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
Pembrolizumab (new therapeutic indication: head and neck squamous cell carcinoma, PD-L1 expression, first-line, in combination with radiotherapy with or without concomitant cisplatin therapy)

From 21 May 2026

At their session on 21 May 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 following information shall be added after No. 5 to the information on the benefit assessment of Pembrolizumab in accordance with the resolution of 16 October 2025:

Pembrolizumab

Resolution of: 21 May 2026
Entry into force on: 21 May 2026
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 24 October 2025):

KEYTRUDA® as monotherapy is indicated for the treatment of resectable locally advanced head and neck squamous cell carcinoma as neoadjuvant treatment, continued as adjuvant treatment in combination with radiation therapy with or without concomitant cisplatin and then as monotherapy in adults whose tumours express PD-L1 with a CPS ≥ 1.

Therapeutic indication of the resolution (resolution of 21 May 2026):

See new therapeutic indication according to marketing authorisation.

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

a) Adults with resectable locally advanced head and neck squamous cell carcinoma whose tumours express PD-L1 with a CPS ≥ 1 and who are eligible for cisplatin-based therapy; neoadjuvant and adjuvant therapy

Appropriate comparator therapy:

A therapy regimen consisting of
- surgery (tumour resection)
- followed by an individualised therapy with selection of:
  - adjuvant chemoradiotherapy with cisplatin and
  - adjuvant radiotherapy

The extent and probability of the additional benefit of pembrolizumab as neoadjuvant therapy and as postoperative adjuvant therapy in combination with radiotherapy, with or without concomitant cisplatin therapy, followed by pembrolizumab monotherapy, compared with postoperative adjuvant radiotherapy, with or without concomitant cisplatin therapy:

Hint for a minor additional benefit

b) Adults with resectable locally advanced head and neck squamous cell carcinoma whose tumours express PD-L1 with a CPS ≥ 1 and who are ineligible for cisplatin-based therapy; neoadjuvant and adjuvant therapy

Appropriate comparator therapy:

A therapy regimen consisting of:
- surgery (tumour resection)
- followed by an individualised therapy with selection of:
  - adjuvant chemoradiotherapy with:

- mitomycin + 5-FU

or

- carboplatin + 5-FU

or

- docetaxel

and

- adjuvant radiotherapy

The extent and probability of the additional benefit of pembrolizumab as neoadjuvant therapy and as postoperative adjuvant therapy in combination with radiotherapy, with or without concomitant cisplatin therapy, followed by pembrolizumab monotherapy, compared with the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:[1]

a) Adults with resectable locally advanced head and neck squamous cell carcinoma whose tumours express PD-L1 with a CPS ≥ 1 and who are eligible for cisplatin-based therapy; neoadjuvant and adjuvant therapy

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	↔	No relevant difference for the benefit assessment
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		

[1] Data from the dossier assessment of the IQWiG (A25-148) and from the addendum (A25-148), unless otherwise indicated.

KEYNOTE 689 study: neoadjuvant pembrolizumab, surgery, adjuvant pembrolizumab + radiotherapy ± cisplatin **vs** surgery, adjuvant radiotherapy ± cisplatin

Relevant sub-population: patients whose tumours express PD-L1 with a CPS ≥ 1

Mortality

Endpoint	**Neoadjuvant pembrolizumab, surgery, adjuvant pembrolizumab + radiotherapy ± cisplatin**		**Surgery, adjuvant radiotherapy ± cisplatin**		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					
	347	n.r. 106 (30.5)	335	61.8 [49.2; n.c.] 128 (38.2)	0.72 [0.56; 0.94] 0.014[b]

Morbidity

Endpoint	**Neoadjuvant pembrolizumab, surgery, adjuvant pembrolizumab + radiotherapy ± cisplatin**		**Surgery, adjuvant radiotherapy ± cisplatin**		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]
Failure of the curative therapeutic approach					
There are no suitable data.					
Symptomatology					
EORTC QLQ-C30, EORTC QLQ-H&N35, symptom scales					
There are no suitable data.					

Endpoint	**Neoadjuvant pembrolizumab, surgery, adjuvant pembrolizumab + radiotherapy ± cisplatin**		**Surgery, adjuvant radiotherapy ± cisplatin**		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]
Health status					
EQ-5D VAS					
There are no suitable data.					

Health-related quality of life

Endpoint	**Neoadjuvant pembrolizumab, surgery, adjuvant pembrolizumab + radiotherapy ± cisplatin**		**Surgery, adjuvant radiotherapy ± cisplatin**		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]
EORTC QLQ-C30, EORTC QLQ-H&N35, functional scales					
There are no suitable data.					

Side effects

Endpoint	**Neoadjuvant pembrolizumab, surgery, adjuvant pembrolizumab + radiotherapy ± cisplatin**		**Surgery, adjuvant radiotherapy ± cisplatin**		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]
Total adverse events[c]					
	345	3.1 [3.0; 3.4] 333 (96.5)	300	0.7 [0.4; 0.9] 291 (97.0)	-
Serious adverse events (SAE)[c]					
	345	37.0 [24.9; n.c.] 171 (49.6)	300	n.r. [30.9; n.c.] 112 (37.3)	n.a.
Severe adverse events (CTCAE grade 3 or 4)[c]					
	345	11.9 [9.3; 14.0] 263 (76.2)	300	9.0 [6.4; 10.0] 224 (74.7)	0.64 [0.54; 0.78] < 0.001[d]
Therapy discontinuation due to adverse events[c]					
	345	n.r. 85 (24.6)	300	n.r. [28.0; n.c.] 45 (15.0)	n.c.

Endpoint	Neoadjuvant pembrolizumab, surgery, adjuvant pembrolizumab + radiotherapy ± cisplatin		Surgery, adjuvant radiotherapy ± cisplatin		Intervention vs control
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95% CI] p value[f]
Specific adverse events					
Immune-mediated AEs[e] (presented additionally)	361	158 (43.8)	315	34 (10.8)	-
Immune-mediated SAEs[e]	361	29 (8.0)	315	1 (0.3)	25.30 [3.47; 184.70] < 0.001
Immune-mediated severe AEs[e]	361	36 (10.0)	315	2 (0.6)	15.71 [3.81; 64.71] < 0.001

[a] Indication of absolute difference (AD) only in case of statistically significant difference; own calculation
[b] Cox proportional hazards model using Efron's method for handling ties; stratified by primary tumour localisation (oropharynx/oral cavity vs larynx vs hyopharynx) and tumour stage (III vs IV A)
[c] Without the PTs: neoplasm progression, malignant neoplasm progression and disease progression
[d] Cox proportional hazards model using Efron's method for handling ties
[e] The information refers to the total population from the study report.
[f] Own calculation of RR, 95% CI (asymptotic) and p value (unconditional exact test)

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.c. = not calculable; n.r. = not reached; RR = relative risk; SAE = serious adverse event; AE= adverse event; vs = versus

b) Adults with resectable locally advanced head and neck squamous cell carcinoma whose tumours express PD-L1 with a CPS ≥ 1 and who are ineligible for cisplatin-based therapy; neoadjuvant and adjuvant therapy

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

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

a) Adults with resectable locally advanced head and neck squamous cell carcinoma whose tumours express PD-L1 with a CPS ≥ 1 and who are eligible for cisplatin-based therapy; neoadjuvant and adjuvant therapy

Approx. 2,190 to 3,640 patients

b) Adults with resectable locally advanced head and neck squamous cell carcinoma whose tumours express PD-L1 with a CPS ≥ 1 and who are ineligible for cisplatin-based therapy; neoadjuvant and adjuvant therapy

Approx. 360 to 600 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 Keytruda (active ingredient: pembrolizumab) at the following publicly accessible link (last access: 25 March 2026):

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

Therapy with pembrolizumab should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of patients with head and neck tumours as well as ear, nose and throat (otorhinolaryngology) specialists and other doctors from other specialist groups participating in the Oncology Agreement.

In accordance with the EMA requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material that contains information for medical professionals and patients. The training material contains, in particular, instructions on the management of immune-mediated side effects potentially occurring with pembrolizumab as well as on infusion-related reactions.

4. Treatment costs

The costs for the first year of treatment are shown for the cost representation in the resolution.

Annual treatment costs:

a) Adults with resectable locally advanced head and neck squamous cell carcinoma whose tumours express PD-L1 with a CPS ≥ 1 and who are eligible for cisplatin-based therapy; neoadjuvant and adjuvant therapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Pembrolizumab (neoadjuvant treatment as monotherapy, followed by adjuvant treatment in combination with radiotherapy, with or without concomitant cisplatin administration, followed by treatment as monotherapy)	
Pembrolizumab	€ 79,566.63
Surgery (tumour resection)	Different from patient to patient
Radiotherapy	€ 4,089.09 - € 4,700.64
Cisplatin	€ 87.64 - € 286.88
Radiotherapy + cisplatin	€ 4,421.35 - € 4,987.52
Total	Pembrolizumab (neoadjuvant treatment as monotherapy, followed by adjuvant treatment in combination with radiotherapy **without** concomitant cisplatin administration, followed by treatment as monotherapy): € 83,655.72 - € 84,267.27 (plus the costs for surgery (tumour resection) different from patient to patient)
	Pembrolizumab (neoadjuvant treatment as monotherapy, followed by adjuvant treatment in combination with radiotherapy **with** concomitant cisplatin administration, followed by treatment as monotherapy): € 83,987.98 - € 84,554.15 (plus the costs for surgery (tumour resection) different from patient to patient)

Designation of the therapy	Annual treatment costs/ patient
Additionally required SHI services[2]	*€ 116.05*
Appropriate comparator therapy:	
A therapy regimen consisting of surgery (tumour resection), followed by an individualised therapy with selection of adjuvant chemoradiotherapy with cisplatin and adjuvant radiotherapy	
Surgery (tumour resection)	Different from patient to patient
Adjuvant radiotherapy	
Radiotherapy	€ 4,089.09 - € 4,700.64 (plus the costs for surgery (tumour resection) different from patient to patient)
Adjuvant chemoradiotherapy	
Radiotherapy	€ 4,333.71 – € 4,700.64
Cisplatin	€ 569.66 - € 2,495.86
Radiotherapy + cisplatin	€ 4,903.37 - € 7,196.50
Total	Adjuvant chemoradiotherapy with cisplatin: € 4,903.37 - € 7,196.50 (plus the costs for surgery (tumour resection) different from patient to patient)
Additionally required SHI services[3]	*€ 203.00 - € 326.88*

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

[2] The additionally required SHI services only result for the case design, in which neoadjuvant treatment with pembrolizumab is followed by an adjuvant treatment consisting of chemoradiotherapy with cisplatin, followed by pembrolizumab monotherapy

[3] The additionally required SHI services only result for the case design of chemoradiotherapy with cisplatin.

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:					
Pembrolizumab (neoadjuvant treatment as monotherapy, followed by adjuvant treatment in combination with radiotherapy, with or without concomitant cisplatin administration, followed by treatment as monotherapy)					
Pembrolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	17.0 (21-day cycle) or 8.5 (42-day cycle)	€ 1,700 (21-day cycle) or € 850 (42-day cycle)
Cisplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	2.0	€ 200
Appropriate comparator therapy					
A therapy regimen consisting of surgery (tumour resection), followed by an individualised therapy with selection of adjuvant chemoradiotherapy with cisplatin and adjuvant radiotherapy					
Cisplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	13.0 – 17.4	€ 1,300 - € 1,740

b) Adults with resectable locally advanced head and neck squamous cell carcinoma whose tumours express PD-L1 with a CPS ≥ 1 and who are ineligible for cisplatin-based therapy; neoadjuvant and adjuvant therapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Pembrolizumab (neoadjuvant treatment as monotherapy, followed by adjuvant treatment in combination with radiotherapy without concomitant cisplatin administration, followed by treatment as monotherapy)	
Pembrolizumab	€ 79,566.63
Surgery (tumour resection)	Different from patient to patient
Radiotherapy	€ 4,089.09 - € 4,700.64
Total	Pembrolizumab (neoadjuvant treatment as monotherapy, followed by adjuvant treatment in combination with radiotherapy **without** concomitant cisplatin administration, followed by treatment as monotherapy): € 83,655.72 - € 84,267.27 (plus the costs for surgery (tumour resection) different from patient to patient)
Appropriate comparator therapy:	
A therapy regimen consisting of surgery (tumour resection), followed by an individualised therapy with selection of adjuvant chemoradiotherapy with mitomycin + 5-FU or carboplatin + 5-FU or docetaxel, and adjuvant radiotherapy	
Surgery (tumour resection)	
Surgery (tumour resection)	Different from patient to patient
Adjuvant radiotherapy	
Radiotherapy	€ 4,089.09 - € 4,700.64 (plus the costs for surgery (tumour resection) different from patient to patient)
Adjuvant chemoradiotherapies	
Radiotherapy	€ 4,333.71 – € 4,700.64 (plus the costs for surgery (tumour resection) different from patient to patient)
Mitomycin	€ 1,222.19 - € 2,922.03
5-FU	€ 1,007.81 - € 2,258.88
mitomycin + 5-FU	€ 2,230.00 - € 5,180.91
Total	Radiotherapy + mitomycin + 5-FU: € 6,563.71 - € 9,881.55 (plus the costs for surgery (tumour resection) different from patient to patient)
Carboplatin	€ 5,061.55 - € 5,419.75

Designation of the therapy	Annual treatment costs/ patient
5-FU	€ 1,882.40 - € 2,015.62
Carboplatin + 5-FU	€ 6,943.95 - € 7,435.37
Total	Radiotherapy + carboplatin + 5-FU: € 11,277.66 - € 12,136.01 (plus the costs for surgery (tumour resection) different from patient to patient)
docetaxel	€ 11,034.78
Total	Radiotherapy + docetaxel: € 15,368.49 - € 15,735.42 (plus the costs for surgery (tumour resection) different from patient to patient)

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

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:					
Pembrolizumab (neoadjuvant treatment as monotherapy, followed by adjuvant treatment in combination with radiotherapy, with or without concomitant cisplatin administration, followed by treatment as monotherapy)					
Pembrolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	17.0 (21-day cycle) or 8.5 (42-day cycle)	€ 1,700 (21-day cycle) or € 850 (42-day cycle)
Cisplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	2.0	€ 200

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Appropriate comparator therapy					
A therapy regimen consisting of surgery (tumour resection), followed by adjuvant chemoradiotherapy with mitomycin + 5-FU or carboplatin + 5-FU or docetaxel					
mitomycin + 5-FU					
Mitomycin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	8.7 – 10.4	€ 870 - € 1,040
5-FU	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	5	10.4	€ 5,200
			4	8.7	€ 3,480
Carboplatin + 5-FU					
Carboplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	5	2.0	€ 1,000
			4	3.0	€ 1,200
5-FU	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	5	13.0	€ 6,500
			4	17.4	€ 6,960
docetaxel					
docetaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	52.1	€ 5,210

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) Adults with resectable locally advanced head and neck squamous cell carcinoma whose tumours express PD-L1 with a CPS ≥ 1 and who are eligible for cisplatin-based therapy; neoadjuvant and adjuvant therapy

- No medicinal product with new active ingredients for use in combination therapy in compliance with the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

b) Adults with resectable locally advanced head and neck squamous cell carcinoma whose tumours express PD-L1 with a CPS ≥ 1 and who are ineligible for cisplatin-based therapy; neoadjuvant and adjuvant therapy

- No medicinal product with new active ingredients for use in combination therapy in compliance with the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

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 entered into force on the day of its publication on the G-BA website on 21 May 2026.

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

Berlin, 21 May 2026

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

Prof. Hecken