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: cervical cancer, PD-L1 expression ≥ 1 (CPS), combination with chemotherapy with or without bevacizumab)

of 2 February 2023

At its session on 2 February 2023, 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. 4 to the information on the benefit assessment Pembrolizumab in accordance with the resolution of 19 January 2023 on the therapeutic indication "as monotherapy is indicated for the treatment of adolescents aged 12 years and older with advanced (unresectable or metastatic) melanoma":**

Pembrolizumab

Resolution of: 2 February 2023
Entry into force on: 2 February 2023
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 25 April 2022):

Keytruda, in combination with chemotherapy with or without bevacizumab, is indicated for the treatment of persistent, recurrent, or metastatic cervical cancer in adults whose tumours express PD-L1 with a CPS ≥ 1.

Therapeutic indication of the resolution (resolution of 2 February 2023):

See new therapeutic indication according to marketing authorisation.

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

a) Adult patients with persistent, recurrent or metastatic cervical cancer, whose tumours express PD-L1 with CPS ≥ 1; first-line

Appropriate comparator therapy:

Therapy according to doctor's instructions

a1) **Extent and probability of the additional benefit of pembrolizumab in combination with cisplatin and paclitaxel with or without bevacizumab or in combination with carboplatin and paclitaxel with or without bevacizumab compared with the appropriate comparator therapy**:

Indication of a considerable additional benefit

a2) **Extent and probability of the additional benefit of pembrolizumab in combination with chemotherapies other than cisplatin and paclitaxel with or without bevacizumab or carboplatin and paclitaxel with or without bevacizumab compared with the appropriate comparator therapy:**

An additional benefit is not proven.

b) Adult patients with persistent, recurrent or metastatic cervical cancer whose tumours express PD-L1 with CPS ≥ 1; after first-line chemotherapy and for whom further antineoplastic therapy is an option

Appropriate comparator therapy:

Therapy according to doctor's instructions

Extent and likelihood of additional benefit of pembrolizumab in combination with chemotherapy with or without bevacizumab compared with the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:[1]

a) Adult patients with persistent, recurrent or metastatic cervical cancer whose tumours express PD-L1 with CPS ≥ 1; first-line

a1) Pembrolizumab in combination with cisplatin and paclitaxel with or without bevacizumab, or in combination with carboplatin and paclitaxel with or without bevacizumab

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↑↑	Advantage in overall survival.
Morbidity	↔	Advantage in health status; disadvantages in the symptom scales dyspnoea and peripheral neuropathies; overall no predominant advantage or disadvantage.
Health-related quality of life	↔	No relevant difference for the benefit assessment.
Side effects	↓↓	Disadvantages in the endpoint discontinuation due to AEs. In detail, disadvantages in 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 ∅: There are no usable data for the benefit assessment. n.c.: not calculable		

KEYNOTE 826:

Comparison: Pembrolizumab + cisplatin + paclitaxel ± bevacizumab or carboplatin + paclitaxel ± bevacizumab **vs** placebo + cisplatin + paclitaxel ± bevacizumab or carboplatin + paclitaxel ± bevacizumab

Study design: double-blind, randomised, controlled phase III study, ongoing

Data cut-off: 1st data cut-off from 03.05.2021

Relevant sub-population: Patients with PD-L1-expressing tumours (CPS ≥ 1)

[1] Data from the dossier assessment of the IQWiG (A22-70) and from the addendum (A12-135), unless otherwise indicated.

Mortality

Endpoint	Pembrolizumab + chemotherapy ± bevacizumab		Placebo + Chemotherapy ± Bevacizumab		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 (%)*	Hazard ratio [95% CI] P value[a] Absolute difference (AD)[b]
Overall survival					
	273	n.a. [19.8; n.c.] 118 (43.2)	275	16.3 [14.5; 19.4] 154 (56.0)	0.64 [0.50; 0.81] < 0.001

Morbidity

Endpoint	Pembrolizumab + chemotherapy ± bevacizumab		Placebo + Chemotherapy ± Bevacizumab		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 (%)*	Hazard ratio [95% CI] P value[a] Absolute difference (AD)[b]
Progression-free survival (PFS)[c]					
	273	12.8 [10.4; 20.6] 139 (50.9)	275	8.3 [7.7; 9.2] 178 (64.7)	0.60 [0.48; 0.75] < 0.001 AD = + 4.5 months
Symptomatology (EORTC QLQ-C30) – time to first deterioration[d]					
Exhaustion	246	1.4 [1.4; 2.1] 199 (80.9)	253	2.0 [1.4; 2.2] 189 (74.7)	1.12 [0.92; 1.37] 0.257
Nausea and vomiting	246	2.9 [2.4; 3.7] 170 (69.1)	253	2.7 [2.1; 3.9] 171 (67.6)	0.99 [0.80; 1.22] 0.912
Pain	246	4.5 [3.4; 5.8] 155 (63.0)	253	3.4 [2.3; 4.7] 164 (64.8)	0.94 [0.76; 1.18] 0.607

(continuation)

Dyspnoea	246	3.6 [2.8; 4.6] 164 (66.7)	253	6.2 [3.6; 8.3] 140 (55.3)	1.30 [1.03; 1.63] 0.025 AD = - 2.6 months
Insomnia	246	5.5 [3.7; 7.6] 141 (57.3)	253	6.3 [4.9; 8.7] 137 (54.2)	1.08 [0.85; 1.36] 0.544
Appetite loss	246	5.5 [4.2; 8.3] 144 (58.5)	253	5.9 [4.5; 7.6] 139 (54.9)	0.99 [0.78; 1.25] 0.925
Constipation	246	4.1 [2.2; 6.9] 142 (57.7)	253	4.7 [3.0; 7.0] 148 (58.5)	0.99 [0.78; 1.25] 0.924
Diarrhoea	246	4.2 [2.9; 7.0] 146 (59.3)	253	6.5 [4.9; 9.9] 131 (51.8)	1.21 [0.95; 1.54] 0.116
Symptomatology (EORTC QLQ-CX24) – time to first deterioration[d]					
Symptom experience	244	n.a. 81 (33.2)	251	n.a. [12.6; n.c.] 88 (35.1)	0.80 [0.59; 1.09] 0.152
Lymphoedema	244	9.7 [6.3; 17.4] 123 (50.4)	251	11.1 [6.2; n.c.] 112 (44.6)	1.06 [0.82; 1.37] 0.654
Peripheral neuropathy	244	1.4 [1.0; 1.6] 207 (84.8)	251	1.7 [1.4; 2.1] 197 (78.5)	1.22 [1.00; 1.49] 0.049 AD = - 0.3 months
Menopausal symptoms	244	5.5 [3.0; 9.1] 134 (54.9)	251	6.9 [5.0; 12.1] 126 (50.2)	1.14 [0.89; 1.46] 0.285
Sexual/vaginal functioning	No usable data available[e]				
Health status (EQ-5D VAS)[d]					
	248	14.7 [8.0; n.c.] 116 (46.8)	254	7.3 [5.0; 13.1] 133 (52.4)	0.76 [0.59; 0.98] 0.034 AD = + 7.4 months

Health-related quality of life

Endpoint	Pembrolizumab + chemotherapy ± bevacizumab		Placebo + Chemotherapy ± Bevacizumab		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 (%)*	Hazard ratio [95% CI] P value[a] Absolute difference (AD)[b]
EORTC QLQ-C30 - time to first deterioration[f]					
Global health status	246	4.1 [3.1; 6.3] 156 (63.4)	253	3.5 [2.8; 4.6] 172 (68.0)	0.85 [0.68; 1.06] 0.149
Physical functioning	246	3.4 [2.8; 4.1] 171 (69.5)	253	3.5 [3.0; 4.8] 166 (65.6)	1.09 [0.88; 1.36] 0.414
Role functioning	246	2.1 [1.5; 2.9] 189 (76.8)	253	2.8 [2.1; 3.3] 188 (74.3)	1.00 [0.81; 1.23] 0.983
Emotional functioning	246	6.9 [5.4; 12.9] 130 (52.8)	253	7.0 [5.7; 13.9] 128 (50.6)	1.02 [0.80; 1.31] 0.860
Cognitive functioning	246	2.8 [2.1; 3.8] 180 (73.2)	253	3.5 [2.8; 4.4] 166 (65.6)	1.10 [0.89; 1.36] 0.394
Social functioning	246	2.8 [2.1; 4.1] 173 (70.3)	253	3.5 [2.7; 4.2] 163 (64.4)	1.12 [0.90; 1.39] 0.322
EORTC QLQ-CX24 - time to first deterioration[f]					
Sexual activity	236	n.a. 41 (17.4)	248	n.a. 33 (13.3)	1.16 [0.73; 1.85] 0.520
Concern about painful sexual intercourse, sexual activity and sexual experience	234	n.a. 73 (31.2)	244	n.a. [16.3; n.c.] 65 (26.6)	1.02 [0.73; 1.43] 0.918
Sexual pleasure	No usable data available[e]				

(continuation)

Body image	244	3.0 [2.0; 4.2] 157 (64.3)	251	2.2 [1.5; 3.3] 169 (67.3)	0.91 [0.73; 1.13] 0.394

Side effects

Endpoint	**Pembrolizumab + chemotherapy ± bevacizumab**		**Placebo + Chemotherapy ± Bevacizumab**		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 (%)*	Hazard ratio [95% CI] P value[a] Absolute difference (AD)[b]
Total adverse events (presented additionally)[g]					
	272	0.6 [0.4; 0.6] 270 (99.3)	275	0.4 [0.4; 0.6] 273 (99.3)	-
Serious adverse events (SAEs)[g]					
	272	68.6 [31.3; n.c.] 137 (50.4)	275	n.a. [57.4; n.c.] 117 (42.5)	1.20 [0.94; 1.54] 0.148
Severe adverse events (CTCAE grade ≥ 3)[g]					
	272	9.1 [7.1; 11.4] 222 (81.6)	275	11.9 [9.1; 13.4] 206 (74.9)	1.19 [0.99; 1.44] 0.067
Therapy discontinuations due to adverse events[g, h]					
	272	n.a. [66.1; n.c.] 106 (39.0)	275	n.a. 69 (25.1)	1.54 [1.14; 2.09] 0.005
Specific adverse events					
Immune-mediated AEs (presented additionally)	No data available[i]				
Immune-mediated SAEs[g]	272	n.a. 23 (8.5)	275	n.a. 10 (3.6)	2.21 [1.05; 4.65] 0.036

(continuation)

Immune-mediated severe AEs (CTCAE grade ≥ 3)[g]	272	n.a. 38 (14.0)	275	n.a. 14 (5.1)	2.61 [1.41; 4.82] 0.002
Skin and subcutaneous tissue disorders (SOC, severe AEs, CTCAE grade ≥ 3)[g, j]	272	n.a. 17 (6.3)	275	n.a. 1 (0.4)	17.46 [2.32; 131.17] 0.005

a CI and p value: Cox proportional hazards model, for endpoints in the mortality, morbidity and health-related quality of life categories stratified by metastasis, PD-L1 status and decision to use bevacizumab by the principal investigator
b Indication of absolute difference (AD) only in case of statistically significant difference; own calculation
c Data from the dossier of the pharmaceutical company (Module 4 A) of 18 July 2022
d An increase in score by ≥ 10 points compared to the start of the study is considered a clinically relevant deterioration (scale range 0 to 100).
e > 50 % missing values at the start of the study.
f A decrease in score by ≥ 10 points compared to the start of the study is considered a clinically relevant deterioration (scale range 0 to 100).
g excluding AEs attributed to progression of the underlying disease, defined as the MedDRA terms "neoplasm progression", "malignant neoplasm progression" and "disease progression"
h Discontinuation of at least 1 active ingredient component
i Data on immune-mediated AEs are only available for the total population (N = 307 vs N = 309): Intervention arm n = 126 (41.0 %) vs comparator arm n = 82 (26.5 %)
j This includes the following PTs in the total population (N = 307 vs. N = 309): Rash maculopapular (intervention arm n = 6 vs comparator arm n = 0), rash (n = 3 vs n = 1) and pruritus (n = 2 vs n = 0).

Abbreviations used:
AD = Absolute difference; CTCAE = Common Terminology Criteria for Adverse Events; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30; EORTC QLQ-CX24 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire - Cervical Cancer Module; HR = hazard ratio; CI = confidence interval; MedDRA = Medical Dictionary for Regulatory Activities; N = number of patients evaluated; n = number of patients with (at least one) event; n.a. = not achieved; PT = preferred term; VAS = visual analogue scale; vs = versus

a2) Pembrolizumab in combination with chemotherapies other than cisplatin and paclitaxel with or without bevacizumab or carboplatin and paclitaxel with or without bevacizumab

No data are available to allow an assessment of the additional benefit.

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 ∅: There are no usable data for the benefit assessment. n.c.: not calculable		

b) Adult patients with persistent, recurrent or metastatic cervical cancer whose tumours express PD-L1 with CPS ≥ 1; after first-line chemotherapy and for whom further antineoplastic therapy is an option

No data are available to allow an assessment of the additional benefit.

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 ∅: There are no usable data for the benefit assessment. n.c.: not calculable		

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

a) Adult patients with persistent, recurrent or metastatic cervical cancer whose tumours express PD-L1 with CPS ≥ 1; first-line

approx. 1,060 – 1,230 patients

b) Adult patients with persistent, recurrent or metastatic cervical cancer whose tumours express PD-L1 with CPS ≥ 1; after first-line chemotherapy and for whom further antineoplastic therapy is an option

approx. 255 - 295 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: 17 January 2023):

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, specialists in obstetrics and gynaecology, and other specialists participating in the Oncology Agreement, all of whom are experienced in the treatment of patients with cervical cancer.

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

Annual treatment costs:

a) Adult patients with persistent, recurrent or metastatic cervical cancer whose tumours express PD-L1 with CPS ≥ 1; first-line

a1) Pembrolizumab in combination with cisplatin and paclitaxel with or without bevacizumab, or in combination with carboplatin and paclitaxel with or without bevacizumab

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Pembrolizumab in combination with	
cisplatin + paclitaxel ± bevacizumab	
Pembrolizumab	€ 93,522.22
Cisplatin	€ 1,247.23
Paclitaxel	€ 15,562.91
Pembrolizumab + cisplatin + paclitaxel total	€ 110,332.36
Bevacizumab	€ 67,616.40
Pembrolizumab + cisplatin + paclitaxel + bevacizumab total	€ 177,948.76
Additionally required SHI services	€ 538.85 - € 629.23
Carboplatin + paclitaxel ± bevacizumab	
Pembrolizumab	€ 93,522.22
Carboplatin	€ 5,516.67
Paclitaxel	€ 15,562.91
Pembrolizumab + carboplatin + paclitaxel total	€ 114,601.80
Bevacizumab	€ 67,616.40
Pembrolizumab + carboplatin + paclitaxel + bevacizumab total	€ 182,218.20
Additionally required SHI services	€ 213.98
Appropriate comparator therapy:	
Therapy according to doctor's instructions[2]	

[2] Costs are only presented for the combination of active ingredients cisplatin + paclitaxel + bevacizumab, cisplatin + topotecan, carboplatin + paclitaxel + bevacizumab and paclitaxel + topotecan + bevacizumab. In addition to these, the following combinations of active ingredients cisplatin + paclitaxel, carboplatin + paclitaxel, carboplatin + topotecan and paclitaxel + topotecan also represent suitable comparators for the present benefit assessment in the context of therapy according to doctor's instructions. However, these combinations of active ingredients products are not approved in the present therapeutic indication, and therefore, no costs are presented for these combinations of active ingredients.

Designation of the therapy	Annual treatment costs/ patient
- Cisplatin + paclitaxel + bevacizumab	
Cisplatin	€ 1,247.23
Paclitaxel	€ 15,562.91
Bevacizumab	€ 67,616.40
Cisplatin + paclitaxel + bevacizumab total	€ 84,426.54
Additionally required SHI services	€ 538.85 - € 629.23
- Cisplatin + topotecan	
Cisplatin	€ 1,247.23
Topotecan	€ 7,939.10
Cisplatin + topotecan total	€ 9,186.33
Additionally required SHI services	€ 324.87 - € 415.25
- Carboplatin + paclitaxel + bevacizumab	
Carboplatin	€ 5,516.67
Paclitaxel	€ 15,562.91
Bevacizumab	€ 67,616.40
Carboplatin + paclitaxel + bevacizumab total	€ 88,695.98
Additionally required SHI services	€ 213.98
- Paclitaxel + topotecan + bevacizumab	
Paclitaxel	€ 15,562.91
Topotecan	€ 7,939.10
Bevacizumab	€ 67,616.40
Total	€ 91,118.41
Additionally required SHI services	€ 213.98

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 January 2023

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	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	8.7 - 17.4	€ 870.00 - € 1,740.00
Bevacizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	17.4	€ 1,740.00
Carboplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740.00
Cisplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740.00
Paclitaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740.00
Appropriate comparator therapy:					
Bevacizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	17.4	€ 1,740.00
Carboplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740.00
Cisplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740.00
Paclitaxel	Surcharge for production of a	€ 100	1	17.4	€ 1,740.00

	parenteral preparation containing cytostatic agents				
Topotecan	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	3	17.4	€ 5,220.00

a2) Pembrolizumab in combination with chemotherapies other than cisplatin and paclitaxel with or without bevacizumab or carboplatin and paclitaxel with or without bevacizumab

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Pembrolizumab in combination with	
another than chemotherapy ± bevacizumab mentioned in the approval study	
Pembrolizumab	€ 93,522.22
Other chemotherapy	Not determinable
Bevacizumab	€ 67,616.40
Appropriate comparator therapy:	
Therapy according to doctor's instructions[2]	
- Cisplatin + paclitaxel + bevacizumab	
Cisplatin	€ 1,247.23
Paclitaxel	€ 15,562.91
Bevacizumab	€ 67,616.40
Cisplatin + paclitaxel + bevacizumab total	€ 84,426.54
Additionally required SHI services	€ 538.85 - € 629.23
- Cisplatin + topotecan	
Cisplatin	€ 1,247.23
Topotecan	€ 7,939.10
Cisplatin + topotecan total	€ 9,186.33
Additionally required SHI services	€ 324.87 - € 415.25
- Carboplatin + paclitaxel + bevacizumab	
Carboplatin	€ 5,516.67
Paclitaxel	€ 15,562.91
Bevacizumab	€ 67,616.40
Carboplatin + paclitaxel + bevacizumab total	€ 88,695.98

Designation of the therapy	Annual treatment costs/ patient
Additionally required SHI services	€ 213.98
- Paclitaxel + topotecan + bevacizumab	
Paclitaxel	€ 15,562.91
Topotecan	€ 7,939.10
Bevacizumab	€ 67,616.40
Total	€ 91,118.41
Additionally required SHI services	€ 213.98

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 January 2023

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	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	8.7 - 17.4	€ 870.00 - € 1,740.00
Bevacizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	17.4	€ 1,740.00
Other chemotherapy	Not determinable				
Appropriate comparator therapy:					
Bevacizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	17.4	€ 1,740.00
Carboplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740.00
Cisplatin	Surcharge for production of a	€ 100	1	17.4	€ 1,740.00

	parenteral preparation containing cytostatic agents				
Paclitaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740.00
Topotecan	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	3	17.4	€ 5,220.00

b) Adult patients with persistent, recurrent or metastatic cervical cancer whose tumours express PD-L1 with CPS ≥ 1; after first-line chemotherapy and for whom further antineoplastic therapy is an option

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Pembrolizumab in combination with	
cisplatin + paclitaxel ± bevacizumab	
Pembrolizumab	€ 93,522.22
Cisplatin	€ 1,247.23
Paclitaxel	€ 15,562.91
Pembrolizumab + cisplatin + paclitaxel total	€ 110,332.36
Bevacizumab	€ 67,616.40
Pembrolizumab + cisplatin + paclitaxel + bevacizumab total	€ 177,948.76
Additionally required SHI services	€ 538.85 - € 629.23
Carboplatin + paclitaxel ± bevacizumab	
Pembrolizumab	€ 93,522.22
Carboplatin	€ 5,516.67
Paclitaxel	€ 15,562.91
Pembrolizumab + carboplatin + paclitaxel total	€ 114,601.80
Bevacizumab	€ 67,616.40

Designation of the therapy	Annual treatment costs/ patient
Pembrolizumab + carboplatin + paclitaxel + bevacizumab total	€ 182,218.20
Additionally required SHI services	€ 213.98
Appropriate comparator therapy:	
Therapy according to doctor's instructions[3]	No data available

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 January 2023

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	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	8.7 - 17.4	€ 870.00 - € 1,740.00
Bevacizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	17.4	€ 1,740.00
Carboplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740.00
Cisplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740.00
Paclitaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740.00

[3] For the present benefit assessment, the monotherapies with nab-paclitaxel, vinorelbine, ifosfamide, topotecan, pemetrexed, irinotecan, pembrolizumab (for patients with PD-L1 positive metastatic cervical cancer) represent a suitable comparator in the context of a therapy according to doctor's instructions. However, these medicinal products are not approved in the present therapeutic indication (as monotherapies), and therefore, no costs are presented for these medicinal products.

5. 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 Pembrolizumab

Medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V are medicinal products with the following new active ingredients which, on the basis of the marketing authorisation under Medicinal Products Act, can be used in a combination therapy with pembrolizumab for the treatment of persistent, recurrent, or metastatic cervical cancer in adults whose tumours express PD-L1 with a CPS ≥ 1:

a) Adult patients with persistent, recurrent or metastatic cervical cancer whose tumours express PD-L1 with CPS ≥ 1; first-line

a1) Pembrolizumab in combination with cisplatin and paclitaxel with or without bevacizumab, or in combination with carboplatin and paclitaxel with or without bevacizumab:

– No active ingredient that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

a2) Pembrolizumab in combination with chemotherapies other than cisplatin and paclitaxel with or without bevacizumab or carboplatin and paclitaxel with or without bevacizumab:

– No active ingredient that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

b) Adult patients with persistent, recurrent or metastatic cervical cancer whose tumours express PD-L1 with CPS ≥ 1; after first-line chemotherapy and for whom further antineoplastic therapy is an option

– No active ingredient that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 2 February 2023.

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

Berlin, 2 February 2023

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

Prof. Hecken