Gemeinsamer Bundesausschuss

Resolution

of the Federal Joint Committee 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

At their session on 5 June 2025, the Federal Joint Committee (G-BA) resolved to amend the Pharmaceuticals Directive (AM-RL) in the version dated 18 December 2008 / 22 January 2009 (Federal Gazette, BAnz. No. 49a of 31 March 2009), as last amended by the publication of the resolution of D Month YYYY (Federal Gazette, BAnz AT DD.MM.YYYY BX), as follows:

I. Annex XII shall be amended in alphabetical order to include the active ingredient Mirvetuximab soravtansine as follows:

Mirvetuximab soravtansine

Resolution of: 5 June 2025
Entry into force on: 5 June 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 14 November 2024):

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, 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 therapeutic indication according to marketing authorisation.

1. Extent of the additional benefit and significance of the evidence

Mirvetuximab soravtansine is approved as a medicinal product for the treatment of rare diseases in accordance with Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999 on orphan drugs. In accordance with 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.

The G-BA determines the extent of the additional benefit for the number of patients and patient groups for which there is a therapeutically significant additional benefit in accordance with Chapter 5 Section 12, paragraph 1, number 1, sentence 2 of its Rules of Procedure (VerfO) in conjunction with Section 5, paragraph 8 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), indicating the significance of the evidence. This quantification of the additional benefit is based on the criteria laid out in Chapter 5 Section 5, paragraph 7, numbers 1 to 4 of the Rules of Procedure (VerfO).

<u>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</u>

Extent of the additional benefit and significance of the evidence of mirvetuximab soravtansine:

Indication of a considerable additional benefit

Study results according to endpoints:[1]

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

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↑↑	Advantage in overall survival
Morbidity	n.a.	There are no assessable data.
Health-related quality of life	n.a.	There are no assessable data.
Side effects	↑↑	Advantages in SAEs, severe AEs and therapy discontinuation due to AEs. Advantages and disadvantages in the specific AEs, in detail. The disadvantages of specific AEs are particularly evident in eye disorders.
Explanations: ↑: statistically significant and relevant positive effect with low/unclear reliability of data ↓: statistically significant and relevant negative effect with low/unclear reliability of data ↑↑: statistically significant and relevant positive effect with high reliability of data ↓↓: statistically significant and relevant negative effect with high reliability of data ↔: no statistically significant or relevant difference ∅: No data available. n.a.: not assessable		

Studies

MIRASOL

- Randomised, open-label, multicentre phase III study
- Mirvetuximab soravtansine vs therapy according to doctor's instructions[2]
- Final data cut-off from 26.09.2024

FORWARD 1

- Randomised, open-label, multicentre phase III study
- Mirvetuximab soravtansine vs therapy according to doctor's instructions[2]
- Relevant sub-population: Post-hoc defined study population (modified ITT, mITT) with high FRα status (≥ 75%)
- Final data cut-off from 18.03.2020

[1] Data from the dossier assessment of the G-BA (published on 17. March 2025), unless otherwise indicated.
[2] A selection of paclitaxel, pegylated liposomal doxorubicin and topotecan

Meta-analysis of the MIRASOL and FORWARD 1 studies

Mortality

Endpoint	Mirvetuximab		Therapy according to doctor's instructions[2]		Intervention vs control
	N	Median survival time in months [95% CI] *Patients with event n (%)*	N	Median survival time in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[a]
Overall survival					
MIRASOL	227	16.9 [14.36; 19.8] *162 (71)*	226	13.3 [11.4; 15.42] 177 (78)	0.67 [0.54; 0.84] 0.0004 AD = + 3.6 months
FORWARD 1 (mITT)	82	16.43 [12.42; 20.50] *51 (62)*	34	11.40 [6.11; 18.10] 25 (74)	0.66 [0.40; 1.08] 0.10
Meta-analysis	309	16.5 [14.7; 19.1]	260	13.3 [11.4; 15.1]	0.67 [0.55; 0.82] 0.0001 AD = + 3.2 months
				Interaction test[b]:	0.92

Morbidity

Endpoint	Mirvetuximab		Therapy according to doctor's instructions[2]		Intervention vs control
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[a]
Progression-free survival according to BICR (primary endpoint – presented additionally)					
MIRASOL	227	5.82 [4.93; 6.97] *164 (72)*	226	4.34 [3.52; 4.99] 127 (56)	0.70 [0.55; 0.89] 0.0043 AD = + 1.48 months
FORWARD 1 (mITT)	82	5.68 [4.04; 8.15] 59 (72)	34	3.22 [1.51; 5.49] 26 (76)	0.62 [0.38; 1.02] 0.069
Meta-analysis	309	5.75 [5.39; 6.87]	260	4.30 [3.22; 4.86]	0.69 [0.56; 0.86] 0.0011 AD = + 1.45 months

Endpoint	Mirvetuximab		Therapy according to doctor's instructions[2]		Intervention vs control
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	Effect estimator [95% CI] p value Absolute difference (AD)[a]
EORTC QLQ-C30	No suitable data available.				
EORTC QLQ-OV28	No suitable data available.				
EQ-5D-VAS	No suitable data available.				
PGIS[c]	No suitable data available.				
FOSI[d]	No suitable data available.				

Health-related quality of life

Endpoint	Mirvetuximab		Therapy according to doctor's instructions[2]		Intervention vs control
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	Effect estimator [95% CI] p value Absolute difference (AD)[a]
EORTC QLQ-C30	No suitable data available.				
EORTC QLQ-OV28	No suitable data available.				

Side effects

Endpoint **MedDRA system organ classes/ preferred terms/ AEs of special interest**	**Mirvetuximab**		**Therapy according to doctor's instructions[2]**		Intervention vs control
	N	Median time to event in weeks [95% CI] *Patients with event n (%)*	N	Median time to event in weeks [95% CI] *Patients with event n (%)*	HR [95% CI] p value
Total adverse events (presented additionally)					
MIRASOL	218	0.50 [0.29; 0.86] 211 (97)	207	1.00 [0.86; 1.14] 194 (94)	-
FORWARD 1 (mITT)	79	0.43 [0.29; 0.57] 79 (100)	32	0.50 [0.29; 1.00] 32 (100)	-
Meta-analysis	297	0.43 [0.29; 0.57] 290 (98)	239	0.86 [0.57; 1.14] 226 (95)	-
Serious adverse events (SAE)					
MIRASOL	218	n.a. [59.9; n.a.] 55 (25)	207	33.7 [28.6; n.a.] 69 (33)	0.55 [0.38; 0.80] 0.0012
FORWARD 1 (mITT)	79	97.29 [97.29; n.a.] 22 (28)	32	30.71 [7.57; n.a.] 13 (41)	0.44 [0.21; 0.92] 0.033 AD = +66.58 weeks
Meta-analysis	297	n.a. [97.3; n.a.] 77 (26)	239	33.71 [28.6; 45.7] 82 (34)	0.51 [0.37; 0.71] 0.0001
				Interaction test[b]:	0.62
Severe adverse events (CTCAE grade 3 or 4)					
MIRASOL	218	31.6 [21.1; 47.7] 97 (44)	207	14.1 [9.71; 17.7] 113 (55)	0.54 [0.41; 0.72] < 0.0001 AD = + 17.5 weeks
FORWARD 1 (mITT)	79	31.86 [19.0; n.a.] 37 (47)	32	9.00 [3.14; 10.43] 20 (62)	0.44 [0.25; 0.79] 0.008 AD = + 22.86 weeks
Meta-analysis	297	31.57 [22.0; 44.7] 134 (45)	239	12.0 [9.14; 16.0] 133 (56)	0.51 [0.40; 0.66] < 0.0001 AD = + 19.57 weeks

				Interaction test[b]:	0.58
Therapy discontinuation due to adverse events					
MIRASOL	218	n.a. [73.86; n.a.] 25 (11)	207	79.14 [55.29; n.a.] 31 (15)	0.44 [0.25; 0.78] 0.0042
FORWARD 1 (mITT)	79	n.a. [61.14; n.a.] 13 (16)	32	18.71 [8.71; n.a.] 15 (47)	0.27 [0.12; 0.59] 0.001
Meta-analysis	297	n.a. 38 (13)	239	79.1 [55.3; n.a.] 46 (19)	0.38 [0.24; 0.60] < 0.0001
				Interaction test[b]:	0.35
Severe adverse events according to MedDRA (with an incidence ≥ 5% in one study arm and statistically significant difference between the treatment arms; SOC and PT)					
Blood and lymphatic system disorders, SOC					
MIRASOL	218	n.a. 6 (3)		n.a. 51 (25)	0.07 [0.03; 0.17] < 0.0001
FORWARD 1	79	n.a. 4 (5)		34.3 [6.29; n.a.] 9 (28)	0.06 [0.01; 0.28] < 0.0001
Meta-analysis	297	n.a. 10 (3)		n.a. [34.3; n.a.] 60 (25)	0.07 [0.03; 0.15] < 0.0001[e]
Anaemia, PT					
MIRASOL	218	n.a. 2 (1)	207	n.a. [48.0; n.a.] 21 (10)	0.04 [0.01; 0.30] < 0.0001
Meta-analysis	297	n.a. 4 (1)	239	n.a. [48.0; n.a.] 23 (10)	0.08 [0.03; 0.29] < 0.0001[e]
Neutropenia, PT					
MIRASOL	218	n.a. 2 (1)	207	n.a. 36 (17)	0.04 [0.01; 0.16] < 0.0001
Meta-analysis	297	n.a. 2 (1)	239	n.a. 44 (18)	0.02 [0.01; 0.09] < 0.0001[e]
Thrombocytopenia, PT					
MIRASOL	218	n.a. 2 (1)	207	n.a. 13 (6)	0.10 [0.02; 0.43] 0.0001
Fatigue, PT					
MIRASOL	218	n.a.	207	n.a.	0.31

		5 (2)		11 (5)	[0.11; 0.90] 0.02
Meta-analysis	297	n.a. 7 (2)	239	n.a. [74.7; n.a.] 13 (5)	0.30 [0.12; 0.78] 0.01[e]
Eye disorder, SOC					
MIRASOL	218	100.7 [98.4; n.a.] 34 (16)	207	n.a. 0 (0)	n.a.[f]
FORWARD 1	79	106.0 [44.7; n.a.] 11 (14)	32	n.a. 0 (0)	n.a.[f]
Meta-analysis	297	106.0 [98.4; n.a.] 45 (15)	239	n.a. 0 (0)	n.a.[f]
General disorders and administration site conditions, SOC					
MIRASOL	218	n.a. 10 (5)	207	n.a. 22 (11)	0.33 [0.15; 0.69] 0.002
FORWARD 1	79	74.1 [n.a.] 4 (5)	32	n.a. 6 (19)	0.20 [0.06; 0.73] 0.014
Meta-analysis	297	n.a. 14 (5)	239	n.a. [74.7; n.a.] 28 (12)	0.29 [0.15; 0.56] 0.0001[e]
Fatigue, PT					
MIRASOL	218	n.a. 5 (2)	207	n.a. 11 (5)	0.31 [0.11; 0.90] 0.02
Meta-analysis	297	n.a. 7 (2)	239	n.a. [74.7; n.a.] 13 (5)	0.30 [0.12; 0.78] 0.01[e]
Investigations, SOC					
MIRASOL	218	n.a. 6 (3)	207	n.a. 17 (8)	0.22 [0.08; 0.61] 0.001
Meta-analysis	297	n.a. 8 (3)	239	n.a. 19 (8)	0.24 [0.10; 0.57] 0.0006[e]
SAEs according to MedDRA (with an incidence ≥ 5% in one study arm and statistically significant difference between the treatment arms; SOC and PT)					
Small bowel obstruction, PT					
MIRASOL	218	n.a. 4 (2)	207	n.a. 10 (5)	0.24 [0.07; 0.76]

					0.01
Meta-analysis	297	n.a. 4 (1)	239	n.a. 12 (5)	0.18 [0.06; 0.56] 0.001[e]
Gastrointestinal disorders, SOC					
Meta-analysis	297	n.a. 32 (11)	239	n.a. [38.3; n.a.] 32 (13)	0.57 [0.34; 0.95] 0.03[e]
Adverse events of special interest (with statistically significant difference between the treatment arms)					
Pneumonitis, AE regardless of severity grade					
MIRASOL	218	n.a. [56.7; n.a.] 26 (12)	207	n.a. 1 (0.5)	12.4 [1.65; 92.9] 0.0004
Peripheral neuropathy, AE regardless of severity grade					
MIRASOL	218	n.a. [19.1; n.a.] 82 (38)	207	n.a. [24.3; n.a.] 47 (23)	1.45 [1.01; 2.08] 0.043
Meta-analysis	297	52.1 [19.1; n.a.] 118 (40)	239	n.a. [24.3; n.a.] 56 (23)	1.40 [1.01; 1.94] 0.041[e]
Cataract, AE regardless of severity grade					
MIRASOL	218	98.43 [52.9; n.a.] 37 (17)	207	n.a. 1 (0.5)	18.1 [2.46; 133.9] < 0.0001
Meta-analysis	297	85.14 [52.14; n.a.] 51 (17)	239	n.a. 2 (1)	10.54 [2.5; 44.0] < 0.0001[e]
Dry eye, AE regardless of severity grade					
MIRASOL	218	98.4 [37.1; n.a.] 64 (29)	207	n.a. 5 (2)	11.1 [4.42; 27.6] < 0.0001
FORWARD 1	79	30.1 [24.1; n.a.] 28 (35)	32	n.a. [23.6; n.a.] 1 (3)	10.5 [1.42; 77.4] 0.001
Meta-analysis	297	68.6 [30.4; n.a.] 92 (31)	239	n.a. 6 (3)	11.0 [4.80; 25.4] < 0.0001[e]
Eye pain, AE regardless of severity grade					
MIRASOL	218	n.a. 21 (10)	207	n.a. 1 (0.5)	15.5 [2.07; 116.0] 0.0001
Meta-analysis	297	n.a.	239	n.a. 1 (0.4)	19.7 [2.7; 145.4]

		[111.1; n.a.] 32 (11)			< 0.0001[e]
Keratopathy, AE regardless of severity grade					
Meta-analysis	297	51.0 [34.43; n.a.] 94 (32)	239	n.a. 1 (0.4)	67.0 [9.32; 482.0] < 0.0001[e]
Photophobia, AE regardless of severity grade					
MIRASOL	218	n.a. [71.3; n.a.] 42 (19)	207	n.a. 1 (0.5)	29.5 [4.05; 215.3] < 0.0001
Meta-analysis	297	102.0 [75.3; n.a.] 56 (19)	239	n.a. 2 (1)	17.0 [4.12; 70.2] < 0.0001[e]
Blurred vision, AE regardless of severity grade					
MIRASOL	218	31.1 [15.1; 39.3] 94 (43)	207	n.a. 5 (2)	16.8 [6.80; 41.4] < 0.0001
FORWARD 1	79	19.0 [11.1; 30.1] 36 (46)	32	n.a. 1 (3)	17.2 [2.34; 125.6] < 0.0001
Meta-analysis	297	23.9 [15.3; 32.3] 130 (44)	239	n.a. 6 (3)	17.0 [7.47; 38.7] < 0.0001[e]
Reduced visual acuity, AE regardless of severity grade					
Meta-analysis	297	n.a. [62.1; n.a.] 49 (16)	239	n.a. 1 (0)	24.7 [3.39; 180.7] < 0.0001[e]

a. Indication of absolute difference (AD) only in case of statistically significant difference; own calculation
b. Interaction test from the data cut-off from 27.10.2023
c. Only collected in the MIRASOL study
d. Only collected in the FORWARD 1 study
e. No information on the interaction test
f. HR not calculable; a significant difference can be assumed, taking into account the high event rate already at an early stage and considering the number and time until the first AESI "Eye disorders" respectively

Abbreviations used:
AD = absolute difference; CTCAE = Common Terminology Criteria for Adverse Events; HR = hazard ratio; CI = confidence interval; N = number of patients evaluated; n = number of patients with (at least one) event; n.a. = not applicable; n.c. = not calculable; n.r. = not reached; vs = versus

2. Number of patients or demarcation of patient groups eligible for treatment

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

Approx. 630 – – 1,300 patients

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.

4. Treatment costs

Annual treatment costs:

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

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Mirvetuximab soravtansine	€ 245,200.10
Additionally required SHI costs	€ 178.69 - € 181.19
Total	€ 245,378.79 - € 245,381.29

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 May 2025)

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Medicinal product to be assessed					
Mirvetuximab soravtansine	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	17.4	€ 1,740

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

In the context of the designation of medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V, the following findings are made:

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.

The designation of combinations exclusively serves the implementation of the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. 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.

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 5 June 2025.

The justification to this resolution will be published on the website of the G-BA at www.g-ba.de.

Berlin, 5 June 2025

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

Prof. Hecken