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)
Tislelizumab (new therapeutic indication: non-small cell lung cancer, after previous therapy)

of 18 June 2025

At their session on 18 June 2025, 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. 5 to the information on the benefit assessment of Tislelizumab in accordance with the resolution of 18 June 2025 for the therapeutic indication: "Non-small cell lung cancer, squamous, first-line, combination with carboplatin and either paclitaxel or nab-paclitaxel":

Tislelizumab

Resolution of: 18 June 2025
Entry into force on: 18 June 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 8 July 2024):

Tevimbra as monotherapy is indicated for the treatment of adult patients with locally advanced or metastatic NSCLC after prior platinum-based therapy. Patients with EGFR-mutated or ALK-positive NSCLC should also have received targeted therapies prior to treatment with tislelizumab.

Therapeutic indication of the resolution (resolution of 18 June 2025):

See new therapeutic indication according to marketing authorisation.

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

Adults with locally advanced or metastatic NSCLC after prior platinum-based 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 tislelizumab compared to docetaxel:

a1) Patients with PD-L1 expression ≥ 1%

An additional benefit is not proven.

a2) Patients with tumour cell PD-L1 < 1%

An additional benefit is not proven.

Study results according to endpoints:[1]

Adults with locally advanced or metastatic NSCLC after prior platinum-based chemotherapy

a1) Patients with PD-L1 expression ≥ 1%

No data available.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	∅	No data available.
Morbidity	∅	No data available.
Health-related quality of life	∅	No data available.
Side effects	∅	No data available.
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 ∅: No data available. n.a.: not assessable		

a2) Patients with PD-L1 expression < 1%

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	There is no relevant difference for the benefit assessment.
Morbidity	↔	Advantage for the endpoint of alopecia collected using EORTC QLQ-LC13. No relevant differences for the benefit assessment overall.
Health-related quality of life	n.a.	There are no assessable data.
Side effects	↑	Advantage in the overall rate of severe AEs. In detail, mainly advantages in specific AEs.
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 ∅: No data available. n.a.: not assessable		

[1] Data from the dossier assessment of the IQWiG (A24-128) and from the addendum (A25-63), unless otherwise indicated.

RATIONALE 303 study:

- Open-label, parallel, randomised controlled phase III study
- Tislelizumab versus docetaxel
- Data cut-off from 18.01.2024

Relevant patient population: Patients with PD-L1 expression < 1%

Mortality

Endpoint	**Tislelizumab**		**Docetaxel**		Intervention vs control
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	Hazard ratio [95% CI] p value[a] Absolute difference (AD)[b]
Overall survival					
	214	15.4 [13.2; 18.2] 166 (77.6)	103	11.7 [8.8; 14.9] 82 (79.6)	0.79 [0.61; 1.03] 0.084

Morbidity

Progression-free survival[2]					
	214	2.3 [2.14; 4.04] 192 (89.7)	103	2.9 [2.14; 4.17] 81 (78.6)	0.85 [0.65; 1.11] 0.232
Symptomatology					
EORTC QLQ-C30 – time to 1st deterioration[c]					
	No suitable data[d]				
EORTC QLQ-LC13 – time to 1st deterioration[c]					
Alopecia	214	n.r. [33.1; n.c.] 34 (15.9)	103	0.8 [0.8; 1.4] 67 (65.0)	0.09 [0.06; 0.14]; < 0.001
Cough, dysphagia, dyspnoea, haemoptysis, pain (arm/ shoulder; chest; other), peripheral neuropathy, mouth pain	No suitable data[d]				
Health status (EQ-5D VAS – time to 1st deterioration)[c]					
	No suitable data[d]				

[2] Data from Module 4 of the benefit assessment dossier from 20 December 2024.

Health-related quality of life

EORTC-QLQ C30	
	No suitable data[d]

Side effects

Endpoint	**Tislelizumab**		**Docetaxel**		Intervention vs control
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	Hazard ratio [95% CI] p value[a] Absolute difference (AD)[b]
Total adverse events (presented additionally)					
	213	0.5 [0.4; 0.7] 209 (98.1)	98	0.2 [0.1; 0.3] 95 (96.9)	-
Serious adverse events (SAE)					
	213	22.4 [16.6; 48.2] 72 (33.8)	98	n.r. 26 (26.5)	0.87 [0.55; 1.37] 0.549
Severe adverse events (CTCAE grade 3 or 4)					
	213	16.4 [10.7; 21.7] 91 (42.7)	98	0.3 [0.3; 1.0] 71 (72.4)	0.25 [0.18; 0.35] < 0.001
Therapy discontinuation due to adverse events					
	213	n.r. 23 (10.8)	98	n.r. 13 (13.3)	0.59 [0.29; 1.19] 0.134
Specific adverse events					
Immune-mediated AEs	No suitable data[e]				
Gastrointestinal disorders (SOC, AE)	213	14.5 [7.4; 20.4] 86 (40.4)	98	2.1 [1.0; 10.6] 53 (54.1)	0.46 [0.32; 0.66] < 0.001
Asthenia (PT, AE)	213	n.r. 33 (15.5)	98	n.r. 22 (22.4)	0.5 [0.28; 0.87] 0.012
Insomnia (PT, AE)	213	n.r. 12 (5.6)	98	n.r. 11 (11.2)	0.36 [0.15; 0.83] 0.013
Alopecia (PT, AE)	213	n.r. 2 (0.9)	98	1.6 [0.7; 5.1] 52 (53.1)	0.01 [0.003; 0.05] < 0.001
Respiratory, thoracic and mediastinal disorders (SOC, SAE)	213	n.r. [48.2; n.c.] 30 (14.1)	98	n.r. 4 (4.1)	2.87 [1.00; 8.21] 0.040

Blood and lymphatic system disorders (SOC, severe AE[f])	213	n.r. 14 (6.6)	98	4.6 [1.6; n.c.] 45 (45.9)	0.09 [0.05; 0.17] < 0.001
included therein:					
Neutropenia (PT, severe AE[f])	213	n.r. 2 (0.9)	98	n.r. [7.2; n.c.] 26 (26.5)	0.03 [0.01; 0.12] < 0.001
Leukopenia (PT, severe AE[f])	213	n.r. 1 (0.5)	98	n.r. 17 (17.3)	RR: 0.03 [0.004; 0.20] < 0.001
Febrile neutropenia (PT, severe AE[f])	213	n.r. 0 (0)	98	n.r. 16 (16.3)	RR: 0.01 [0.001; 0.23] < 0.001
Investigations (SOC, severe AE[f])	213	n.r. 15 (7.0)	98	n.r. [5.4; n.c.] 36 (36.7)	0.13 [0.07; 0.24] < 0.001
included therein:					
Neutropenia (PT, severe AE[f])	213	n.r. 2 (0.9)	98	n.r. 28 (28.6)	0.01 [0.002; 0.10] < 0.001
Leukopenia (PT, severe AE[f])	213	n.r. 1 (0.5)	98	n.r. 25 (25.5)	0.02 [0.002; 0.11]; < 0.001
Infections and infestations (SOC, severe AE[f])	213	n.r. [48.5; n.c.] 19 (8.9)	98	n.r. 16 (16.3)	0.37 [0.19; 0.74] 0.004
Metabolism and nutrition disorders (SOC, severe AE[f])	213	n.r. 14 (6.6)	98	n.r. 13 (13.3)	0.45 [0.21; 0.96] 0.034

[a] Cox proportional hazards model and log-rank test; each stratified by histology (squamous cell carcinoma vs non-squamous cell carcinoma), and line of therapy (second vs third line of therapy)
[b] Data on absolute difference (AD) only in the case of statistically significant difference; own calculation
[c] An increase by ≥ 10 points compared to the start of the study is considered a clinically relevant deterioration (scale range: 0 to 100).
[d] for explanation, see section I 4.1 of IQWiG's benefit assessment and section 2.1 of the addendum
[e] for explanation, see section I 4.1 of IQWiG's benefit assessment and section 2.3 of the addendum
[f] operationalised as CTCAE grade ≥ 3

Abbreviations used:
AD = absolute difference; CTCAE = Common Terminology Criteria for Adverse Events; EORTC = European Organisation for Research and Treatment of Cancer; HR = hazard ratio; CI = confidence interval; N = number of patients evaluated; n = number of patients with (at least one) event; n.c. = not calculable; n.r. = not reached; QLQ-C30 = Quality of life Questionnaire - Core 30; QLQ-LC13 = Quality of Life Questionnaire – Lung Cancer 13; PT = preferred term; RCT = randomised controlled trial; RR = relative risk; SOC = system organ class; SAE = serious adverse event; AE = adverse event; VAS = visual analogue scale; vs = versus

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

Adults with locally advanced or metastatic NSCLC after prior platinum-based chemotherapy

a1) Patients with PD-L1 expression ≥ 1%

Approx. 440 to 970 patients

a2) Patients with PD-L1 expression < 1%

Approx. 250 to 650 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 Tevimbra (active ingredient: tislelizumab) agreed upon in the context of the marketing authorisation at the following publicly accessible link (last access: 20 February 2025):

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

Therapy with tislelizumab 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 carcinoma, 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.

In accordance with the EMA requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material that contains information for medical professionals and patients (including patient identification card). The training material contains, in particular, instructions on the management of immune-mediated side effects potentially occurring with tislelizumab.

4. Treatment costs

Annual treatment costs:

Adults with locally advanced or metastatic NSCLC after prior platinum-based chemotherapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Tislelizumab	€ 75,142.25
Appropriate comparator therapy:	
Docetaxel (only for patients with PD-L1 negative tumours)	
Docetaxel	€ 8,527.22
Additionally required SHI costs	*€ 75.55*

Designation of the therapy	Annual treatment costs/ patient
Pemetrexed (only for patients with PD-L1 negative tumours and except in cases of predominantly squamous histology)	
Pemetrexed	€ 18,621.48
Additionally required SHI costs	*€ 133.14 – € 186.43*
Nivolumab	
Nivolumab	€ 75,862.26
Pembrolizumab (only for patients with PD-L1 expressing tumours (TPS ≥ 1%))	
Pembrolizumab	€ 81,438.79
Atezolizumab	
Atezolizumab	€ 67,771.78
Docetaxel in combination with nintedanib (only for patients with PD-L1 negative tumours and adenocarcinoma histology)	
Docetaxel	€ 8,527.22
Nintedanib	€ 32,010.55
Total:	€ 40,537.77
Additionally required SHI costs	*€ 75.55*

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 June 2025)

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Tislelizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	17.4	€ 1,740
Docetaxel (monotherapy or combination therapy)	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740
Nivolumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	26.1	€ 2,610
Pembrolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	17.4	€ 1,740
Pemetrexed	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	17.4	€ 1,740

5. Designation of 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 the assessed medicinal product

In the context of the designation of medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V, the following findings are made:

Adults with locally advanced or metastatic non-small cell lung cancer (NSCLC) after prior platinum-based chemotherapy

- No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient authorised in monotherapy.

The designation of combinations exclusively serves the implementation of the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 18 June 2025.

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

Berlin, 18 June 2025

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

Prof. Hecken