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 Tepotinib (advanced non-small cell lung cancer, METex14 skipping, pretreated patients)

of 1 September 2022

At its session on 1 September 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. **Annex XII shall be amended in alphabetical order to include the active ingredient Tepotinib as follows:**

Tepotinib

Resolution of: 1 September 2022
Entry into force on: 1 September 2022
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 16 February 2022):

TEPMETKO as monotherapy is indicated for the treatment of adult patients with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14) skipping, who require systemic therapy following prior treatment with immunotherapy and/or platinum-based chemotherapy.

Therapeutic indication of the resolution (resolution of 1 September 2022):

See therapeutic indication according to marketing authorisation.

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

a) Adults with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14-) skipping following first-line therapy with a PD-1/PD-L1 antibody as monotherapy

Appropriate comparator therapy for tepotinib as monotherapy:

– 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 (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 tepotinib compared to the appropriate comparator therapy:

An additional benefit is not proven.

b) Adults with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14-) skipping following first-line therapy with a platinum-containing chemotherapy

Appropriate comparator therapy for tepotinib as monotherapy:

– 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, Tumour Proportion Score (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 tepotinib compared to the appropriate comparator therapy:

An additional benefit is not proven.

c) Adults with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14-) skipping following first-line therapy with a PD-1/PD-L1 antibody in combination with a platinum-based chemotherapy or after sequential therapy with a PD-1/PD-L1 antibody and a platinum-containing chemotherapy

Appropriate comparator therapy for tepotinib as monotherapy:

Patient-individual therapy, taking into account previous therapy and histology with selection of afatinib, pemetrexed, erlotinib, docetaxel, docetaxel in combination with ramucirumab and docetaxel in combination with nintedanib and vinorelbine.

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

An additional benefit is not proven.

Study results according to endpoints:[1]

a) Adults with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14-) skipping following first-line therapy with a PD-1/PD-L1 antibody as monotherapy

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 advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14-) skipping following first-line therapy with a platinum-containing chemotherapy

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.
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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		

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A22-30) unless otherwise indicated.

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

c) Adults with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14-) skipping following first-line therapy with a PD-1/PD-L1 antibody in combination with a platinum-based chemotherapy or after sequential therapy with a PD-1/PD-L1 antibody and a platinum-containing chemotherapy

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
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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		

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

a) Adults with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14-) skipping following first-line therapy with a PD-1/PD-L1 antibody as monotherapy

approx. 80 to 130 patients

b) Adults with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14-) skipping following first-line therapy with a platinum-containing chemotherapy

approx. 60 to 100 patients

c) Adults with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14-) skipping

following first-line therapy with a PD-1/PD-L1 antibody in combination with a platinum-based chemotherapy or after sequential therapy with a PD-1/PD-L1 antibody and a platinum-containing chemotherapy

approx. 400 to 680 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 Tepmetko (active ingredient: tepotinib) at the following publicly accessible link (last access: 16 August 2022):

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

Treatment with tepotinib 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.

METex14 skipping test
Before starting treatment with tepotinib, the presence of alterations leading to METex14 skipping must be confirmed using a validated test method.

4. Treatment costs

Annual treatment costs:

a) Adults with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14-) skipping following first-line therapy with a PD-1/PD-L1 antibody as monotherapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Tepotinib	€ 120,198.15
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

[2] except in the case of predominantly squamous histology

Designation of the therapy	Annual treatment costs/ patient
Vinorelbine	€ 4,750.55 - € 6,004.04
Total	€ 6,766.34 - € 8,498.51
Additionally required SHI costs	€ 328.58 - € 421.62
Cisplatin + gemcitabine	
Cisplatin	€ 2,015.79 - € 2,494.46
Gemcitabine	€ 8,218.72
Total	€ 10,234.51 - € 10,713.18
Additionally required SHI costs	€ 328.58 - € 421.62
Cisplatin + docetaxel	
Cisplatin	€ 2,015.79
Docetaxel	€ 13,742.17
Total	€ 15,757.96
Additionally required SHI costs	€ 328.58 - € 421.62
Cisplatin + paclitaxel	
Cisplatin	€ 2,284.10
Paclitaxel	€ 17,485.96
Total	€ 19,770.05
Additionally required SHI costs	€ 545.55 - € 638.59
Cisplatin + pemetrexed	
Cisplatin	€ 2,015.79
Pemetrexed	€ 8,802.66
Total	€ 10,818.45
Additionally required SHI costs	€ 457.07 - € 599.20
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	€ 4,750.55 - € 6,004.04
Total	€ 12,825.02 - € 14,078.51
Carboplatin + gemcitabine	
Carboplatin	€ 8,074.47
Gemcitabine	€ 8,218.72
Total	€ 16,293.19

Designation of the therapy	Annual treatment costs/ patient
Carboplatin + docetaxel	
Carboplatin	€ 8,074.47
Docetaxel	€ 13,742.17
Total	€ 21,816.64
Carboplatin + paclitaxel	
Carboplatin	€ 8,074.47
Paclitaxel	€ 17,485.96
Total	€ 25,560.43
Additionally required SHI costs	€ 216.97
Carboplatin + pemetrexed	
Carboplatin	€ 8,074.47
Pemetrexed	€ 8,802.66
Total	€ 16,877.13
Additionally required SHI costs	€ 128.49 - € 177.58
Carboplatin in combination with nab-paclitaxel	
Carboplatin	€ 8,074.47
nab-paclitaxel	€ 39,113.46
Total	€ 47,187.93
Monotherapy with gemcitabine or vinorelbine[3]	
Gemcitabine	€ 7,166.25
Vinorelbine	€ 7,112.17 - € 8,988.81

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

b) Adults with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14-) skipping following first-line therapy with a platinum-containing chemotherapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Tepotinib	€ 120,198.15
Appropriate comparator therapy:	
Docetaxel (only for patients with PD-L1 negative tumours)	

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

Designation of the therapy	Annual treatment costs/ patient
Docetaxel	€ 13,742.17
Pemetrexed[4]	
Pemetrexed	€ 8,802.66
Additionally required SHI costs	€ 128.49 - € 177.58
Nivolumab	
Nivolumab	€ 76,217.74
Pembrolizumab	
Pembrolizumab[5]	€ 99,671.38
Atezolizumab	
Atezolizumab	€ 68,139.62
Docetaxel in combination with nintedanib[6]	
Docetaxel	€ 13,742.17
Nintedanib	€ 32,010.08
Total	€ 45,752.25

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

c) Adults with advanced non-small cell lung cancer (NSCLC) harbouring alterations leading to mesenchymal-epithelial transition factor gene exon 14 (METex14-) skipping following first-line therapy with a PD-1/PD-L1 antibody in combination with a platinum-based chemotherapy or after sequential therapy with a PD-1/PD-L1 antibody and a platinum-containing chemotherapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Tepotinib	€ 120,198.15
Appropriate comparator therapy:	
Patient-individual therapy, taking into account previous therapy and histology with selection of afatinib, pemetrexed, erlotinib, docetaxel, docetaxel in combination with ramucirumab, docetaxel in combination with nintedanib and vinorelbine.	
Afatinib	
Afatinib	€ 30,935.18
Pemetrexed	
Pemetrexed	€ 8,802.66

[4] only for patients with PD-L1 negative tumours and except in the case of predominantly squamous cell histology
[5] only for patients with PD-L1 expressing tumours, Tumour Proportion Score (TPS) ≥ 1%
[6] only for patients with PD-L1 negative tumours and adenocarcinoma histology

Designation of the therapy	Annual treatment costs/ patient
Additionally required SHI costs	€ 128.49 - € 177.58
Erlotinib	
Erlotinib	€ 9,851.84
Docetaxel in combination with ramucirumab	
Docetaxel	€ 13,742.17
Ramucirumab	€ 56,850.15
Total	€ 70,592.32
Docetaxel in combination with nintedanib	
Docetaxel	€ 13,742.17
Nintedanib	€ 32,010.08
Total	€ 45,752.25
Vinorelbine	
Vinorelbine	€ 7,509.17 - € 9,373.83

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

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number / cycle	Number / patient/ year	Costs/ patient/ year
Appropriate comparator therapy:					
Atezolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1	17.4	€ 1,235.40
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
Docetaxel (monotherapy or combination therapy)	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	17.4	€ 1,409.40

Designation of the therapy	Type of service	Costs/ unit	Number / cycle	Number / patient/ year	Costs/ patient/ year
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
nab-paclitaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	3	52.2	€ 4,228.20
Nivolumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1	26.1	€ 1,853.10
Paclitaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	17.4	€ 1,409.40
Pembrolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1	8.7 - 17.4	€ 617.70 - € 1,235.40
Pemetrexed	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	17.4	€ 1,409.40
Ramucirumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1	17.4	€ 1,235.40
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

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 1 September 2022.

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

Berlin, 1 September 2022

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

Prof. Hecken