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: Renal cell carcinoma, first-line treatment, combination with cabozantinib)

of 21 October 2021

At its session on 21 October 2021, 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 DD. 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 of 16 September 2021:

Nivolumab

Resolution of: 21 October 2021
Entry into force on: 21 October 2021
BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 13 April 2021):

Opdivo in combination with cabozantinib is indicated for the first-line treatment of adult patients with advanced renal cell carcinoma

Therapeutic indication of the resolution (resolution of 21 October 2021):

- see therapeutic indication according to marketing authorisation

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

a) Adult patients with previously untreated, advanced renal cell carcinoma with favourable risk profile (IMDC score 0)

Appropriate comparator therapy:

- Pembrolizumab in combination with axitinib

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

An additional benefit is not proven.

b) Adult patients with previously untreated, advanced renal cell carcinoma with intermediate (IMDC score 1-2) or poor-risk profile (IMDC score ≥ 3)

Appropriate comparator therapy:

- Avelumab in combination with axitinib (only for patients with a poor-risk profile)

  or
- Nivolumab in combination with ipilimumab

  or
- Pembrolizumab in combination with axitinib

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

An additional benefit is not proven.

Study results according to endpoints: [1]

a) Adult patients with previously untreated, advanced renal cell carcinoma with favourable risk profile (IMDC score 0)

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	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 ∅: There are no usable data for the benefit assessment. n.a.: not assessable		

b) Adult patients with previously untreated, advanced renal cell carcinoma with intermediate (IMDC score 1-2) or poor-risk profile (IMDC score ≥ 3)

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	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 ∅: There are no usable data for the benefit assessment.		

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A21-59) unless otherwise indicated.

n.a.: not assessable

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

a) Adult patients with previously untreated, advanced renal cell carcinoma with favourable risk profile (IMDC score 0)

approx. 400 – 760 patients

b) Adult patients with previously untreated, advanced renal cell carcinoma with intermediate (IMDC score 1-2) or poor-risk profile (IMDC score ≥ 3)

approx. 2390 – 3420 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: 15 September 2021):

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, as well as specialists in internal medicine and nephrology, and other specialists participating in the Oncology Agreement experienced in the treatment of patients with advanced renal cell carcinoma.

In accordance with the Medicines Agency requirements regarding additional risk minimisation measures, the pharmaceutical company must provide healthcare professionals and patients with a patient card. The patient card contains, in particular, instructions on the management of immune-mediated side effects potentially occurring with nivolumab as well as on infusion-related reactions. The prescribing doctor must discuss the risks of therapy with nivolumab with the patient. The patient card should be made available to the patient.

In the CheckMate 9ER study, only patients with renal cell carcinoma with clear cell histology were examined. No data are available for patients with non-clear cell renal cell carcinoma.

4. Treatment costs

Annual treatment costs:

a) Adult patients with previously untreated, advanced renal cell carcinoma with favourable risk profile (IMDC score 0)

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Nivolumab in combination with cabozantinib	
Nivolumab	€ 79,308.84 - € 79,613.87
Cabozantinib	€ 65,515.31
Total	€ 144,824.15 - 145,129.18
Appropriate comparator therapy:	
Pembrolizumab in combination with axitinib	
Pembrolizumab	€ 99,706.18
Axitinib	€ 46,868.22
Total	€ 146,574.39

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1st October 2021)

Costs for additionally required SHI services: not applicable

Other SHI services:

Designation of therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Nivolumab	Surcharge for the preparation of parenteral solutions containing monoclonal antibodies	€ 71	1	13.0	€ 923
				26.1	€ 1,853.10
Pembrolizumab	Surcharge for the preparation of parenteral solutions containing monoclonal antibodies	€ 71	1	8.7	€ 617.70
				17.4	€ 1,235.40

b) Adult patients with previously untreated, advanced renal cell carcinoma with intermediate (IMDC score 1-2) or poor-risk profile (IMDC score ≥ 3)

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Nivolumab in combination with cabozantinib	
Nivolumab	€ 79,308.84 - € 79,613.87

Designation of the therapy	Annual treatment costs/ patient
Cabozantinib	€ 65,515.31
Total	€ 144,824.15 - 145,129.18
Appropriate comparator therapy:	
Avelumab in combination with axitinib (only for patients with a poor-risk profile)	
Avelumab	€ 82,182.64
Axitinib	€ 46,868.22
Total	€ 129,050.85
Nivolumab in combination with ipilimumab	
Initial treatment	
Nivolumab	€ 12,201.36
Ipilimumab	€ 29,046.08
Total initial treatment	€ 41,247.44
Follow-up treatment	
Nivolumab	€ 56,736.32 - € 61,311.83
Initial treatment + total follow-up treatment	€ 97,983.76 - € 102,559.27
Pembrolizumab in combination with axitinib	
Pembrolizumab	€ 99,706.18
Axitinib	€ 46,868.22
Total	€ 146,574.39

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1st October 2021)

Costs for additionally required SHI services: not applicable

Other SHI services:

Designation of therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Nivolumab (in combination with cabozantinib)	Surcharge for the preparation of parenteral solutions containing monoclonal antibodies	€ 71	1	13.0	€ 923
				26.1	€ 1,853.10
Pembrolizumab	Surcharge for the preparation of parenteral solutions containing monoclonal antibodies	€ 71	1	8.7	€ 617.70
				17.4	€ 1,235.40
Avelumab	Surcharge for the preparation of parenteral solutions	€ 71	1	26.1	€ 1,853.10

	containing monoclonal antibodies				
Nivolumab in combination with ipilimumab					
Nivolumab (follow-up treatment with nivolumab in a 14-day cycle)	Surcharge for the preparation of parenteral solutions containing monoclonal antibodies	€ 71	1	24.1	€ 1,711.10
Nivolumab (follow-up treatment with nivolumab in a 28-day cycle)	Surcharge for the preparation of parenteral solutions containing monoclonal antibodies	€ 71	1	13.3	€ 944.30
Ipilimumab	Surcharge for the preparation of parenteral solutions containing monoclonal antibodies	€ 71	1	4	€ 284.00
Total					€ 1,228.30 - € 1,995.10

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 21 October 2021.

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

Berlin, 21 October 2021

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

Prof. Hecken