Gemeinsamer Bundesausschuss

Resolution

of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive (AM-RL):

Annex XII - Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V Selpercatinib (lung cancer, non-small cell, RET fusion-positive, after platinum-based chemotherapy and/or immunotherapy)

of 2 September 2021

At its session on 2 September 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 on DD. Month YYYY (Federal Gazette, BAnz AT DD.MM.YYYY BX), as follows:

I. Annex XII shall be amended in alphabetical order to include the active ingredient selpercatinib as follows:

Selpercatinib

Resolution of: 02.09.2021
Entry into force on: 02.09.2021
BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 11 February 2021):

Retsevmo as monotherapy is indicated for the treatment of adults with advanced RET fusion-positive non-small cell lung cancer (NSCLC) who require systemic therapy following prior treatment with immunotherapy and/or platinum-based chemotherapy.

Retsevmo as monotherapy is indicated for the treatment of adults and adolescents 12 years and older with advanced RET-mutant medullary thyroid cancer (MTC) who require systemic therapy following prior treatment with cabozantinib and/or vandetanib.

Retsevmo as monotherapy is indicated for the treatment of adults with advanced RET fusion-positive thyroid cancer who require systemic therapy following prior treatment with sorafenib and/or lenvatinib.

Therapeutic indication of the resolution (resolution from the 2 September 2021):

Retsevmo as monotherapy is indicated for the treatment of adults with advanced RET fusion-positive non-small cell lung cancer (NSCLC) who require systemic therapy following prior treatment with immunotherapy and/or platinum-based chemotherapy.

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

a) <u>Adults with advanced RET fusion-positive non-small cell lung cancer (NSCLC) for whom systemic therapy is indicated; after first-line therapy with an anti-PD-1/PD-L1 antibody as monotherapy</u>

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

- 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.

b) Adults with advanced RET fusion-positive non-small cell lung cancer (NSCLC) for whom systemic therapy is indicated; after first-line cytotoxic chemotherapy

Appropriate comparator therapy:

- Docetaxel (only for patients with PD-L1 negative tumours)

or

- Pemetrexed (only for patients with PD-L1 negative tumours and except in cases of predominantly squamous histology)

or

- Nivolumab

or

- Pembrolizumab (only for patients with PD-L1 expressing tumours (TPS ≥ 1 %))

or

- Atezolizumab

or

- Docetaxel in combination with nintedanib (only for patients with PD-L1 negative tumours and adenocarcinoma histology)

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

An additional benefit is not proven.

c) Adults with advanced RET fusion-positive non-small cell lung cancer (NSCLC) for whom systemic therapy is indicated; after first-line therapy with an anti-PD-1/PD-L1 antibody in combination with platinum-containing chemotherapy or after sequential therapy with an anti-PD-1/PD-L1 antibody and platinum-containing chemotherapy

Appropriate comparator therapy:

Patient-individual therapy taking into account prior therapy and histology; selecting afatinib, pemetrexed, erlotinib, docetaxel, docetaxel in combination with ramucirumab, docetaxel in combination with nintedanib and vinorelbine.

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 advanced RET fusion-positive non-small cell lung cancer (NSCLC) for whom systemic therapy is indicated; after first-line therapy with an anti-PD-1/PD-L1 antibody as monotherapy

There are no suitable data that would allow for the assessment of the additional benefit.

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A21-27) 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	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) <u>Adults with advanced RET fusion-positive non-small cell lung cancer (NSCLC) for whom systemic therapy is indicated; after first-line cytotoxic chemotherapy</u>

There are no suitable data that would allow for the assessment of the additional benefit.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
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c) Adults with advanced RET fusion-positive non-small cell lung cancer (NSCLC) for whom systemic therapy is indicated; after first-line therapy with an anti-PD-1/PD-L1 antibody in combination with platinum-containing chemotherapy or after sequential therapy with an anti-PD-1/PD-L1 antibody and platinum-containing chemotherapy

There are no suitable data that would allow for the 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.
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2. Number of patients or demarcation of patient groups eligible for treatment

a) Adults with advanced RET fusion-positive non-small cell lung cancer (NSCLC) for whom systemic therapy is indicated; after first-line therapy with an anti-PD-1/PD-L1 antibody as monotherapy

approx. 5 – 20 patients

b) Adults with advanced RET fusion-positive non-small cell lung cancer (NSCLC) for whom systemic therapy is indicated; after first-line cytotoxic chemotherapy

approx. 20 – 80 patients

c) Adults with advanced RET fusion-positive non-small cell lung cancer (NSCLC) for whom systemic therapy is indicated; after first-line therapy with an anti-PD-1/PD-L1 antibody in combination with platinum-containing chemotherapy or after sequential therapy with an anti-PD-1/PD-L1 antibody and platinum-containing chemotherapy

approx. 30 – 100 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: 29 July 2021):
https://www.ema.europa.eu/en/documents/product-information/retsevmo-epar-product-information_de.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 doctors from other specialist groups participating in the Oncology Agreement.

This medicinal product has been authorised under a so-called “conditional approval” scheme. This means that further evidence of the benefit of the medicinal product is anticipated. The European Medicines Agency (EMA) will assess new information on this medicinal product at least annually and update the product information for healthcare professionals as necessary.

RET testing

A validated test should confirm the presence of RET gene fusion prior to initiation of treatment with selpercatinib.

4. Treatment costs

Annual treatment costs:

a) Adults with advanced RET fusion-positive non-small cell lung cancer (NSCLC) for whom systemic therapy is indicated; after first-line therapy with an anti-PD-1/PD-L1 antibody as monotherapy

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Selpercatinib	€ 169,382.39
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))	
Cisplatin + docetaxel	
Cisplatin	€ 2,007.44
Docetaxel	€ 21,230.61
Total:	€ 23,238.05
Additionally required SHI costs	€ 328.58 - € 421.62
Cisplatin + gemcitabine	
Cisplatin	€ 2,007.44 - 2,486.11
Gemcitabine	€ 8,193.66
Total:	€ 10,201.10 - € 10,679.77
Additionally required SHI costs	€ 328.58 - € 421.62
Cisplatin + paclitaxel	
Cisplatin	€ 2,271.74
Paclitaxel	€ 17,473.78
Total:	€ 19,745.52
Additionally required SHI costs	€ 582.64 - € 675.68
Cisplatin + pemetrexed	
Cisplatin	€ 2,007.44
Pemetrexed	€ 19,894.46
Total:	€ 21,901.90
Additionally required SHI costs	€ 455.34 - € 595.97
Cisplatin + vinorelbine	
Cisplatin	€ 2,007.44 - 2,486.11
Vinorelbine	€ 4,742.20 - € 5,987.34

Designation of the therapy	Annual treatment costs/patient
Total:	€ 6,749.64 - € 8,473.45
Additionally required SHI costs	€ 328.58 - € 421.62
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	
Carboplatin + docetaxel	
Carboplatin	€ 8,209.32
Docetaxel	€ 21,230.61
Total:	€ 29,439.93
Carboplatin + gemcitabine	
Carboplatin	€ 8,209.32
Gemcitabine	€ 8,193.66
Total:	€ 16,402.98
Carboplatin + paclitaxel	
Carboplatin	€ 8,209.32
Paclitaxel	€ 17,473.78
Total:	€ 25,683.10
Additionally required SHI costs	€ 254.06
Carboplatin + pemetrexed	
Carboplatin	€ 8,209.32
Pemetrexed	€ 19,894.46
Total:	€ 28,103.78
Additionally required SHI costs	€ 126.76 - € 174.35
Carboplatin + vinorelbine	
Carboplatin	€ 8,209.32
Vinorelbine	€ 4,742.20 - € 5,987.34
Total:	€ 12,951.52 - € 14,196.66
Carboplatin in combination with nab-paclitaxel	
Carboplatin	€ 8,209.32
nab-paclitaxel	€ 39,088.40
Total:	€ 47,297.72
Monotherapy with gemcitabine or vinorelbine (only for patients with ECOG performance status 2 as an alternative to platinum-based combination treatment)	
Gemcitabine	€ 7,156.89
Vinorelbine	€ 7,099.67 - € 8,963.81

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 August 2021)

Other SHI services:

Designation of 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	€ 81	1	17.4	€ 1,409.40
Cisplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	17.4	€ 1,409.40
Vinorelbine (combination therapy)	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	2	34.8	€ 2,818.80
Vinorelbine (Monotherapy)	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	52.1	€ 4,220.10
Gemcitabine (combination therapy)	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	2	34.8	€ 2,818.80
Gemcitabine (Monotherapy)	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	3	39	€ 3,159.00
Docetaxel	Surcharge for production of a parenteral	€ 81	1	17.4	€ 1,409.40

Designation of therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
	preparation containing cytostatic agents				
Paclitaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	17.4	€ 1,409.40
Pemetrexed	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	17.4	€ 1,409.40
Nab-paclitaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	3	52.2	€ 4,228.20

b) <u>Adults with advanced RET fusion-positive non-small cell lung cancer (NSCLC) for whom systemic therapy is indicated; after first-line cytotoxic chemotherapy</u>

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Selpercatinib	€ 169,382.39
Appropriate comparator therapy:	
Docetaxel	€ 21,230.61
Pemetrexed	€ 19,894.46
Additionally required SHI costs	€ 126.76 - € 174.35
Nivolumab	€ 79,613.87
Pembrolizumab	€ 99,706.18
Atezolizumab	€ 67,766.91
Docetaxel in combination with nintedanib	
Docetaxel	€ 21,230.61

Designation of the therapy	Annual treatment costs/patient
Nintedanib	€ 32,007.42
Total:	€ 53,238.03

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 August 2021)

Other SHI services:

Designation of therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Pembrolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1	8.7 - 17.4	€ 617.70 - € 1,235.40
Atezolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1	17.4	€ 1,235.40
Docetaxel (mono- or combination therapy)	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	17.4	€ 1,409.40
Nivolumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1	26.1	€ 1,853.10
Pemetrexed	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	17.4	€ 1,409.40

c) Adults with advanced RET fusion-positive non-small cell lung cancer (NSCLC) for whom systemic therapy is indicated; after first-line therapy with an anti-PD-1/PD-L1 antibody in combination with platinum-containing chemotherapy or after sequential therapy with an anti-PD-1/PD-L1 antibody and platinum-containing chemotherapy

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Selpercatinib	€ 169,382.39
Appropriate comparator therapy:	
Afatinib	€ 30,932.06
Pemetrexed	€ 19,894.46
Additionally required SHI costs	€ 126.76 - € 174.35
Erlotinib	€ 8,728.49
Vinorelbine	€ 7,099.67 - € 8,963.81
Docetaxel	€ 21,230.61
Docetaxel in combination with ramucirumab	
Docetaxel	€ 21,230.61
Ramucirumab	€ 56,833.97
Total:	€ 78,064.58
Docetaxel in combination with nintedanib	
Docetaxel	€ 21,230.61
Nintedanib	€ 32,007.42
Total:	€ 53,238.03

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 August 2021)

Other SHI services:

Designation of therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Pemetrexed	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	17.4	€ 1,409.40
Docetaxel (mono- or combination therapy)	Surcharge for production of a parenteral preparation	€ 81	1	17.4	€ 1,409.40

Designation of therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
	containing cytostatic agents				
Vinorelbine (Monotherapy)	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	52.1	€ 4,220.10
Ramucirumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1	17.4	€ 1,235.40

II. The resolution will enter into force on the day of its publication on the internet on the website of the G-BA on 2 September 2021.

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

Berlin, 2 September 2021

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

Prof. Hecken