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
Nivolumab (new therapeutic indication: mismatch repair deficient (dMMR) or microsatellite instability-high (MSI-H) colorectal cancer, first-line, combination with ipilimumab)

of 18 December 2025

At their session on 18 December 2025, the Federal Joint Committee (G-BA) resolved not 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 Nivolumab in accordance with the resolution "Nivolumab (reassessment after the deadline: oesophageal or gastro-oesophageal junction cancer, pretreated patients, adjuvant treatment)" of 18 December 2025:

Nivolumab

Resolution of: 18 December 2025
Entry into force on: 18 December 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 19 December 2024):

OPDIVO in combination with ipilimumab is indicated for the treatment of adult patients with mismatch repair deficient or microsatellite instability-high colorectal cancer in the following settings:

– first-line treatment of unresectable or metastatic colorectal cancer

Therapeutic indication of the resolution (resolution of 18 December 2025):

See new therapeutic indication according to marketing authorisation

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

Adults with unresectable or metastatic mismatch repair deficient or microsatellite instability-high colorectal cancer; first-line treatment

Appropriate comparator therapy:

– Pembrolizumab as monotherapy

Extent and probability of the additional benefit of nivolumab in combination with ipilimumab compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:[1]

Adults with unresectable or metastatic mismatch repair deficient or microsatellite instability-high colorectal cancer; first-line treatment

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

[1] Data from the dossier assessment of the IQWiG (A25-80) and from the addendum (A25-135), unless otherwise indicated.

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	∅	No data available.
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

Adults with unresectable or metastatic mismatch repair deficient or microsatellite instability-high colorectal cancer; first-line treatment

Approx. 560 – 1,800 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 Opdivo (active ingredient: nivolumab) at the following publicly accessible link (last access: 29 October 2025):

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

Treatment with nivolumab should only be initiated and monitored by specialists in internal medicine, haematology, and oncology, internal medicine and gastroenterology, and specialists participating in the Oncology Agreement experienced in the treatment of patients with colorectal 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 (including patient identification card).

The training material contains, in particular, information and warnings about immune-mediated side effects as well as infusion-related reactions.

4. Treatment costs

Annual treatment costs:

Adults with unresectable or metastatic mismatch repair deficient or microsatellite instability-high colorectal cancer; first-line treatment

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed: Nivolumab in combination with ipilimumab	
First year of treatment	
Initial treatment	
Nivolumab	€ 11,626.40
Ipilimumab	€ 26,331.84
Initial treatment: total	€ 37,958.24
Follow-up treatment	
Nivolumab	€ 58,132.00
Initial treatment + follow-up treatment: Total	€ 96,090.24
Second year of treatment	
Nivolumab	€ 75,571.60
Appropriate comparator therapy:	
First year of treatment and subsequent years	
Pembrolizumab	€ 81,438.79

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 15 October 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					
First year of treatment					
Nivolumab	Surcharge for the production of parenteral solutions with monoclonal antibodies	€ 100	1	14 – 24	€ 1,400 - € 2,400
Ipilimumab	Surcharge for the production of parenteral solutions with monoclonal antibodies	€ 100	1	4	€ 400
Second year of treatment					
Nivolumab	Surcharge for the production of parenteral solutions with monoclonal antibodies	€ 100	1	13 - 26	€ 1,300 - € 2,600
Appropriate comparator therapy					
First year of treatment and subsequent years					
Pembrolizumab	Surcharge for the production of parenteral solutions with monoclonal antibodies	€ 100	1	8.7 – 17.4	€ 870 - € 1,740

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:

Adults with unresectable or metastatic mismatch repair deficient or microsatellite instability-high colorectal cancer; first-line treatment

– 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.

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 18 December 2025.

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

Berlin, 18 December 2025

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

Prof. Hecken