NCPE Assessment Summary

Mirvetuximab soravtansine (Elahere®)

HTA ID: 24051

June 2026

Applicant: Abbvie

Mirvetuximab soravtansine as monotherapy 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.

NCPE
National Centre for Pharmacoeconomics, Ireland

The National Centre for Pharmacoeconomics (NCPE) has issued a recommendation regarding the cost-effectiveness of mirvetuximab soravtansine (Elahere®).

Following assessment of the Applicant's submission, the NCPE recommends that mirvetuximab soravtansine (Elahere®) be considered for reimbursement if cost effectiveness can be improved relative to existing treatments*.

The Health Service Executive (HSE) asked the NCPE to carry out an evaluation of the Applicant's (Abbvie) Health Technology Assessment of mirvetuximab soravtansine (Elahere®). The NCPE uses a decision framework to systematically assess whether a technology is cost-effective. This includes comparative clinical effectiveness and health related quality of life benefits, which the new treatment may provide and whether the cost requested by the pharmaceutical company is justified.

Following the recommendation from the NCPE, the HSE examines all the evidence which may be relevant for the decision; the final decision on reimbursement is made by the HSE. In the case of cancer drugs the NCPE recommendation is also considered by the National Cancer Control Programme (NCCP) Technology Review Group.

About the National Centre for Pharmacoeconomics

The NCPE are a team of clinicians, pharmacists, pharmacologists and statisticians who evaluate the benefit and costs of medical technologies and provide advice to the HSE. We also obtain valuable support from clinicians with expertise in the specific clinical area under consideration. Our aim is to provide impartial advice to help decision makers provide the most effective, safe and value for money treatments for patients. Our advice is for consideration by anyone who has a responsibility for commissioning or providing healthcare, public health or social care services.

Summary

In November 2025, AbbVie submitted a dossier which investigated the comparative clinical effectiveness, cost-effectiveness and budget impact of mirvetuximab soravtansine (Elahere®) as monotherapy 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. AbbVie is seeking reimbursement of mirvetuximab soravtansine on the Oncology Drugs Management System.

Epithelial ovarian, fallopian tube, and primary peritoneal cancer are collectively referred to as epithelial ovarian cancer (EOC). Despite initial therapy, the majority of patients with advanced EOC relapse and develop platinum-resistant disease which has a poor prognosis. FRα is a protein that is overexpressed on the surface of the majority of EOC tumours. High FRα expression in EOC is associated with more aggressive tumours and resistance to chemotherapy.

Mirvetuximab soravtansine is an antibody drug conjugate that targets and binds to FRα. After binding to FRα, mirvetuximab soravtansine is internalised followed by intracellular release of cytotoxic DM4 resulting in cell cycle arrest and apoptotic cell death. The recommended dose of mirvetuximab soravtansine is 6mg/kg, based on adjusted ideal body weight (AIBW), administered once every 21 days by intravenous infusion. The summary of product characteristic (SmPC) for mirvetuximab soravtansine states that eligible patients should have FRα tumour status defined as ≥75% viable tumour cells demonstrating moderate (2+) and/or strong (3+) membrane staining by immunohistochemistry (≥75% of cells with PS2+), assessed by a Conformité Européenne (CE)-marked in-vitro diagnostic (IVD) with the corresponding intended purpose. If a CE-marked IVD is not available, an alternative validated test should be used. The SmPC recommends that mirvetuximab soravtansine is continued until disease progression or unacceptable toxicity.

Standard of care therapies in the management of platinum resistant ovarian cancer in Ireland are single agent (non-platinum) chemotherapies. Paclitaxel, topotecan, and

pegylated liposomal doxorubicin (PLD) are commonly used and were included as comparators in this submission, which the Review Group considered appropriate.

1. Comparative effectiveness of mirvetuximab soravtansine

The clinical efficacy and safety of mirvetuximab soravtansine was assessed in MIRASOL; a randomised, open label, phase III, multi-centre trial of mirvetuximab soravtansine versus investigator's choice of chemotherapy (ICC) in adult female participants (n=453) with platinum-resistant, recurrent high-grade serous EOC, who had received one to three prior systemic anticancer therapies and had high FRα tumour expression (≥75% of cells with PS2+) assessed using the Ventana FOLR1 assay. Platinum resistance was defined as progression of disease between more than three months and less than or equal to six months after the date of the last platinum dose (if only one line of prior platinum therapy) or within six months after the date of the last platinum dose (if two or three prior lines of platinum). Participants with primary platinum refractory disease were excluded. Participants were randomised 1:1 to receive either mirvetuximab soravtansine at a dose of 6mg/kg based on AIBW administered once every 21 days (n = 227) or ICC (n= 226), consisting of paclitaxel (40.7%), PLD (35.8%) or topotecan (23.5%) selected before random assignment. The primary endpoint was progression-free survival (PFS) using RECIST 1.1 criteria as determined by investigator assessment (PFS_{INV}). Key secondary endpoints were overall survival (OS), objective response rate by investigator (ORR_{INV}) and patient reported outcomes (PROs) using the Abdominal/ Gastrointestinal Scale of the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire – Ovarian Cancer Module 28 (QLQ-OV28-Ab/GI).

At the final analysis (26 September 2024), mirvetuximab soravtansine demonstrated statistically significant improvements in PFS (median PFS_{INV}: 5.59 versus 3.98 months, hazard ratio [HR] 0.63, 95% confidence interval (95% CI) 0.51 to 0.79), OS (median OS: 16.85 versus 13.34 months, HR 0.68, 95% CI 0.54 to 0.84) and ORR (odds ratio 3.75, 95% CI 2.40 to 5.85), compared with ICC. No statistically significant difference was found with mirvetuximab soravtansine in patient-reported outcomes (EORTC QLQ-QV28 Ab/GI), compared with ICC. Given the open label nature of MIRASOL, PFS by blinded independent central review (PFS_{BICR}) was provided as a sensitivity analysis of the primary endpoint (PFS_{INV}). Although the

median PFS and HRs were similar between PFS_{INV} and PFS_{BICR}, overall, there was poor concordance between PFS_{INV} and PFS_{BICR} based on individual PFS determinations at the final analysis. Given the open label nature of MIRASOL, the Review Group considered there was a risk of bias using investigator classification of progression without any mechanism to compare PFS_{INV} and PFS_{BICR} results. This limitation in the endpoint methodology is a source of bias in the BICR analysis. Informative censoring impacted the interpretation of the MIRASOL trial results; a greater number of participants did not receive study treatment in the ICC arm compared to the mirvetuximab soravtansine arm (n=19/226 versus n=9/227 respectively) or withdrew following at least one dose of study drug (n=26/226 versus n=8/227 respectively). The impact of this bias on time to event outcomes (PFS, OS) could not be addressed or accurately quantified. There were also notable differences between the mirvetuximab soravtansine and ICC arms in the proportions of participants treated with mirvetuximab soravtansine (<1% versus 7%) as a subsequent therapy which may have introduced bias for the efficacy estimates of OS. However, the magnitude and direction of this bias on OS is not known. Furthermore, mirvetuximab soravtansine as a subsequent treatment is not reimbursed in Ireland and is not reflective of clinical practice.

2. Safety of mirvetuximab soravtansine

The safety of mirvetuximab soravtansine was informed by the safety population for MIROSOL at the final analysis (26 September 2024). Grade three or higher (≥ 3) study drug-related treatment-emergent adverse events (TEAEs) occurred in 27% of participants in the mirvetuximab soravtansine arm and 37% of participants in the ICC arm. Grade ≥3 drug related eye disorders TEAEs occurred in 0% of participants in the ICC arm and 14% of participants in the mirvetuximab soravtansine arm including blurred vision (8%) and keratopathy (9%). Participants treated with mirvetuximab soravtansine were reported to have more dose reductions than participants treated with ICC (34.9% versus 24.6%); adverse events were the primary reason for any dose modifications among both treatment groups. Fewer participants treated with mirvetuximab soravtansine (3%) had study drug related grade ≥ 3 TEAEs leading to discontinuation of study drug compared to those treated with ICC (5%). Four deaths in the mirvetuximab soravtansine arm and five deaths in the ICC arm were reported due to TEAEs, of which none in the mirvetuximab soravtansine arm and one in the ICC arm were deemed to be study drug related. The mean duration of exposure was longer

in the mirvetuximab soravtansine arm compared to the ICC arm (30.5 weeks versus 17.7 weeks respectively). Extensive recommendations have been included in the SmPC including advice on baseline ophthalmic examinations, patient counselling including the use of prophylactic lubricating eye drops, ocular monitoring and management of ocular disorders.

3. Cost effectiveness of mirvetuximab soravtansine

Methods

Cost effectiveness was assessed, from the perspective of the HSE, using a partitioned survival model. The cost-effectiveness model (CEM) included three mutually exclusive health states: pre-progression, post-progression and death. The modelled population was based on MIRASOL trial participants. The intervention was mirvetuximab soravtansine and the comparator was pooled chemotherapy informed by the ICC arm of the MIRASOL trial. The treatment effects captured by the model were the delay of disease progression and death. In each cycle, patients accrued quality-adjusted life years (QALYs) and incurred costs specific to the treatment arm and the health state occupied. The CEM considers a lifetime horizon of 37.2 years. A half cycle correction was applied.

The key efficacy inputs to the model were PFS_{INV} and OS, which were endpoints in the MIRASOL trial. Time to treatment discontinuation data from MIRASOL were used to model duration of treatment and to calculate treatment costs for mirvetuximab soravtansine and pooled chemotherapy. Parametric models were fitted to the Kaplan Meier (KM) data for PFS_{INV} and OS. The independent lognormal distribution was selected by the Applicant as the base case model for PFS_{INV} for both mirvetuximab soravtansine and pooled chemotherapy. The Review Group note that all potential models and the KM PFS data produce similar cost effectiveness results and were therefore satisfied with the Applicant's choice of curves for modelling PFS_{INV}. The gamma and Weibull distributions were selected by the Applicant to extrapolate OS in the mirvetuximab soravtansine and pooled chemotherapy arms respectively. However, the Review Group note that all parametric curves imply a much longer tail than seen in the KM data for OS, which have reached 0% and 4% remaining alive in the MIRV and the pooled chemotherapy arm respectively, with less than 30% of patients censored in each arm. Therefore, the Review Group considered it more appropriate to use the observed KM data to model OS. The Review Group requested functionality to include

treatment waning for the parametric curves for OS at preliminary review. However, the Applicant declined to implement this request. The Applicant modelled time-on-treatment (ToT) for mirvetuximab soravtansine and each component of the pooled chemotherapy arm to reflect differences in dosing regimens and cycle lengths, which were expected to result in distinct treatment duration patterns over time. The Applicant used the exponential curve to model mirvetuximab soravtansine and ToT data to model each component of the pooled chemotherapy arm. The Review Group considered that choosing different approaches to model the duration of treatment for the intervention and the comparator was inappropriate. However, the Review Group did not change the choice of curve in the NCPE adjusted base case as it had a relatively small impact on cost-effectiveness results.

The CEM included drug acquisition costs, drug administration costs, subsequent treatment costs, adverse event costs and disease management costs. Additional treatment arm-specific monitoring costs and pre-medication costs were included for mirvetuximab soravtansine only, in line with the SmPC. A once-off, end-of life cost was applied to a proportion of patients entering the death health state. FRα testing costs were assumed to be incurred by patients in the mirvetuximab soravtansine arm only. Positive and negative FRα tests were accounted for; 32% of patients with platinum resistant ovarian cancer are assumed to test positive for FR-α expression, therefore, it was assumed that approximately three tests are required to identify one eligible patient. The Applicant applied a relative dose intensity (RDI) to the modelled dosing for mirvetuximab soravtansine and pooled chemotherapy to account for reduced drug exposure in the MIRASOL trial. The RDI implemented in the Applicant's CEM was based on a revised definition of RDI which differed from the RDI reported in the MIRASOL clinical study report (final analysis). The Applicant derived utility (quality of life) values in the CEM using EQ-5D-5L data from the MIRASOL trial, converted to utility values using the EQ-5D-5L Irish value set. The Applicant's base case used a 'time-to-death' approach for utilities adjusted for adverse events. The 'time-to-death' sub-states were further stratified according to treatment type and according to pre-progression and post-progression health status.

Several changes were made to inform the NCPE adjusted base case, specifically the use of observed KM data from the MIRASOL trial to model OS, implementation of RDI values for

study treatments as reported in the MIRASOL trial clinical study report (final analysis), implementation of utility values based on progression status only and implementation of utility values generated using the EQ-5D-3L descriptive system and UK value set, in line with previous HTAs and current NCPE guidelines.

Results

Deterministic incremental cost effectiveness ratios (ICERs) for mirvetuximab soravtansine versus pooled chemotherapy, generated under Applicant base case assumptions and NCPE adjusted base case assumptions are presented in Table 1 and in Table 2 respectively.

Table 1: Applicant base case incremental cost-effectiveness results[a, b, d, e]

Treatments	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
Pooled chemotherapy[c]	35,604	0.80			
Mirvetuximab soravtansine	116,718	1.17	81,114	0.37	218,983

CIC: commercial-in-confidence; ICER: incremental cost-effectiveness ratio; PLD: pegylated liposomal doxorubicin; QALY: quality adjusted life year

[a] Corresponding probabilistic ICER using 1,000 iterations = €216,532/QALY. Figures in the table are rounded, calculations may not be directly replicable

[b] A CIC PAS has been offered for mirvetuximab soravtansine, which has not been included in this table.

[C] Pooled chemotherapy comprised of PLD (35.8%), topotecan (23.5%) and paclitaxel (40.7%). The distribution of comparators was informed by the MIRASOL trial.

[d] There was an error in the Applicant's cost effectiveness model whereby the Framework Agreement rebate (9%) was applied to PLD, topotecan and paclitaxel which are available as generic medicines. This error was rectified by the NCPE in this table.

[e] Discount rate of 4% was applied to costs and outcomes.

Table 2: NCPE adjusted base case incremental cost-effectiveness results [a,b,d]

Treatments	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
Pooled chemotherapy[c]	37,070	0.81			
Mirvetuximab soravtansine	125,422	1.06	88,352	0.25	354,306

CIC: commercial-in-confidence; ICER: incremental cost-effectiveness ratio; PLD: pegylated liposomal doxorubicin; QALY: quality adjusted life year

[a] Corresponding probabilistic ICER using 1,000 iterations = €349,138/QALY. Figures in the table are rounded, calculations may not be directly replicable

[b] A CIC PAS has been offered for mirvetuximab soravtansine, which has not been included in this table.

[C] Pooled chemotherapy comprised of PLD (35.8%), topotecan (23.5%) and paclitaxel (40.7%). The distribution of comparators was informed by the MIRASOL trial.

[d] Discount rate of 4% was applied to costs and outcomes.

Sensitivity analysis

Cost-effectiveness results were most sensitive to modelling assumptions related to extrapolation of OS, and the use of time to death, progression status and treatment specific utilities. Under NCPE adjusted base case assumptions, the probability of cost-effectiveness

of mirvetuximab soravtansine versus pooled chemotherapy was 0% at both the €45,000/QALY and €20,000/QALY thresholds. A price-ICER analysis, using NCPE adjusted base case assumptions, indicated that an 80.5% and 86.2% reduction to the price to wholesaler (PtW) of mirvetuximab soravtansine would be required for mirvetuximab soravtansine to be cost-effective at the €45,000/QALY and the €20,000/QALY thresholds respectively.

4. Budget impact of **mirvetuximab soravtansine**

The PtW for one vial (20ml) of mirvetuximab soravtansine is €2,930. Costs in the budget impact model (BIM) were informed by the duration of treatment based on the area under the curve in the CEM capped by PFS. The Applicant estimated the cost per patient, per treatment course of mirvetuximab soravtansine to be €107,274 (including VAT) which incorporated a revised RDI which differed from the RDI reported in the MIRASOL clinical study report (final analysis). The Applicant estimated the five-year cumulative gross and net drug budget impacts to be €21.48 million (including VAT) and €19.96 million (including VAT), respectively. The NCPE estimated the cost per patient, per treatment course of mirvetuximab soravtansine to be €116,984 (including VAT). The Review Group made a number of corrections in the BIM specifically the application of the overall average age-standardised incidence rate for ovarian cancer (2020-2022) as reported by the National Cancer Registry of Ireland to the overall female population (as opposed to the adult only female population), the removal of the Framework Agreement rebate (9%) for PLD and updates to the RDIs for mirvetuximab soravtansine and ICC to align with those reported in the MIRASOL clinical study report (final analysis). Using the Review Group assumptions, the estimated five-year cumulative gross and net drug budget impacts were €29.60 million (including VAT) and €27.41 million (including VAT), respectively. Budget impact estimates were sensitive to patient number estimates which were very uncertain. Costs associated with FRα testing were accounted for in line with the approach taken in the CEM. The Applicant and NCPE adjusted five-year cumulative net healthcare budget impacts (inclusive of drug and non-drug costs [VENTANA FOLR1 companion diagnostic test]) were €20.10 million (including VAT) and €27.62 million (including VAT), respectively.

5. Patient Organisation Submission

A patient organisation submission was received from OvaCare. This submission will form part of the information that the HSE considers when making their drug funding decision.

6. Conclusion

The NCPE recommends that mirvetuximab soravtansine as monotherapy for the treatment of 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 be considered for reimbursement if cost-effectiveness can be improved relative to existing treatments*.

*Next steps: The NCPE Assessment Report and recommendation and Patient Organisation submission, will be considered by the HSE when making their decision on reimbursement, while also having regard to the criteria specified in the Health (Pricing and Supply of Medical Goods) Act 2013.

Further information on this process may be found here.