Gemeinsamer Bundesausschuss

Blinatumomab (New Therapeutic Indication: B-precursor acute lymphoblastic leukaemia, relapsed or refractory, Ph+ CD19+)

Resolution of: 15 July 2021 Valid until: unlimited
Entry into force on: 15 July 2021
BAnz AT 25 08 2021 B5

New therapeutic indication (according to the marketing authorisation of 22 December 2020):

Blincyto is indicated as monotherapy for the treatment of adults with CD19 positive relapsed or refractory B-precursor acute lymphoblastic leukaemia (ALL). Patients with Philadelphia chromosome positive B-precursor ALL should have failed treatment with at least 2 tyrosine kinase inhibitors (TKIs) and have no alternative treatment options.

Therapeutic indication of the resolution (resolution of 15 July 2021):

Blincyto is indicated as monotherapy for the treatment of adults with Philadelphia chromosome positive CD19 positive relapsed or refractory B-precursor acute lymphoblastic leukaemia (ALL). Patients with Philadelphia chromosome positive B-precursor ALL should have failed treatment with at least 2 tyrosine kinase inhibitors (TKIs) and have no alternative treatment options.

1. Extend 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 German Social Code, Book Five (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).

Adults with Philadelphia chromosome positive CD19 positive relapsed or refractory B-precursor acute lymphoblastic leukaemia (ALL), in whom treatment with at least 2 tyrosine kinase inhibitors (TKIs) has failed and who have no alternative treatment options

Extend of the additional benefit and significance of the evidence of blinatumomab:

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

Study results according to endpoints:[1]

Adults with Philadelphia chromosome positive CD19 positive relapsed or refractory B-precursor acute lymphoblastic leukaemia (ALL)in whom treatment with at least 2 tyrosine kinase inhibitors (TKIs) has failed and who have no alternative treatment options

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a	not assessable
Morbidity	n.a	not assessable
Health-related quality of life	∅	No data available
Side effects	n.a	not assessable
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.a.: not assessable		

Study 20100216 (ALCANTARA): Single-arm, multicenter Phase II study

Final data cut-off from 06.01.2017, Full Analysis Set

Mortality

Endpoint	ALCANTARA N=45[a]
	Median time to event in months [95% CI] *Patients with event n (%)*
Overall survival	9.0 [5.7; 13.5] *37 (82.2)*

[1]Data from the dossier assessment of the G-BA (published on the 3. Mai 2021), unless otherwise indicated.

Morbidity

	Patients with event n (%)
Complete remission	
CR after 2 treatment cycles	*14 (31.1)*
CR/CRh after 2 treatment cycles	*16 (35.6)*
CR/CRh/CRi after 2 treatment cycles	*18 (40.0)*
MRD remission	
MRD remission after 2 treatment cycles	*18 (40.0)*
Complete MRD remission	*18 (40.0)*

Health-related quality of life

There are no data.

Side effects

Endpoint	**ALCANTARA N = 45**
	Patients with event n (%)
Adverse events (AE) in total	*45 (100)*
Serious adverse events (SAEs)	*28 (62.2)*
Severe adverse events (CTCAE grade ≥ 3)	*38 (84.4)*
AE that led to study discontinuation	*3 (6.7)*
AE of CTCAE grade ≥ 3 with an incidence ≥ 5% **SOC** PT	
Blood and lymphatic system disorders	*28 (62.2)*
Febrile neutropenia	*12 (26.7)*
Thrombocytopenia	*10 (22.2)*
Anaemia	*7 (15.6)*

Leukocytosis	*3 (6.7)*
Neutropenia	*3 (6.7)*
Cardiac disorders	*3 (6.7)*
Gastrointestinal disorders	*3 (6.7)*
General disorders and administration site conditions	*11 (24.4)*
Pyrexia	*5 (11.1)*
Pain	*4 (8.9)*
Infections and infestations	*11 (24.4)*
Sepsis	*4 (8.9)*
Infection in connection with a medical product	*3 (6.7)*
Investigations	*9 (20.0)*
Alanine aminotransferase increased	*5 (11.1)*
Elevated aspartate aminotransferase	*5 (11.1)*
Metabolism and nutrition disorders	*5 (11.1)*
Musculoskeletal and connective tissue disorders	*6 (13.3)*
Nervous system disorders	*7 (15.6)*
Headache	*3 (6.7)*
Respiratory, thoracic and mediastinal disorders	*5 (11.1)*
Vascular disorders	*4 (8.9)*
SAE with an incidence ≥ 5% **SOC** PT	
Blood and lymphatic system disorders	*8 (17.8)*
Febrile neutropenia	*4 (8.9)*
General disorders and administration site conditions	*6 (13.3)*
Infections and infestations	*9 (20.0)*
Infection in connection with a medical product	*3 (6.7)*
Sepsis	*3 (6.7)*
Musculoskeletal and connective tissue disorders	*3 (6.7)*

Nervous system disorders	*7 (15.6)*		
Tremor	*3 (6.7)*		
Respiratory, thoracic and mediastinal disorders	*3 (6.7)*		
AE of special interest			
	Any CTCAE grade n (%)	*CTCAE grade ≥ 3) n (%)*	*SAE n (%)*
Acute pancreatitis[b]	*0 (0)*	*0 (0)*	*0 (0)*
Haematopoietic cytopenia[b]	*29 (64.4)*	*24 (53.3)*	*4 (8.9)*
Capillary Leak Syndrome[c]	*0 (0)*	*0 (0)*	*0 (0)*
Neurologic events[d]	*28 (62.2)*	*6 (13.3)*	*6 (13.3)*
Cytokine release syndrome[c]	*4 (8.9)*	*0 (0)*	*1 (2.2)*
Decreased immunoglobulin levels[c]	*4 (8.9)*	*0 (0)*	*0 (0)*
Elevated liver enzymes[e]	*8 (17.8)*	*6 (13.3)*	*1 (2.2)*
Immunogenicity	*0 (0)*	*0 (0)*	*0 (0)*
Infections[f]	*22 (48.9)*	*11 (24.4)*	*9 (20.0)*
Infusion reaction[c] taking into account the infusion duration	*21 (46.7)*	*3 (6.7)*	*1 (2.2)*
Infusion reaction[c] without consideration of the infusion duration	*22 (48.9)*	*3 (6.7)*	*1 (2.2)*
Lymphopenia[c]	*0 (0)*	*0 (0)*	*0 (0*
Medication Error[g]	*2 (4.4)*	*0 (0)*	*2 (4.4)*
Neutropenia[c]	*21 (46.7)*	*15 (33.3)*	*4 (8.9)*
Progressive multifocal leukoencephalopathy[g]	*1 (2.2)*	*0 (0)*	*0 (0)*
Tumour Lysis Syndrome[b]	*1 (2.2)*	*1 (2.2)*	*1 (2.2)*

[a] Full Analysis Set
[b] SMQ, narrow search
[c] MedDRA query of the sponsor, narrow search
[d] MedDRA query of the sponsor, all terms
[e] SMQ liver-related investigations, signs and symptoms
[f] System Organ Class
[g] MedDRA query of the sponsor, broad search

Abbreviations used:
CTCAE = Common Terminology Criteria for Adverse Events; CI = confidence interval; MedDRA: Medical Dictionary for Regulatory Activities; N = number of patients evaluated; n = number of patients with (at least one) event; SMQ: Standardised MedDRA Queries

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

Adults with Philadelphia chromosome positive CD19 positive relapsed or refractory B-precursor acute lymphoblastic leukaemia (ALL), in whom treatment with at least 2 tyrosine kinase inhibitors (TKIs) has failed and who have no alternative treatment options

approx. 5 to 10 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: 28 May 2021):
https://www.ema.europa.eu/documents/product-information/blincyto-epar-product-information_de.pdf

Initiation and monitoring of treatment with blinatumomab should be performed only by specialists in internal medicine and haematology and oncology experienced in the therapy of patients with acute lymphoblastic leukaemia.

In accordance with the requirements of the EMA regarding additional risk minimisation measures, the pharmaceutical company must provide training material for physicians, pharmacists, healthcare professionals and patients/healthcare professionals, as well as a patient reminder 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 Philadelphia chromosome positive CD19 positive relapsed or refractory B-precursor acute lymphoblastic leukaemia (ALL), in whom treatment with at least 2 tyrosine kinase inhibitors (TKIs) has failed and who have no alternative treatment options

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Blinatumomab	
Induction	€ 129,382.76
Consolidation	€ 0 - € 209,002.92
Total:	€ 129,382.76 - € 338,385.68

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 June 2021)

Costs for additionally required SHI services: not applicable