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 (reassessment after the deadline: non-small cell lung cancer, PD-L1 expression ≥ 50%, adjuvant therapy after resection and chemotherapy)

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. Annex XII is amended as follows:

1. **The information on Atezolizumab in the version of the resolution of 5 January 2023 (BAnz AT 17.02.2023 B4), last modified on 17 August 2023, is repealed.**

2. **In Annex XII, the following information shall be added after No. 5 to the information on the benefit assessment of Atezolizumab in accordance with the resolution of 20 March 2025 (non-small cell lung cancer, first-line):**

Atezolizumab

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

Therapeutic indication (according to the marketing authorisation of 7 June 2022):

Tecentriq as monotherapy is indicated as adjuvant treatment following complete resection and platinum-based chemotherapy for adult patients with NSCLC with a high risk of recurrence whose tumours have PD-L1 expression on ≥ 50% of tumour cells (TC) and who do not have EGFR mutant or ALK-positive NSCLC.

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

See therapeutic indication according to marketing authorisation.

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

Adults with completely resected NSCLC with a high risk of recurrence after platinum-based chemotherapy whose tumours have PD-L1 expression on ≥ 50% of tumour cells (TC) and who do not have EGFR mutant or ALK-positive NSCLC; adjuvant treatment

Appropriate comparator therapy:

Monitoring wait-and-see approach

Extent and probability of the additional benefit of atezolizumab compared to monitoring wait-and-see approach:

Hint for a considerable additional benefit

Study results according to endpoints:[1]

Adults with completely resected NSCLC with a high risk of recurrence after platinum-based chemotherapy whose tumours have PD-L1 expression on ≥ 50% of tumour cells (TC) and who do not have EGFR mutant or ALK-positive NSCLC; adjuvant treatment

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↑	Advantage in overall survival.
Morbidity	↑↑	Advantages in the prevention of recurrences.
Health-related quality of life	∅	No data available.
Side effects	↓↓	Disadvantages in the endpoints of SAEs and therapy discontinuation due to AEs. In detail, disadvantages 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		

IMpower010 study

- Study design: RCT, open-label, parallel
- Comparison: Atezolizumab versus Best Supportive Care (BSC)
- Data cut-off: 26 January 2024

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A24-102) unless otherwise indicated.

Mortality

Endpoint	**Atezolizumab**		**BSC**		Atezolizumab vs BSC
	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 (%)*	HR [95% CI]; p value[a]
Overall survival					
	106	n.r. *22 (20.8)*	103	87.1 [72.0; n.r.] *41 (39.8)*	0.47 [0.28; 0.80] 0.005

Morbidity

Endpoint	**Atezolizumab**		**BSC**		Atezolizumab vs BSC
	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 (%)*	HR [95% CI]; p value[a]
Recurrences					
Recurrence rate	106	- *34 (32.1)*	103	- *55 (53.4)*	RR: 0.61 [0.44; 0.84] 0.002[b]
Local recurrence	106	- *4 (3.8[c])*	103	- *8 (7.8)*	-
Regional recurrence	106	- *12 (11.3[c])*	103	- *8 (7.8)*	-
Distant recurrence[d]	106	- *11 (10.4[c])*	103	- *28 (27.2)*	-
New primary lung cancer	106	- *1 (0.9[c])*	103	- *3 (2.9)*	-
Death without recurrence	106	- *6 (5.7)*	103	- *8 (7.8)*	-
Disease-free survival	106	n.r. *34 (32.1)*	103	42.9 [32.0; n.c.] *55 (53.4)*	0.52 [0.33; 0.80] 0.003

Health-related quality of life

Endpoint	**Atezolizumab**		**BSC**		Atezolizumab vs BSC
	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 (%)*	HR [95% CI]; p value
No endpoint assessed in this category					

Side effects

Endpoint	**Atezolizumab**		**BSC**		Atezolizumab vs BSC
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95% CI]; p value[e]
Total adverse events (presented additionally)					
	104	*99 (95.2)*	101	*71 (70.3)*	-
Serious adverse events (SAE)					
	104	*16 (15.4)*	101	*4 (4.0)*	3.88 [1.34; 11.22] 0.006
Severe adverse events (CTCAE grade ≥ 3)					
	104	*21 (20.2)*	101	*11 (10.9)*	1.85 [0.94; 3.65] 0.070
Therapy discontinuation due to adverse events					
	104	*20 (19.2)*	101	*0[f] (0)*	39.83 [2.44; 649.84] < 0.001
Specific adverse events					
Immune-mediated AEs (AEs, SAEs, severe AEs)	No usable data available				
Fever (PT, AE)	104	*11 (10.6)*	101	*0 (0)*	22.34 [1.33; 374.20] < 0.001
Skin and subcutaneous tissue disorders (SOC, AE)	104	*36 (34.6)*	101	*6 (5.9)*	5.83 [2.57; 13.23] < 0.001

Infections and infestations (SOC, SAEs)	104	*7 (6.7)*	101	*0 (0)*	– 0.008

a. HR and CI calculated using the Cox proportional hazards model, p value calculated using the log-rank test; each stratified by sex, tumour histology and stage of the disease
b. RR, CI and p value calculated with the log-binomial model; adjusted for sex, tumour histology and stage of the disease
c. Calculation by IQWiG
d. Of the patients with distant recurrence, 1 and 11 patients in the intervention and comparator arms respectively had CNS recurrences
e. Calculation by IQWiG; RR, CI (asymptotic) and p value (unconditional exact test, CSZ method according to Martín Andrés et al. [2]). In the case of 0 events in one study arm, the correction factor 0.5 was used in both study arms when calculating effect and CI.
f. The presentation was taken from Module 4 A of the pharmaceutical company. The discontinuation relates to treatment with atezolizumab. In the comparator arm, 1 patient had discontinued BSC therapy. It is unclear exactly which supportive measure was discontinued.

Abbreviations used:
AD = absolute difference; BSC = Best supportive care; CTCAE = Common Terminology Criteria for Adverse Events; HR = hazard ratio; CI = confidence interval; N = number of patients evaluated; n = number of patients with event; n.c. = not calculable; n.a. = not achieved; PT = preferred term; RCT = randomised controlled trial; RR = relative risk; SOC = system organ class; SAE = serious adverse event; AE= adverse event; CNS = central nervous system

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

Adults with completely resected NSCLC with a high risk of recurrence after platinum-based chemotherapy whose tumours have PD-L1 expression on ≥ 50% of tumour cells (TC) and who do not have EGFR mutant or ALK-positive NSCLC; adjuvant treatment

Approx. 700 to 890 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 March 2025):

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.

[2] Martín Andrés A, Silva Mato A. Choosing the optimal unconditioned test for comparing two independent proportions. Computat Stat Data Anal 1994; 17(5): 555-574. https://doi.org/10.1016/0167-9473(94)90148-1.

Patients are to be selected for treatment with atezolizumab as monotherapy on the basis of tumour PD-L1 expression, confirmed by a validated test.

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. The training material contains, in particular, instructions on the management of immune-mediated side effects potentially occurring with atezolizumab as well as on infusion-related reactions.

4. Treatment costs

Annual treatment costs:

Adults with completely resected NSCLC with a high risk of recurrence after platinum-based chemotherapy whose tumours have PD-L1 expression on ≥ 50% of tumour cells (TC) and who do not have EGFR mutant or ALK-positive NSCLC; adjuvant treatment

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Atezolizumab	€ 66,213.81
Appropriate comparator therapy:	
Monitoring wait-and-see approach	Not calculable

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

Costs for additionally required SHI services: not applicable

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 completely resected NSCLC with a high risk of recurrence after platinum-based chemotherapy whose tumours have PD-L1 expression on ≥ 50% of tumour cells (TC) and who do not have EGFR mutant or ALK-positive NSCLC; adjuvant treatment

– 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