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
Mosunetuzumab (follicular lymphoma, after ≥ 2 prior therapies)

of 15 December 2022

At its session on 15 December 2022, 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 Mosunetuzumab as follows:**

Mosunetuzumab

Resolution of: 15 December 2022
Entry into force on: 15 December 2022
Federal Gazette, BAnz AT DD MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 3 June 2022):

Lunsumio as monotherapy is indicated for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL) who have received at least two prior systemic therapies.

Therapeutic indication of the resolution (resolution of 15 December 2022):

See therapeutic indication according to marketing authorisation.

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

Mosunetuzumab is approved as a medicinal product for the treatment of rare diseases under 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 follicular lymphoma (FL) who have received at least two prior systemic therapies</u>

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

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

Study results according to endpoints:[1]

Adults with relapsed or refractory follicular lymphoma (FL) who have received at least two prior systemic therapies

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.c.	There are no assessable data.
Morbidity	n.c.	There are no assessable data.
Health-related quality of life	n.c.	There are no assessable data.
Side effects	n.c.	There are no assessable data.
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		

GO29781 study:

- single-arm phase I/II study
- Assessment-relevant sub-population: Subjects with relapsed or refractory FL after at least two prior systemic therapies who were treated with mosunetuzumab monotherapy at the pivotal dose (FL-RP2D cohort)
- Data cut-off of 27 August 2021

Mortality

Endpoint	N	Median survival time in months [95% CI][a,b] *Patients with event n (%)*
Overall survival		
	90	n.a. [n.a.; n.a.] 8 (8.9)

[1] Data from the dossier assessment of the G-BA (published on 4. Oktober 2022), unless otherwise indicated.

Morbidity

Endpoint	N	Patients with event n (%) [95%- CI][c]
Complete remission (presented additionally)[d]		
	90	54 (60) [49.1; 70.2]
Endpoint	N	MV (SD)
Health status (EQ-5D VAS) – change to baseline[e]		
Cycle 2 day 1	90	-0.2 (11.1)
Cycle 4 day 1	90	5.3 (15.2)
EORTC-QLQ-C30 (symptom scales)		
No assessable data available.[f]		

Health-related quality of life

Endpoint	N	MV (SD)
FACT-LymS – change to baseline[e]		
Cycle 2 day 1	90	-1.0 (7.7)
Cycle 4 day 1	90	2.7 (6.7)
Cycle 6 day 1	90	2.8 (7.4)
EORTC-QLQ-C30 (functional scales)		
No assessable data available.[f]		

Side effects

Endpoint	N	Patients with event n (%)
Adverse events in total	90	90 (100)
Serious adverse events (SAE)	90	42 (46.7)
Severe adverse events (CTCAE grade ≥ 3)	90	63 (70.0)
Therapy discontinuation due to adverse events	90	4 (4.4)
AE with CTCAE grade ≥ 3 with incidence ≥ 5% (SOC, *PT*)		
Blood and lymphatic system disorders	90	25 (27.8)
Neutropenia[g]	*90*	*17 (18.9)*
Anaemia[g]	*90*	*7 (7.8)*

Endpoint	N	Patients with event n (%)
Metabolism and nutrition disorders	90	25 (27.8)
Hypophosphataemia	*90*	*15 (16.7)*
Hyperglycaemia	*90*	*7 (7.8)*
Infections and infestations	90	15 (16.7)
Investigations	90	15 (16.7)
Alanine aminotransferase increased[g]	*90*	*5 (5.6)*
Neutropenia[g]	*90*	*7 (7.8)*
Serious adverse events (SAE) with incidence ≥ 5% (SOC, *PT*)		
Immune system disorders	90	21 (23.3)
Cytokine release syndrome[g]	*90*	*21 (23.3)*
Metabolism and nutrition disorders	90	5 (5.6)
Infections and infestations	90	18 (20.0)
Adverse events of special interest		
Cytokine release syndrome (Lee Grade; 2014) Grade ≥ 3 SAE	90	 3 (3.3) 21 (23.3)
Flare reaction grade ≥ 3 SAE	90	 2 (2.2) 2 (2.2)
Hepatic events grade ≥ 3 SAE	90	 6 (6.7) 1 (1.1)
Infections grade ≥ 3 SAE	90	 15 (16.7) 18 (20.0)
Pneumonitis/ interstitial lung disease grade ≥ 3 SAE	90	 1 (1.1) 1 (1.1)
Anaemia and reduced haemoglobin Grade ≥ 3 SAE	90	 7 (7.8) 0
DI-CCNAE events[h] Grade ≥ 3 SAE	90	 1 (1.1) 2 (2.2)

Endpoint	N	Patients with event n (%)
Nervous system disorders and psychiatric disorders Grade ≥ 3 SAE	90	 4 (4.4) 4 (4.4)
Neutropenia Grade ≥ 3 SAE	90	 24 (26.7) 1 (1.1)
Thrombocytopenia Grade ≥ 3 SAE	90	 4 (4.4) 0

a. Median: Kaplan-Meier method; 95% CI: Brookmeyer and Crowley
b. Duration of observation (days), median (min; max): 556 (60; 837)
c. 95% CI according to the Clopper-Pearson method
d. Subjects for whom response assessments were missing were classified as non-complete responders.
e. Only questionnaires from subjects who received the study medication at the respective cycle were considered. Any questionnaires collected from subjects who had already discontinued therapy were not considered.
f. In the dossier, only the fatigue and physical functioning scales were evaluated for the data cut-off of 27 August 2021. With regard to the responder analyses for all scales of the EORTC QLQ-C30 questionnaire submitted in the written statement procedure, the return rates are below 70% from cycle 4 or cycle 6. The data submitted is therefore considered to be unusable overall.
g. Defined as AE of special interest.
h. Neurologic events, including neurological events impairing driving ability.

Abbreviations used:
CRS = cytokine release syndrome; CTCAE = Common Terminology Criteria for Adverse Events EQ-5D = European Quality of Life 5 Dimension - 5 Level; FACT-LymS = Functional Assessment of Cancer Therapy-Lymphoma subscale; FL = follicular lymphoma; CI = confidence interval; N = number of patients evaluated; n = number of patients with (at least one) event; MV = mean value; n.c. = not calculable; n.a. = not achieved; PT = preferred term; RP2D= recommended phase II dose; SD = standard deviation; SOC = system organ class; (S)AE = (serious) adverse event; VAS = visual analogue scale; vs = versus

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

Adults with relapsed or refractory follicular lymphoma (FL) who have received at least two prior systemic therapies

approx. 650 – 690 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 Lunsumio (active ingredient: mosunetuzumab) at the following publicly accessible link (last access: 2 November 2022):

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

Treatment with mosunetuzumab should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of patients with follicular lymphoma. In addition, mosunetuzumab must only be administered in a setting that is sufficiently medically equipped to treat severe reactions such as cytokine release syndrome (CRS).

This medicinal product was approved under "special conditions". This means that further evidence of the benefit of the medicinal product is anticipated. The European Medicines Agency 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 requirements of the European Medicines Agency (EMA) regarding additional measures to minimise risks, the pharmaceutical company must ensure that each subject treated with mosunetuzumab receives a patient pass which informs and clarifies the risks of CRS and includes a warning for the healthcare professionals treating the subjects.

Patients with grade 3b follicular lymphoma were not investigated in the dose expansion phase of the GO29781 study.

4. Treatment costs

Annual treatment costs:

Adults with relapsed or refractory follicular lymphoma (FL) who have received at least two prior systemic therapies

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Mosunetuzumab	€ 86,135.44 - € 162,844.15[2]
Additionally required SHI costs	€ 46.66 - € 221.64

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 December 2022

[2] Treatment with mosunetuzumab takes place over 8 cycles. If necessary, it may be administered for a maximum of 17 cycles. The annual treatment costs are thus presented as a range.

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Mosunetuzumab	Surcharge for production of parenteral preparations containing cytostatic agents	€ 100	1 - 3	10 - 19	€ 1,000 - € 1,900

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 Mosunetuzumab

Medicinal products with new active ingredients pursuant to 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 mosunetuzumab for the treatment of adults with relapsed or refractory follicular lymphoma (FL) who have received at least two prior systemic therapies:

Adults with relapsed or refractory follicular lymphoma (FL) who have received at least two prior systemic therapies

- 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. The resolution will enter into force on the day of its publication on the website of the G-BA on 15 December 2022.

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

Berlin, 15 December 2022

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

Prof. Hecken