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
Blinatumomab (new therapeutic indication: acute lymphoblastic B-cell leukaemia, Ph-, CD19+, newly diagnosed)

From 21. August 2025

At their session on 21. August 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. **In Annex XII, the following information shall be added after No. 5 to the information on the benefit assessment of Blinatumomab in the version of the resolution of 21 August 2025 on the therapeutic indication "indicated as monotherapy for the treatment of paediatric patients aged ≥ 1 month to < 1 year with high-risk first relapsed Philadelphia chromosome-negative CD19 positive B-cell precursor acute lymphoblastic leukaemia (ALL) as part of the consolidation therapy":**

Blinatumomab

Resolution of: 21. August 2025
Entry into force on: 21. August 2025
BAnz AT TT. MM JJJJ Bx

New therapeutic indication (according to the marketing authorisation of 23. January 2025):

BLINCYTO is indicated as monotherapy as part of consolidation therapy for the treatment of adult patients with newly diagnosed Philadelphia chromosome negative CD19 positive B-cell precursor ALL.

Therapeutic indication of the resolution (resolution of 21. August 2025):

See new therapeutic indication according to marketing authorisation.

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

Blinatumomab 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 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 Ordinance on the Benefit Assessment of Pharmaceuticals (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 newly diagnosed Philadelphia chromosome negative CD19 positive B-cell precursor ALL; consolidation therapy</u>

Extent of the additional benefit and significance of the evidence of Blinatumomab as monotherapy:

Hint for a considerable additional benefit

Study results according to endpoints:[1]

Adults with newly diagnosed Philadelphia chromosome negative CD19 positive B-cell precursor ALL; consolidation therapy

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↑↑	Advantage in overall survival.
Morbidity	↑	Advantage in recurrence-free survival.
Health-related quality of life	∅	No data available.
Side effects	↔	There are no assessable data for SAEs. No relevant difference for the benefit assessment for severe AEs. Advantages and disadvantages in the specific AE, in detail. In detail, there is a disadvantage for neurological events (AEs of special interest)
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		

E1910 study: Blinatumomab monotherapy (alternating with chemotherapy) vs chemotherapy

- Ongoing, multicentre, randomised, controlled, open-label, phase III study
- Data cut-off: Interim data cut-off from 23.06.2023 for the step 3 Analysis Set

[1] Data from the dossier assessment of the G-BA (published on 2. June 2025), unless otherwise indicated.

Mortality

Endpoint	Blinatumomab/ chemotherapy[a]		Chemotherapy[b]		Blinatumomab/ chemotherapy vs chemotherapy
	N[c]	Median survival time in months [95% CI] *Patients with event n (%)*	N[c]	Median survival time in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value
Overall survival					
	152	n.a. *30 (19.7)*	134	n.a. [4.2; n.a.] *53 (39.6)*	0.47 [0.30; 0.74] < 0.001

Morbidity

Endpoint	Blinatumomab/ chemotherapy[1]		Chemotherapy[2]		Blinatumomab/ chemotherapy vs chemotherapy
	N[c]	Median time in months [95% CI] *Patients with event n (%)*	N[c]	Median time in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value
Recurrence-free survival					
	152	n.a. *36 (23.7)*	134	n.a. [3.7; n.a.] *56 (41.8)*	0.53 [0.35; 0.81] 0.003

Health-related quality of life

Endpoint	Blinatumomab/ chemotherapy		Chemotherapy		Blinatumomab/ chemotherapy vs chemotherapy
	N	Median time in months [95% CI] *Patients with event n (%)*	N	Median time in months [95% CI] *Patients with event n (%)*	Effect estimator [95% CI] p value
No data on quality of life were assessed.					

Side effects

Endpoint	Blinatumomab/ chemotherapy[1]		Chemotherapy[2]		Blinatumomab/ chemotherapy vs chemotherapy
	N[d]	*Patients with event n (%)*	N[d]	*Patients with event n (%)*	RR [95% CI] p value
Total adverse events (presented additionally)	-[e]				
Serious adverse events (SAE)	-[e]				
Severe adverse events (CTCAE grade ≥ 3)	147	*139 (94.6)*	128	*125 (97.7)*	0.97 [0.82; 1.15] 0.73
Therapy discontinuation due to adverse events	-[f]				
Severe adverse events according to MedDRA (with an incidence ≥ 5% in one study arm and statistically significant difference between the treatment arms; SOC and PT)					
Leukopenia (PT)	147	*74 (50.3)*	128	*81 (63.3)*	0.78 [0.64; 0.96] 0.019
Nervous system disorders (SOC)	147	*33 (22.4)*	128	*13 (10.2)*	2.15 [1.18; 3.92] 0.012
Adverse events of special interest (with statistically significant difference between the treatment arms)					
Neurologic events	147	42 (28.6)	128	14 (10.9)	2.65 [1.52; 4.62] < 0.001

Endpoint	Blinatumomab/ chemotherapy[1]		Chemotherapy[2]		Blinatumomab/ chemotherapy vs chemotherapy
	N[d]	*Patients with event n (%)*	N[d]	*Patients with event n (%)*	RR [95% CI] p value

a From step 3, the participants were stratified, among others, by "MRD status" (positive: ≥ 0.01%; negative: < 0.01%) and randomised into the treatment arms. By amendment 14 (23.05.2018), after FDA marketing authorisation of blinatumomab in MRD-positive subjects, randomisation was only described in MRD-negative subjects. MRD-positive subjects (n = 18) could immediately be enrolled in the intervention arm.

b Outside the protocol, 34 subjects (25.4%) in the control arm received blinatumomab. No further information on the reasons or the time could be identified.

c Step 3 Analysis Set. The number corresponds to those subjects who were used to calculate the respective statistics.

d Step 3 Safety Analysis Set.

e A complete survey was only planned for AEs of CTCAE grade ≥ 3 and AEs of interest

f Data not assessable, especially as it is unclear to what extent AEs that led to therapy discontinuation were collected in full

Abbreviations used:
CTCAE = Common Terminology Criteria for Adverse Events; HR = hazard ratio; n.d.: no data available; CI = confidence interval; N = number of patients evaluated; n = number of patients with (at least one) event; n.a. = not applicable; RR = relative risk; vs = versus

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

Adults with newly diagnosed Philadelphia chromosome negative CD19 positive B-cell precursor ALL; consolidation therapy

Approx. 160 to 270 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 Blincyto (active ingredient: Blinatumomab) at the following publicly accessible link (last access: 30. Mai 2025):

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

Treatment with blinatumomab should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of patients with acute lymphoblastic leukaemia.

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 (including a patient card).

In particular, the training material contains instructions on the administration of Blincyto and on neurological events.

4. Treatment costs

Annual treatment costs:

Adults with newly diagnosed Philadelphia chromosome negative CD19 positive B-cell precursor ALL; consolidation therapy

According to the product information, blinatumomab monotherapy is used alternately with chemotherapy as part of the consolidation therapy.

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Blinatumomab	€ 69,006.56 - € 276,026.24

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

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Blinatumomab	Surcharge for the production of a parenteral solution with monoclonal antibodies	€ 100	Cycle 1: 28 Cycle 2 - 4: each 28	28 - 112	€ 2800 - € 11200

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 newly diagnosed Philadelphia chromosome negative CD19 positive B-cell precursor ALL; consolidation 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 21. August 2025.

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

Berlin, 21. August 2025

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

Prof. Hecken