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 Selpercatinib (new therapeutic indication: first-line RET fusion-positive non-small cell lung cancer)

of 15 December 2022

At its session on 15 December 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 shall be added after No. 4 to the information on the benefit assessment of Selpercatinib in accordance with the resolution of 2 September 2021:

Selpercatinib

Resolution of: 15 December 2022
Entry into force on: 15 December 2022
Federal Gazette, BAnz AT DD MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 21 June 2022):

Retsevmo as monotherapy is indicated for the treatment of adults with:

– advanced RET fusion-positive non-small cell lung cancer (NSCLC) not previously treated with an RET inhibitor.

Therapeutic indication of the resolution (resolution of 15 December 2022):

This is an extension of the indication for selpercatinib as monotherapy for the treatment of adults with advanced RET fusion-positive non-small cell lung cancer (NSCLC) in first-line not previously treated with an RET inhibitor.

The indication for the treatment of adults with advanced RET fusion-positive non-small cell lung cancer (NSCLC) who require systemic therapy after platinum-containing chemotherapy and/or treatment with immunotherapy is the subject of the resolution on the benefit assessment of selpercatinib dated 2 September 2021.

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

a) Adults with an advanced RET fusion-positive non-small cell lung cancer (NSCLC) with PD-L1 expression ≥ 50% of tumour cells; first-line therapy

Appropriate comparator therapy:

- Pembrolizumab as monotherapy

Extent and probability of the additional benefit of selpercatinib compared to the appropriate comparator therapy:

An additional benefit is not proven.

b) Adults with an advanced RET fusion-positive non-small cell lung cancer (NSCLC) with PD-L1 expression < 50% of tumour cells; first-line therapy

Appropriate comparator therapy:

- Cisplatin in combination with a third-generation cytostatic (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed (except in the case of predominantly squamous histology))

or

- Carboplatin in combination with a third-generation cytostatic drug (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed (except in the case of predominantly squamous histology)) cf. Annex VI to Section K of the Pharmaceuticals Directive

or

- Carboplatin in combination with nab-paclitaxel

or

- Pembrolizumab in combination with pemetrexed and platinum-containing chemotherapy (only for patients without EGFR or ALK-positive tumour mutations and with non-squamous histology)

or

- Pembrolizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel (only for squamous histology)

or

- Monotherapy with gemcitabine or vinorelbine (only for patients with ECOG performance status 2 as an alternative to platinum-based combination treatment)

Extent and probability of the additional benefit of selpercatinib compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:[1]

a) Adults with an advanced RET fusion-positive non-small cell lung cancer (NSCLC) with PD-L1 expression ≥ 50% of tumour cells; first-line therapy

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

Summary of results for relevant clinical endpoint

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: ↑: 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.c.: not calculable		

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A22-65) unless otherwise indicated.

b) Adults with an advanced RET fusion-positive non-small cell lung cancer (NSCLC) with PD-L1 expression < 50% of tumour cells; first-line therapy

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

Summary of results for relevant clinical endpoint

Endpoint category	Direction of effect/ risk of bias	Summary
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2. Number of patients or demarcation of patient groups eligible for treatment

a) Adults with an advanced RET fusion-positive non-small cell lung cancer (NSCLC) with PD-L1 expression ≥ 50% of tumour cells; first-line therapy

approx. 30 to 90 patients

b) Adults with an advanced RET fusion-positive non-small cell lung cancer (NSCLC) with PD-L1 expression < 50% of tumour cells; first-line therapy

approx. 85 to 220 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 Retsevmo (active ingredient: selpercatinib) at the following publicly accessible link (last access: 6 December 2022):

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

Treatment with selpercatinib should only be initiated and monitored by specialists in internal medicine, haematology and oncology who are experienced in the treatment of patients with non-small cell lung cancer, as well as specialists in internal medicine and pulmonology or

specialists in pulmonary medicine and other doctors from specialist groups participating in the Oncology Agreement.

This medicine has been given 'conditional approval'. This means that further evidence of the benefit of the medicinal product is anticipated. The European Medicines Agency will evaluate new information on this medicinal product at a minimum once per year and update the product information where necessary.

RET testing

The selection of patients for treatment of advanced RET fusion-positive NSCLC should be based on a validated test method.

4. Treatment costs

Annual treatment costs:

a) Adults with an advanced RET fusion-positive non-small cell lung cancer (NSCLC) with PD-L1 expression ≥ 50% of tumour cells; first-line therapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Selpercatinib	€ 50,695.13
Appropriate comparator therapy:	
Pembrolizumab	€ 99,671.38

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

b) Adults with an advanced RET fusion-positive non-small cell lung cancer (NSCLC) with PD-L1 expression < 50% of tumour cells; first-line therapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Selpercatinib	€ 50,695.13
Appropriate comparator therapy:	
Cisplatin in combination with a third-generation cytostatic (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed[2])	
Cisplatin + vinorelbine	
Cisplatin	€ 2,015.79 - € 2,494.46
Vinorelbine	€ 5,015.72 - € 6,261.22
Total	€ 7,031.51 - € 8,755.68

[2] except in the case of predominantly squamous histology

Designation of the therapy	Annual treatment costs/ patient
Additionally required SHI costs	€ 324.87 - € 416.67
Cisplatin + gemcitabine	
Cisplatin	€ 2,015.79 - € 2,494.46
Gemcitabine	€ 8,218.72
Total	€ 10,234.51 - € 10,713.18
Additionally required SHI costs	€ 324.87 - € 416.67
Cisplatin + docetaxel	
Cisplatin	€ 2,015.79
Docetaxel	€ 13,742.17
Total	€ 15,757.96
Additionally required SHI costs	€ 324.87 - € 416.67
Cisplatin + paclitaxel	
Cisplatin	€ 2,284.10
Paclitaxel	€ 17,485.96
Total	€ 19,770.05
Additionally required SHI costs	€ 540.45 - € 632.25
Cisplatin + pemetrexed	
Cisplatin	€ 2,015.79
Pemetrexed	€ 37,075.40
Total	€ 39,091.19
Additionally required SHI costs	€ 453.66 - € 594.84
Carboplatin in combination with a third-generation cytostatic (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed[2])	
Carboplatin + vinorelbine	
Carboplatin	€ 8,074.47
Vinorelbine	€ 5,015.72 - € 6,261.22
Total	€ 13,090.19 - € 14,335.69
Carboplatin + gemcitabine	
Carboplatin	€ 8,074.47
Gemcitabine	€ 8,218.72
Total	€ 16,293.19
Carboplatin + docetaxel	
Carboplatin	€ 8,074.47
Docetaxel	€ 13,742.17

Designation of the therapy	Annual treatment costs/ patient
Total	€ 21,816.64
Carboplatin + paclitaxel	
Carboplatin	€ 8,074.47
Paclitaxel	€ 17,485.96
Total	€ 25,560.43
Additionally required SHI costs	€ 215.58
Carboplatin + pemetrexed	
Carboplatin	€ 8,074.47
Pemetrexed	€ 37,075.40
Total	€ 45,149.87
Additionally required SHI costs	€ 128.79 - € 178.17
Carboplatin in combination with nab-paclitaxel	
Carboplatin	€ 8,074.47
nab-paclitaxel	€ 39,113.46
Total	€ 47,187.93
Pembrolizumab in combination with pemetrexed and platinum-containing chemotherapy[3]	
Pembrolizumab + pemetrexed + cisplatin	
Pembrolizumab	€ 99,671.38
Pemetrexed	€ 37,075.40
Cisplatin	€ 2,015.79
Total	€ 138,762.57
Additionally required SHI costs	€ 453.66 - € 594.84
Pembrolizumab + pemetrexed + carboplatin	
Pembrolizumab	€ 99,671.38
Pemetrexed	€ 37,075.40
Carboplatin	€ 8,074.47
Total	€ 144,821.25
Additionally required SHI costs	€ 128.79 - € 178.17
Pembrolizumab in combination with carboplatin and either paclitaxel or nab-paclitaxel[4]	
Pembrolizumab + carboplatin + paclitaxel	
Pembrolizumab	€ 99,671.38
Carboplatin	€ 8,074.47

[3] Only for patients without EGFR or ALK-positive tumour mutations and with non-squamous histology
[4] only for squamous histology

Designation of the therapy	Annual treatment costs/ patient
Paclitaxel	€ 17,485.96
Total	€ 125,231.81
Additionally required SHI costs	€ 215.58
Pembrolizumab + carboplatin + nab-paclitaxel	
Pembrolizumab	€ 99,671.38
Carboplatin	€ 8,074.47
nab-paclitaxel	€ 39,113.46
Total	€ 146,859.31
Monotherapy with gemcitabine or vinorelbine[5]	
Gemcitabine	€ 7,166.25
Vinorelbine	€ 7,509.17 - € 9,373.83

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

[5] only for patients with ECOG performance status 2 as an alternative to platinum-based combination treatment

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number / patient/ year	Costs/ patient/ year
Appropriate comparator therapy:					
Carboplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740.00
Cisplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740.00
Docetaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740.00
Gemcitabine (combination therapy)	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	2	34.8	€ 3,480.00
Gemcitabine (monotherapy)	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	3	39	€ 3,900.00
nab-paclitaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	3	52.2	€ 5,220.00
Paclitaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740.00
Pembrolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	8.7 - 17.4	€ 870.00 - € 1,740.00
Pemetrexed	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740.00
Vinorelbine (combination therapy)	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	2	34.8	€ 3,480.00
Vinorelbine (monotherapy)	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	52.1	€ 5,210.00

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 Selpercatinib

Medicinal products with new active ingredients pursuant to Section 35a, para. 3, sentence 4 SGB V are medicinal products with the following new active ingredients which, on the basis of the marketing authorisation under Medicinal Products Act, can be used in a combination therapy with selpercatinib for the first-line treatment of adults with advanced RET fusion-positive non-small cell lung cancer (NSCLC) who have not previously been treated with an RET inhibitor:

Adults with an advanced RET fusion-positive non-small cell lung cancer (NSCLC) with PD-L1 expression ≥ 50% of tumour cells; first-line 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.

Adults with an advanced RET fusion-positive non-small cell lung cancer (NSCLC) with PD-L1 expression < 50% of tumour cells; first-line 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 15 December 2022.

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

2. The period of validity of the resolution is limited to 31 December 2025.

Berlin, 15 December 2022

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

Prof. Hecken