Epcoritamab (diffuse large B-cell lymphoma, after ≥ 2 prior therapies)

Resolution of: 4 April 2024 valid until: unlimited
Entry into force on: 4 April 2024
Federal Gazette, BAnz AT 16 05 2024 B4

Therapeutic indication (according to the marketing authorisation of 22 September 2023):

Tepkinly as monotherapy is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy.

Therapeutic indication of the resolution (resolution of 4 April 2024):

See therapeutic indication according to marketing authorisation.

1. Extent of the additional benefit and significance of the evidence

Epcoritamab is approved as a medicinal product for the treatment of rare diseases in accordance with Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999 on orphan drugs. In accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V, the additional medical benefit is considered to be proven through the grant of the marketing authorisation.

The Federal Joint Committee (G-BA) determines the extent of the additional benefit for the number of patients and patient groups for which there is a therapeutically significant additional benefit in accordance with Chapter 5 Section 12, paragraph 1, number 1, sentence 2 of its Rules of Procedure (VerfO) in conjunction with Section 5, paragraph 8 AM-NutzenV, indicating the significance of the evidence. This quantification of the additional benefit is based on the criteria laid out in Chapter 5 Section 5, paragraph 7, numbers 1 to 4 of the Rules of Procedure (VerfO).

<u>Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy</u>

Extent of the additional benefit and significance of the evidence of epcoritamab:

Hint for a non-quantifiable additional benefit since the scientific data does not allow quantification.

Study results according to endpoints:[1]

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	No data available in comparison with the control group.
Morbidity	n.a.	No data available in comparison with the control group.
Health-related quality of life	n.a.	No data available in comparison with the control group.
Side effects	n.a.	No data available in comparison with the control group.
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		

<u>GCT3013-01 study</u>

- open-label, single-arm phase I/II study
- Relevant sub-population: Cohort of patients with relapsed or refractory DLBCL in the expansion phase
- Data cut-off: 21.04.2023

Mortality

Endpoint	Epcoritamab	
	N	Patients with event n (%)
Overall survival		
Deaths	139[a]	77 (55.4)
		Kaplan-Meier estimator overall survival rate (%) [95% CI][b]
At month 6	139	70.6 [62.2; 77.5]
At month 12	139	58.4 [49.6; 66.2]
At month 18	139	51.5 [42.7; 59.6]
Endpoint	N	Median survival time in months [95% CI]
	139	19.4 [11.7; 27.7]

[1] Data from the dossier assessment of the G-BA (published on 15. January 2024), unless otherwise indicated.

Morbidity

Endpoint	Epcoritamab	
	N	Median time in months [95% CI] Patients with event n (%)
Progression-free survival (PFS)[c] – presented additionally (assessed by IRC using the Lugano criteria (2014))		
	139	4.4 [3.0; 8.8] 94 (67.6)
		Patients with event n (%) [95% CI]
Overall response rate (ORR)[d] – presented additionally (assessed by IRC using the Lugano criteria (2014))		
Total response rate (CR + PR)	139	86 (61.9) [53.3; 70.0]
CR	139	56 (40.3)
PR	139	30 (21.6)
Health status		
EQ-5D VAS		
There are no usable data.		

Health-related quality of life

Endpoint	Epcoritamab	
	N	Patients with event n (%)
FACT-Lym		
There are no usable data.		

Side effects

Endpoint	Epcoritamab	
	N	**Patients with event n (%)**
Adverse events in total (presented additionally)	139	138 (99.3)
Serious adverse events (SAE)	139	95 (68.3)
Severe adverse events (CTCAE grade ≥ 3)[e]	139	96 (69.1)
Therapy discontinuation due to adverse events[f]	139	22 (15.8)

Endpoint	Epcoritamab	
	N	Patients with event n (%)
SAEs according to MedDRA system organ class (with an incidence ≥ 10%)		
Immune system disorders	139	40 (28.8)
Infections and infestations	139	41 (29.5)
Severe adverse events according to MedDRA system organ class (with an incidence ≥ 10%)		
Blood and lymphatic system disorders	139	41 (29.5)
Infections and infestations	139	35 (25.2)[g]
Investigations	139	19 (13.7)
AEs of special interest (with an incidence ≥ 10%)		
Cytokine Release Syndrome (CRS)		
AE (regardless of severity grade)	139	69 (49.6)
SAE	139	40 (28.8)

a. Corresponds to the FAS and the safety population. An ITT population was not defined; all screened subjects who met the inclusion criteria received at least one dose of epcoritamab, according to the study report.
b. Calculated probability that a subject is alive at a given time.
c. Information from the dossier of the pharmaceutical company.
d. Primary endpoint. Assessed by IRC according to Lugano criteria (Lugano classification, Cheson et al. 2014).
e. AEs are classified according to MedDRA (version 25.0) and CTCAE (version 5.0). CRS and ICANS are categorised according to the criteria of the American Society for Transplantation and Cellular Therapy (Lee et al. 2019) and CTLS according to Cairo-Bishop (Coiffier et al. 2008).
f. Criteria defined in the study protocol for discontinuation of study medication due to unacceptable toxicity from the study medication are CRS grade 4, CRS combined with MAS/HLH or ICANS grade ≥ 3. In addition, other AEs may have led to discontinuation of the study medication.
g. Information from the study report. In module 4 of the dossier of the pharmaceutical company, the incidence of this AE is given as n = 42 (30.2%).

Abbreviations used:
CRS = cytokine release syndrome; CTCAE = Common Terminology Criteria for Adverse Events; CTLS = clinical tumour lysis syndrome; ICANS = immune effector cell-associated neurotoxicity syndrome; EQ-5D VAS = European Quality of Life 5-Dimension Visual Analogue Scale; FACT-Lym = Functional Assessment of Cancer Therapy - Lymphoma; FAS = full analysis set; ITT = intention-to-treat; CI = confidence interval; MAS/HLH = macrophage activation syndrome / haemophagocytic lymphohistiocytosis; MedDRA = Medical Dictionary for Regulatory Activities; N = number of patients evaluated; n = number of patients with (at least one) event; n.a. = not applicable; n.c. = not calculable; n.r. = not reached; PFS = progression-free survival; SAS = safety population; SOC = system organ class; (S)AE = (serious) adverse event.

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

Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy

approx. 1,050 – 1,900 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 Tepkinly (active ingredient: epcoritamab) at the following publicly accessible link (last access: 22 December 2023):

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

Treatment with epcoritamab should only be initiated and monitored by specialists in internal medicine, haematology and oncology, experienced in the treatment of patients with diffuse large B-cell lymphoma (DLBCL).

This medicinal product received a conditional marketing authorisation. This means that further evidence of the benefit of the medicinal product is anticipated. The European Medicines Agency EMA will evaluate new information on this medicinal product at a minimum once per year and update the product information where necessary.

In accordance with the EMA's requirements for additional risk minimisation measures, the pharmaceutical company must ensure that all healthcare professionals who may prescribe epcoritamab and each subject treated with epcoritamab receive a patient pass containing information on risks associated with cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) as well as a warning for healthcare professionals treating the subjects and the contact details of the healthcare professional prescribing epcoritamab.

The pivotal study GCT3013-01 did not enrol any patients who were eligible for curative intensive salvage therapy followed by high-dose chemotherapy with haematopoietic stem cell transplantation (HSCT).

4. Treatment costs

Annual treatment costs:

The annual treatment costs shown refer to the first year of treatment.

Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Epcoritamab	€ 205,873.58
Additionally required SHI services	€ 54.34 - € 54.67
Total	€ 205,927.92 – € 205,928.25

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 March 2024)

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 relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic 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.