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: endometrial carcinoma, first-line, combination with carboplatin and paclitaxel)

of 15 May 2025

At their session on 15 May 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. **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 15 May 2025 "Pembrolizumab (new therapeutic indication: Cervical cancer (stage III - IVA), first-line, combination with chemoradiotherapy)":**

Pembrolizumab

Resolution of: 15 May 2025
Entry into force on: 15 May 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 21 October 2024):

KEYTRUDA, in combination with carboplatin and paclitaxel, is indicated for the first-line treatment of primary advanced or recurrent endometrial carcinoma in adults who are candidates for systemic therapy.

Therapeutic indication of the resolution (resolution of 15 May 2025):

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 stage III - IV primary advanced endometrial carcinoma, or mismatch repair **deficient** (**d**MMR) or microsatellite instability-high (MSI-H) recurrent endometrial carcinoma who

- have not yet received systemic therapy as postoperative or adjuvant therapy for treatment of the primary advanced disease,
- have not yet received chemotherapy for treatment of the recurrence.

Appropriate comparator therapy:

- Dostarlimab in combination with carboplatin and paclitaxel followed by Dostarlimab as monotherapy

Extent and probability of the additional benefit of pembrolizumab in combination with carboplatin and paclitaxel, followed by treatment with pembrolizumab, compared with the appropriate comparator therapy:

An additional benefit is not proven.

b) Adult patients with stage III - IV primary advanced endometrial carcinoma or mismatch repair **proficient** (**p**MMR) recurrent endometrial carcinoma who:

- have not yet received systemic therapy as postoperative or adjuvant therapy for treatment of the primary advanced disease,
- have not yet received chemotherapy for treatment of the recurrence.

Appropriate comparator therapy:

- Durvalumab in combination with carboplatin and paclitaxel, followed by durvalumab in combination with olaparib

Extent and probability of the additional benefit of pembrolizumab in combination with carboplatin and paclitaxel, followed by treatment with pembrolizumab, compared with the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:[1]

a) Adult patients with stage III - IV primary advanced endometrial carcinoma, or mismatch repair **deficient** (**d**MMR) or microsatellite instability-high (MSI-H) recurrent endometrial carcinoma who
   - have not yet received systemic therapy as postoperative or adjuvant therapy for treatment of the primary advanced disease,
   - have not yet received chemotherapy for treatment of the recurrence.

No suitable data available.

Summary of results for relevant clinical endpoints

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		

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A24-111) unless otherwise indicated.

b) Adult patients with stage III - IV primary advanced endometrial carcinoma or mismatch repair **proficient** (**p**MMR) recurrent endometrial carcinoma who:

- have not yet received systemic therapy as postoperative or adjuvant therapy for treatment of the primary advanced disease,
- have not yet received chemotherapy for treatment of the recurrence.

No suitable data available.

Summary of results for relevant clinical endpoints

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		

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

a) Adult patients with stage III - IV primary advanced endometrial carcinoma, or mismatch repair **deficient** (**d**MMR) or microsatellite instability-high (MSI-H) recurrent endometrial carcinoma who

- have not yet received systemic therapy as postoperative or adjuvant therapy for treatment of the primary advanced disease,
- have not yet received chemotherapy for treatment of the recurrence.

Approx. 380 to 1,520 patients

b) Adult patients with stage III - IV primary advanced endometrial carcinoma or mismatch repair **proficient** (**p**MMR) recurrent endometrial carcinoma who:

- have not yet received systemic therapy as postoperative or adjuvant therapy for treatment of the primary advanced disease,
- have not yet received chemotherapy for treatment of the recurrence.

Approx. 990 to 1,810 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: 7 January 2025):

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

Treatment 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 endometrial carcinoma.

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:

The annual treatment costs shown refer to the first year of treatment.

a) Adult patients with stage III - IV primary advanced endometrial carcinoma, or mismatch repair **deficient** (**d**MMR) or microsatellite instability-high (MSI-H) recurrent endometrial carcinoma who
   - have not yet received systemic therapy as postoperative or adjuvant therapy for treatment of the primary advanced disease,
   - have not yet received chemotherapy for treatment of the recurrence.

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Pembrolizumab in combination with carboplatin and paclitaxel	
Pembrolizumab	€ 31,055.16
Carboplatin	€ 1,902.90
Paclitaxel	€ 5,360.58
Maintenance treatment with pembrolizumab as monotherapy	
Pembrolizumab	€ 59,004.80
Total	€ 97,323.44
Appropriate comparator therapy:	
Dostarlimab in combination with carboplatin and paclitaxel	

Designation of the therapy	Annual treatment costs/ patient
Dostarlimab	€ 25,794.18
Carboplatin	€ 1,902.90
Paclitaxel	€ 5,360.58
Maintenance treatment with dostarlimab as monotherapy	
Dostarlimab	€ 49,008.94
Total	€ 82,066.60

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 April 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:					
Pembrolizumab in combination with carboplatin and paclitaxel					
Pembrolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	6	€ 600
Paclitaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	6	€ 600
Carboplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	6	€ 600
Maintenance treatment with pembrolizumab as monotherapy					
Pembrolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	5.7	€ 570
Appropriate comparator therapy:					
Dostarlimab in combination with carboplatin and paclitaxel					

Dostarlimab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	6	€ 600
Paclitaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	6	€ 600
Carboplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	6	€ 600
Maintenance treatment with dostarlimab as monotherapy					
Dostarlimab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	5.7	€ 570

b) Adult patients with stage III - IV primary advanced endometrial carcinoma or mismatch repair **proficient** (**p**MMR) recurrent endometrial carcinoma who:
   - have not yet received systemic therapy as postoperative or adjuvant therapy for treatment of the primary advanced disease,
   - have not yet received chemotherapy for treatment of the recurrence.

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Pembrolizumab in combination with carboplatin and paclitaxel	
Pembrolizumab	€ 31,055.16
Carboplatin	€ 1,902.90
Paclitaxel	€ 5,360.58
Maintenance treatment with pembrolizumab as monotherapy	
Pembrolizumab	€ 59,004.80
Total	€ 97,323.44
Appropriate comparator therapy:	
Durvalumab in combination with carboplatin and paclitaxel	
Durvalumab	€ 17,845.36 – € 26,768.04
Carboplatin	€ 1,268.60 – € 2,370.24
Paclitaxel	€ 3,573.72 – € 5,360.58
Maintenance treatment with durvalumab and olaparib	
Durvalumab	€ 50,655.24 – € 59,594.40
Olaparib	€ 38,349.68 - € 45,088.96
Total	€ 111,692.60 - € 139,182.22

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 April 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:					
Pembrolizumab in combination with carboplatin and paclitaxel					
Pembrolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	6	€ 600
Paclitaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	6	€ 600

Carboplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	6	€ 600
Maintenance treatment with pembrolizumab as monotherapy					
Pembrolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	5.7	€ 570
Appropriate comparator therapy:					
Durvalumab in combination with carboplatin and paclitaxel					
Durvalumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	4 – 6	€ 400 – € 600
Paclitaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	4 – 6	€ 400 – € 600
Carboplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	4 – 6	€ 400 – € 600
Maintenance treatment with durvalumab and olaparib					
Durvalumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	8.5 – 10.0	€ 850 – € 1,000

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) Adult patients with stage III - IV primary advanced endometrial carcinoma, or mismatch repair **deficient** (**d**MMR) or microsatellite instability-high (MSI-H) recurrent endometrial carcinoma who
   - have not yet received systemic therapy as postoperative or adjuvant therapy for treatment of the primary advanced disease,
   - have not yet received chemotherapy for treatment of the recurrence.

   – No medicinal product with new active ingredients that can be used in a combination therapy and fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

b) Adult patients with stage III - IV primary advanced endometrial carcinoma or mismatch repair **proficient** (**p**MMR) recurrent endometrial carcinoma who:
   - have not yet received systemic therapy as postoperative or adjuvant therapy for treatment of the primary advanced disease,
   - have not yet received chemotherapy for treatment of the recurrence.

   – No medicinal product with new active ingredients that can be used in a combination therapy that fulfils 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.

The resolution will enter into force on the day of its publication on the internet on the website of the Federal Joint Committee on 15 May 2025.

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

Berlin, 15 May 2025

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

Prof. Hecken