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
Atezolizumab (new therapeutic indication: non-small cell lung cancer, first-line)

of 20 March 2025

At its session on 20 March 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. 4 to the information on the benefit assessment of Atezolizumab in accordance with the resolution of 5 January 2023 last modified on 17 August 2023:

Atezolizumab

Resolution of: 20 March 2025
Entry into force on: 20 March 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 26 August 2024):

Tecentriq as monotherapy is indicated for the first-line treatment of adult patients with advanced NSCLC who are ineligible for platinum-based therapy.

Therapeutic indication of the resolution (resolution of 20 March 2025):

See new therapeutic indication according to marketing authorisation.

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

a) Adults with advanced NSCLC with PD-L1 expression ≥ 50% on TC considered ineligible for platinum; first-line therapy

Appropriate comparator therapy for atezolizumab as monotherapy:

− Pembrolizumab as monotherapy

or

− Cemiplimab as monotherapy

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

An additional benefit is not proven.

b) Adults with locally advanced NSCLC with PD-L1 expression < 50% on TC considered ineligible for platinum; first-line therapy

Appropriate comparator therapy for atezolizumab as monotherapy:

− Gemcitabine as monotherapy

or

− Vinorelbine as monotherapy

Extent and probability of the additional benefit of atezolizumab over monotherapy with gemcitabine or vinorelbine:

Indication of a minor additional benefit

Study results according to endpoints:[1]

a) Adults with advanced NSCLC with PD-L1 expression ≥ 50% on TC considered ineligible for platinum; first-line therapy

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		

b) Adults with locally advanced NSCLC with PD-L1 expression < 50% on TC considered ineligible for platinum; first-line therapy

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↑↑	Advantage in overall survival.
Morbidity	n.a.	There are no assessable data.
Health-related quality of life	n.a.	There are no assessable data.
Side effects	↑↑	Advantages in the endpoints of severe AEs (in detail 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 (A24-97) and from the addendum (A25-25), unless otherwise indicated.

IPSOS study

- Atezolizumab vs vinorelbine or gemcitabine
- Study design: multicentre, open-label randomised controlled trial
- Data cut-offs:
  - 15 May 2020 (pre-specified interim analysis of overall survival after 304 events)
  - 30 April 2022 (pre-specified final analysis of overall survival after 379 events in the entire study population)

Mortality

Endpoint	**Atezolizumab**		**Gemcitabine or vinorelbine**		Intervention vs control
	N	Median survival time in months [95% CI][b] *Patients with event n (%)*	N	Median survival time in months [95% CI][b] *Patients with event n (%)*	Effect estimator [95% CI] [b] p value[c] Absolute difference (AD)[a]
Overall survival/ mortality					
Overall survival	229	10.2 [8.5; 12.0] 197 (86.0)	115	8.0 [5.8; 10.9] 102 (88.7)	0.76 [0.59; 0.97] 0.025 2.2

Morbidity

Endpoint	**Atezolizumab**		**Gemcitabine or vinorelbine**		Intervention vs control
	N	Median time to event in months [95% CI][b] *Patients with event n (%)*	N	Median time to event in months [95% CI][b] *Patients with event n (%)*	Effect estimator [95% CI][d] p value[c] Absolute difference (AD)[a]
Progression-free survival (PFS)					
PFS based on the principal investigator	229	4.2 [3.3; 5.5] 216 (94.3)	115	4.2 [3.0; 5.7] 104 (90.4)	0.86 [0.68; 1.10][b] 0.2223
Symptomatology					
EORTC QLQ-C30	No suitable data available.				
EORTC QLQ-LC13	No suitable data available.				
Health status					
EQ-5D VAS	No suitable data available.				

Health-related quality of life

EORTC QLQ-C30	
	No suitable data available.

Side effects

Endpoint	**Atezolizumab**		**Gemcitabine or vinorelbine**		Intervention vs control
	N	Median time to event in months [95% CI][b] *Patients with event n (%)*	N	Median time to event in months [95% CI][b] *Patients with event n (%)*	Effect estimator [95% CI][d] p value[c] Absolute difference (AD)[a]
Total adverse events (presented additionally)					
	228	n.d. 212 (93.0)	113	n.d. 111 (98.2)	
Serious adverse events (SAE)					
	228	n.d. 119 (52.2)	113	n.d. 44 (38.9)	1.11 [0.78; 1.58] 0.560
Severe adverse events[e]					
	228	n.d. 135 (59.2)	113	n.d. 70 (61.9)	0.66 [0.49; 0.89] 0.006
Therapy discontinuation due to adverse events					
	228	n.d. 34 (14.9)	113	n.d. 17 (15.0)	0.59 [0.32; 1.09] 0.089
Specific adverse events					
Immune-mediated AEs (presented additionally)	228	n.d. 128 (55.7)	113	n.d. 26 (23.0)	
Immune-mediated SAEs	No suitable data available.				
Immune-mediated severe AEs[e]	No suitable data available.				
Neutropenia (PT, severe AEs[e])	228	n.d. 2 (0.9)	113	n.d. 12 (10.6)	0.05 [0.01; 0.23] < 0.001
Skin reactions[f]	228	n.d. 45 (19.7)	113	n.d. 16 (14.2)	1.21 [0.68; 2.15] 0.522
Gastrointestinal disorders (SOC, AEs)	228	n.d. 99 (43.4)	113	n.d. 61 (54.0)	0.51 [0.37; 0.71] < 0.001

[a] Indication of absolute difference (AD) only in case of statistically significant difference; own calculation

[b] HR and 95% CI: Cox regression model, stratified by tumour histology (IxRS) and presence of brain metastases (IxRS);
[c] p value: log-rank test
[d] HR and 95% CI: unstratified Cox regression model
[e] Operationalised as CTCAE grade ≥ 3.
[f] Operationalised as skin and subcutaneous tissue disorders (SOC, AEs)
Abbreviations used:
AD = absolute difference; CTCAE = Common Terminology Criteria for Adverse Events; 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; vs = versus

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

a) Adults with advanced NSCLC with PD-L1 expression ≥ 50% on TC considered ineligible for platinum; first-line therapy

Approx. 550 - 2,190 patients

b) Adults with locally advanced NSCLC with PD-L1 expression < 50% on TC considered ineligible for platinum; first-line therapy

Approx. 1,350 – 5,380 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: 9 December 2024):

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

Treatment with atezolizumab 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.

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, information and warnings about immune-mediated side effects as well as infusion-related reactions.

4. Treatment costs

Annual treatment costs:

a) Adults with locally advanced or metastatic NSCLC with PD-L1 expression ≥ 50% on TC who are considered ineligible for platinum and whose disease does not have an EGFR mutation or ALK translocation; first-line therapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Atezolizumab	€ 67,771.78
Appropriate comparator therapy:	
Pembrolizumab as monotherapy	
Pembrolizumab	€ 90,059.96
Cemiplimab as monotherapy	
Cemiplimab	€ 71,009.05

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

Costs for additionally required SHI services: not applicable

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Appropriate comparator therapy					
Pembrolizumab as monotherapy					
Pembrolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	8.7 - 17.4	€ 870 - € 1,740
Cemiplimab as monotherapy					
Cemiplimab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	17.4	€ 1,740

b) Adults with locally advanced or metastatic NSCLC with PD-L1 expression ≥ 50% on TC who are considered ineligible for platinum and whose disease does not have an EGFR mutation or ALK translocation; first-line therapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Atezolizumab	€ 67,771.78
Appropriate comparator therapy:	
Monotherapy with gemcitabine	
Gemcitabine	€ 7,016.88
Monotherapy with vinorelbine	
Vinorelbine	€ 7,510.74 - € 9,376.96

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

Costs for additionally required SHI services: not applicable

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Appropriate comparator therapy					
Monotherapy with gemcitabine					
Gemcitabine	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	1	39.0	€ 3,900
Monotherapy with vinorelbine					
Vinorelbine	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	1	52.1	€ 5,210

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:

a) Adults with advanced NSCLC with PD-L1 expression ≥ 50% on TC considered ineligible for platinum; first-line therapy

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.

b) Adults with locally advanced NSCLC with PD-L1 expression < 50% on TC considered ineligible for platinum; first-line therapy

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 20 March 2025.

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

Berlin, 20 March 2025

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

Prof. Hecken