Resolution

Gemeinsamer Bundesausschuss

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

Atezolizumab (New Therapeutic Indication: NSCLC, Non-Squamous, First Line, Combination with Bevacizumab, Paclitaxel, and Carboplatin)

of 2 April 2020

On 2 April 2020, the Federal Joint Committee (G-BA) resolved by written statement to amend the Directive on the Prescription of Medicinal Products in SHI-accredited Medical Care (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. In Annex XII, the following information shall be added after No. 4 to the information on the benefit assessment of atezolizumab in accordance with the resolution of 20 June 2019:

Atezolizumab

Resolution of: 2 April 2020
Entry into force on: 2 April 2020
Federal Gazette, BAnz AT DD MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 5 March 2019):

Tecentriq, in combination with bevacizumab, paclitaxel, and carboplatin, is indicated for the first-line treatment of adult patients with metastatic non-squamous non-small cell lung cancer (NSCLC). In patients with EGFR mutant or ALK-positive NSCLC, Tecentriq, in combination with bevacizumab, paclitaxel, and carboplatin, is indicated only after failure of appropriate targeted therapies.

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

a) Adults with metastatic non-squamous non-small cell lung cancer and a Tumour Proportion Score [TPS] of ≥ 50% (PD-L1 expression) and without EGFR mutations or ALK translocations; first-line therapy

Appropriate comparator therapy:

Pembrolizumab as monotherapy

Extent and probability of the additional benefit of atezolizumab compared with the appropriate comparator therapy:

An additional benefit is not proven.

b) Adults with metastatic non-squamous non-small cell lung cancer; and a Tumour Proportion Score [TPS] of ≥ 50% (PD-L1 expression); first-line therapy; or a EGFR mutant or ALK-positive NSCLC independent of the tumour proportion score [TPS] after pretreatment with an appropriate targeted therapy.

Appropriate comparator therapy:

- Cisplatin in combination with a third-generation cytostatic agent (vinorelbine or gemcitabine or docetaxel or paclitaxel or pemetrexed), taking into account the authorisation status.

  or

- Carboplatin in combination with a third-generation cytostatic agent (only for patients with an increased risk of cisplatin-induced side effects as part of a combination therapy; *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)

Extent and probability of the additional benefit of atezolizumab compared with the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:[1]

a) Adults with metastatic non-squamous non-small cell lung cancer and a Tumour Proportion Score [TPS] of ≥ 50% (PD-L1 expression) and without EGFR mutations or ALK translocations; first-line therapy

There is no 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	∅	No data were submitted.
Morbidity	∅	No data were submitted.
Health-related quality of life	∅	No data were submitted.
Side effects	∅	No data were submitted.
Explanations: ↑↑ positive statistically significant and relevant effect with high reliability of data ↑ positive statistically significant and relevant effect with low/unclear reliability of data ↔ no statistically significant or relevant difference ↓ negative statistically significant and relevant effect with low/unclear reliability of data ↓↓ negative statistically significant and relevant effect with high reliability of data ∅ there are no usable data for the benefit assessment n.a.: not assessable [with justification]		

b) Adults with metastatic non-squamous non-small cell lung cancer; and a Tumour Proportion Score [TPS] of ≥ 50% (PD-L1 expression); first-line therapy; or a EGFR mutant or ALK-positive NSCLC independent of the tumour proportion score [TPS] after pre-treatment with an appropriate targeted therapy:

There is no 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.	The data presented were not used for the benefit assessment.
Morbidity	n.a.	The data presented were not used for the benefit assessment.
Health-related quality of life	n.a.	The data presented were not used for the benefit assessment.
Side effects	n.a.	The data presented were not used for the benefit assessment.
Explanations: ↑↑ positive statistically significant and relevant effect with high reliability of data ↑ positive statistically significant and relevant effect with low/unclear reliability of data ↔ no statistically significant or relevant difference ↓ negative statistically significant and relevant effect with low/unclear reliability of data ↓↓ negative statistically significant and relevant effect with high reliability of data ∅ there are no usable data for the benefit assessment n.a.: not assessable [with justification]		

[1] Data from the dossier evaluation of the IQWiG (A19-83) unless otherwise indicated.

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

a) Adults with metastatic non-squamous non-small cell lung cancer and a Tumour Proportion Score [TPS] of ≥ 50% (PD-L1 expression) and without EGFR mutations or ALK translocations, first-line therapy

approx. 2,320 to 2,640 patients

b) Adults with metastatic non-squamous non-small cell lung cancer; and a Tumour Proportion Score [TPS] of ≥ 50% (PD-L1 expression); first-line therapy; or a EGFR mutant or ALK-positive NSCLC independent of the tumour proportion score [TPS] after pre-treatment with an appropriate targeted therapy

approx. 6,670 to 6,950 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 Tecentriq® (active ingredient: atezolizumab) at the following publicly accessible link (last access: 11 February 2020):

https://www.ema.europa.eu/en/documents/product-information/tecentriq-epar-product-information_de.pdf

Treatment with atezolizumab may only be initiated and monitored by specialists in internal medicine, haematology, and oncology, specialists in internal medicine and pneumology, specialists in pulmonary medicine, and specialists participating in the Oncology Agreement who are experienced in the treatment of patients with non-small cell lung cancer.

According to the requirements for risk minimisation activities in the EPAR (European Public Assessment Report), the pharmaceutical company must provide the following information material on atezolizumab:

− Training material for health professionals
− Patient pass

The training material includes, in particular, instructions on how to deal with the immune mediated side effects potentially occurring under atezolizumab treatment as well as infusion-related reactions.

4. Treatment costs

Annual treatment costs:

a) Adults with metastatic non-squamous non-small cell lung cancer and a Tumour Proportion Score [TPS] of ≥ 50% (PD-L1 expression) and without EGFR mutations or ALK translocations; first-line therapy

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Induction therapy	
Atezolizumab	€ 17,702.36 – 26,553.54
Carboplatin	€ 2,003.88 – 3,005.82
Paclitaxel	€ 4,770.08 – 7,155.12
Bevacizumab	€ 9,953.52 – 14,930.28 or € 19,138.32 – 28,707.48
Maintenance treatment	
Atezolizumab	€ 50,451.73 – 59,302.91
Bevacizumab	€ 28,367.53 – 33,344.29 or € 54,544.21 – 64,113.37
Total:	€ 127,077.04 – 170,417.90
Appropriate comparator therapy:	
Pembrolizumab	€ 101,243.99

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 March 2020

Costs for additionally required SHI services: not applicable

Other services covered by SHI funds:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Medicinal product to be assessed:					
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	4–6	€ 324 – 486

Designation of the therapy	Type of service	Costs/ unit	Num-ber/ cycle	Num-ber/ patient/ year	Costs/ patient/ year
Paclitaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	4–6	€ 324 – 486
Bevacizumab	Surcharge for the prepara-tion of a parenteral solu-tion containing monoclonal antibodies	€ 71	1	17.4	€ 1,235.40
Appropriate comparator therapy:					
Pembrolizumab	Surcharge for the prepara-tion of a parenteral solu-tion containing monoclonal antibodies	€ 71	1	17.4	€ 1,235.40

b) Adults with metastatic non-squamous non-small cell lung cancer; and a Tumour Proportion Score [TPS] of ≥ 50% (PD-L1 expression); first-line therapy; or a EGFR mutant or ALK-positive NSCLC independent of the tumour proportion score [TPS] after pre-treatment with an appropriate targeted therapy.

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Induction therapy	
Atezolizumab	€ 17,702.36 – 26,553.54
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Paclitaxel	€ 4,770.08 – 7,155.12
Bevacizumab	€ 9,953.52 – 14,930.28 or € 19,138.32 – 28,707.48
Maintenance treatment	
Atezolizumab	€ 50,451.73 – 59,302.91
Bevacizumab	€ 28,367.53 – 33,344.29 or € 54,544.21 – 64,113.37
Total:	€ 127,077.04 – 170,417.90
Appropriate comparator therapy:	
Cisplatin in combination with a third-generation cytostatic agent (docetaxel or gemcitabine or paclitaxel or pemetrexed or vinorelbine)	
Cisplatin plus docetaxel	
Cisplatin	€ 2,007.44
Docetaxel	€ 21,230.61

Designation of the therapy	Annual treatment costs/patient
Total	€ 23,238.05
Additionally required SHI service	€ 328.58 – 421.62
Cisplatin plus gemcitabine	
Cisplatin	€ 2,007.44 – 2,486.11
Gemcitabine	€ 8,193.66
Total	€ 10,201.10 – 10,679.77
Additionally required SHI service	€ 328.58 – 421.62
Cisplatin plus paclitaxel	
Cisplatin	€ 2,271.74
Paclitaxel	€ 20,749.85
Total	€ 23,021.59
Additionally required SHI service	€ 559.12 – 652.16
Cisplatin plus pemetrexed	
Cisplatin	€ 2,007.44
Pemetrexed	€ 68,656.57
Total	€ 70,664.01
Additionally required SHI service	€ 454.67 – 594.50
Cisplatin plus vinorelbine	
Cisplatin	€ 2,007.44 – 2,486.11
Vinorelbine	€ 4,716.97 – 5,686.32
Total	€ 6,724.41 – 8,172.43
Additionally required SHI service	€ 328.58 – 421.62
Carboplatin in combination with a third-generation cytostatic agent (docetaxel or gemcitabine or paclitaxel or pemetrexed or vinorelbine)	
Carboplatin plus docetaxel	
Carboplatin	€ 8,716.88
Docetaxel	€ 21,230.61
Total	€ 29,947.49
Carboplatin plus gemcitabine	
Carboplatin	€ 8,716.88
Gemcitabine	€ 8,193.66
Total	€ 16,910.54
Carboplatin plus paclitaxel	
Carboplatin	€ 8,716.88
Paclitaxel	€ 20,749.85
Total	€ 29,466.73
Additionally required SHI service	€ 230.54

Designation of the therapy	Annual treatment costs/patient
Carboplatin plus pemetrexed	
Carboplatin	€ 8,716.88
Pemetrexed	€68,656.57
Total	€ 77,373.45
Additionally required SHI service	€ 126.09 – 172.88
Carboplatin plus vinorelbine	
Carboplatin	€ 8,716.88
Vinorelbine	€ 4,716.97 – 5,686.32
Total	€ 13,433.85 – 14,403.20
Carboplatin in combination with nab-paclitaxel	
Carboplatin	€ 8,716.88
Nab-paclitaxel	€ 39,088.40
Total	€ 47,805.28

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 March 2020

Costs for additionally required SHI services: not applicable

Other services covered by SHI funds:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Medicinal product to be assessed:					
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	4–6	€ 324 – 486
Paclitaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	4–6	€ 324 – 486
Bevacizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1	17.4	€ 1,235.40

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	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	2	34.8	€ 2,818.80
Gemcitabine	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	2	34.8	€ 2,818.80
Docetaxel	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	17.4	€ 1,409.40
Paclitaxel	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	1	52.2	€ 4,228.20
Pemetrexed	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	17.4	€ 1,409.40

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 April 2020.

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

Berlin, 2 April 2020

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Prof. Hecken