and that it provides an additional treatment option for patients with FR α positive, platinum-resistant high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who are not suitable for bevacizumab.

4.4. Service implications

Diagnostic testing for FR α status is not currently established in Scotland and there may be potential service implications with the introduction of this testing. Ophthalmic exams should be conducted before the initiation of mirvetuximab soravtansine and if a patient develops any new or worsening ocular symptoms before the next dose. This may impact the service.

Diagnostic test required to identify patients eligible for treatment: contact local laboratory for information.

5. Patient and clinician engagement (PACE)

A patient and clinician engagement (PACE) meeting with patient group representatives and clinical specialists was held to consider the added value of mirvetuximab soravtansine, as an orphan equivalent and end of life medicine, in the context of treatments currently available in NHSScotland.

The key points expressed by the group were:

- Ovarian cancer is a devastating disease for patients and their families and friends, with a poor prognosis for the many women diagnosed at a late stage. Patients and their families face a great deal of anxiety over the efficacy and durability of treatment, and whether the disease will recur. This is compounded when the disease becomes platinum-resistant. For patients with platinum-resistant ovarian cancer, treatment options are very limited and prognosis is extremely poor.
- Many patients face debilitating symptoms which include ascites or pleural effusions, abdominal pain, changes in bowel habit and eventually bowel obstruction resulting in an impaired ability to eat and drink. Surgical procedures can have long-term effects on abdominal organs. Removal of both ovaries results in immediate surgical menopause. These physically and psychologically debilitating symptoms and side effects impact independence and can affect work, finances, family, and caring roles permanently. Uncertainty affects everyday decisions and future planning. Many describe feeling isolated and lonely and are reluctant to socialise or spend time in public places due to concerns about acquiring infections.

- Many patients will have had several rounds of chemotherapy +/- bevacizumab and often have residual side effects from this treatment, alongside the burden of the disease. Chemotherapy has a severe physical and mental toll on patients, which can impact on a patient's ability to care for themselves and carry out daily activities. Nausea and alopecia, pain, peripheral neuropathy, joint pain, fatigue and reduced mobility, as well as cumulative haematological side effects including compromised immunity all negatively impact on patients' well-being. There is thus an unmet need for treatments for women whose disease has become platinum-resistant.
- Mirvetuximab soravtansine is the first treatment to improve PFS and OS in patients with folate receptor-alpha high disease. This time can be very important for women in this situation. It could help them to organise their affairs and spend a few additional months with loved ones without the debilitating effects of chemotherapy.
- It is associated with notable benefits over currently available treatments. It is given once every three weeks, while often other treatments are given weekly. It has a different side effect profile than chemotherapy, such as less alopecia, neutropenia, and peripheral neuropathy. The immunosuppression caused by chemotherapy greatly restricts patients. It is expected to provide better symptom control, which would give patients greater independence, dignity, and improve quality of life. Greater symptom control would grant patients the opportunity to spend time with family, travel, socialise, continue working, and do the things that matter to them. Access to mirvetuximab soravtansine would remove some of the burden for family and carers due to reduced travel for appointments, reduced side effects, reduced anxiety, and more good quality time with their loved ones.
- Because of the above benefits, some patients who might consider refusing more chemotherapy may consider treatment with mirvetuximab soravtansine. Many women value the opportunity to play an active role in decisions about their treatment. Having access to a wider range of treatment options and being able to make decisions about the treatment they receive, can provide a sense of agency at an otherwise uncertain and challenging time.
- Safety monitoring is a critical component of mirvetuximab soravtansine delivery due to the potential for ocular AE. Although many of the ocular issues seen were mild in severity, rarely ocular side effects can be serious and may not return to normal if the medicine is discontinued. Potential side effects and monitoring requirements need to be clearly explained to patients when considering whether to proceed with this medicine.

Additional Patient and Carer Involvement

We received patient group submissions from Ovacom Ovarian Cancer Charity, Ovarian Cancer Action and Target Ovarian Cancer. All three organisations are registered charities. Ovacom Ovarian Cancer Charity has received 11.48% pharmaceutical company funding in the past two years, including from the submitting company. Ovarian Cancer Action has received 2.9% pharmaceutical company funding in the past two years, including from the submitting company. Target Ovarian Cancer has received 0.59% pharmaceutical company funding in the past two years, including from the submitting company. Representatives from all three patient groups

participated in the PACE meeting. The key points of their submissions have been included in the full PACE statement considered by SMC.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

An overview of economic analysis is presented in Table 6.1.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility analysis.
Time horizon	Lifetime. Starting age of 62.8 years (mean age from MIRASOL ITT population) modelled to 100 years.
Population	Adult patients with 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. The eligible population aligns with the MHRA marketing authorisation and the MIRASOL study ITT population. Subgroup analyses were explored for bevacizumab-unsuitable subgroups: (a) prior bevacizumab treatment exposure; (b) received three prior lines of therapy.
Comparators	(a) Chemotherapy: a basket of chemotherapies including paclitaxel, PLD, and topotecan based on clinical study investigators choice (IC); (b) bevacizumab plus chemotherapy: bevacizumab in combination with paclitaxel, PLD or topotecan.
Model description	A three-state partitioned survival model was used, with pre-progression, post-progression, and death states. A one-week cycle length, with half-cycle correction, was applied to the model.
Clinical data	The MIRASOL clinical study was the primary data source for PFS, OS, and duration of treatment (DoT) for mirvetuximab soravtansine and the chemotherapy comparator used in the economic analysis. MIRASOL is a phase 3, randomised open-label study of mirvetuximab soravtansine <i>versus</i> IC chemotherapy. In the absence of direct comparative evidence for mirvetuximab soravtansine <i>versus</i> bevacizumab plus chemotherapy, an anchored MAIC was conducted to provide indirect comparisons of PFS and OS outcomes for mirvetuximab soravtansine (using MIRASOL patient-level data) and bevacizumab plus chemotherapy (using aggregate data from AURELIA, a phase 3, randomised open-label trial for bevacizumab plus chemotherapy <i>versus</i> chemotherapy).¹⁵ The indirect treatment comparison results numerically favoured mirvetuximab soravtansine for OS (HR <1) but numerically favoured bevacizumab for PFS (HR >1). As there are no DoT data reported in the AURELIA study, bevacizumab plus chemotherapy DoT was assumed to be equivalent to PFS. Grade 3+ TEAEs with incidence $\geq 5\%$ in either MIRASOL arm were included; bevacizumab AEs were sourced from the AURELIA study.¹⁵
Extrapolation	PFS and OS were extrapolated in the economic analysis for mirvetuximab soravtansine and the comparators (with PFS also serving as a proxy for DoT for bevacizumab plus chemotherapy), using standard parametric distributions. Parametric curves were fitted independently to each arm. Base case extrapolation approaches were selected based on a combined assessment of statistical fit (AIC and BIC) and clinical plausibility informed by UK clinical expert opinion. Base case selections were OS: log-logistic for mirvetuximab soravtansine and Weibull for chemotherapy; PFS: lognormal for both arms; DoT: exponential for mirvetuximab soravtansine and Kaplan-Meier data directly applied for each chemotherapy component (paclitaxel, PLD, topotecan). For bevacizumab plus chemotherapy, relative OS and

	PFS were derived by applying inverse MAIC HRs to mirvetuximab soravtansine, (OS HR 1.37[CI: 0.93-1.51]; PFS HR: 0.90 [CI:0.53-1.52]). Bevacizumab plus chemotherapy DoT was assumed to be equivalent to PFS in the base case. Alternative distributions were explored in scenario analyses.
Quality of life	Health state utility values were derived from EQ-5D-5L data collected in the MIRASOL clinical study. Utility values were estimated using a mixed model with a repeated measure approach to account for missing observations in the study data. Treatment specific utility values were applied, with the values for bevacizumab plus chemotherapy assumed to be equal to those applied in the chemotherapy arm. For patients receiving mirvetuximab soravtansine, utility values applied in the base case for pre-progression and post-progression states were 0.822 and 0.742, respectively. For patients receiving chemotherapy or bevacizumab plus chemotherapy, pre-progression and post-progression utilities were 0.798 and 0.718, respectively. Utilities were age adjusted, and one-off disutilities for grade 3+ AEs (anaemia, cataract, fatigue, keratopathy, neutropenia, thrombocytopenia, blurred vision) were applied additively, using values sourced from published literature.
Costs and resource use	Medicine acquisition costs were included for all medicines included in the economic analysis. Pre-medication, administration (based on infusion duration in the SPC), and 50% vial sharing for all treatments were applied in the base case. Relative dose intensities reported in the MIRASOL study were incorporated in the model. It was assumed that subsequent treatments were received by 67% of patients in mirvetuximab soravtansine arm and 65% in comparator arms following disease progression. Post-progression medicines included taxanes, topotecan, anthracyclines, gemcitabine and mirvetuximab soravtansine, and were costed based on median treatment durations (converted to means assuming an exponential distribution) derived from the MIRASOL study and published literature.¹⁷ Disease management resource use estimates (healthcare professional visits, CT scans) were sourced from NICE TA285.¹⁸ Adverse event costs were included, and additional monitoring and treatment costs for ocular AEs were applied to patients receiving mirvetuximab soravtansine. FRα testing costs were applied for mirvetuximab soravtansine patients. A one-off terminal care cost was applied at death for all patients.
PAS/contract price	A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a discount was offered on the list price of mirvetuximab soravtansine. Contract prices are in place for paclitaxel, PLD, bevacizumab, and gemcitabine (post-progression treatment) and these were included in the results used for decision-making.

6.2. Results

The results were presented for the base case versus chemotherapy and bevacizumab plus chemotherapy. In addition, results of two subgroup analyses were presented relating to bevacizumab-unsuitable patients, defined as: (a) those previously treated with bevacizumab; (b) those who had previously received three prior lines of therapy. For both subgroups mirvetuximab soravtansine was compared with chemotherapy only.

Disaggregated incremental results showed that life year and quality-adjusted life year (QALY) gains *versus* both of the comparators (chemotherapy, bevacizumab plus chemotherapy) are achieved primarily through additional time spent in the post-progression state, with lower QALYs estimated than bevacizumab plus chemotherapy in the pre-progression state.

Disaggregated cost results show that incremental costs of mirvetuximab soravtansine relative to comparators are primarily due to increased total medicine treatment costs and pre-progression disease management costs, these differences being partially offset by lower post-progression treatment costs.

SMC would wish to present the with PAS cost-effectiveness results that were used for decision-making. However, SMC is unable to publish these results due to commercial in confidence concerns regarding the PAS. SMC considered results for decision-making that considered all relevant PAS/contract prices. SMC is unable to present these results due to competition law issues.

*Other data were also assessed but remain confidential.**

6.3. Sensitivity analyses

A range of sensitivity and scenario analyses were considered and descriptions of these key scenarios are provided in Table 6.2.

Table 6.2 Selected scenario analysis results

	Base case	Scenarios
1.	Independently fitted models for OS. Mirvetuximab soravtansine: Log-logistic; Chemotherapy: Weibull; bevacizumab plus chemotherapy: HR vs mirvetuximab soravtansine	a) Jointly fitted models for OS. Weibull (best statistical fit by AIC & BIC) b) Jointly fitted models for OS. Gamma (2 nd best statistical fit by AIC & BIC)
2.	Independently fitted models for PFS. Mirvetuximab soravtansine: Lognormal; Chemotherapy: Lognormal; bevacizumab: HR vs mirvetuximab soravtansine	Jointly fitted models for PFS. Lognormal (best statistical fit by AIC & BIC)
3.	Mirvetuximab soravtansine OS distribution: Log-logistic (4 th in AIC/3 rd in BIC)	a) mirvetuximab soravtansine OS - Gamma (1 st best fit) b) mirvetuximab soravtansine OS - Weibull (2 nd best fit) c) mirvetuximab soravtansine OS - Gen Gamma (3 rd in AIC/4 th in BIC)
4.	Chemotherapy OS distribution: Weibull (1 st best fit)	a) Chemotherapy OS - Gamma (2 nd best fit) b) Chemotherapy OS - Generalised Gamma (3 rd best fit) c) Chemotherapy OS - Gompertz (4 th best fit)
5.	Bevacizumab plus chemotherapy: inverse HRs obtained from ITC	Apply one to both PFS and OS HRs (assume equal efficacy)
6.	HSUVs: sourced from MIRASOL, via MMRM	a) Progression status and treatment type (with interaction term) b) Progression status only (adjusted for AEs) c) No treatment specific HSUVs. Apply the same HSUVs for mirvetuximab soravtansine and comparators (pre-progression, 0.822; post-progression, 0.742)
7.	50% of vial sharing	Vial sharing applied to paclitaxel and PLD only
8.	Lifetime horizon (37.2 years)	a) Time horizon: 10 years b) Time horizon: 15 years
9.	Chemotherapy dosing schedules: clinical expert opinion	Chemotherapy dosing schedules: aligned with SPC
10.	9% of patient receiving mirvetuximab soravtansine as chemotherapy subsequent treatment	Excluded patients from receiving mirvetuximab soravtansine as chemotherapy subsequent treatment
11.	Combined scenarios	a) Scenario 1a and 8a b) Scenario 1b and 8b c) Scenario 3a and 8a d) Scenario 3b and 8a

Abbreviations: DoT, duration of treatment; HSUVs, health state utility values; ICER, incremental cost-effectiveness ratio; MMRM, mixed model repeated measure; OS, overall survival; PFS, progression free survival; PLD, pegylated liposomal doxorubicin; SPC, summaries of product characteristics.

6.4. Key strengths

- The model uses direct data from the Phase 3 MIRASOL study for mirvetuximab soravtansine versus chemotherapy comparisons, with statistically significant and clinically meaningful OS and PFS benefits demonstrated in the licensed population.
- Relevant comparators were used in the model, reflecting current practice in Scotland.

6.5. Key uncertainties

- There is uncertainty surrounding the 5- and 10-year OS estimates for patients receiving mirvetuximab soravtansine. A log-logistic distribution was selected by the company for base case OS extrapolation for mirvetuximab soravtansine, based primarily on company's advisory board clinical experts. However, alternative parametric curves with a superior statistical fit (gamma, Weibull, and generalised gamma), which generated more pessimistic 5- and 10-year OS estimates consistent with the Scottish clinical expert opinion, substantially increased the ICER against both comparators and in particular *versus* chemotherapy (Table 6.2, scenarios 3 and 11c-d). This highlights the uncertainty associated with the long-term mirvetuximab soravtansine OS extrapolations.
- The approach to parametric curve fitting was a further source of uncertainty in OS extrapolations. Jointly fitted models, in which parametric curves for mirvetuximab soravtansine and comparators were fitted based on a pooled analysis across study arms, were explored as a scenario. This had a substantial upward impact on the ICER (Table 6.2, scenario 1 and 11a-b), indicating that the choice between independently fitted functions and joint models is a key structural uncertainty. However, the company provided justification for using independent models due to the different mechanism of action and pattern of hazards of the individual treatments meaning jointly fitted models were considered less relevant for decision-making.
- There is uncertainty over the relative PFS and OS benefits versus bevacizumab plus chemotherapy associated with limitations with the indirect treatment comparison. The population was not fully aligned with the licensed indication (FR α status not specified in AURELIA). The degree of adjustment required to account for limited overlap between studies leads to a significant loss of effective sample size after matching. Additionally, confidence intervals for PFS and OS estimates cross a value of one indicating uncertainty around differences between arms in PFS/OS outcomes. Scenario analyses in which a hazard ratio of 1 (denoting equivalence) was used for both endpoints had a large impact on the cost-effectiveness estimates (Table 6.2, scenario 5).
- Although the utility data were sourced directly from the EQ-5D-5L data of the MIRASOL study, the values appear high when compared to general population at age 62.8 years (model analysis starting age). Additionally, utility increments were applied for mirvetuximab soravtansine patients relative to comparator patients for both pre- and post-progression states (0.024 increment for either state). In the absence of direct data,

bevacizumab plus chemotherapy utilities were assumed to be consistent with those for chemotherapy. Treatment-based utility increments are associated with uncertainty especially in relation to progressed disease. The exclusion of treatment specific utilities was explored as a scenario analysis (Table 6.2, scenario 6c).

- There is uncertainty over the use of mirvetuximab soravtansine as a subsequent therapy in the comparator arms (assumed to be 9% of patients in the base case). The base case assumption increased comparator post-progression costs, and thereby reduced the ICER, relative to scenario results in which mirvetuximab soravtansine was not included as potential comparator subsequent therapy (Table 6.2, scenario 10).

7. Conclusion

The Committee considered the benefits of mirvetuximab soravtansine in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that as mirvetuximab soravtansine is an orphan equivalent medicine, SMC can accept greater uncertainty in the economic case.

After considering all the available evidence and the output from the PACE process, the Committee accepted mirvetuximab soravtansine for use in NHSScotland.

8. Guidelines and Protocols

The British Gynaecological Cancer Society (BGCS) published 'BGCS ovarian, tubal and primary peritoneal cancer guidelines: Recommendations for practice update 2024' in October 2024.⁸

The European Society of Medical Oncology (ESMO) published 'Newly diagnosed and relapsed epithelial ovarian cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up' in October 2023.⁴

ESMO published 'ESMO Clinical Practice Guideline Express Update on the management of epithelial ovarian cancer' in February 2026.¹⁹

The Scottish Intercollegiate Guidelines Network (SIGN) published the guideline 'Management of epithelial ovarian cancer' (SIGN 135) in November 2013. This guideline was revised in October 2018.²⁰

9. Additional Information

9.1. Product availability date

24 June 2026

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per cycle (£)
mirvetuximab soravtansine	6 mg/kg per AIBW once every 3 weeks intravenously until disease progression or unacceptable toxicity	19,800

Costs from BNF online on 01 June 2026. Costs calculated assuming an adjusted ideal body weight of 59 kg. Costs calculated using the full cost of vials assuming wastage. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS. This template does not incorporate any PAS/contract price discounts associated with comparator medicines.

[Other data were also assessed but remain confidential.*](#)

References

1. AbbVie Ltd. Mirvetuximab soravtansine concentrate for solution for infusion (ELAHERE®) Summary of product characteristics. Electronic Medicines Compendium www.medicines.org.uk/emc/ Last updated 08 December 2025.
2. Public Health Scotland. Cancer incidence and prevalence in Scotland. To December 2023. Publication date: 30 September 2025. www.publichealthscotland.scot.
3. Cancer Research UK. Ovarian cancer incidence. Latest cancer incidence statistics for the years 2019, 2021-2022. Last reviewed 23 April 2026. www.cancerresearchuk.org.
4. Gonzalez-Martin A, Harter P, Leary A, Lorusso D, Miller RE, Pothuri B, et al. Newly diagnosed and relapsed epithelial ovarian cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. *Ann Oncol*. 2023;34(10):833–48.
5. The European Medicines Agency (EMA). European Public Assessment Report. Mirvetuximab soravtansine (Elahere®). 19/09/2024, EMEA/H/C/005036/0000. www.ema.europa.eu.
6. The European Medicines Agency (EMA). European Public Assessment Report. Mirvetuximab soravtansine (Elahere®). 19/09/24, EMEA/H/C/005036/0000 www.ema.europa.eu.
7. Davis A, Tinker AV, Friedlander M. "Platinum resistant" ovarian cancer: what is it, who to treat and how to measure benefit? *Gynecol Oncol*. 2014;133(3):624–31.
8. Moss E, Taylor A, Andreou A, Ang C, Arora R, Attygalle A, et al. British Gynaecological Cancer Society (BGCS) ovarian, tubal and primary peritoneal cancer guidelines: Recommendations for practice update 2024. *Eur J Obstet Gynecol Reprod Biol*. 2024;300:69–123.
9. Van Gorp T, Angelergues A, Konecny G, Garcia-Garcia Y, Banerjee S, Moroney J, et al. Final overall survival analysis among patients with folate receptor alpha-positive, platinum-resistant ovarian cancer treated with mirvetuximab soravtansine versus investigator's choice chemotherapy in phase II MIRASOL (GOG-3045/ENGOT-ov55) study. *Gynecologic Oncology*. 2025;200(Supplement 1):349 EP – 50.
10. AbbVie. A Study of Mirvetuximab Soravtansine vs. Investigator's Choice (IC) of Chemotherapy in Platinum-Resistant, Advanced High-Grade Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Cancers With High Folate Receptor-Alpha (FR α) Expression (MIRASOL). NCT04209855. Last updated: 27 August 2025. Available from: www.clinicaltrials.gov.
11. Moore KN, Angelergues A, Konecny GE, Garcia Y, Banerjee S, Lorusso D, et al. Mirvetuximab Soravtansine in FR α -Positive, Platinum-Resistant Ovarian Cancer. *N Engl J Med*. 2023;389(23):2162–74.
12. Van Gorp T, Moore KN, Konecny GE, Leary A, Garcia-Garcia Y, Banerjee S, et al. Patient-reported outcomes from the MIRASOL trial evaluating mirvetuximab soravtansine versus chemotherapy in patients with folate receptor alpha-positive, platinum-resistant ovarian cancer: a randomised, open-label, phase 3 trial. *Lancet Oncol*. 2025;26(4):503–15.
13. Moore KN, Oza AM, Colombo N, Oaknin A, Scambia G, Lorusso D, et al. Phase III, randomized trial of mirvetuximab soravtansine versus chemotherapy in patients with platinum-resistant ovarian cancer: primary analysis of FORWARD I. *Ann Oncol*. 2021;32(6):757–65.
14. AbbVie. New Product Assessment Form. Mirvetuximab soravtansine (ELAHERE®) monotherapy for the treatment of folate receptor alpha-positive platinum-resistant advanced epithelial ovarian, fallopian tube or primary peritoneal cancer. July 2025. Submitted May 2026.
15. Pujade-Lauraine E, Hilpert F, Weber B, Reuss A, Poveda A, Kristensen G, et al. Bevacizumab combined with chemotherapy for platinum-resistant recurrent ovarian cancer: The AURELIA open-label randomized phase III trial. *J Clin Oncol*. 2014;32(13):1302–8.
16. ImmunoGen, AbbVie. Data on File. Final clinical study report. MIRASOL: A randomized, open-label, phase 3 study of mirvetuximab soravtansine vs. Investigator's choice of chemotherapy

in platinum-resistant advanced highgrade epithelial ovarian, primary peritoneal, or fallopian tube cancers with high folate receptoralpha expression. 2024.

17. Mutch DG, Orlando M, Goss T, Teneriello MG, Gordon AN, McMeekin SD, et al. Randomized phase III trial of gemcitabine compared with pegylated liposomal doxorubicin in patients with platinum-resistant ovarian cancer. *J Clin Oncol*. 2007;25(19):2811–8.
18. National Institute for Health and Care Excellence. Bevacizumab in combination with gemcitabine and carboplatin for treating the first recurrence of platinum-sensitive advanced ovarian cancer [TA285]. Published September 2012. Available from: www.nice.org.uk.
19. González-Martín A, Ledermann JA. ESMO Clinical Practice Guideline Express Update on the management of epithelial ovarian cancer. *ESMO Open*. 2026;11(2).
20. Scottish Intercollegiate Guidelines Network (SIGN). SIGN 135. Management of epithelial ovarian cancer. Published November 2013. Revised 2018. Available at: www.sign.ac.uk.

This assessment is based on data submitted by the applicant company up to and including 17 July 2026.

*[*Agreement between the Association of the British Pharmaceutical Industry \(ABPI\) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:https://www.scottishmedicines.org.uk/about-us/policies-publications/](https://www.scottishmedicines.org.uk/about-us/policies-publications/)*

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC includes Scottish national contract prices in its decision-making. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document.

Patient Access Schemes (PAS): A PAS is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. The Patient Access Scheme Assessment Group (PASAG), established under the auspices of Public Services Delivery Scotland, reviews and advises NHS Scotland on the feasibility and acceptability on implementing proposed schemes. PASAG operates separately from SMC to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHS Scotland on the basis of a PAS that has been considered acceptable for implementation by PASAG, a set of guidance notes on the operation of the scheme will be circulated to health boards' Area Drugs and Therapeutics Committees prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.