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) and Annex XIIa – Combinations of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Zanubrutinib (New therapeutic indication: follicular lymphoma, after ≥ 2 prior therapies, combination with obinutuzumab)

of 6 June 2024

At its session on 6 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. In Annex XII, the following information shall be added after No. 5 to the information on the benefit assessment of Zanubrutinib in accordance with the resolution of 15 June 2023:

Zanubrutinib

Resolution of: 6 June 2024
Entry into force on: 6 June 2024
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 15 November 2023):

BRUKINSA in combination with obinutuzumab is indicated for the treatment of adult patients with refractory or relapsed follicular lymphoma (FL) who have received at least two prior systemic therapies.

Therapeutic indication of the resolution (resolution of 6 June 2024):

See new therapeutic indication according to marketing authorisation.

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

Adults with refractory or relapsed grade 1 to 3a follicular lymphoma who have received at least two prior systemic therapies

Appropriate comparator therapy:

Patient-individual therapy with selection of:

- bendamustine + obinutuzumab followed by obinutuzumab maintenance treatment in accordance with the marketing authorisation,
- lenalidomide + rituximab,
- rituximab monotherapy,
- mosunetuzumab,
- tisagenlecleucel

taking into account prior therapy, course of the disease and general condition.

Extent and probability of the additional benefit of zanubrutinib in combination with obinutuzumab compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:[1]

Adults with refractory or relapsed grade 1 to 3a follicular lymphoma, who have received at least two prior systemic therapies

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

Adults with refractory or relapsed grade 1 to 3a follicular lymphoma who have received at least two prior systemic therapies

Approx. 370 - 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 Brukinsa (active ingredient: zanubrutinib) at the following publicly accessible link (last access: 13 March 2024):

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

Treatment with zanubrutinib should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of patients with follicular lymphoma.

[1] Data from the dossier evaluation of the Institute for Quality and Efficiency in Health Care (IQWiG) (A23-130) unless otherwise indicated.

4. Treatment costs

Annual treatment costs:

Adults with refractory or relapsed grade 1 to 3a follicular lymphoma, who have received at least two prior systemic therapies

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Zanubrutinib + obinutuzumab	
Zanubrutinib	€ 67,428.15
Obinutuzumab	€ 27,491.64
Total	€ 94,919.79
Additionally required SHI costs	*€ 11.40*
Appropriate comparator therapy:	
Bendamustine + obinutuzumab	
Bendamustine	€ 6,023.10
Obinutuzumab	€ 27,491.64
Total	€ 33,514.74
Additionally required SHI costs	*€ 11.40*
Lenalidomide + rituximab	
Lenalidomide	€ 427.76
Rituximab	€ 21,709.80
Total	€ 22,137.56
Additionally required SHI costs	*€ 79.80 - € 80.13*
Rituximab monotherapy	
Rituximab	€ 10,854.90
Additionally required SHI costs	*€ 46.94 - € 47.27*
CAR-T cell therapy	
tisagenlecleucel	€ 239,000.00
Additionally required SHI costs	*€ 417.95*
Mosunetuzumab monotherapy	
Mosunetuzumab	€ 73,879.76 - € 139,671.65
Additionally required SHI costs	*€ 64.50 - € 64.83*

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 01 May 2024)

Costs for additionally required SHI services: not applicable

Other SHI benefits:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Cost/ patient/ year
Medicinal product to be assessed					
Zanubrutinib + obinutuzumab					
Obinutuzumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	11.0	€ 1,100
Appropriate comparator therapy					
Bendamustine + obinutuzumab					
Bendamustine	Surcharge for production of a parenteral solution containing cytostatic agents	€ 100	2	6	€ 1,200
Obinutuzumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	Cycle 1: 3 Cycle 2 - 9: 1	11	€ 1,100
Lenalidomide + rituximab					
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	Induction therapy: 4 Maintenance treatment: 1	Induction therapy: 1 Maintenance treatment: 4	€ 800
Rituximab monotherapy					
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	4	€ 400
Tisagenlecleucel - Lymphocyte depletion					
Cyclophos-phamide	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

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Cost/ patient/ year
Mosunetuzumab monotherapy					
Mosunetuzu-mab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	Cycle 1: 3 From cycle 2 onwards: 1	10 - 19	€ 1,000 - € 1,900

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 refractory or relapsed grade 1 to 3a follicular lymphoma,
who have received at least two prior systemic therapies

The following medicinal products with new active ingredients that can be used in a combination therapy with zanubrutinib in the therapeutic indication of the resolution on the basis of the marketing authorisation under Medicinal Products Act are named (active ingredients and invented names) in accordance with Section 35a, paragraph 3, sentence 4 SGB V:

obinutuzumab (Gazyvaro)

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. **In Annex XIIa of the Pharmaceuticals Directive, the following information shall be added in alphabetical order:**

"Active ingredient of the assessed medicinal product

Zanubrutinib

Resolution according to Section 35a paragraph 3 SGB V from

06 June 2024

Therapeutic indication of the resolution

BRUKINSA in combination with obinutuzumab is indicated for the treatment of adult patients with refractory or relapsed follicular lymphoma (FL) who have received at least two prior systemic therapies.

Patient group a

Adults with refractory or relapsed grade 1 to 3a follicular lymphoma,
who have received at least two prior systemic therapies

Naming of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V (active ingredients and invented names[2])

obinutuzumab (Gazyvaro)

Period of validity of the designation (since... or from... to)

Since 6 June 2024"

III. Entry into force

1. **The resolution will enter into force on the day of its publication on the website of the G-BA on 6 June 2024.**

2. **The period of validity of the resolution is limited to 1 July 2029.**

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

Berlin, 6 June 2024

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

Prof. Hecken