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
Trastuzumab deruxtecan (new scientific findings Section 14: gastric or gastroesophageal junction adenocarcinoma, HER2-positive, following trastuzumab-based therapy)

From 19 March 2026

At their session on 19 March 2026, 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. In Annex XII, the information on the benefit assessment of Trastuzumab deruxtecan in the version of the resolution of 20 July 2023 (BAnz AT 12.09.2023 B1) shall be amended as follows:

1. After the information:

   "Resolution of: 20 July 2023
   Entry into force on: 20 July 2023
   BAnz AT 12.9.2023 B1", the following information is inserted:

   "Resolution of: 19 March 2026
   Entry into force on: 19 March 2026
   Federal Gazette, BAnz AT DD. MM YYYY Bx“

2. In the heading "Therapeutic indication of the resolution (resolution of 20 July 2023): See new therapeutic indication according to marketing authorisation", the word "resolution" is replaced by the word "resolutions". After the date specification "20 July 2023", the phrase "and of 19 March 2026" shall be added, and the following information shall be added:

"Therapeutic indication of the resolution (resolution of 19 March 2026):

Enhertu as monotherapy is indicated for the treatment of adult patients with advanced HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior trastuzumab-based first-line therapy."

3. In Number 1 "Additional benefit of the medicinal product in relation to the appropriate comparator therapy", the information shall be amended as follows:

   a) After the information "- Ramucirumab in combination with paclitaxel", the information

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

      An additional benefit is not proven." is replaced by the information "Extent and probability of the additional benefit of trastuzumab deruxtecan compared with ramucirumab in combination with paclitaxel:

      Indication of a minor additional benefit".

   b) The heading "Study results according to endpoints:" is marked with a superscript footnote "1", which is indicated as follows: "Data from the dossier assessment of the IQWiG (A25-128) and from the addenda (A25-128 and A26-10), unless otherwise indicated."

   c) After the information "Study results according to endpoints", the information shall be amended as follows:

      aa) After the information "a) Adults with advanced HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior trastuzumabbased first-line therapy", the information "There are no assessable data" is deleted.

      bb) Before the information "b) Adults with advanced HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma; after at least two prior treatment regimens, including trastuzumab", the information

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Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	There are no assessable data.
Morbidity	n.a.	There are no assessable data.
Health-related quality of life	n.a.	There are no assessable data.
Side effects	n.a.	There are no assessable data.
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		

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shall be replaced by the following information:

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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	↑	Advantage in the discontinuation due to 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		

The DESTINY-Gastric04 study:

- ongoing randomised controlled trial
- Trastuzumab deruxtecan **versus** ramucirumab + paclitaxel

Mortality

Endpoint	Trastuzumab deruxtecan		Ramucirumab + paclitaxel		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 Absolute difference (AD)[a]
Overall survival					
Overall survival	246	14.7 [12.1; 16.6] 124 (50.4)	248	11.4 [9.9; 15.5] 142 (57.3)	0.70 [0.55; 0.90] 0.004 AD: +3.3 months

Morbidity

Endpoint	Trastuzumab deruxtecan		Ramucirumab + paclitaxel		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 Absolute difference (AD)[a]
Progression-free survival (PFS)					
	246	6.7 [5.6; 7.1] 166 (67.5)	248	5.6 [4.9; 5.8] 156 (62.9)	0.74 [0.59; 0.92] 0.0074 AD: +1.1 months
Symptomatology					
Symptomatology (PGIS)	No suitable data[b]				
Health status (EQ-5D VAS, PGIC)	No suitable data[b]				

Health-related quality of life

Endpoint	Trastuzumab deruxtecan		Ramucirumab + paclitaxel		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
FACT-Ga	No suitable data[b]				

Side effects

Endpoint	Trastuzumab deruxtecan		Ramucirumab + paclitaxel		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
Adverse events					
	244	0.1 [0.1; 0.2] 244 (100)	233	0.2 [0.2; 0.2] 228 (97.9)	-
Serious adverse events (SAEs)					

	244	13.7 [6.6; n.r.] 99 (40.6)	233	8.5 [6.3; 12.3] 96 (41.2)	0.91 [0.69; 1.21] 0.510
Severe adverse events (CTCAE grade 3 or 4)					
	244	2.3 [1.6; 3.5] 166 (68.0)	233	1.6 [1.0; 2.3] 169 (72.5)	0.81 [0.65; 1.00] 0.052
Therapy discontinuation due to adverse events					
	244	22.1 [17.1; n.c.] 35 (14.3)	233	n.r. 40 (17.2)	0.61 [0.39; 0.98] 0.038[e]
Specific adverse events					
Cardiac disorders (SOC, severe AEs[c])	244	n.d. 1 (0.4)	233	n.d. 4 (1.7)	–[f]
Thrombocytopenia (PT, severe AEs[c])	244	n.r. [23.1; n.c.] 17 (7.0)	233	n.r. 8 (3.4)	1.88 [0.81; 4.37] 0.139[e]
ILD / pneumonitis (SAEs)[g]	244	n.r. 5 (2.0)	233	n.r. 3 (1.3)	1.49 [0.36; 6.22] 0.585[h]
Vomiting (PT, AEs)	244	n.r. 64 (26.2)	233	n.r. 33 (14.2)	1.92 [1.26; 2.93] 0.002[e]
Stomatitis (PT, AEs)	244	n.r. 14 (5.7)	233	n.r. 31 (13.3)	0.38 [0.20; 0.71] 0.002[e]
Epistaxis (PT, AEs)	244	n.r. 4 (1.6)	233	n.r. 34 (14.6)	0.10 [0.03; 0.27] < 0.001[e]
Musculoskeletal and connective tissue disorders and bone and joint injuries (SOC, AEs)	244	n.r. 41 (16.8)	233	14.6 [14.6; n.c.] 63 (27.0)	0.51 [0.34; 0.76] < 0.001[e]
Renal and urinary disorders (SOC, AEs)	244	n.r. 12 (4.9)	233	n.r. 31 (13.3)	0.30 [0.15; 0.58] < 0.001[e]
Nausea (PT, severe AEs[c])	244	n.r. 13 (5.3)	233	n.r. 0 (0)	n.c. < 0.001[i]
Hypertension (PT, severe AEs[c])	244	n.r. 1 (0.4)	233	n.r. 25 (10.7)	0.03 [0.004; 0.24] < 0.001[e]

Nervous system disorders (SOC, severe AEs[c])	244	n.r. 8 (3.3)	233	n.r. 16 (6.9)	0.41 [0.18; 0.96] 0.034[e]

a Effect and CI: Cox proportional hazards model, stratified by HER2 status (IHC 3+ vs IHC 2+ / ISH+); p value: Log-rank test stratified by HER2 status (IHC 3+ vs IHC 2+ / ISH+)
b For justification, see section I 4.1 of the present dossier assessment
c Operationalised as CTCAE grade ≥ 3
d Discontinuation of at least 1 component
e Effect: unstratified Cox proportional hazards model with treatment as the sole categorical variable; CI: based on the Wald test; p value: based on the unstratified log-rank test
f The pharmaceutical company did not submit any calculations on the HR, CI and p value.
g For operationalisation, see section I 4.1
h Effect: Cox proportional hazards model with treatment as a categorical variable; inclusion of stratification factors according to a pre-specified pooling strategy; CI: based on the Wald test; p value: based on the log-rank test; inclusion of stratification factors according to a pre-specified pooling strategy
i p value: based on the unstratified log-rank test
j Indication of absolute difference (AD) only in case of statistically significant difference; own calculation
k Information from the dossier of the pharmaceutical company

Abbreviations used:
AD = absolute difference; CTCAE = Common Terminology Criteria for Adverse Events; FACT-Ga = Functional Assessment of Cancer Therapy-Gastric; HR = hazard ratio; HER2 = human epidermal growth factor receptor; IHC = immunohistochemistry; ILD = interstitial lung disease; ISH = in situ hybridisation; n.d. = no data available; CI = confidence interval; N = number of patients evaluated; n = number of patients with (at least one) event; n.c. = not calculable; n.r. = not reached; PGIC = Patient Global Impression of Change; PGIS = Patient Global Impression of Severity; PT = preferred term; RCT = randomised controlled trial; SOC = system organ class; SAE = serious adverse event; AE = adverse event; VAS = visual analogue scale; vs = versus

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4. In Number 2 "Number of patients or demarcation of patient groups eligible for treatment", the information "approx. 360 – 600" after the information "a) Adults with advanced HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior trastuzumab-based first-line therapy" is replaced by the information "530 – 1,560".

5. In Number 4 "Treatment costs", the information shall be amended as follows:

   aa) After the information "Annual treatment costs:", the information "The costs for the first year of treatment are shown for the cost representation in the resolution." shall be inserted.

   bb) After the information "a) Adults with advanced HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma who have received a prior trastuzumab-based first-line therapy", the information

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Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Trastuzumab deruxtecan	€ 189,123.21
Appropriate comparator therapy:	
Ramucirumab + paclitaxel	
Ramucirumab	€ 71,031.74
Paclitaxel	€ 17,573.79
Additionally required SHI services	€ 241.99
Total	€ 88,847.52
For monotherapies, cf. Annex VI to Section K of the Pharmaceuticals Directive	
Paclitaxel	
Paclitaxel	€ 23,476.78
Additionally required SHI services	€ 241.99
Total	€ 23,718.77
Docetaxel	€ 13,734.17
Irinotecan	€ 15,482.52

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 1 July 2023)
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is replaced by the following information:

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Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Trastuzumab deruxtecan	€ 124,560.51
Appropriate comparator therapy:	
Ramucirumab + paclitaxel	
Paclitaxel	€ 17,600.70
Ramucirumab	€ 74,146.80
Total	€ 91,747.50
Additionally required SHI services	€ 259.00
For monotherapies, cf. Annex VI to Section K of the Pharmaceuticals Directive	
Docetaxel	€ 8,527.22
Irinotecan	€ 13,051.31
Paclitaxel	€ 23,512.73

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 15 January 2026)

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II. The resolution will enter into force on the day of its publication on the G-BA website on 19 March 2026.

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

Berlin, 19 March 2026

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Prof. Hecken