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 indication: biliary cancer with MSI-H or 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 of Pembrolizumab in accordance with the resolution of 19 January 2023: "as monotherapy for the treatment of unresectable or metastatic small intestine cancer with MSI-H or a dMMR and disease progression on or following at least one prior 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:

- unresectable or metastatic gastric, small intestine, or biliary cancer, who have disease progression on or following at least one prior therapy.

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

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

- unresectable or metastatic biliary cancer with disease progression, who have disease progression on or following at least one prior therapy.

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

Adults with unresectable or metastatic biliary cancer with microsatellite instability-high (MSI-H) or with mismatch repair deficiency (dMMR) and disease progression on or following at least one prior therapy

**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]

Adults with unresectable or metastatic biliary cancer with microsatellite instability-high (MSI-H) or with mismatch repair deficiency (dMMR) and disease progression on or following at least one prior therapy

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) (A22-79) 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:<br>↑ statistically significant and relevant positive effect with low/unclear reliability of data<br>↓ statistically significant and relevant negative effect with low/unclear reliability of data<br>↑↑ statistically significant and relevant positive effect with high reliability of data<br>↓↓ statistically significant and relevant negative effect with high reliability of data<br>↔: no statistically significant or relevant difference<br>∅: There are no usable data for the benefit assessment.<br>n.c.: not calculable | | |

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

Adults with unresectable or metastatic biliary cancer with microsatellite instability-high (MSI-H) or with mismatch repair deficiency (dMMR) and disease progression on or following at least one prior therapy

approx. 20 – 150 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

Treatment with pembrolizumab should only be initiated and monitored by specialists in internal medicine, haematology and oncology as well as specialists in internal medicine and gastroenterology and other specialists participating in the Oncology Agreement, all of whom are experienced in the treatment of patients with biliary cancer.

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

**Annual treatment costs:**

Adults with unresectable or metastatic biliary cancer with microsatellite instability-high (MSI-H) or with mismatch repair deficiency (dMMR) and disease progression on or following at least one prior therapy

| 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] | |
| Best supportive care[3] | Different from patient to patient |

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

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 | Surcharge for the preparation of a parenteral solution containing | € 100 | 1 | 8.7 - 17.4 | € 870 - € 1,740 |

[2] In addition to BSC, the following treatment option is also considered a suitable comparator in the context of a clinical study: 5-fluorouracil + folinic acid + oxaliplatin (FOLFOX).
However, the active ingredients mentioned are not approved in the present therapeutic indication, which is why the costs are not presented.
[3] In the case of a comparison with best supportive care, also to be used additionally for the medicinal product to be assessed.

| Designation of the therapy | Type of service | Costs/ unit | Number/ cycle | Number/ patient/ year | Costs/ patient/ year |
|---|---|---|---|---|---|
| | monoclonal antibodies | | | | |

**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 unresectable or metastatic biliary cancer with microsatellite instability-high (MSI-H) or with a mismatch repair deficiency (dMMR) and progression of the disease on or following at least one previous therapy:

Adults with unresectable or metastatic biliary cancer with microsatellite instability-high (MSI-H) or with mismatch repair deficiency (dMMR) and disease progression on or following at least one prior therapy

- 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