Gemeinsamer Bundesausschuss

Justification

of the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive:

Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Mirvetuximab soravtansine

(ovarian, fallopian tube, or primary peritoneal cancer, FRα-positive, platinum-resistant, after 1 to 3 prior therapies)

of 5 June 2025

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assesses the benefit of all reimbursable medicinal products with new active ingredients.

For medicinal products for the treatment of rare diseases (orphan drugs) that are approved according to Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999, the additional medical benefit is considered to be proven through the grant of the marketing authorisation according to Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V, the additional medical benefit is considered to be proven through the grant of the marketing authorisation. Evidence of the medical benefit and the additional medical benefit in relation to the appropriate comparator therapy do not have to be submitted (Section 35a, paragraph 1, sentence 11, 2nd half of the sentence SGB V). Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V thus guarantees an additional benefit for an approved orphan drug, although an assessment of the orphan drug in accordance with the principles laid down in Section 35a, paragraph 1, sentence 3, No. 2 and 3 SGB V in conjunction with Chapter 5 Sections 5 et seq. of the Rules of Procedure (VerfO) of the G-BA has not been carried out. In accordance with Section 5, paragraph 8 AM-NutzenV, only the extent of the additional benefit is to be quantified indicating the significance of the evidence.

However, the restrictions on the benefit assessment of orphan drugs resulting from the statutory obligation to the marketing authorisation do not apply if the turnover of the medicinal product with the SHI at pharmacy sales prices and outside the scope of SHI-accredited medical care, including VAT exceeds € 30 million in the last 12 calendar months. According to Section 35a paragraph 1, sentence 12 SGB V, the pharmaceutical company must then, within three months of being requested to do so by the G-BA, submit evidence according to Chapter 5, Section 5, subsection 1–6 VerfO, in particular regarding the additional medical benefit in relation to the appropriate comparator therapy as defined by the G-BA according to Chapter 5 Section 6 VerfO and prove the additional benefit in comparison with the appropriate comparator therapy.

In accordance with Section 35a, paragraph 2 SGB V, the G-BA decides whether to carry out the benefit assessment itself or to commission the Institute for Quality and Efficiency in Health Care (IQWiG). Based on the legal requirement in Section 35a, paragraph 1, sentence 11 SGB V that the additional benefit of an orphan drug is considered to be proven through the grant of the marketing authorisation the G-BA modified the procedure for the benefit assessment of orphan drugs at their session on 15 March 2012 to the effect that, for orphan drugs, the G-BA initially no longer independently determines an appropriate comparator therapy as the basis for the solely legally permissible assessment of the extent of an additional benefit to be assumed by law. Rather, the extent of the additional benefit is assessed exclusively on the basis of the approval studies by the G-BA indicating the significance of the evidence.

Accordingly, at their session on 15 March 2012, the G-BA amended the mandate issued to the IQWiG by the resolution of 1 August 2011 for the benefit assessment of medicinal products with new active ingredients in accordance with Section 35a, paragraph 2 SGB V to that effect that, in the case of orphan drugs, the IQWiG is only commissioned to carry out a benefit assessment in the case of a previously defined comparator therapy when the sales volume of the medicinal product concerned has exceeded the turnover threshold according to Section 35a, paragraph 1, sentence 12 SGB V and is therefore subject to an unrestricted benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment by the G-BA must be completed within three months of the relevant date for submission of the evidence and published on the internet.

According to Section 35a paragraph 3 SGB V, the G-BA decides on the benefit assessment within three months of its publication. The resolution is to be published on the internet and is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The relevant date for the start of the benefit assessment procedure was the first placing on the (German) market of the active ingredient mirvetuximab soravtansine on 15 December 2024 in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure (VerfO) of the G-BA. The pharmaceutical company submitted the final dossier to the G-BA in accordance with Section 4, paragraph 3, number 1 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5 Section 8, paragraph 1, number 1 VerfO on 4 December 2024.

Mirvetuximab soravtansine for the treatment of ovarian, fallopian tube or primary peritoneal cancer is approved as a medicinal product for the treatment of a rare disease under Regulation (EC) No 141/2000 of the European Parliament and the Council of 16 December 1999.

In accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V, the additional benefit is considered to be proven through the grant of the marketing authorisation. The extent of the additional benefit and the significance of the evidence are assessed on the basis of the approval studies by the G-BA.

The G-BA carried out the benefit assessment and commissioned the IQWiG to assess the information provided by the pharmaceutical company in Module 3 of the dossier on treatment costs and patient numbers. The benefit assessment was published on 17 March 2025 together with the IQWiG assessment on the website of the G-BA (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA has adopted its resolution on the basis of the dossier of the pharmaceutical company, the dossier assessment carried out by the G-BA, the assessment of treatment costs and patient numbers (IQWiG G24-36) prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure.

In order to determine the extent of the additional benefit, the G-BA has evaluated the studies relevant for the marketing authorisation with regard to their therapeutic relevance (qualitative) in accordance with the criteria laid down in Chapter 5 Section 5, paragraph 7, sentence 1, numbers 1 – 4 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of mirvetuximab soravtansine.

2.1 Additional benefit of the medicinal product

2.1.1 Approved therapeutic indication of Mirvetuximab soravtansine (Elahere) in accordance with the product information

ELAHERE as monotherapy is indicated for the treatment of adult patients with folate receptor-alpha (FRα) positive, platinum-resistant high grade serous epithelial ovarian, fallopian tube,

[1] General Methods, version 7.0 from 19.09.2023. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

or primary peritoneal cancer who have received one to three prior systemic treatment regimens

Therapeutic indication of the resolution (resolution of 5 June 2025):

See the approved therapeutic indication.

2.1.2 Extent of the additional benefit and significance of the evidence

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

In summary, the additional benefit of mirvetuximab soravtansine is assessed as follows:

Indication of a considerable additional benefit

Justification:

For the assessment of the extent of the additional benefit of mirvetuximab in the therapeutic indication of high grade serous epithelial ovarian cancer after one to three prior therapies, the pharmaceutical company presented data from the multicentre, open-label, randomised phase III MIRASOL and FORWARD 1 studies as well as a meta-analysis of these two studies.

MIRASOL study

The MIRASOL study is a multicentre, open-label, randomised phase III study conducted between 2020 and 2024 to investigate the efficacy and safety of mirvetuximab in adult patients with high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received one to three prior systemic treatment regimens and whose tumours have a high folate receptor-alpha (FRα) level. The study is being conducted in 136 study sites in Asia, Australia, Europe and the USA.

A total of 453 patients were enrolled in the study and randomised in a 1:1 ratio into the intervention arm (mirvetuximab soravtansine, N = 227) and the comparator arm (therapy according to doctor's instructions with selection of paclitaxel, pegylated liposomal doxorubicin and topotecan, N = 226).

The primary endpoint of the study was progression-free survival (PFS). Other endpoints were overall survival and endpoints in the categories morbidity, health-related quality of life and side effects.

For the benefit assessment, the results of the final data cut-off from 26.09.2024 are used.

FORWARD 1 study

The FORWARD 1 study is a multicentre, open-label, randomised phase III study conducted between 2017 and 2020 to investigate the efficacy and safety of mirvetuximab in adult patients with high grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received one to three prior systemic treatment regimens and whose tumours are folate receptor-alpha (FRα) positive (medium or high expression). The study is being conducted in 101 study sites, mainly in Europe and the USA.

A total of 366 patients were enrolled in the study and randomised in a 2:1 ratio into the intervention arm (mirvetuximab soravtansine, N = 248) and the comparator arm (therapy

according to doctor's instructions with selection of paclitaxel, pegylated liposomal doxorubicin and topotecan, N = 118). Randomisation was stratified according to "number of prior therapies (1 vs 2 vs 3)", "FRα-level (≥ 75% tumour staining at ≥ 2+ intensity [high] vs ≥ 50% to < 75% tumour staining at > 2+ intensity [medium]" and according to "IC chemo (paclitaxel vs pegylated liposomal doxorubicin (PLD) vs topotecan)".

The primary endpoint of the study was progression-free survival (PFS). Other endpoints were overall survival and endpoints in the categories morbidity, health-related quality of life and side effects.

In the dossier, the pharmaceutical company presented data on the benefit assessment-relevant sub-population of patients with ovarian cancer and high FRα-expression, corresponding to the therapeutic indication according to the product information. This post-hoc defined modified (mITT) population comprises 116 patients in total, with 82 patients in the treatment arm and 34 patients in the control arm.

For the benefit assessment, the results of the final data cut-off from 18.03.2020 are used.

Comparator therapies in the MIRASOL and FORWARD 1 studies

In both studies, the comparators paclitaxel, pegylated liposomal doxorubicin and topotecan were used as part of a therapy according to doctor's instructions. In the EPAR, the EMA describes that the selection of comparators is almost in line with the current guideline recommendations, but also points out that chemotherapy in combination with bevacizumab is recommended for patients without contraindications and without prior exposure to bevacizumab.

39% (MIRASOL) and 50% (FORWARD 1) of patients in the intervention arm and 37% (MIRASOL) and 47% (FORWARD 1) in the control arm had not received any prior bevacizumab-containing therapy. It is not clear from the data presented in the benefit assessment procedure why bevacizumab-naïve patients in the study did not receive bevacizumab-containing chemotherapy, especially since up to 18.5% of patients received bevacizumab as part of the subsequent therapy. It therefore remains unclear whether a relevant percentage of patients would have been eligible for bevacizumab-containing therapy and to what extent these patients were treated in accordance with the currently generally recognised treatment standard.

Meta-analysis

In addition to the results of the individual studies, the pharmaceutical company presented a post-hoc meta-analytical evaluation of the MIRASOL and FORWARD 1 studies in the dossier.

Comparison between the MIRASOL and FORWARD 1 studies

In the MIRASOL study, 46% and 48% of patients respectively received three lines of therapy, in the FORWARD 1 study the figures were 35% and 41%. The prior therapies in the MIRASOL study also comprised 10-40% higher percentages of the active ingredients bevacizumab, PARP inhibitors and doxorubicin/ PLD.

In addition, there was a difference in the definition of platinum-resistant disease in patients with only one prior therapy between the two studies. In the MIRASOL study, this was defined as progression between 3 or 6 months after the date of the last platinum dose, whereas in the FORWARD 1 study, progression could occur before month 3. In the MIRASOL study, a non-response or progression within 3 months of initial platinum-based treatment and within 4 weeks for the FORWARD 1 study was categorised as platinum refractoriness.

The summary of the two studies is considered appropriate overall and the results of the meta-analysis are used as a basis for the benefit assessment alongside the results of the individual studies.

Subgroup analyses

As part of the written statement procedure, the pharmaceutical company subsequently submitted subgroup analyses of the meta-analysis.

The meta-analysis showed a statistically significant interaction term (0.0382) for overall survival for the subgroup "BRCA status", with a statistically significant advantage in favour of mirvetuximab soravtansine for both subgroups. The subgroup analyses were conducted purely descriptively and the subgroup of patients with a positive BRCA status is small (N=40 vs N=39). Although the effects differed in extent, they are aligned in direction. Also for SAEs, there was a statistically significant interaction with analogue results for BRCA status.

In the overall analysis, the effect modification by the characteristic "BRCA status" is considered inadequate to derive corresponding separate conclusions on the additional benefit.

On the study results:

Mortality

Overall survival in the MIRASOL and FORWARD 1 studies was operationalised as the time from randomisation to death from any cause.

For the endpoint of overall survival, the MIRASOL study and the meta-analysis showed a statistically significant advantage in favour of mirvetuximab soravtansine. The extent of the prolongation achieved in overall survival is assessed as a relevant improvement.

Morbidity

Progression-free survival

Progression-free survival (PFS) was operationalised in the MIRASOL and FORWARD 1 studies as the time from randomisation to occurrence of radiological disease progression or death from any cause, whichever occurred first. The endpoint was collected in both studies by principal investigators on site as well as using BICR, and was assessed according to the RECIST criteria version 1.1. For the PFS endpoint, both the MIRASOL study and the meta-analysis showed a statistically significant advantage in favour of mirvetuximab soravtansine.

The PFS endpoint is a composite endpoint composed of endpoints of the mortality and morbidity categories. The endpoint component "mortality" was already assessed as an independent endpoint in the present study via the endpoint "overall survival". The morbidity component assessment was not done in a symptom-related manner but exclusively by means of imaging (disease progression assessed by radiology according to the RECIST version 1.1 criteria).

Taking into account the aspects mentioned above, there are different opinions within the G-BA regarding the patient-relevance of the endpoint PFS. The overall statement on the additional benefit remains unaffected.

Symptomatology

Symptomatology was assessed using the instruments EORTC QLQ-C30, EORTC QLQ-OV28, EQ-5D-VAS, PGIS (only in the MIRASOL study) and FOSI (only in the FORWARD 1 study).

The return rates are < 70% as early as week 8/9 and thus for the first survey after baseline for all instruments.

As part of the written statement procedure, the pharmaceutical company subsequently submitted data for all enrolled patients from amendment 2 of the MIRASOL study. However, the return rates here also remain at < 70% in relation to the ITT or mITT population, which is why the results for the patient-reported outcomes are unsuitable for the benefit assessment.

Quality of life

EORTC QLQ-C30 and EORTC QLQ-OV28

Health-related quality of life was assessed using the EORTC QLQ-C30 and EORTC QLQ-OV28 instruments.

The return rates are < 70% and are therefore unsuitable for the benefit assessment (detailed presentation in the section on symptomatology).

Side effects

Adverse events (AEs) in total

In the MIRASOL and FORWARD 1 studies, AEs occurred in both study arms in almost all patients. The results were only presented additionally.

Serious adverse events (SAE); severe AEs (CTCAE grade 3 or 4) and therapy discontinuation due to adverse events

For the endpoints of SAEs, severe AEs and therapy discontinuation due to AEs, there were statistically significant differences to the advantage of mirvetuximab soravtansine.

Specific AEs

In detail, for the severe AEs (with an incidence ≥ 5% in at least one study arm), there were statistically significant advantages in the intervention arm for "Blood and lymphatic system disorders, SOC" (MIRASOL and FORWARD 1 studies as well as meta-analysis), "General disorders and administration site conditions, SOC" (MIRASOL and FORWARD 1 studies as well as meta-analysis), "Investigations, SOC" (MIRASOL study and meta-analysis), "Anaemia, PT" (MIRASOL study and meta-analysis), "Neutropenia, PT" (MIRASOL study and meta-analysis), "Thrombocytopenia, PT" (MIRASOL study) as well as "Fatigue, PT" (MIRASOL study and meta-analysis).

For the SAEs (with an incidence ≥ 5% in at least one study arm), there was a statistically significant advantage in the intervention arm for "Small bowel obstruction, PT" (MIRASOL study and meta-analysis) and "Gastrointestinal disorders, SOC" (meta-analysis).

For the AEs of special interest, there were statistically significant disadvantages in the intervention arm for "Pneumonitis, AE regardless of severity grade" (MIRASOL study) and "Peripheral neuropathy, AE regardless of severity grade" (MIRASOL study and meta-analysis) as well as in the following PT for "Eye disorder", "Cataract, AE regardless of severity grade" (MIRASOL study and meta-analysis), "Dry eye, AE regardless of severity grade" (MIRASOL and FORWARD 1 studies as well as meta-analysis), "Eye pain, AE regardless of severity grade" (MIRASOL study and meta-analysis), "Keratopathy, AE regardless of severity grade" (meta-analysis), "Photophobia, AE regardless of severity grade" (MIRASOL study and meta-analysis), "Blurred vision, AE regardless of severity grade" (MIRASOL and FORWARD 1 studies as well as meta-analysis) and "Reduced visual acuity, AE regardless of severity grade" (meta-analysis).

Overall, there was a clear advantage of mirvetuximab soravtansine in the endpoint category of side effects compared to therapy according to doctor's instructions with selection of paclitaxel, pegylated liposomal doxorubicin and topotecan.

Overall assessment

For the benefit assessment, results on mortality, morbidity, quality of life and side effects from the open-label, randomised, controlled phase III MIRASOL and FORWARD 1 studies as well as the meta-analysis of these two studies comparing mirvetuximab soravtansine with a therapy according to doctor's instructions with selection of paclitaxel, pegylated liposomal doxorubicin and topotecan are available.

For the endpoint of overall survival, the MIRASOL study and the meta-analysis showed a statistically significant advantage in favour of mirvetuximab soravtansine. The extent of the prolongation achieved in overall survival is assessed as a relevant improvement.

No assessable data on morbidity and health-related quality of life are available.

For the endpoint category of side effects, there were statistically significant advantages for SAEs, severe AEs and therapy discontinuation due to AEs, which are assessed as a significant improvement. In detail, there were advantages and disadvantages for specific AEs.

In the overall assessment, the G-BA identified a considerable additional benefit of mirvetuximab soravtansine for 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 due to relevant advantages in overall survival and clear advantages in side effects.

Significance of the evidence

This benefit assessment is based on the results of the open-label, randomised, controlled phase III MIRASOL and FORWARD 1 studies as well as the meta-analysis of these two studies.

The risk of bias is considered to be low at study level and for the endpoints of overall survival and side effects.

No assessable data on morbidity and health-related quality of life are available. In view of the fact that high significance is attributed to statements on quality of life especially in the advanced palliative situation, there is uncertainty regarding the significance of the evidence.

Overall, the G-BA derives an indication of the identified additional benefit with regard to the significance of the evidence.

2.1.3 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Elahere with the active ingredient mirvetuximab soravtansine.

Mirvetuximab soravtansine (Elahere) as monotherapy was approved 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.

The results from the open-label, randomised, controlled phase III MIRASOL and FORWARD 1 studies as well as a meta-analysis of these two studies are available for the benefit assessment. In both studies, mirvetuximab soravtansine was compared with a therapy according to doctor's instructions with selection of paclitaxel, pegylated liposomal doxorubicin and topotecan.

For the endpoint of overall survival, there was a statistically significant difference to the advantage of mirvetuximab soravtansine, the extent of which was assessed as a relevant improvement.

No assessable data on morbidity and health-related quality of life are available.

In terms of side effects, there were clear advantages for the SAEs, severe AEs and therapy discontinuation due to AEs, as well as advantages and disadvantages for specific AEs in detail.

In the overall assessment, there were relevant advantages in overall survival and clear advantages in side effects. No assessable data on morbidity and health-related quality of life are available. Overall, a considerable additional benefit of mirvetuximab soravtansine was identified.

The significance of the evidence for the additional benefit identified is classified in the "indication" category overall.

2.2 Number of patients or demarcation of patient groups eligible for treatment

The information on the number of patients is based on the target population in statutory health insurance (SHI).

The G-BA base their resolution generally on the pharmaceutical company's information on the total population.

These are however subject to uncertainties. The pharmaceutical company chose the incidence approach for its derivation. This is plausible in principle, but it can be assumed that some patients do not suffer disease progression during second or third-line systemic therapy or a relapse thereafter in the same year, but later.

Further uncertainties lie in particular in the unclear transferability and imprecision of a large proportion of the percentage values used by the pharmaceutical company.

2.3 Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Elahere (active ingredient: mirvetuximab soravtansine) at the following publicly accessible link (last access: 23 May 2025):

https://www.ema.europa.eu/en/documents/product-information/elahere-epar-product-information_en.pdf

Treatment with mirvetuximab soravtansine should only be initiated and monitored by specialists in internal medicine, haematology, and oncology, specialists in gynaecology, and other specialists participating in the Oncology Agreement, all of whom are experienced in the treatment of patients with ovarian cancer.

Prior to treatment with mirvetuximab soravtansine and in the event of eye symptoms, an eye examination should be carried out by an ophthalmologist. Prior to each cycle, patients should also be advised to report any new or deteriorating eye symptoms to the treating doctor or specialist staff.

2.4 Treatment costs

The treatment costs are based on the requirements in the product information and the information listed in the LAUER-TAXE® (last revised: 1 May 2025).

For the cost representation, one year is assumed for all medicinal products.

For the cost representation, only the dosages of the general case are considered. Patient-individual dose adjustments (e.g. because of side effects or co-morbidities) are not taken into account when calculating the annual treatment costs.

Treatment period:

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Mirvetuximab soravtansine	1 x per 21-day cycle	17.4	1	17.4

Consumption:

For dosages depending on body weight (BW) or body surface area (BSA), the average body measurements from the official representative statistics "Microcensus 2021 – body measurements of the population" were applied (average body height of women: 1.66 m, average body weight of women: 69.2 kg).[2]

According to the product information, the recommended dose of mirvetuximab soravtansine is 6 mg/kg adjusted ideal body weight (AIBW) once every 3 weeks as an intravenous infusion. The use of the AIBW reduces the variability between underweight and overweight patients.

The AIBW is calculated using the ideal body weight (IBW) as follows:

AIBW = ideal body weight (IBW [kg]) + 0.4 x (actual body weight [kg] - IBW) IBW = 0.9 x body height [cm] - 92

An adult woman's average body height of 166 cm and the average body weight of 69.2 kg from the currently available data of the 2021 Microcensus are used to calculate the average annual consumption per patient for medicinal products for which individual dosing is based on body weight.

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Mirvetuximab soravtansine	6 mg/kg AIBW = 372.72 mg	372.72 mg	4 x 100 mg	1	69.6 x 100 mg

Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Section 130 and Section 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis

[2] Federal Health Reporting. Average body measurements of the population (2021, both sexes, 15 years and older), www.gbe-bund.de

of consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates. Any reference prices shown in the cost representation may not represent the cheapest available alternative.

Costs of the medicinal products:

Medicinal product to be assessed					
Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Mirvetuximab soravtansine 100 mg	1 INF	€ 3,734.76	€ 1.77	€ 210.00	€ 3,522.99
Abbreviations: INF = infusion solution					

Costs for additionally required SHI services:

Only costs directly related to the use of the medicinal product are taken into account. If there are regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, the costs incurred for this must be taken into account as costs for additionally required SHI services.

Medical treatment costs, medical fee services, and costs incurred for routine examinations (e.g. regular laboratory services such as blood count tests) that do not exceed the standard expenditure in the course of the treatment are not shown.

Non-prescription medicinal products that are reimbursable at the expense of the statutory health insurance according to Annex I of the Pharmaceuticals Directive (so-called OTC exception list) are not subject to the current medicinal products price regulation. Instead, in accordance with Section 129 paragraph 5aSGB V, when a non-prescription medicinal product is dispensed and invoiced in accordance with Section 300, a medicinal product dispensing price in the amount of the dispensing price of the pharmaceutical company plus the surcharges in accordance with Sections 2 and 3 of the Pharmaceutical Price Ordinance in the version valid on 31 December 2003 applies to the insured.

Prophylactic premedication

According to the product information, premedication with a corticosteroid (e.g. dexamethasone, IV), an antihistamine (e.g. diphenhydramine, PO or IV), an antipyretic (e.g. paracetamol, PO or IV) and an anti-emetic (e.g. a 5HT3 serotonin receptor antagonist, PO or IV) is needed prior to the administration of mirvetuximab soravtansine.

Therefore, the costs for dexamethasone, dimetindene and paracetamol with the dosage for premedication given in the product information are presented as an example. The costs may vary depending on the active ingredient and the dosage form used.

The product information does not provide any specific information on the premedication with antiemetics, which is why the necessary costs cannot be quantified.

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates	Treatment days/ year	Costs/ patient / year
Medicinal product to be assessed							
Mirvetuximab soravtansine							
Dexamethasone IV 10 mg	10 ILO at 5 mg	€ 17.43	€ 0.00	€ 1.77	€ 15.66	17.4	€ 54.50
Dimetindene IV 1 mg/ 10 kg = 6.96 mg	5 ILO at 4 mg	€ 26.24	€ 1.77	€ 7.02	€ 17.45	17.4	€ 121.45
Paracetamol 500 mg – 1,000 mg	20 TAB at 500 mg 10 TAB at 1,000 mg	€ 3.47 € 3.32	€ 0.17 € 0.17	€ 0.15 € 0.14	€ 3.15 € 3.01	17.4	€ 2.74 - € 5.24
Abbreviations: SFI = solution for injection; TAB = tablets							

LAUER-TAXE® last revised: 1 May 2025

Other SHI services:

The special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe) (Sections 4 and 5 of the Pharmaceutical Price Ordinance) from 1 October 2009 is not fully used to calculate costs. Alternatively, the pharmacy sales price publicly accessible in the directory services according to Section 131 paragraph 4 SGB V is a suitable basis for a standardised calculation.

According to the currently valid version of the special agreement on contractual unit costs of retail pharmacist services (Hilfstaxe), surcharges for the production of parenteral preparations containing cytostatic agents a maximum amount of € 100 per ready-to-use preparation, and for the production of parenteral solutions containing monoclonal antibodies a maximum of € 100 per ready-to-use unit are to be payable. These additional other costs are not added to the pharmacy sales price but rather follow the rules for calculating in the Hilfstaxe. The cost representation is based on the pharmacy retail price and the maximum surcharge for the preparation and is only an approximation of the treatment costs. This presentation does not take into account, for example, the rebates on the pharmacy purchase price of the active ingredient, the invoicing of discards, the calculation of application containers, and carrier solutions in accordance with the regulations in Annex 3 of the Hilfstaxe.

2.5 Designation of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with the assessed medicinal product

According to Section 35a, paragraph 3, sentence 4, the G-BA designates all medicinal products with new active ingredients that can be used in a combination therapy with the assessed

medicinal product for the therapeutic indication to be assessed on the basis of the marketing authorisation under Medicinal Products Act.

Basic principles of the assessed medicinal product

A designation in accordance with Section 35a, paragraph 3, sentence 4 SGB V requires that it is examined based on the product information for the assessed medicinal product whether it can be used in a combination therapy with other medicinal products in the assessed therapeutic indication. In the first step, the examination is carried out on the basis of all sections of the currently valid product information for the assessed medicinal product.

If the assessed medicinal product contains an active ingredient or a fixed combination of active ingredients in the therapeutic indication of the resolution (assessed therapeutic indication) and is approved exclusively for use in monotherapy, a combination therapy is not considered due to the marketing authorisation under Medicinal Products Act, which is why no designation is made.

A designation is also not considered if the G-BA has decided on an exemption as a reserve antibiotic for the assessed medicinal product in accordance with Section 35a, paragraph 1c, sentence 1 SGB V. The additional benefit is deemed to be proven if the G-BA has decided on an exemption for a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V; the extent of the additional benefit and its therapeutic significance are not to be assessed by the G-BA. Due to the lack of an assessment mandate by the G-BA following the resolution on an exemption according to Section 35a, paragraph 1c, sentence 1 SGB V with regard to the extent of the additional benefit and the therapeutic significance of the reserve antibiotic to be assessed, there is a limitation due to the procedural privileging of the pharmaceutical companies to the effect that neither the proof of an existing nor an expected at least considerable additional benefit is possible for exempted reserve antibiotics in the procedures according to Section 35a paragraph 1 or 6 SGB V and Section 35a paragraph 1d SGB V. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V must therefore also be taken into account at the level of designation according to Section 35a, paragraph 3, sentence 4 SGB V in order to avoid valuation contradictions.

With regard to the further examination steps, a differentiation is made between a "determined" or "undetermined" combination, which may also be the basis for a designation.

A "determined combination" exists if one or more individual active ingredients which can be used in combination with the assessed medicinal product in the assessed therapeutic indication are specifically named.

An "undetermined combination" exists if there is information on a combination therapy, but no specific active ingredients are named. An undetermined combination may be present if the information on a combination therapy:

- names a product class or group from which some active ingredients not specified in detail can be used in combination therapy with the assessed medicinal product, or
- does not name any active ingredients, product classes or groups, but the assessed medicinal product is used in addition to a therapeutic indication described in more

detail in the relevant product information, which, however, does not include information on active ingredients within the scope of this therapeutic indication.

Concomitant active ingredient

The concomitant active ingredient is a medicinal product with new active ingredients that can be used in combination therapy with the assessed medicinal product for the therapeutic indication to be assessed.

For a medicinal product to be considered as a concomitant active ingredient, it must be classified as a medicinal product with new active ingredients according to Section 2 paragraph 1 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with the corresponding regulations in Chapter 5 of the Rules of Procedure of the G-BA as of the date of the present resolution. In addition, the medicinal product must be approved in the assessed therapeutic indication, whereby a marketing authorisation is sufficient only for a sub-area of the assessed therapeutic indication.

Based on an "undetermined combination", the concomitant active ingredient must be attributable to the information on the product class or group or the therapeutic indication according to the product information of the assessed medicinal product in the assessed therapeutic indication, whereby the definition of a product class or group is based on the corresponding requirements in the product information of the assessed medicinal product.

In addition, there must be no reasons for exclusion of the concomitant active ingredient from a combination therapy with the assessed medicinal product, in particular no exclusive marketing authorisation as monotherapy.

In addition, all sections of the currently valid product information of the eligible concomitant active ingredient are checked to see whether there is any information that excludes its use in combination therapy with the assessed medicinal product in the assessed therapeutic indication under marketing authorisation regulations. Corresponding information can be, for example, dosage information or warnings. In the event that the medicinal product is used as part of a determined or undetermined combination which does not include the assessed medicinal product, a combination with the assessed medicinal product shall be excluded.

Furthermore, the product information of the assessed medicinal product must not contain any specific information that excludes its use in combination therapy with the eligible concomitant active ingredient in the assessed therapeutic indication under marketing authorisation regulations.

Medicinal products with new active ingredients for which the G-BA has decided on an exemption as a reserve antibiotic in accordance with Section 35a, paragraph 1c, sentence 1 SGB V are ineligible as concomitant active ingredients. The procedural privileging of the reserve antibiotics exempted according to Section 35a, paragraph 1c, sentence 1 SGB V also applies accordingly to the medicinal product eligible as a concomitant active ingredient.

Designation

The medicinal products which have been determined as concomitant active ingredients in accordance with the above points of examination are named by indicating the relevant active ingredient and the invented name. The designation may include several active ingredients,

provided that several medicinal products with new active ingredients may be used in the same combination therapy with the assessed medicinal product or different combinations with different medicinal products with new active ingredients form the basis of the designation.

If the present resolution on the assessed medicinal product in the assessed therapeutic indication contains several patient groups, the designation of concomitant active ingredients shall be made separately for each of the patient groups.

Exception to the designation

The designation excludes combination therapies for which - patient group-related - a considerable or major additional benefit has been determined by resolution according to Section 35a, paragraph 3, sentence 1 SGB V or it has been determined according to Section 35a, paragraph 1d, sentence 1 SGB V that at least considerable additional benefit of the combination can be expected. In this context, the combination therapy that is excluded from the designation must, as a rule, be identical to the combination therapy on which the preceding findings were based.

In the case of designations based on undetermined combinations, only those concomitant active ingredients - based on a resolution according to Section 35a, paragraph 3, sentence 1 SGB V on the assessed medicinal product in which a considerable or major additional benefit had been determined - which were approved at the time of this resolution are excluded from the designation.

Legal effects of the designation

The designation of combinations is carried out in accordance with the legal requirements according to Section 35a, paragraph 3, sentence 4 and is used exclusively to implement the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The designation is not associated with a statement as to the extent to which a therapy with the assessed medicinal products in combination with the designated medicinal products corresponds to the generally recognised state of medical knowledge. The examination was carried out exclusively on the basis of the possibility under Medicinal Products Act to use the medicinal products in combination therapy in the assessed therapeutic indication based on the product information; the generally recognised state of medical knowledge or the use of the medicinal products in the reality of care were not the subject of the examination due to the lack of an assessment mandate of the G-BA within the framework of Section 35a, paragraph 3, sentence 4 SGB V.

The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

Justification for the findings on designation in the present resolution:

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

No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient authorised in monotherapy.

3. Bureaucratic costs calculation

The proposed resolution does not create any new or amended information obligations for care providers within the meaning of Annex II to Chapter 1 VerfO and, accordingly, no bureaucratic costs.

4. Process sequence

On 4 December 2024, the pharmaceutical company submitted a dossier for the benefit assessment of mirvetuximab soravtansine to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 VerfO.

The benefit assessment of the G-BA was published on 17 March 2025 together with the IQWiG assessment of treatment costs and patient numbers on the website of the G-BA (www.g-ba.de), thus initiating the written statement procedure. The deadline for submitting statements was 7 April 2025.

The oral hearing was held on 22 April 2025.

In order to prepare a recommendation for a resolution, the Subcommittee on Medicinal Products commissioned a working group (Section 35a) consisting of the members nominated by the leading organisations of the care providers, the members nominated by the SHI umbrella organisation, and representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions.

The evaluation of the written statements received and the oral hearing was discussed at the session of the subcommittee on 27 May 2025, and the draft resolution was approved.

At their session on 5 June 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	11 March 2025	Information of the benefit assessment of the G-BA
Working group Section 35a	15 April 2025	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	22 April 2025	Conduct of the oral hearing
Working group Section 35a	29.04.2025; 13 May 2025	Consultation on the dossier assessment by the G-BA, the assessment of treatment costs and patient numbers by the IQWiG, and the

		evaluation of the written statement procedure
Subcommittee on Medicinal Products	27 May 2025	Concluding discussion of the draft resolution
Plenum	5 June 2025	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 5 June 2025

Federal Joint Committee (G-BA)
in accordance with Section 91 SGB V
The Chair

Prof. Hecken