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: Lenvatinib (new therapeutic indication: advanced renal cell carcinoma, first-line, combination with pembrolizumab)

of 7 July 2022

At its session on 7 July 2022, 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 lenvatinib in accordance with the resolution of 7 July 2022 for the therapeutic indication:"... in combination with pembrolizumab is indicated for the treatment of adult patients with advanced or recurrent endometrial carcinoma (EC) who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and are not candidates for curative surgery or radiation":**

Lenvatinib

Resolution of: 7 July 2022
Entry into force on: 7 July 2022
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 26 November 2021):

Kisplyx is indicated for the treatment of adults with advanced renal cell carcinoma (RCC) in combination with pembrolizumab, as first-line treatment.

Therapeutic indication of the resolution (resolution of 7 July 2022):

See new therapeutic indication according to marketing authorisation.

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

a) Adults 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 lenvatinib in combination with pembrolizumab compared to the appropriate comparator therapy:

An additional benefit is not proven.

b) Adults 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 lenvatinib in combination with pembrolizumab compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:[1]

a) Adults 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) Adults 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

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[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A21-160) unless otherwise indicated.

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

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

approx. 400 – 760 patients

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

approx. 2,390 – 3,420 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 Kisplyx (active ingredient: lenvatinib) at the following publicly accessible link (last access: 26 April 2022):

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

Treatment with lenvatinib in combination with pembrolizumab 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, all of whom are experienced in the treatment of adults with advanced renal cell carcinoma.

In the CLEAR 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) Adults 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:	
Lenvatinib in combination with pembrolizumab	
Lenvatinib	€ 34,378.62
Pembrolizumab	€ 99,714.53
Total	€ 134,093.15
Appropriate comparator therapy:	
Pembrolizumab in combination with axitinib	

Designation of the therapy	Annual treatment costs/ patient
Pembrolizumab	€ 99,714.53
Axitinib	€ 46,871.34
Total	€ 146,585.87

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 June 2022)

Costs for additionally required SHI services: not applicable

b) Adults 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:	
Lenvatinib in combination with pembrolizumab	
Lenvatinib	€ 34,378.62
Pembrolizumab	€ 99,714.53
Total	€ 134,093.15
Appropriate comparator therapy:	
Avelumab in combination with axitinib (only for patients with a poor risk profile)	
Avelumab	€ 82,207.69
Axitinib	€ 46,871.34
Total	€ 129,079.04
Nivolumab in combination with ipilimumab	
Initial treatment	
Nivolumab	€ 11,680.88
Ipilimumab	€ 26,331.60
Total initial treatment	€ 38,012.48
Follow-up treatment	
Nivolumab	€ 54,316.09 - € 58,696.42
Initial treatment + total follow-up treatment	€ 92,328.57 - € 96,708.90
Pembrolizumab in combination with axitinib	
Pembrolizumab	€ 99,714.53
Axitinib	€ 46,871.34
Total	€ 146,585.87

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 June 2022)

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:					
Lenvatinib in combination with pembrolizumab					
Pembrolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1	8.7	€ 617.70
				17.4	€ 1,235.40
Appropriate comparator therapy					
Avelumab in combination with axitinib (only for patients with a poor risk profile)					
Avelumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1	26.1	€ 1,853.10
Nivolumab in combination with ipilimumab					
Nivolumab (follow-up treatment with nivolumab in a 14-day cycle)	Surcharge for the preparation of a parenteral solution 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 a parenteral solution containing	€ 71	1	13.3	€ 944.30

	monoclonal antibodies				
Ipilimumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1	4	€ 284
Pembrolizumab in combination with axitinib					
Pembrolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1	8.7	€ 617.70
				17.4	€ 1,235.40

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 7 July 2022.

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

Berlin, 7 July 2022

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

Prof. Hecken