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, PD-L1 expression ≥ 50%, adjuvant therapy after resection and chemotherapy)

of 5 January 2023

At its session on 5 January 2023, 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 19 November 2021:

Atezolizumab

Resolution of: 5 January 2023
Entry into force on: 5 January 2023
Federal Gazette, BAnz AT DD MM YYYY Bx

New 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 (see section 5.1 for selection criteria).

Therapeutic indication of the resolution (resolution of 5 January 2023):

See new 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

Appropriate comparator therapy:

Monitoring wait-and-see approach

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

Hint for a non-quantifiable 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

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↑	Advantage in overall survival.
Morbidity	n.c.	There are no assessable data.
Health-related quality of life	∅	No data available.
Side effects	↓↓	Disadvantages in the endpoints of SAE, therapy discontinuations due to 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
∅: There are no usable data for the benefit assessment.
n.c.: not calculable

IMpower010 study

- Study design: RCT, open-label, parallel
- Comparison: Atezolizumab vs BSC
- Data cut-offs:

  21.01.2021 (interim analysis DFS)

  18.04.2022 (interim analysis OS)

1 Data from the dossier assessment of the IQWiG (A22-67) and from the addendum (A22-124), unless otherwise indicated.

Mortality

Endpoint	Atezolizumab		Best supportive care		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
Overall survival					
	106	n.a. *15 (14.2)*	103	n.a. *30 (29.1)*	0.45 [0.24; 0.85] 0.012

Morbidity

Endpoint	Atezolizumab		Best supportive care		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
Recurrences	No usable data available				

Health-related quality of life

Endpoint	Atezolizumab		Best supportive care		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 collected in this category					

Side effects

Endpoint	Atezolizumab		Best supportive care		Atezolizumab vs BSC
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	RR [95% CI]; p value
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 (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, AEs)	104	*11 (10.6)*	101	*0 (0)*	22.34 [1.33; 374.20] < 0.001
Skin and subcutaneous tissue disorders (SOC, AEs)	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

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.a. = not achieved; PT = preferred term; RCT = randomised controlled trial; RR = relative risk; SOC = system organ class; SAE = serious adverse event; AE= adverse event; vs = versus

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

approx. 700 to 790 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: 16 November 2022):

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.

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

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 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

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Atezolizumab	€ 66,573.19 - € 71,708
Appropriate comparator therapy:	

Designation of the therapy	Annual treatment costs/ patient
Monitoring wait-and-see approach	incalculable

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 01 December 2022)

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
Atezolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	13 – 26	€ 1,300 - € 2,600

5. 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 Atezolizumab

Medicinal products with new active ingredients as defined in Section 35a, paragraph 3, sentence 4 SGB V are medicinal products with the following new active ingredients which, on the basis of the marketing authorisation under Medicinal Products Act, can be used in a combination therapy with atezolizumab for the 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:

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

No active ingredient that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

II. Entry into force

1. The resolution will enter into force on the day of its publication on the internet on the website of the Federal Joint Committee on 5 January 2023.

2. The period of validity of the resolution is limited to 1 April 2024.

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

Berlin, 5 January 2023

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

Prof. Hecken