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 with MSI-H or with dMMR, pretreated)

of 19 January 2023

At its session on 19 January 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 for the treatment of unresectable or metastatic colorectal cancer with MSI-H or dMMR after previous fluoropyrimidine-based combination therapy":**

Pembrolizumab

Resolution of: 19 January 2023
Entry into force on: 19 January 2023
Federal Gazette, BAnz AT DD. MM YYYY Bx

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

Keytruda as monotherapy is indicated for the treatment of the following MSI-H or dMMR tumours in adults with:

- advanced or recurrent endometrial carcinoma, who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and who are not candidates for curative surgery or radiation.

Therapeutic indication of the resolution (resolution of 19 January 2023):

See new therapeutic indication according to marketing authorisation.

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

Adult patients with advanced or recurrent endometrial cancer with microsatellite instability-high (MSI-H) or mismatch repair deficiency (dMMR), who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and who are not candidates for curative surgery or radiation

Appropriate comparator therapy:

Therapy according to doctor's instructions

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

An additional benefit is not proven.

Study results according to endpoints:[1]

Adult patients with advanced or recurrent endometrial cancer with microsatellite instability-high (MSI-H) or mismatch repair deficiency (dMMR), who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and who are not candidates for curative surgery or radiation

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

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A22-76) unless otherwise indicated.

Summary of results for relevant clinical endpoints

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

Adult patients with advanced or recurrent endometrial cancer with microsatellite instability-high (MSI-H) or mismatch repair deficiency (dMMR), who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and who are not candidates for curative surgery or radiation

approx. 230 to 3,360 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: 3 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 endometrial carcinoma.

Before initiation of therapy with pembrolizumab, the presence of microsatellite instability-high (MSI-H) or mismatch repair deficiency (dMMR) should be confirmed by a validated test in a tumour sample.

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

Annual treatment costs:

Adult patients with advanced or recurrent endometrial cancer with microsatellite instability-high (MSI-H) or mismatch repair deficiency (dMMR), who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and who are not candidates for curative surgery or radiation

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Pembrolizumab	€ 93,522.22
Appropriate comparator therapy:	
Therapy according to doctor's instructions[2]	
Medroxyprogesterone acetate	€ 687.30 - € 1172.64
Megestrol acetate	€ 2,268.06 - € 9,072.25
Cisplatin monotherapy	€ 931.84 - € 3,594.84
Additionally required SHI services	€ 242.72 - € 2,076.26
Doxorubicin monotherapy	€ 2,241.40 - € 2,915.85
Cisplatin + doxorubicin	
Cisplatin	€ 430.08
Doxorubicin	€ 1,921.20
Total:	€ 2,351.28
Additionally required SHI services	€ 112.03 - € 143.19

[2] The active ingredients paclitaxel and carboplatin in combination with paclitaxel are also suitable comparators for the present benefit assessment in the context of therapy according to doctor's instructions. However, these medicinal products are not approved in the present therapeutic indication, and therefore, no costs are presented for these medicinal products.

Designation of the therapy	Annual treatment costs/ patient
Best supportive care[3]	Different from patient to patient

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 January 2023)

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Pembrolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	8.7 - 17.4	€ 870 - € 1,740
Cisplatin (monotherapy)	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1 or 5	13.0 - 17.4 or 65.0 - 87.0	€ 1,300.00 - € 1,740.00 or € 6,500.00 - € 8,700.00
Cisplatin (in combination with doxorubicin)	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	6	€ 600.00
Doxorubicin (monotherapy)	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740.00
Doxorubicin (in combination with cisplatin)	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	6	€ 600.00

[3] In the case of a comparison with best supportive care, also to be used additionally for the medicinal product to be assessed.

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 that can be used in a combination therapy with pembrolizumab for the treatment of advanced or recurrent endometrial carcinoma, with disease progression on or following prior treatment with a platinum-containing therapy in any setting and when curative surgery or radiation is not an option:

Adult patients with advanced or recurrent endometrial cancer with microsatellite instability-high (MSI-H) or mismatch repair deficiency (dMMR), who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and who are not candidates for curative surgery or radiation

- 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 19 January 2023.

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

Berlin, 19 January 2023

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

Prof. Hecken