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
Zanubrutinib (new therapeutic indication: marginal zone lymphoma (MZL), after min. 1 prior anti-CD20 therapy)

of 15 June 2023

At its session on 15 June 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 Zanubrutinib in accordance with the resolution of 15 June 2023 for the therapeutic indication: "for the treatment of adult patients with relapsed/ refractory chronic lymphocytic leukaemia (CLL)":**

Zanubrutinib

Resolution of: 15 June 2023
Entry into force on: 15 June 2023
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 28 October 2022):

Brukinsa as monotherapy is indicated for the treatment of adult patients with marginal zone lymphoma (MZL) who have received at least one prior anti-CD20-based therapy.

Therapeutic indication of the resolution (resolution of 15 June 2023):

See new therapeutic indication according to marketing authorisation

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

Adults with marginal zone lymphoma who have received at least one prior anti-CD20 therapy

Appropriate comparator therapy for zanubrutinib:

Patient-individual therapy with selection of:

- Bendamustine
- CHOP (cyclophosphamide + doxorubicin + vincristine + prednisone)
- CVP (cyclophosphamide + vincristine + prednisone)
- FCM (fludarabine + cyclophosphamide + mitoxantrone) + rituximab (in subjects with resistance to CHOP)
- Chlorambucil
- Cyclophosphamide

taking into account the prior therapy, the course of the disease (including duration of remission since prior therapy) and the general condition

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

An additional benefit is not proven.

Study results according to endpoints:

Adults with marginal zone lymphoma who have received at least one prior anti-CD20 therapy

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		

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

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

Adults with marginal zone lymphoma who have received at least one prior anti-CD20 therapy

approx. 590 – 1,760 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: 1 March 2023):

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 marginal zone lymphoma.

4. Treatment costs

Annual treatment costs:

Patients with marginal zone lymphoma (MZL) with at least one prior therapy anti-CD20 therapy

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Zanubrutinib	€ 65,843.20
Appropriate comparator therapy:	
A patient-individual therapy taking into account the prior therapy, the course of the disease (including the duration of remission since prior therapy) and the general condition [1].	
Monotherapies	
Cyclophosphamide	€ 320.48 - € 720.59
Chlorambucil	€ 388.67
Bendamustine	€ 24,356.94
R-FCM (fludarabine + cyclophosphamide + mitoxantrone + rituximab) cf. Annex VI to Section K of the Pharmaceuticals Directive	
Fludarabine	€ 1,569.66 - € 2,616.10
Cyclophosphamide	€ 111.74 - € 167.61
Mitoxantrone	€ 891.60 - € 1,783.20
Rituximab	€ 10,630.44 - € 21,260.88
Total	€ 13,203.44 - € 25,827.79
Additionally required SHI services	€ 45.80 - € 77.85
CHOP (cyclophosphamide + doxorubicin + vincristine + prednisone)	
Cyclophosphamide	€ 187.55
Doxorubicin	€ 1,572.24
Vincristine	€ 206.28
Prednisolone	€ 33.22
Total	€ 1,999.29
CVP (cyclophosphamide + vincristine + prednisone)	
Cyclophosphamide	€ 187.55
Vincristine	€ 275.04
Prednisolone	€ 37.54

[1] Only the therapy options approved for the present therapeutic indication were presented, whereby the annual treatment costs cannot be exactly quantified due to individual treatment regimens.

Designation of the therapy	Annual treatment costs/ patient
Total	€ 500.13

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

Costs for additionally required SHI services:

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ Cycle	Number/ patient/ year	Costs/ patient/ year
Monotherapies					
Bendamustine	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	2	35	€ 3500
Cyclophosphamide		€ 100	1	13 - 18	€ 1300 - € 1800
R-FCM (fludarabine + cyclophosphamide + mitoxantrone + rituximab) cf. Annex VI to Section K of the Pharmaceuticals Directive					
Fludarabine	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	3	12 - 24	€ 1,200 - € 2,400
Cyclophosphamide		€ 100	3	12 - 24	€ 1200 - € 2400
Mitoxantrone		€ 100	1	4 - 8	€ 400 - € 800
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	4 - 8	€ 400 - € 800
CHOP (cyclophosphamide + doxorubicin + vincristine + prednisone)					
Cyclophosphamide	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	6	€ 600
Doxorubicin		€ 100	1	6	€ 600
Vincristine		€ 100	1	6	€ 600
CVP (cyclophosphamide + vincristine + prednisone)					
Cyclophosphamide		€ 100	1	8	€ 800

Designation of the therapy	Type of service	Costs/ unit	Number/ Cycle	Number/ patient/ year	Costs/ patient/ year
Vincristine	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	8	€ 800

5. 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 Zanubrutinib

Medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V are medicinal products with the following new active ingredients that can be used in a combination therapy with zanubrutinib for the treatment of marginal zone lymphoma on the basis of the marketing authorisation granted under Medicinal Products Act:

Adults with marginal zone lymphoma who have received at least one prior anti-CD20 therapy

- 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 15 June 2023.

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

Berlin, 15 June 2023

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

Prof. Hecken