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)
Polatuzumab vedotin (reassessment of an orphan drug after exceeding the EUR 30 million turnover limit: relapsed/ refractory diffuse large B-cell lymphoma)

of 20 June 2024

At its session on 20 June 2024, 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 is amended as follows:

1. The information on polatuzumab vedotin in the version of the resolutions of 20 August 2020 (BAnz AT 28.09.2020 B5) and 1 December 2022 (BAnz AT 25.01.2023 B2) is repealed.
2. Annex XII shall be amended in alphabetical order to include the active ingredient polatuzumab vedotin as follows:

Polatuzumab vedotin

Resolution of: 20 June 2024
Entry into force on: 20 June 2024
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 16 January 2020):

Polivy in combination with bendamustine and rituximab is indicated for the treatment of adult patients with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) who are not candidates for haematopoietic stem cell transplant.

Therapeutic indication of the resolution (resolution of 20 June 2024):

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/refractory diffuse large B-cell lymphoma (DLBCL) after failure of one line of systemic therapy who are not candidates for haematopoietic stem cell transplant

Appropriate comparator therapy:

- Tafasitamab in combination with lenalidomide

Extent and probability of the additional benefit of polatuzumab vedotin in combination with bendamustine and rituximab compared with the appropriate comparator therapy:

An additional benefit is not proven.

b1) Adults with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) after failure of two or more lines of systemic therapy who are candidates for CAR-T cell therapy and are not candidates for haematopoietic stem cell transplant

Appropriate comparator therapy:

- tisagenlecleucel
  or
- axicabtagene ciloleucel
  or
- lisocabtagene maraleucel

Extent and probability of the additional benefit of polatuzumab vedotin in combination with bendamustine and rituximab compared with the appropriate comparator therapy:

An additional benefit is not proven.

b2) Adults with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) after failure of two or more lines of systemic therapy who are not candidates for CAR-T cell therapy and haematopoietic stem cell transplant

Appropriate comparator therapy:

Therapy according to doctor's instructions under consideration of:

- tafasitamab in combination with lenalidomide,
- pixantrone monotherapy *and*
- radiation.

Extent and probability of the additional benefit of polatuzumab vedotin in combination with bendamustine and rituximab compared with the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:[1]

a) Adults with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) after failure of one line of systemic therapy who are not candidates for haematopoietic stem cell transplant

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	∅	No data available.
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		

b1) Adults with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) after failure of two or more lines of systemic therapy who are candidates for CAR-T cell therapy and are not candidates for haematopoietic stem cell transplant

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

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A23-140) unless otherwise indicated.

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	∅	No data available.
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		

b2) Adults with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) after failure of two or more lines of systemic therapy who are not candidates for CAR-T cell therapy and haematopoietic stem cell transplant

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	∅	No data available.
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/refractory diffuse large B-cell lymphoma (DLBCL) after failure of one line of systemic therapy who are not candidates for haematopoietic stem cell transplant

Approx. 1,200 – 1,330 patients

b1) Adults with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) after failure of two or more lines of systemic therapy who are candidates for CAR-T cell therapy and are not candidates for haematopoietic stem cell transplant

Approx. 720 – 950 patients

b2) Adults with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) after failure of two or more lines of systemic therapy who are not candidates for CAR-T cell therapy and haematopoietic stem cell transplant

Approx. 630 – 840 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 Polivy (active ingredient: polatuzumab vedotin) at the following publicly accessible link (last access: 2 May 2024):

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

Treatment with polatuzumab vedotin 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).

4. Treatment costs

Annual treatment costs:

a) Adults with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) after failure of one line of systemic therapy who are not candidates for haematopoietic stem cell transplant

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Polatuzumab vedotin in combination with bendamustine and rituximab	
Polatuzumab vedotin	€ 64,070.34
Bendamustine	€ 6,023.10
Rituximab	€ 16,282.35
Total	€ 86,375.79
Additionally required SHI services	*€ 63.37 - € 63.70*
Appropriate comparator therapy:	
Tafasitamab in combination with lenalidomide	
Tafasitamab	€ 101,783.55
Lenalidomide	€ 427.76

Designation of the therapy	Annual treatment costs/ patient
Total	€ 102,211.31

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 June 2024)

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:					
Polatuzumab vedotin in combination with bendamustine and rituximab					
Polatuzumab vedotin	Surcharge for the preparation of parenteral solutions containing polatuzumab vedotin	€ 100	1	6	€ 600
Bendamustine	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	2	12	€ 1,200
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	6	€ 600
Appropriate comparator therapy					
Tafasitamab in combination with 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

<u>b1) Adults with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) after failure of two or more lines of systemic therapy who are candidates for CAR-T cell therapy and are not candidates for haematopoietic stem cell transplant</u>

Axicabtagene ciloleucel, tisagenlecleucel and lisocabtagene maraleucel are administered as a single intravenous infusion according to the requirements in the underlying product information.

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Polatuzumab vedotin in combination with bendamustine and rituximab	
Polatuzumab vedotin	€ 64,070.34
Bendamustine	€ 6,023.10

Designation of the therapy	Annual treatment costs/ patient
Rituximab	€ 16,282.35
Total	€ 86,375.79
Additionally required SHI services	*€ 63.37 - € 63.70*
Appropriate comparator therapy:	
Tisagenlecleucel	€ 239,000.00
Additionally required SHI services	*€ 417.95*
Axicabtagene ciloleucel	€ 272,000.00
Additionally required SHI services	*€ 767.54*
Lisocabtagene maraleucel	€ 345,000.00
Additionally required SHI services	*€ 752.30*

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 June 2024)

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:					
Polatuzumab vedotin in combination with bendamustine and rituximab					
Polatuzumab vedotin	Surcharge for the preparation of parenteral solutions containing polatuzumab vedotin	€ 100	1	6	€ 600
Bendamustine	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	2	12	€ 1,200
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	6	€ 600
Appropriate comparator therapy					
Tisagenlecleucel: lymphocyte depletion					
Fludarabine	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	3	3	€ 300
Cyclophosphamide	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	3	3	€ 300
Axicabtagene ciloleucel: lymphocyte depletion					

Fludarabine	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	3	3	€ 300
Cyclophosphamide	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	3	3	€ 300
Lisocabtagene maraleucel: lymphocyte depletion					
Fludarabine	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	3	3	€ 300
Cyclophosphamide	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	3	3	€ 300

b2) Adults with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) after failure of two or more lines of systemic therapy who are not candidates for CAR-T cell therapy and haematopoietic stem cell transplant

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Polatuzumab vedotin in combination with bendamustine and rituximab	
Polatuzumab vedotin	€ 64,070.34
Bendamustine	€ 6,023.10
Rituximab	€ 16,282.35
Total	€ 86,375.79
Additionally required SHI services	*€ 63.37 - € 63.70*
Appropriate comparator therapy:	
Therapy according to doctor's instructions under consideration of – tafasitamab in combination with lenalidomide, - pixantrone monotherapy and – radiation	
Tafasitamab in combination with lenalidomide	
Tafasitamab	€ 101,783.55
Lenalidomide	€ 427.76
Total	€ 102,211.31
Pixantrone monotherapy	
Pixantrone	€ 5,801.28 - € 34,807.68
Radiation	
Radiation	Different from patient to patient

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 June 2024)

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:					
Polatuzumab vedotin in combination with bendamustine and rituximab					
Polatuzumab vedotin	Surcharge for the preparation of parenteral solutions containing polatuzumab vedotin	€ 100	1	6	€ 600
Bendamustine	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	2	12	€ 1,200
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	6	€ 600
Appropriate comparator therapy					
Tafasitamab in combination with 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 – 18	€ 300 - € 1,800

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/refractory diffuse large B-cell lymphoma (DLBCL) after failure of one line of systemic therapy who are not candidates for haematopoietic stem cell transplant

- 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.

b1) Adults with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) after failure of two or more lines of systemic therapy who are candidates for CAR-T cell therapy and are not candidates for haematopoietic stem cell transplant

- 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.

b2) Adults with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) after failure of two or more lines of systemic therapy who are not candidates for CAR-T cell therapy and haematopoietic stem cell transplant

- 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. The resolution will enter into force on the day of its publication on the website of the G-BA on 20 June 2024.

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

Berlin, 20 June 2024

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

Prof. Hecken