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)
Loncastuximab tesirine (diffuse large B-cell lymphoma and high-grade B-cell lymphoma, after ≥ 2 prior therapies)

of 2 November 2023

At its session on 2 November 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. Annex XII shall be amended in alphabetical order to include the active ingredient Loncastuximab tesirine as follows:

Loncastuximab tesirine

Resolution of: 2 November 2023
Entry into force on: 2 November 2023
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 20 December 2022):

Zynlonta as monotherapy is indicated for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL), after two or more lines of systemic therapy.

Therapeutic indication of the resolution (resolution of 2 November 2023):

See therapeutic indication according to marketing authorisation

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

a) Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL), after two or more lines of systemic therapy, who are eligible for CAR-T cell therapy or stem cell transplantation

Appropriate comparator therapy:

Therapy according to doctor's instructions under consideration of

- Tisagenlecleucel,
- axicabtagene ciloleucel,
- an induction therapy with
  - R-GDP (rituximab, gemcitabine, dexamethasone, cisplatin and carboplatin) *or*
  - R-DHAP (rituximab, dexamethasone, cisplatin, cytarabine) *or*
  - R-ICE (rituximab, ifosfamide, carboplatin, etoposide)

  followed by high-dose therapy with **autologous** stem cell transplantation if there is a response to induction therapy,
- an induction therapy with
  - R-GDP (rituximab, gemcitabine, dexamethasone, cisplatin and carboplatin) *or*
  - R-DHAP (rituximab, dexamethasone, cisplatin, cytarabine) *or*
  - R-ICE (rituximab, ifosfamide, carboplatin, etoposide)

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

Extent and probability of the additional benefit of loncastuximab tesirine compared to the appropriate comparator therapy:

An additional benefit is not proven.

b) Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL), after two or more lines of systemic therapy, who are **not** eligible for CAR-T cell therapy or stem cell transplantation

Appropriate comparator therapy:

Therapy according to doctor's instructions under consideration of

- Polatuzumab vedotin + bendamustine + rituximab,
- tafasitamab + lenalidomide,
- pixantrone monotherapy,
- radiation

Extent and probability of the additional benefit of loncastuximab tesirine compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:

a) Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL), after two or more lines of systemic therapy, who are eligible for CAR-T cell therapy or stem cell transplantation

No adequate 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

b) Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL), after two or more lines of systemic therapy, who are **not** eligible for CAR-T cell therapy or stem cell transplantation

No adequate 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 relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL), after two or more lines of systemic therapy, who are eligible for CAR-T cell therapy or stem cell transplantation

Approx. 680 to 1,200 patients

b) Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL), after two or more lines of systemic therapy, who are **not** eligible for CAR-T cell therapy or stem cell transplantation

Approx. 680 to 700 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 Zynlonta (active ingredient: loncastuximab tesirine) at the following publicly accessible link (last access: 19 July 2023):

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

Treatment with loncastuximab tesirine 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) and high-grade B-cell lymphoma.

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 EMA's requirements for additional risk minimisation measures, the pharmaceutical company must ensure that all healthcare professionals who may prescribe loncastuximab tesirine and each subject treated with loncastuximab tesirine receive a patient pass containing safety information on the risks of photosensitivity reactions and a warning for the healthcare professional treating the person. Patients should carry their patient pass with them at all times.

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 relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL), after two or more lines of systemic therapy, who are eligible for CAR-T cell therapy or stem cell transplantation

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Loncastuximab tesirine	€ 427,142.80
Appropriate comparator therapy:	
CAR-T cell therapies	
Axicabtagene ciloleucel	€ 272,000.00
Additionally required SHI costs	*€ 762.04*
Tisagenlecleucel	€ 239,000.00
Additionally required SHI costs	*€ 414.38*
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	

Designation of the therapy	Annual treatment costs/ patient
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	
Rituximab	€ 5,315.42 - € 8,313.20
Ifosfamide	€ 671.48 - € 1,007.22
Carboplatin	€ 633.30 - € 949.95 (2 cycles) – € 822.60 - € 1,233.90 (3 cycles)
Etoposide	€ 459.30 - € 688.95
R-ICE	€ 7,079.50 - € 7,268.80 (2 cycles) – € 10,959.32 - € 11,243.27 (3 cycles)
Additionally required SHI costs	*€ 156.13 - € 175.65*
R-DHAP (rituximab + dexamethasone + cytarabine + cisplatin); 2-3 cycles	
Rituximab	€ 5,315.42 - € 8,313.20
Dexamethasone	€ 44.29 - € 79.59
Cytarabine	€ 575.52 - € 863.28
Cisplatin	€ 285.96 - € 428.94
R-DHAP	€ 6,221.19 - € 9,685.01
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
Total: *Additionally required SHI costs*	*€ 143.16 - € 192.26*
Total: R-ICE induction chemotherapy + High-dose chemotherapy with autologous stem cell transplantation	€ 45,943.36 - € 46,132.66 (2 cycles R-ICE) – € 49,823.18 - € 50,107.13 (3 cycles R-ICE)
Total:	*€ 156.13 - € 175.65*

Designation of the therapy	Annual treatment costs/ patient
Additionally required SHI costs	
Total: R-DHAP induction chemotherapy + High-dose chemotherapy with autologous stem cell transplantation	€ 45,085.05 - € 48,548.87
Total: *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	
Rituximab	€ 5,315.42 - € 8,313.20
Ifosfamide	€ 671.48 - € 1,007.22
Carboplatin	€ 633.30 - € 949.95 (2 cycles) – € 822.60 - € 1,233.90 (3 cycles)
Etoposide	€ 459.30 - € 688.95
R-ICE	€ 7,079.50 - € 7,268.80 (2 cycles) – € 10,959.32 - € 11,243.27 (3 cycles)
Additionally required SHI costs	*€ 156.13 - € 175.65*
R-DHAP (rituximab + dexamethasone + cytarabine + cisplatin); 2-3 cycles	
Rituximab	€ 5,315.42 - € 8,313.20
Dexamethasone	€ 44.29 - € 79.59
Cytarabine	€ 575.52 - € 863.28
Cisplatin	€ 285.96 - € 428.94
R-DHAP	€ 6,221.19 - € 9,685.01
Additionally required SHI costs	*€ 143.16 - € 192.26*
High-dose chemotherapy with allogeneic stem cell transplantation	

Designation of the therapy	Annual treatment costs/ patient
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
Total: *Additionally required SHI costs*	*€ 143.16 - € 192.26*
Total: R-ICE induction chemotherapy + High-dose chemotherapy with allogeneic stem cell transplantation	€ 64,643.13 - € 64,832.43 (2 cycles R-ICE) – € 68,522.95 - € 68,806.90 (3 cycles R-ICE)
Total: *Additionally required SHI costs*	*€ 156.13 - € 175.65*
Total: R-DHAP induction chemotherapy + High-dose chemotherapy with allogeneic stem cell transplantation	€ 63,784.82 - € 67,248.64
Total: *Additionally required SHI costs*	*€ 143.16 - € 192.26*

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 October 2023)

Costs for additionally required SHI services: not applicable

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					
Loncastuximab tesirine	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	17.4	€ 1,740
Appropriate comparator therapy					
CAR-T cell therapies					
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
Tisagenlecleucel *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
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	1	2.0 – 3.0	€ 200 – € 300
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					
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	2.0 – 3.0	€ 200 – € 300
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	1	2.0 – 3.0	€ 200 – € 300
R-DHAP (rituximab + dexamethasone + cytarabine + cisplatin); 2-3 cycles					
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	2.0 – 3.0	€ 200 – € 300

Cytarabine	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	1	2.0 – 3.0	€ 200 – € 300
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	1	2.0 – 3.0	€ 200 – € 300
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					
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	2.0 – 3.0	€ 200 – € 300
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	1	2.0 – 3.0	€ 200 – € 300
R-DHAP (rituximab + dexamethasone + cytarabine + cisplatin); 2-3 cycles					
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	2.0 – 3.0	€ 200 – € 300
Cytarabine	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	1	2.0 – 3.0	€ 200 – € 300
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: 15 October 2023)

b) Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL), after two or more lines of systemic therapy, who are **not** eligible for CAR-T cell therapy or stem cell transplantation

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Loncastuximab tesirine	€ 427,142.80
Appropriate comparator therapy:	
Polatuzumab vedotin + bendamustine + rituximab	
Polatuzumab vedotin	€ 61,470.36
Bendamustine	€ 5,906.30
Rituximab	€ 15,946.26

Designation of the therapy	Annual treatment costs/ patient
Total	€ 83,322.92
Total: *Additionally required SHI costs*	*€ 62.65 – € 62.98*
Tafasitamab + lenalidomide	
Tafasitamab	€ 97,585.95
Lenalidomide	€ 427.72
Total	€ 98,013.67
Pixantrone monotherapy	
Pixantrone	€ 5,576.28 - € 33,457.68
radiation	
radiation	varies from patient to patient

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 October 2023)

Costs for additionally required SHI services: not applicable

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					
Loncastuximab tesirine	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	17.4	€ 1,740
Appropriate comparator therapy					
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	€ 100	2	12.0	€ 1,200

	containing cytostatic agents				
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
Pixantrone monotherapy					
Pixantrone	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	3	3.0 – 18.0	€ 300 – € 1,800

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 October 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 relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL), after two or more lines of systemic therapy, who are eligible for CAR-T cell therapy or stem cell transplantation

– 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.

b) Adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL), after two or more lines of systemic therapy, who are **not** eligible for CAR-T cell therapy or stem cell transplantation

- 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 2 November 2023.

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

Berlin, 2 November 2023

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

Prof. Hecken