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
Pirtobrutinib (new therapeutic indication: chronic lymphocytic leukaemia (CLL), relapsed or refractory, monotherapy)

of 2 October 2025

At their session on 2 October 2025, 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 Pirtobrutinib in accordance with the resolution of 7 August 2025:

Pirtobrutinib

Resolution of: 2 October 2025
Entry into force on: 2 October 2025
Federal Gazette, BAnz AT DD. MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 28 March 2025):

Jaypirca as monotherapy is indicated for the treatment of adult patients with relapsed or refractory chronic lymphocytic leukaemia (CLL) who have been previously treated with a BTK inhibitor.

Therapeutic indication of the resolution (resolution of 2 October 2025):

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 relapsed or refractory chronic lymphocytic leukaemia (CLL) who have been previously treated with a Bruton's tyrosine kinase inhibitor (BTKi) and not with a B-cell lymphoma-2 (BCL-2) inhibitor

Appropriate comparator therapy:

- Venetoclax in combination with rituximab

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

An additional benefit is not proven.

b) Adults with relapsed or refractory chronic lymphocytic leukaemia (CLL) who have been previously treated with a Bruton's tyrosine kinase inhibitor (BTKi) and with a B-cell lymphoma-2 (BCL-2) inhibitor

Appropriate comparator therapy:

Individualised therapy with selection of

- idelalisib in combination with rituximab,
- venetoclax in combination with rituximab and
- bendamustine in combination with rituximab

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

b1) Adults with relapsed or refractory chronic lymphocytic leukaemia (CLL), who have been previously treated with a Bruton's tyrosine kinase inhibitor (BTKi) and with a B-cell lymphoma-2 (BCL-2) inhibitor and for whom idelalisib + rituximab or bendamustine + rituximab is the appropriate individualised therapy

Hint for a minor additional benefit

b2) Adults with relapsed or refractory chronic lymphocytic leukaemia (CLL) who have been previously treated with a Bruton's tyrosine kinase inhibitor (BTKi) and with a B-cell lymphoma-2 (BCL-2) inhibitor and for whom venetoclax + rituximab is the appropriate individualised therapy

An additional benefit is not proven.

Study results according to endpoints:[1]

a) Adults with relapsed or refractory chronic lymphocytic leukaemia (CLL) who have been previously treated with a Bruton's tyrosine kinase inhibitor (BTKi) and not with a B-cell lymphoma-2 (BCL-2) inhibitor

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		

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A25-50) unless otherwise indicated.

b) Adults with relapsed or refractory chronic lymphocytic leukaemia (CLL) who have been previously treated with a Bruton's tyrosine kinase inhibitor (BTKi) and with a B-cell lymphoma-2 (BCL-2) inhibitor

b1) Adults with relapsed or refractory chronic lymphocytic leukaemia (CLL), who have been previously treated with a Bruton's tyrosine kinase inhibitor (BTKi) and with a B-cell lymphoma-2 (BCL-2) inhibitor and for whom indelalisib + rituximab or bendamustine + rituximab is the appropriate individualised therapy

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No relevant difference for the benefit assessment.
Morbidity	n.a.	There are no assessable data.
Health-related quality of life	n.a.	There are no assessable data.
Side effects	↑	Advantages in severe AEs and therapy discontinuation due to AEs. In detail, advantages in the specific AEs.
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		

Open-label, randomised phase III BRUIN CLL-321 study:

- Pirtobrutinib vs investigator's choice (idelalisib + rituximab or bendamustine + rituximab)
- Data cut-off of 29.08.2024
- Relevant sub-population: patients pretreated with BTK and BCL-2 inhibitors

Mortality

Endpoint	**Pirtobrutinib**		**Idelalisib + rituximab or bendamustine + rituximab**[a]		Pirtobrutinib vs idelalisib + rituximab or bendamustine + rituximab[a]
	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					
	60	26.3 [16.0; 29.7] *26 (43.3)*	62	n.c. [28.0; n.r.] *19 (30.6)*	1.39 [0.77; 2.52] 0.279

Morbidity

Endpoint	**Pirtobrutinib**		**Idelalisib + rituximab or bendamustine + rituximab**[a]		Pirtobrutinib vs idelalisib + rituximab or bendamustine + rituximab[a]
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[b]
Progression-free survival (PFS)[c]					
	60	11.4 [8.48; 16.53] *41 (68.3)*	62	8.2 [4.47; 9.92] *45 (72.6)*	0.48 [0.30; 0.75] < 0.001 AD: 3.2 months
Symptomatology (EORTC QLQ-C30)					
No suitable data					
Health status (EQ-5D VAS)					
No suitable data					

Health-related quality of life

Endpoint	**Pirtobrutinib**		**Idelalisib + rituximab or bendamustine + rituximab**[a]		Pirtobrutinib vs idelalisib + rituximab or bendamustine + rituximab[a]
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[b]
EORTC-QLQ C30					
No suitable data					

Side effects

Endpoint	**Pirtobrutinib**		**Idelalisib + rituximab or bendamustine + rituximab**[a]		Pirtobrutinib vs idelalisib + rituximab or bendamustine + rituximab[a]
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	HR [95% CI] p value Absolute difference (AD)[b]
Adverse events (presented additionally)					
	58	0.6 [0.3; 1.2] *53 (91.4)*	56	0.3 [0.1; 0.5] *55 (98.2)*	–
Serious adverse events (SAEs)					
	58	13.5 [6.9; 18.9] *32 (55.2)*	56	6.8 [3.0; n.r.] *28 (50.0)*	0.72 [0.42; 1.22] 0.213
Severe adverse events (CTCAE grade ≥ 3)					
	58	5.1 [2.8; n.r.] *34 (58.6)*	56	2.3 [1.8; 3.3] *43 (76.8)*	0.49 [0.31; 0.78] 0.003 AD: 2.8 months

Therapy discontinuation due to adverse events[d]					
	58	29.4 [n.r.; n.r.] *10 (17.2)*	56	13.0 [8.8; n.r.] *18 (32.1)*	0.31 [0.14; 0.71] 0.004 AD: 16.4 months
Specific adverse events					
Infections and infestations (SOC, AE[e])	58	n.r. [15.2; n.r.] *20 (34.5)*	56	24.5 [n.r.; n.r.] *12 (21.4)*	1.17 [0.56; 2.43] 0.683
Severe bleeding (SMQ, severe AE)	No suitable data				
Bleeding (SMQ, AE)	No suitable data				
Cardiac disorders (SOC, AE)	58	n.r. *5 (8.6)*	56	24.5 [24.5; n.r.] *8 (14.3)*	0.46 [0.15; 1.43] 0.172
Bronchitis (PT, AE)	58	n.r. *1 (1.7)*	56	n.r. *8 (14.3)*	0.09 [0.01; 0.70] 0.004
Fever (PT, AE)	58	n.r. *8 (13.8)*	56	n.r. [7.8.; n.r.] *15 (26.8)*	0.28 [0.11; 0.73] 0.006
Injury, poisoning and procedural complications (SOC, SAE)	58	n.r. *0 (0.0)*	56	n.r. *5 (8.9)*	n.a. 0.018
Renal and urinary disorders (SOC, SAE)	58	n.r. *0 (0.0)*	56	n.r. [13.0; n.r.] *3 (5.4)*	n.a. 0.039
Diarrhoea (PT, SAE)	58	n.r. *0 (0.0)*	56	n.r. *3 (5.4)*	n.a. < 0.001
Investigations (SOC, severe AE)	58	n.r. *5 (8.6)*	56	n.r. *5 (8.6)*	0.32 [0.10; 1.00] 0.040
Skin and subcutaneous tissue disorders (SOC, severe AE)	58	n.r. *2 (3.4)*	56	n.r. *7 (12.5)*	0.19 [0.04; 0.96] 0.027
Metabolism and nutrition disorders (SOC, severe AE)	58	n.r. *1 (1.7)*	56	n.r. *4 (7.1)*	0.09 [0.01; 1.12] 0.035

Hepatobiliary disorders (SOC, severe AE)	58	n.r. *0 (0.0)*	56	n.r. *3 (5.4)*	n.a. 0.031
Vascular disorders (SOC, severe AE)	58	n.r. *0 (0.0)*	56	n.r. *4 (7.1)*	n.a. 0.043

a. Individualised therapy with selection of idelalisib + rituximab and bendamustine + rituximab
b. Absolute difference (AD) given only in the case of a statistically significant difference; own calculation
c. Information provided by the pharmaceutical company
d. Discontinuation of at least one active ingredient component
e. Operationalised as CTCAE grade ≥ 3

Abbreviations used:
AD = absolute difference; CTCAE = Common Terminology Criteria for Adverse Events; HR = hazard ratio; 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; vs = versus

b2) Adults with relapsed or refractory chronic lymphocytic leukaemia (CLL) who have been previously treated with a Bruton's tyrosine kinase inhibitor (BTKi) and with a B-cell lymphoma-2 (BCL-2) inhibitor and for whom venetoclax + rituximab is the appropriate individualised therapy

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 chronic lymphocytic leukaemia (CLL) who have been previously treated with a Bruton's tyrosine kinase inhibitor (BTKi) and not with a B-cell lymphoma-2 (BCL-2) inhibitor

Approx. 4,620 – 6,060 patients

b) Adults with relapsed or refractory chronic lymphocytic leukaemia (CLL) who have been previously treated with a Bruton's tyrosine kinase inhibitor (BTKi) and with a B-cell lymphoma-2 (BCL-2) inhibitor

Approx. 770 – 1,430 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 Jaypirca (active ingredient: pirtobrutinib) at the following publicly accessible link (last access: 23 September 2025):

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

Treatment with pirtobrutinib should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of patients with chronic lymphocytic leukaemia.

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 will evaluate new information on this medicinal product at a minimum once per year and update the product information where necessary.

4. Treatment costs

Annual treatment costs:

a) Adults with relapsed or refractory chronic lymphocytic leukaemia (CLL) who have been previously treated with a Bruton's tyrosine kinase inhibitor (BTKi) and not with a B-cell lymphoma-2 (BCL-2) inhibitor

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Pirtobrutinib	€ 143,363.92
Appropriate comparator therapy:	
Venetoclax in combination with rituximab	
Venetoclax	€ 72,230.25
Rituximab	€ 39,261.06
Total:	€ 111,491.31
Additionally required SHI costs	€ 96.88

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 August 2025)

b) Adults with relapsed or refractory chronic lymphocytic leukaemia (CLL) who have been previously treated with a Bruton's tyrosine kinase inhibitor (BTKi) and with a B-cell lymphoma-2 (BCL-2) inhibitor

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Pirtobrutinib	€ 143,363.92
Appropriate comparator therapy:	
Idelalisib in combination with rituximab	
Idelalisib	€ 52,044.13
Rituximab	€ 49,996.16
Total:	€ 102,040.29
Additionally required SHI costs	€ 92.38
Venetoclax in combination with rituximab	

Designation of the therapy	Annual treatment costs/ patient
Venetoclax	€ 72,230.25
Rituximab	€ 39,261.06
Total:	€ 111,491.31
Additionally required SHI costs	€ 120.31
Bendamustine in combination with rituximab	
Bendamustine	€ 6,148.05
Rituximab	€ 19,803.68
Total:	€ 25,951.73
Additionally required SHI costs	€ 66.15

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 August 2025)

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Appropriate comparator therapy:					
Idelalisib in combination with rituximab					
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	15.0	€ 1500
Venetoclax in combination with rituximab					
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	11.8	€ 1180
Bendamustine in combination with rituximab [BR]					
Bendamustine	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	2	12.0	€ 1200
Rituximab	Surcharge for the preparation of a	€ 100	1	6.0	€ 600

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
	parenteral solution containing monoclonal antibodies				

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 chronic lymphocytic leukaemia (CLL) who have been previously treated with a Bruton's tyrosine kinase inhibitor (BTKi) and not with a B-cell lymphoma-2 (BCL-2) inhibitor

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 chronic lymphocytic leukaemia (CLL) who have been previously treated with a Bruton's tyrosine kinase inhibitor (BTKi) and with a B-cell lymphoma-2 (BCL-2) inhibitor

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 October 2025.**

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

Berlin, 2 October 2025

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

Prof. Hecken