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)
Axicabtagene ciloleucel (new therapeutic indication: diffuse large B-cell lymphoma, high-grade B-cell lymphoma, after 1 prior therapy, relapsed within 12 months or refractory)

of 21 December 2023

At its session on 21 December 2023, 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 Axicabtagene ciloleucel in accordance with the resolution of 21 December 2023 on the therapeutic indication: "for the treatment of adult patients with relapsed or refractory (r/r) follicular lymphoma (FL) after three or more lines of systemic therapy.":**

Axicabtagene ciloleucel

Resolution of: 21 December 2023
Entry into force on: 21 December 2023
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 14 October 2022):

Yescarta is indicated for the treatment of adult patients with diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) that relapses within 12 months from completion of, or is refractory to, first-line chemoimmunotherapy.

Therapeutic indication of the resolution (resolution of 21 December 2023):

See new therapeutic indication according to marketing authorisation.

1. Additional benefit of the medicinal product in relation to the appropriate comparator therapy

a) Adults with diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) who are eligible for high-dose therapy and who relapse within 12 months from completion of, or are refractory to, first-line therapy

Appropriate comparator therapy:

Induction therapy with

- R-GDP (rituximab, gemcitabine, cisplatin, dexamethasone)

or

- R-ICE (rituximab, ifosfamide, carboplatin, etoposide)

or

- R-DHAP (rituximab, dexamethasone, cytarabine, cisplatin)[1]

followed by high-dose therapy with autologous or allogeneic stem cell transplantation if there is a response to induction therapy

Extent and probability of the additional benefit of axicabtagene ciloleucel compared to the appropriate comparator therapy:

Hint for a non-quantifiable additional benefit.

[1] Taking into account the requirements of the Guideline for Inpatient Treatment Methods (last revised 18 October 2023): Section 4, paragraph 2, number 4

b) Adults with diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) who are ineligible for high-dose therapy and who relapse within 12 months from completion of, or are refractory to, first-line therapy

Appropriate comparator therapy:
Therapy according to doctor's instructions under consideration of

– polatuzumab in combination with bendamustine and rituximab

and

– tafasitamab in combination with lenalidomide

Extent and probability of the additional benefit of axicabtagene ciloleucel compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:[2]

a) Adults with diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) who are eligible for high-dose therapy and who relapse within 12 months from completion of, or are refractory to, first-line 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 the endpoint of failure of the curative therapeutic approach (event-free survival)
Health-related quality of life	n.a.	There are no assessable data.
Side effects	n.a.	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 ∅: No data available. n.a.: not assessable		

2 Data from the dossier assessment of the IQWiG (A23-66) and from the addendum (A23-106), unless otherwise indicated.

ZUMA-7 study:

- open-label, randomised phase III study
- Axicabtagene ciloleucel versus induction chemotherapy with R-ICE, R-DHAP, R-ESHAP or R-GDP followed by high-dose therapy (HDT) with autologous stem cell transplantation (autoSCT)
- 1st data cut-off: 18 March 2021
- 2nd data cut-off: 25 January 2023

Mortality

Endpoint	**Axicabtagene ciloleucel**		**Induction therapy + HDT + autoSCT**		Intervention vs control
	N	Median survival time in months [95% CI] *Patients with event n (%)*	N	Median survival time in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value
Overall survival[a]					
	180	n.r. [28.6; n.c.] *82 (46)*	179	31.1 [17.1; n.c.] *95 (53)*	0.726 [0.540; 0.98] 0.017

Morbidity

Endpoint	**Axicabtagene ciloleucel**		**Induction therapy + HDT + autoSCT**		Intervention vs control
	N	Median time in months [95% CI] *Patients with event n (%)*	N	Median time in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[b]
Failure of the curative therapeutic approach					
Event-free survival (EFS) according to centralised assessment (data cut-off from 18.03.2021)					
Event rate[c]	180	– *108 (60)*	179	– *144 (80)*	RR: 0.75 [0.65; 0.86] < 0.001[d]
Disease progression	180	– *82 (46)*	179	– *75 (42)*	
SD as best response until day 150	180	– *4 (2)*	179	– *0 (0)*	
Start of a new lymphoma therapy	180	– *11 (6)*	179	– *63 (35)*	

Endpoint	Axicabtagene ciloleucel		Induction therapy + HDT + autoSCT		Intervention vs control
	N	Median time in months [95% CI] *Patients with event n (%)*	N	Median time in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[b]
Death from any cause	180	– *11 (6)*	179	– *6 (3)*	
EFS	180	8.3 [4.5; 15.8] *108 (60)*	179	2.0 [1.6; 2.8] *144 (80)*	0.40 [0.31; 0.51] < 0.001
Sensitivity analysis - Start of a new lymphoma therapy due to efficacy concerns					
Event rate[c]	180	- *104 (58)*	179	- *136 (76)*	RR: 0.76 [0.65; 0.88] < 0.001[d]
Disease progression	180	n.d.	179	n.d.	
Death from any cause	180	n.d.	179	n.d.	
Residual disease leading to the start of a new lymphoma therapy	180	n.d.	179	n.d.	
EFS	180	11.2 [5.0; 21.5] *104 (58)*	179	2.0 [1.7; 2.7] *136 (76)*	0.40 [0.31; 0.53] < 0.001
Sensitivity analyses by IQWiG (data cut-off from 18.03.2021)					
Sensitivity analysis 1: minimum possible number of occurred qualifying events that mean failure of the curative therapeutic approach					
Event rate[c]	180	– *106 (59)[d]*	179	– *107 (60)[d]*	RR: 0.99 [0.83; 1.17] 0.912[d]
Disease progression	180	– *82 (46)*	179	– *75 (42)*	
SD according to centralised assessment as best response until day 150	180	– *4 (2)*	179	– *0 (0)*	

Endpoint	Axicabtagene ciloleucel		Induction therapy + HDT + autoSCT		Intervention vs control
	N	Median time in months [95% CI] *Patients with event n (%)*	N	Median time in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[b]
Start of a new lymphoma therapy	180	– *9 (5)*[d,e]	179	– –	
SD according to centralised assessment as best response on day 50[f]	180	– –	179	– *26 (15)*	
Death from any cause	180	– *11 (6)*	179	– *6 (3)*	
Event-free survival (EFS)	180	n.d. *106 (59)*[d]	179	n.d. *107 (60)*[d]	n.d.
Sensitivity analysis 2: maximum possible number of occurred qualifying events that mean failure of the curative therapeutic approach					
Event rate[c]	180	– *106 (59)*[d]	179	– *128 (72)*[d]	RR: 0.82 [0.71; 0.96] 0.012[d]
Disease progression	180	– *82 (46)*	179	– *75 (42)*	
SD as best response until day 150	180	– *4 (2)*	179	– *0 (0)*	
Start of a new lymphoma therapy	180	– *9 (5)*[d,e]	179	– –	
Start of a new lymphoma therapy for SD according to the principal investigator	180	– –	179	– *21 (12[d])*	
Start of a new lymphoma therapy for PD according to the principal investigator				– *26 (15[d])*	

Endpoint	Axicabtagene ciloleucel		Induction therapy + HDT + autoSCT		Intervention vs control
	N	Median time in months [95% CI] *Patients with event n (%)*	N	Median time in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[b]
Death from any cause	180	– *11 (6)*	179	– *6 (3)*	
Event-free survival (EFS)	180	n.d. *106 (59)*[d]	179	n.d. *128 (72)*[d]	n.d.
EORTC QLQ-C30 (symptomatology)					
No suitable data[g]					
Health status (EQ-5D VAS)					
No suitable data[g]					

Health-related quality of life

Endpoint	Axicabtagene ciloleucel		Induction therapy + HDT + autoSCT		Intervention vs control
	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 Absolute difference (AD)
EORTC QLQ-C30	No suitable data[g]				

Side effects

Endpoint	Axicabtagene ciloleucel		Induction therapy + HDT + autoSCT		Intervention vs control
	N	Median in months [95% CI] *Patients with event n (%)*	N	Median in months [95% CI] *Patients with event n (%)*	Effect estimator [95% CI] p value Absolute difference (AD)
No suitable data[h]					

a Analyses by the pharmaceutical company
b Indication of absolute difference (AD) only in case of statistically significant difference; own calculation
c Individual components - if available - are shown in the rows below; since only the qualifying events are included in the event rate (total), effect estimators of the individual components are not shown.
d IQWiG calculation
e In the intervention arm, 2 patients received a new lymphoma therapy without prior disease assessment (for 1 patient, axicabtagene ciloleucel therapy was found unsuitable due to cardiac lymphoma and 1 patient did not receive axicabtagene ciloleucel due to elevated grade 2 alanine aminotransferase). These

two patients were not included in the present evaluation, as these situations do not represent a failure of the curative therapeutic approach.

f It is assumed that a new lymphoma therapy was started on day 50 for SD as best response and that there is therefore no overlap between these patients and those with SD as best response until day 150.

g Missing data and high differential percentage of patients missing from the evaluation

h Incomplete analysis population

Abbreviations used:
AD = absolute difference; CTCAE = Common Terminology Criteria for Adverse Events; EFS = event-free survival; HDCT = high-dose chemotherapy; 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.c. = not calculable; n.r. = not reached; RR = relative risk; SD = stable disease; SCT = stem cell transplantation; vs = versus

b) Adults with diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) who are ineligible for high-dose therapy and who relapse within 12 months from completion of, or are refractory to, first-line therapy

No data are available to allow an assessment of the additional benefit.

Summary of results for relevant clinical endpoints

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

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

a) Adults with diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) who are eligible for high-dose therapy and who relapse within 12 months from completion of, or are refractory to, first-line therapy

approx. 800 – 1,130 patients

b) Adults with diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) who are ineligible for high-dose therapy and who relapse within 12 months from completion of, or are refractory to, first-line therapy

approx. 800 – 1,130 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 Yescarta (active ingredient: axicabtagene ciloleucel) at the following publicly accessible link (last access: 20 September 2023):

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

In accordance with the EMA requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material and a patient pass. Training material for all healthcare professionals who will prescribe, dispense, and administer axicabtagene ciloleucel includes instructions for identifying, treating, and monitoring cytokine release syndrome and neurological side effects. It also includes instructions on the cell thawing process, availability of 1 dose of tocilizumab at the point of treatment, provision of relevant information to patients, and full and appropriate reporting of side effects.

The patient training programme should explain the risks of cytokine release syndrome and serious neurologic side effects, the need to report symptoms immediately to the treating physician, to remain close to the treatment facility for at least 4 weeks after infusion of axicabtagene ciloleucel, and to carry the patient emergency card at all times.

Axicabtagene ciloleucel must be used in a qualified treatment facility. For the infusion of axicabtagene ciloleucel in the present therapeutic indication, the quality assurance measures for the use of CAR-T cells in B-cell neoplasms apply (ATMP Quality Assurance Guideline, Annex 1).

4. Treatment costs

Annual treatment costs:

The costs for the first year of treatment are shown for the cost representation in the resolution.

a) Adults with diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) who are eligible for high-dose therapy and who relapse within 12 months from completion of, or are refractory to, first-line therapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Axicabtagene ciloleucel	€ 272,000.00
Additionally required SHI costs	*€ 762.04*
Appropriate comparator therapy:	
Induction chemotherapy followed by high-dose chemotherapy with autologous stem cell transplantation if there is a response to induction chemotherapy	
Induction chemotherapies	
R-GDP (rituximab + gemcitabine + dexamethasone + cisplatin); 2-3 cycles	
Rituximab	€ 5,315.42 - € 8,313.20
Gemcitabine	€ 734.20 - € 1,101.30
Dexamethasone	€ 44.29 - € 79.59
Cisplatin	€ 228.06 - € 342.09
R-GDP	€ 6,321.97 - € 9,836.18
Additionally required SHI costs	*€ 143.16 - € 192.26*
R-ICE (rituximab + ifosfamide + carboplatin + etoposide); 2-3 cycles including a single dose of rituximab before the start of treatment	
Rituximab	€ 8,313.20 - € 10,630.84
Ifosfamide	€ 671.48 - € 1,007.22
Carboplatin	€ 633.30 - € 822.60 (2 cycles) – € 949.95 - € 1,233.90 (3 cycles)
Etoposide	€ 459.30 - € 688.95
R-ICE	€ 10,077.28 - € 10,266.58 (2 cycles) – € 13,276.96 - € 13,560.91 (3 cycles)
Additionally required SHI costs	*€ 105.00 - € 433.37*
R-DHAP (rituximab + dexamethasone + cytarabine + cisplatin); 2-3 cycles including optional single dose of rituximab before the start of treatment	
Rituximab	€ 5,315.42 - € 10,630.84
Dexamethasone	€ 44.29 - € 79.59
Cytarabine	€ 575.52 - € 863.28

Designation of the therapy	Annual treatment costs/ patient
Cisplatin	€ 285.96 - € 428.94
R-DHAP	€ 6,221.19 - € 12,002.65
Additionally required SHI costs	*€ 143.16 - € 192.26*
High-dose chemotherapy with autologous stem cell transplantation	
High-dose chemotherapy with autologous stem cell transplantation	€ 38,863.86
Total	
R-GDP induction chemotherapy + High-dose chemotherapy with autologous stem cell transplantation	€ 45,185.83 - € 48,700.04
Additionally required SHI costs	*€ 143.16 - € 192.26*
R-ICE induction chemotherapy + High-dose chemotherapy with autologous stem cell transplantation	€ 48,941.14 - € 49,130.44 (2 cycles R-ICE) – € 52,140.82 - € 52,424.77 (3 cycles R-ICE)
Additionally required SHI costs	*€ 105.00 - € 433.37*
R-DHAP induction chemotherapy + High-dose chemotherapy with autologous stem cell transplantation	€ 45,085.05 - € 50,866.51
Additionally required SHI costs	*€ 143.16 - € 192.26*
Induction chemotherapy followed by *high-dose chemotherapy with allogeneic stem cell transplantation if there is a response to induction chemotherapy*	
Induction chemotherapies	
R-GDP (rituximab + gemcitabine + dexamethasone + cisplatin); 2-3 cycles	
Rituximab	€ 5,315.42 - € 8,313.20
Gemcitabine	€ 734.20 - € 1,101.30
Dexamethasone	€ 44.29 - € 79.59
Cisplatin	€ 228.06 - € 342.09
R-GDP	€ 6,321.97 - € 9,836.18
Additionally required SHI costs	*€ 143.16 - € 192.26*
R-ICE (rituximab + ifosfamide + carboplatin + etoposide); 2-3 cycles including a single dose of rituximab before the start of treatment	
Rituximab	€ 8,313.20 - € 10,630.84
Ifosfamide	€ 671.48 - € 1,007.22
Carboplatin	€ 633.30 - € 822.60 (2 cycles) – € 949.95 - € 1,233.90 (3 cycles)
Etoposide	€ 459.30 - € 688.95
R-ICE	€ 10,077.28 - € 10,266.58 (2 cycles)

Designation of the therapy	Annual treatment costs/ patient
	– € 13,276.96 - € 13,560.91 (3 cycles)
Additionally required SHI costs	*€ 105.00 - € 433.37*
R-DHAP (rituximab + dexamethasone + cytarabine + cisplatin); 2-3 cycles including optional single dose of rituximab before the start of treatment	
Rituximab	€ 5,315.42 - € 10,630.84
Dexamethasone	€ 44.29 - € 79.59
Cytarabine	€ 575.52 - € 863.28
Cisplatin	€ 285.96 - € 428.94
R-DHAP	€ 6,221.19 - € 12,002.65
Additionally required SHI costs	*€ 143.16 - € 192.26*
High-dose chemotherapy with allogeneic stem cell transplantation	
High-dose chemotherapy with allogeneic stem cell transplantation	€ 57,563.63
Total	
R-GDP induction chemotherapy + High-dose chemotherapy with allogeneic stem cell transplantation	€ 63,885.60 - € 67,399.81
Additionally required SHI costs	*€ 143.16 - € 192.26*
R-ICE induction chemotherapy + High-dose chemotherapy with allogeneic stem cell transplantation	€ 67,640.91 - € 67,830.21 (2 cycles R-ICE) – € 70,840.59 - € 71,124.54 (3 cycles R-ICE)
Additionally required SHI costs	*€ 105.00 - € 433.37*
R-DHAP induction chemotherapy + High-dose chemotherapy with allogeneic stem cell transplantation	€ 63,784.82 - € 69,566.28
Additionally required SHI costs	*€ 143.16 - € 192.26*

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 December 2023

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					
Axicabtagene ciloleucel - Lymphocyte depletion					
Cyclophosphamide	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	3	3.0	€ 300
Fludarabine	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	3	3.0	€ 300
Appropriate comparator therapy					
Induction chemotherapy followed by high-dose chemotherapy with autologous stem cell transplantation if there is a response to induction chemotherapy					
Induction chemotherapies					
R-GDP (rituximab + gemcitabine + dexamethasone + cisplatin); 2-3 cycles					
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	2.0 – 3.0	€ 200 – € 300
Gemcitabine	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	2	4.0 – 6.0	€ 400 – € 600
Cisplatin	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	1	2.0 – 3.0	€ 200 – € 300
R-ICE (rituximab + ifosfamide + carboplatin + etoposide); 2-3 cycles including a single dose of rituximab before the start of treatment					
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	3.0 – 4.0	€ 300 – € 400
Ifosfamide	Surcharge for production of a parenteral solution	€ 100	1	2.0 – 3.0	€ 200 – € 300

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
	containing cytostatic agents				
Carboplatin	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	1	2.0 – 3.0	€ 200 – € 300
Etoposide	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	3	6.0 – 9.0	€ 600 – € 900
Mesna	Surcharge for production of other parenteral solutions	€ 54	2	4.0 – 6.0	€ 216 - € 324
R-DHAP (rituximab + dexamethasone + cytarabine + cisplatin); 2-3 cycles including optional single dose of rituximab before the start of treatment					
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	2.0 – 4.0	€ 200 – € 400
Cytarabine	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	2	4.0 – 6.0	€ 400 – € 600
Cisplatin	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	1	2.0 – 3.0	€ 200 – € 300
Induction chemotherapy followed by high-dose chemotherapy with allogeneic stem cell transplantation if there is a response to induction chemotherapy					
Induction chemotherapies					
R-GDP (rituximab + gemcitabine + dexamethasone + cisplatin); 2-3 cycles					
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	2.0 – 3.0	€ 200 – € 300
Gemcitabine	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	2	4.0 – 6.0	€ 400 – € 600

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Cisplatin	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	1	2.0 – 3.0	€ 200 – € 300
R-ICE (rituximab + ifosfamide + carboplatin + etoposide); 2-3 cycles including a single dose of rituximab before the start of treatment					
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	3.0 – 4.0	€ 300 – € 400
Ifosfamide	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	1	2.0 – 3.0	€ 200 – € 300
Carboplatin	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	1	2.0 – 3.0	€ 200 – € 300
Etoposide	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	3	6.0 – 9.0	€ 600 – € 900
Mesna	Surcharge for production of other parenteral solutions	€ 54	2	4.0 – 6.0	€ 216 - € 324
R-DHAP (rituximab + dexamethasone + cytarabine + cisplatin); 2-3 cycles including optional single dose of rituximab before the start of treatment					
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	2.0 – 4.0	€ 200 – € 400
Cytarabine	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	2	4.0 – 6.0	€ 400 – € 600
Cisplatin	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	1	2.0 – 3.0	€ 200 – € 300

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 December 2023

b) Adults with diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) who are ineligible for high-dose therapy and who relapse within 12 months from completion of, or are refractory to, first-line therapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Axicabtagene ciloleucel	€ 272,000.00
Additionally required SHI costs	*€ 762.04*
Appropriate comparator therapy:	
Polatuzumab vedotin + bendamustine + rituximab	
Polatuzumab vedotin	€ 61,470.36
Bendamustine	€ 6,023.10
Rituximab	€ 15,946.26
Total	€ 83,439.72
Additionally required SHI costs	*€ 62.65 – € 62.98*
Tafasitamab + lenalidomide	
Tafasitamab	€ 97,585.95
Lenalidomide	€ 427.76
Total	€ 98,013.71

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 December 2023

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					
Axicabtagene ciloleucel - Lymphocyte depletion					
Cyclophosphamide	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	3	3.0	€ 300
Fludarabine	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	3	3.0	€ 300
Appropriate comparator therapy					

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Polatuzumab vedotin + bendamustine + rituximab					
Polatuzumab vedotin	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	6.0	€ 600
Bendamustine	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	2	12.0	€ 1,200
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	6.0	€ 600
Tafasitamab + lenalidomide					
Tafasitamab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	Cycle 1: 5 Cycle 2 and 3: 4 From cycle 4 onwards: 2	33.0	€ 3,300

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 December 2023

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:

a) Adults with diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) who are eligible for high-dose therapy and who relapse within 12 months from completion of, or are refractory to, first-line therapy

No medicinal product with new active ingredients that can be used in a combination therapy and fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

b) Adults with diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) who are ineligible for high-dose therapy and who relapse within 12 months from completion of, or are refractory to, first-line therapy

No medicinal product with new active ingredients that can be used in a combination therapy that fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

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. Entry into force

1. The resolution will enter into force on the day of its publication on the website of the G-BA on 21 December 2023.
2. The period of validity of the resolution is limited in accordance with the following regulations:

   The statements made for the patient group

   a) Adults with diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) who are eligible for high-dose therapy and who relapse within 12 months from completion of, or are refractory to, first-line therapy

   in numbers 1, 2, 3, 4 and 5 are limited until 1 July 2024.

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

Berlin, 21 December 2023

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

Prof. Hecken