

# 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: melanoma,  
adolescents  $\geq 12$  to 18 years, monotherapy or combination  
with ipilimumab)

of 21 December 2023

At its session on 21 December 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 is added after no. 4 to the information on the benefit assessment of Nivolumab according to the resolution of 20 October 2022 on the therapeutic indication "first-line treatment of adults with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma with tumour cell PD-L1 expression  $\geq 1\%$ ":**

## **Nivolumab**

Resolution of: 21 December 2023  
Entry into force on: 21 December 2023  
Federal Gazette, BAnz AT DD. MM YYYY Bx

### **New therapeutic indication (according to the marketing authorisation of 31 May 2023):**

Opdivo as monotherapy or in combination with ipilimumab is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults and adolescents 12 years of age and older.

Relative to nivolumab monotherapy, an increase in progression-free survival (PFS) and overall survival (OS) for the combination of nivolumab with ipilimumab is established only in patients with low tumour PD-L1 expression.

### **Therapeutic indications of the resolution (resolution of 21 December 2023):**

- a) Nivolumab as monotherapy is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adolescents 12 years of age and older.
- b) Nivolumab in combination with ipilimumab is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adolescents 12 years of age and older.

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

- a) Adolescents 12 years of age and older with advanced (unresectable or metastatic) melanoma

#### **Appropriate comparator therapy:**

- Pembrolizumab (monotherapy)

#### **Extent and probability of the additional benefit of nivolumab (monotherapy) compared to the appropriate comparator therapy:**

An additional benefit is not proven.

- b) Adolescents 12 years of age and older with advanced (unresectable or metastatic) melanoma

#### **Appropriate comparator therapy:**

- Pembrolizumab (monotherapy)  
or
- Nivolumab (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:<sup>1</sup>**

Adolescents 12 years of age and older with advanced (unresectable or metastatic) melanoma

a) Nivolumab as monotherapy is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adolescents 12 years of age and older.

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 ∅: No data available. n.a.: not assessable		

b) Nivolumab in combination with ipilimumab is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adolescents 12 years of age and older.

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

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<sup>1</sup> Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A23-58) unless otherwise indicated.

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

a) and b) Adolescents 12 years of age and older with advanced (unresectable or metastatic) melanoma

approx. 1 - 4 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: 8 December 2023):

[https://www.ema.europa.eu/en/documents/product-information/opdivo-epar-product-information\\_en.pdf](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 who are experienced in the treatment of patients with melanoma, as well as specialists in skin and sexually transmitted diseases, and specialists in paediatrics and adolescent medicine with specialisation in paediatric haematology and oncology, and other specialists participating in the Oncology Agreement.

In accordance with the European Medicines Agency (EMA) requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material that contains information for medical professionals and patients (incl. 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:

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

##### Adolescents 12 years of age and older with advanced (unresectable or metastatic) melanoma

- a) Nivolumab as monotherapy is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adolescents 12 years of age and older.

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Nivolumab monotherapy	
Nivolumab	€ 45,552.39 - € 73,035.63
Appropriate comparator therapy:	
Pembrolizumab	€ 46,757.63 - € 93,515.26

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 December 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					
Nivolumab (monotherapy)					
Nivolumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	13.0 – 26.1	€ 1,300 - € 2,610
Appropriate comparator therapy:					
Pembrolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	17.4	€ 1,740

b) Nivolumab in combination with ipilimumab is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adolescents 12 years of age and older.

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Nivolumab in combination with ipilimumab	
Nivolumab <sup>2</sup>	€ 36,369.88 - € 60,028.23
Ipilimumab	€ 37,815.24 - € 62,357.56
Total	€ 74,185.12 - € 122,385.79
Appropriate comparator therapy:	
Pembrolizumab	€ 46,757.63 - € 93,515.26
Nivolumab	€ 45,552.39 - € 73,035.63

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 December 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					
Nivolumab in combination with ipilimumab					
Nivolumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	13.3 – 24.1	€ 1,330 - € 2,410
Ipilimumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	4.0	€ 400
Appropriate comparator therapy:					
Pembrolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	17.4	€ 1,740

<sup>2</sup> Includes the costs of the initial phase and follow-up treatment.

Nivolumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	13.0 – 26.1	€ 1,300 - € 2,610
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**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:

Adolescents 12 years of age and older with advanced (unresectable or metastatic) melanoma

- a) Nivolumab as monotherapy is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adolescents 12 years of age and older.
  - No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient authorised in monotherapy.
- b) Nivolumab in combination with ipilimumab is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adolescents 12 years of age and older.
  - 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.

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 21 December 2023.**

The justification to this resolution will be published on the website of the G-BA at [www.g-ba.de](http://www.g-ba.de).

Berlin, 21 December 2023

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

Prof. Hecken