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

of 1 February 2024

At its session on 1 February 2024, 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 shall be amended in alphabetical order to include the active ingredient Glofitamab as follows:

Glofitamab

Resolution of: 1 February 2024
Entry into force on: 1 February 2024
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 7 July 2023):

Columvi 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 1 February 2024):

See therapeutic indication according to marketing authorisation.

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

Glofitamab 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 glofitamab:

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

NP30179 study

- Open-label, single-arm phase I/II dose escalation and dose expansion study
- Relevant sub-population: Cohorts D2 (only subcohort 2 [sub.2]), D3 and D5, which comprise the therapeutic indication in accordance with the marketing authorisation or product information and received the corresponding dosage regimen of glofitamab, pretreatment with obinutuzumab and premedication and prophylaxis for cytokine release syndrome.
- Data cut-off: 2nd Data cut-off from 15 June 2022

Mortality

Endpoint	Glofitamab	
	N	Patients with event n (%)
Overall survival		
Death from any cause	115[a]	65 (56.5)
		Kaplan-Meier estimator (%) [95% CI][b]
At month 12	115	48.7 [39.2; 58.2]
Endpoint	N	Median survival time (in months) [95% CI][c]
	115	10.2 [7.5; 15.7]

[1] Data from the dossier assessment of the G-BA (published on 1. November 2023), unless otherwise indicated.

Morbidity

Endpoint	Glofitamab	
	N	Patients with event n (%) Median PFS (Independent Review Committee) in months [95% CI][d]
Progression-free survival (PFS)[e]		
	115	74 (64.3) 3.8 [3.3; 7.6]
		Patients with event n (%) [95% CI]
Tumour response (complete response assessed by IRC using Lugano criteria (2014))[f,g,h] (presented additionally)		
CR achieved	155	62 (40.0) [32.2; 48.2][i]
EORTC QLQ-C30 (symptom scales)		
		There are no usable data.

Quality of life

Endpoint	Glofitamab	
	N	
EORTC QLQ-C30 (functional scales)		
		There are no usable data.
FACT-LymS		
		There are no usable data.

Side effects

Endpoint	Glofitamab	
	N	**Patients with event n (%)**
Total adverse events (presented additionally)		
	154[k]	152 (98.7)[m]
Serious adverse events (SAE)[j]		
	154[k]	75 (48.7)[m]
Severe adverse events (CTCAE grade ≥ 3)[l]		
	154[k]	99 (64.3)[m]

Endpoint	Glofitamab	
	N	Patients with event n (%)
Therapy discontinuation due to adverse events		
	154[k]	14 (9.1)[m]
SAE with incidence ≥ 5% of patients by system organ class (SOC)		
Immune system disorders	154[k]	34 (22.1)
Infections and infestations	154[k]	28 (18.2)
Blood and lymphatic system disorders	154[k]	10 (6.5)
Neoplasms benign, malignant and unspecified (including cysts and polyps)	154[k]	8 (5.2)
Severe adverse events (CTCAE grade ≥ 3) with incidence ≥ 5% of patients by system organ class (SOC)		
Blood and lymphatic system disorders	154[k]	54 (35.1)
Infections and infestations	154[k]	26 (16.9)
Investigations	154[k]	18 (11.7)
Metabolism and nutrition disorders	154[k]	17 (11.0)

a. ITT population of the pooled cohorts D2 [Sub.2] and D3
b. 95% CI: Greenwood formula.
c. 95% CI: Brookmeyer and Crowley.
d. Median: Kaplan-Meier method; 95% CI: Brookmeyer and Crowley
e. Information from the dossier of the pharmaceutical company
f. Primary endpoint. Assessed by IRC according to Lugano criteria (Lugano classification, Cheson et al. 2014).
g. Subjects for whom the PET-CT assessment is missing or not available are categorised as non-responders (N = 75 [48.4%]).
h. Population D2 [Sub.2], D3 and D5
i. 95% CI according to the Clopper-Pearson method.
j. After a period of 90 days following the last dose of study medication, investigators should report any deaths, serious adverse events, or other adverse events of concern assumed to be related to prior treatment with the study medication. However, investigators are not required to actively monitor subjects for adverse events after the end of the adverse event reporting period (defined as 90 days after the last dose of study medication or until start of another anti-cancer therapy, whichever comes first).
k. Safety population (D2 [Sub.2], D3 and D5): N = 154. This includes all subjects who have received at least one dose of the study medication (obinutuzumab or glofitamab). The safety population in Cohort D3 includes one R/R-FL subject who was mistakenly enrolled in this cohort and excludes one subject who did not receive study treatment with Gpt or glofitamab (mistakenly enrolled).
l. AEs, unrelated to the study medication, were reported up to 90 days after the last administration of glofitamab.
m. Data cut-off from 10 October 2022

Abbreviations used:
ASTCT: American Society for Blood and Marrow Transplantation; CR = complete response; CRS: cytokine release syndrome; CTCAE = Common Terminology Criteria for Adverse Events; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer, Quality of Life Questionnaire - Core 30; FACT-LymS = Functional Assessment of Cancer Therapy - Lymphoma subscale; IRC = Independent Review Committee; ITT = Intention to treat; CI = confidence interval; N = number of patients evaluated; n = number of patients with (at least one) event; PFS: progression-free survival; SOC: system organ class (MedDRA)

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. 1,360 – 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 Columvi (active ingredient: glofitamab) at the following publicly accessible link (last access: 21 December 2023):

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

Treatment with glofitamab 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 European Medicines Agency (EMA) requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material that contains information for medical professionals and patients (incl. patient identification card).

The training material contains, in particular, information and warnings about the cytokine release syndrome.

In the pivotal study NP30179, only patients for whom no available treatment options that would prolong survival were available at the time the study was conducted were enrolled.

Obinutuzumab is not approved for pretreatment prior to starting therapy with glofitamab. The application for marketing authorisation was withdrawn. Obinutuzumab is not reimbursable for this indication.

4. Treatment costs

Annual treatment costs:

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:	
Glofitamab	€ 159,875.24
Additionally required SHI services	€ 36.06 - € 38.93
Total	€ 159,911.30 - € 159,914.17

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

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Medicinal product to be assessed					
Glofitamab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	Cycle 1: 2 Cycles 2 - 12: 1	13	€ 1,300

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.

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 1 February 2024.

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

Berlin, 1 February 2024

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

Prof. Hecken