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
Datopotamab deruxtecan (breast cancer, HR-positive, HER2-negative, after at least 1 prior therapy)

of 20 November 2025

At their session on 20 November 2025, the Federal Joint Committee (G-BA) resolved not 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 Datopotamab deruxtecan as follows:

Datopotamab deruxtecan

Resolution of: 20 November 2025
Entry into force on: 20 November 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 04 April 2025):

Datroway as monotherapy is indicated for the treatment of adult patients with unresectable or metastatic hormone receptor (HR)-positive, HER2-negative breast cancer who have received endocrine therapy and at least one line of chemotherapy in the advanced setting.

Therapeutic indication of the resolution (resolution of 20 November 2025):

See therapeutic indication according to marketing authorisation.

1. Additional benefit of the medicinal product in relation to the appropriate comparator therapy

a) Adults with unresectable or metastatic HR-positive and **HER2-negative (IHC 0)** breast cancer who have received endocrine therapy and **one** line of chemotherapy in the advanced setting

Appropriate comparator therapy:

- Capecitabine
  or
- eribulin
  or
- vinorelbine
  or
- an anthracycline or taxane-containing therapy (only for patients who have not yet received anthracycline and/or taxane-containing therapy or who are eligible for renewed anthracycline or taxane-containing treatment).

Extent and probability of the additional benefit of datopotamab deruxtecan over capecitabine, eribulin or vinorelbine:

An additional benefit is not proven.

b) Adults with unresectable or metastatic HR-positive and **HER2-low (IHC 1+ or IHC 2+/ISH-)** breast cancer who have received endocrine therapy and **one** line of chemotherapy in the advanced setting

Appropriate comparator therapy:

- Trastuzumab deruxtecan

Extent and probability of the additional benefit of datopotamab deruxtecan compared to the appropriate comparator therapy:

An additional benefit is not proven.

c) Adults with unresectable or metastatic HR-positive and **HER2-low (IHC 1+ or IHC 2+/ISH-) and HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH-)** breast cancer who have received endocrine therapy and **at least two** lines of chemotherapy in the advanced setting

Appropriate comparator therapy:

- Sacituzumab govitecan

  or
- trastuzumab deruxtecan (only patients with HER2-low tumour status)

Extent and probability of the additional benefit of datopotamab deruxtecan compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:[1]

a) Adults with unresectable or metastatic HR-positive and **HER2-negative (IHC 0)** breast cancer who have received endocrine therapy and **one** line of chemotherapy in the advanced setting

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No relevant difference for the benefit assessment.
Morbidity	n.a.	There are no assessable data.
Health-related quality of life	n.a.	There are no assessable data.
Side effects	↑	Advantages for severe AEs and in detail advantages and disadvantages for specific AEs.
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		

TROPION-Breast01 study:

- Ongoing, randomised, controlled, open-label, parallel phase III study
- Datopotamab deruxtecan **versus** chemotherapy according to the doctor's instructions[2]

Relevant sub-population: Datopotamab deruxtecan **versus** capecitabine, eribulin or vinorelbine

[1] Data from the dossier assessment of the IQWiG (A25-69) and from the addendum (A25-130), unless otherwise indicated.
[2] A selection of capecitabine, eribulin, gemcitabine and vinorelbine.

Mortality

Endpoint	Datopotamab deruxtecan		Capecitabine, eribulin or vinorelbine		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 (%)*	Hazard ratio [95% CI] p value[a] Absolute difference (AD)[b]
Overall survival					
	63	17.5 [15.2; 20.2] 44 (69.8)	55	14.1 [11.1; 23.0] 36 (65.5)	1.05 [0.67; 1.64] 0.837

Morbidity

Progression-free survival (PFS)[c]					
	63	7.6 [4.4; 9.7] 37 (58.7)	55	4.5 [4.0; 6.0] 36 (65.5)	0.61 [0.38; 0.98] 0.0395 AD: 3.1 months
Symptomatology (EORTC QLQ-C30)					
	No suitable data[d]				
Health status (EQ-5D VAS)					
	No suitable data[d]				

Health-related quality of life

EORTC QLQ-C30	
	No suitable data[d]

Side effects

Endpoint	Datopotamab deruxtecan		Capecitabine, eribulin or vinorelbine		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 (%)*	Hazard ratio [95% CI] p value[a] Absolute difference (AD)[b]
Total adverse events (presented additionally)					
	63	0.2 [0.1; 0.3] 61 (96.8)	55	0.3 [0.2; 0.5] 53 (96.4)	-
Serious adverse events (SAE)					

	63	n.r. 7 (11.1)	55	n.r. [12.2; n.c.] 9 (16.4)	0.51 [0.19; 1.37] 0.173
Severe adverse events (CTCAE grade 3 or 4)					
	63	n.r. [7.6; n.c.] 17 (27.0)	55	2.8 [0.9; 11.7] 31 (56.4)	0.35 [0.19; 0.64] < 0.001[e]
Therapy discontinuation due to adverse events					
	63	n.r. 2 (3.2)	55	n.r. [12.2; n.c.] 4 (7.3)	0.25 [0.04; 1.39] 0.089
PRO-CTCAE					
	No suitable data[f]				
Specific adverse events					
ILD and pneumonitis[g] (AEs)	63	n.r. 2 (3.2)	55	n.r. 0 (0.0)	n.a. 0.292
Keratitis	No suitable data[h]				
Hand-foot syndrome[i] (PT, AEs)	63	n.r. 2 (3.2)	55	n.r. 6 (10.9)	0.28 [0.06; 1.38] 0.095
Nausea (PT, AEs)	63	4.9 [0.8; n.c.] 32 (50.8)	55	n.r. 11 (20.0)	2.82 [1.41; 5.64] 0.002
Stomatitis (PT, AEs)	63	4.5 [2.1; n.c.] 30 (47.6)	55	n.r. 9 (16.4)	3.50 [1.66; 7.39] < 0.001
Loss of appetite (PT, AEs)	63	n.r. 6 (9.5)	55	n.r. 13 (23.6)	0.27 [0.10; 0.77] 0.009[j]
Neutropoenia (PT, severe AEs[k])	63	n.r. 0 (0.0)	55	n.r. 10 (18.2)	n.c.; < 0.001[l]

[a] HR and CI from Cox proportional hazards model; p value from log-rank test. Each stratified by number of previous lines of chemotherapy (1 vs 2), geographical region (USA, Canada and Europe vs rest of the world) and previous use of a CDK4/6 inhibitor (yes vs no).
[b] Data on absolute difference (AD) only in the case of statistically significant difference; own calculation.
[c] Data from the dossier of the pharmaceutical company; results are based on the 1st data cut-off (17.07.2023).
[d] The results presented by the pharmaceutical company on the patient-reported endpoints are unsuitable for use in the benefit assessment due to the high percentage of missing values.
[e] Differences in the magnitude of the results in the analysis of the HR and own calculations of the RR (RR: 0.48 [0.30; 0.76]; p = 0.001); see Table 16.
[f] Only data on PT punctate keratitis and PT ulcerative keratitis are available. No data is available on PT keratitis.
[g] Operationalised via the SMQ Interstitial lung disease (narrow) and other relevant PTs, adjudicated by an independent review committee; see Section I 3.2.1 of the present benefit assessment.
[h] The evaluations submitted by the pharmaceutical company cannot be used due to insufficient responses.
[i] Operationalised via the PT palmar-plantar erythrodysaesthesia syndrome
[j] Differences in the magnitude of the results in the analysis of the HR and own calculations of the RR (RR: 0.40 [0.16; 0.99]; p = 0.043); see Table 16 of the benefit assessment.
[k] Operationalised as CTCAE grade ≥ 3.

[l] Comparison between HR (not implementable) and own calculations of the RR (RR: 0.04 [0.002; 0.70]; p < 0.001); see Table 16 of the benefit assessment.

Abbreviations used:
AD = absolute difference; CDK = cyclin-dependent kinase; CTCAE = Common Terminology Criteria for Adverse Events; EORTC = European Organisation for Research and Treatment of Cancer; HR = hazard ratio; ILD = interstitial lung disease; CI = confidence interval; N = number of evaluated patients; n = number of patients with (at least one) event; n.c. = not calculable; n.r. = not reached; PGI-S = Patient Global Impression of Severity; PRO-CTCAE = Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events; PT = preferred term; QLQ-C30 = Quality of Life Questionnaire – Core 30; RCT = randomised controlled trial; RR = relative risk; SMQ = standardised MedDRA query; SAE = serious adverse event; AE = adverse event; VAS = visual analogue scale; vs = versus

b) Adults with unresectable or metastatic HR-positive and HER2-low **(IHC 1+ or IHC 2+/ISH-)** breast cancer who have received endocrine therapy and **one** line of chemotherapy in the advanced setting

No data available.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	∅	No data available.
Morbidity	∅	No data available.
Health-related quality of life	∅	No data available.
Side effects	∅	No data available.

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

c) Adults with unresectable or metastatic HR-positive and **HER2-low (IHC 1+ or IHC 2+/ISH-) and HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH-)** breast cancer who have received endocrine therapy and **at least two** lines of chemotherapy in the advanced setting

No data available.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	∅	No data available.
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↑↑: 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

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

a) Adults with unresectable or metastatic HR-positive and **HER2-negative (IHC 0)** breast cancer who have received endocrine therapy and **one** line of chemotherapy in the advanced setting

Approx. 1,220 to 2,780 patients

b) Adults with unresectable or metastatic HR-positive and **HER2-low (IHC 1+ or IHC 2+/ISH-)** breast cancer who have received endocrine therapy and **one** line of chemotherapy in the advanced setting

Approx. 1,300 to 3,140 patients

c) Adults with unresectable or metastatic HR-positive and **HER2-low (IHC 1+ or IHC 2+/ISH-) and HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH-)** breast cancer who have received endocrine therapy and **at least two** lines of chemotherapy in the advanced setting

Approx. 1,620 to 8,240 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 Datroway (active ingredient: datopotamab deruxtecan) at the following publicly accessible link (last access: 24 September 2025):

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

Treatment with datopotamab deruxtecan should only be initiated and monitored by specialists in internal medicine, haematology, and oncology who are experienced in the treatment of patients with breast cancer, as well as specialists in obstetrics and gynaecology, and other specialists from other specialist groups participating in the Oncology Agreement.

4. Treatment costs

Annual treatment costs:

a) Adults with unresectable or metastatic HR-positive and **HER2-negative (IHC 0)** breast cancer who have received endocrine therapy and **one** line of chemotherapy in the advanced setting

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Datopotamab deruxtecan	€ 167,545.47
Appropriate comparator therapy:	
Capecitabine as monotherapy	
Capecitabine	€ 2,455.61
Eribulin as monotherapy	
Eribulin	€ 18,417.03
Vinorelbine as monotherapy	
Vinorelbine	€ 7,510.74 – € 9,376.96
An anthracycline or taxane-containing therapy (only for patients who have not yet received anthracycline and/or taxane-containing therapy or who are eligible for renewed anthracycline or taxane-containing treatment)	
Taxanes	
Docetaxel	€ 15,420.05

Designation of the therapy	Annual treatment costs/ patient
Paclitaxel	€ 15,545.68
Additionally required SHI services (Paclitaxel)	€ 271.07
Nab-paclitaxel	€ 35,474.25
Anthracyclines	
Doxorubicin	€ 1,868.45 – € 2,740.39
Doxorubicin PEG-liposomal	€ 36,557.82
Eprirubicin	€ 4,685.70 – € 5,154.27

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 15 September 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:					
Datopotamab deruxtecan	Surcharge for the preparation of a parenteral solution with datopotamab deruxtecan	€ 100	1	17.4	€ 1,740
Appropriate comparator therapy:					
Docetaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740
Doxorubicin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	5 - 11	€ 500 – € 1,100
Doxorubicin PEG-liposomal	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	13.0	€ 1,300
Epirubicin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	10 - 16	€ 1,000 – € 1,600
Eribulin	Surcharge for production of a parenteral	€ 100	2	34.8	€ 3,480

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
	preparation containing cytostatic agents				
Paclitaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740
Nab-paclitaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740
Vinorelbine	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	52.1	€ 5,210

b) Adults with unresectable or metastatic HR-positive and **HER2-low (IHC 1+ or IHC 2+/ISH-)** breast cancer who have received endocrine therapy and one line of chemotherapy in the advanced setting

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Datopotamab deruxtecan	€ 167,545.47
Appropriate comparator therapy:	
Trastuzumab deruxtecan	€ 99,648.41

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 15 September 2025)

Costs for additionally required SHI services: not applicable

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:					
Datopotamab deruxtecan	Surcharge for the preparation of a parenteral solution with datopotamab deruxtecan	€ 100	1	17.4	€ 1,740
Appropriate comparator therapy:					
Trastuzumab deruxtecan	Surcharge for the preparation of a parenteral solution with trastuzumab deruxtecan	€ 100	1	17.4	€ 1,740

c) Adults with unresectable or metastatic HR-positive and **HER2-low (IHC 1+ or IHC 2+/ISH-) and HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH-)** breast cancer who have received endocrine therapy and **at least two** lines of chemotherapy in the advanced setting

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Datopotamab deruxtecan	€ 167,545.47
Appropriate comparator therapy:	
Sacituzumab govitecan	
Sacituzumab govitecan	€ 146,464.85
Trastuzumab deruxtecan (only patients with HER2-low tumour status)	
Trastuzumab deruxtecan	€ 99,648.41

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 15 September 2025)

Costs for additionally required SHI services: not applicable

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:					
Datopotamab deruxtecan	Surcharge for the preparation of a parenteral solution with datopotamab deruxtecan	€ 100	1	17.4	€ 1,740
Appropriate comparator therapy:					
Sacituzumab govitecan	Surcharge for the preparation of a parenteral solution with sacituzumab govitecan	€ 100	2	34.8	€ 3,480
Trastuzumab deruxtecan	Surcharge for the preparation of a parenteral solution with trastuzumab deruxtecan	€ 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:

a) Patient group adults with unresectable or metastatic HR-positive and **HER2-negative (IHC 0)** breast cancer who have received endocrine therapy and **one** line of chemotherapy in the advanced setting

- 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.

b) Adults with unresectable or metastatic HR-positive and **HER2-low (IHC 1+ or IHC 2+/ISH-)** breast cancer who have received endocrine therapy and **one** line of chemotherapy in the advanced setting

- 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.

c) Adults with unresectable or metastatic HR-positive and **HER2-low (IHC 1+ or IHC 2+/ISH-) and HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH-)** breast cancer who have received endocrine therapy and **at least two** lines of chemotherapy in the advanced setting

- 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.

6. Percentage of study participants at study sites within the scope of SGB V in accordance with Section 35a, paragraph 3, sentence 5 SGB V

The medicinal product Datroway is a medicinal product placed on the market from 1 January 2025.

The percentage of study participants in the clinical studies of the medicinal product conducted or commissioned by the pharmaceutical company in the therapeutic indication to be assessed who participated at study sites within the scope of SGB V (German Social Security Code) is < 5 per cent of the total number of study participants.

The clinical studies of the medicinal product in the therapeutic indication to be assessed were therefore not conducted to a relevant extent within the scope of SGB V.

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 20 November 2025.

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

Berlin, 20 November 2025

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

Prof. Hecken