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 (relapsed or refractory mantle cell lymphoma); requirement of routine practice data collection and evaluations

From 4 June 2026

At their session on 4 June 2026, 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 2 October 2025:**

**Pirtobrutinib**

Resolution of: 4 June 2026
Entry into force on: 4 June 2026
Federal Gazette, BAnz AT DD. MM YYYY Bx

Requirement of routine data collection and evaluations according to Section 35a, paragraph 3b, sentence 1 SGB V for the active ingredient pirtobrutinib:

**Therapeutic indication (according to the marketing authorisation of 30 October 2023):**

Jaypirca as monotherapy is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) who have been previously treated with a Bruton's tyrosine kinase (BTK) inhibitor.

**Therapeutic indication for the requirement of routine practice data collection and evaluations (resolution of 4 June 2026):**

see marketing authorisation

## 1. Requirements for routine practice data collection and evaluations

With reference to the justification for the requirement of routine practice data collection for the active ingredient pirtobrutinib for the purpose of the benefit assessment, which forms the basis of the procedure-initiating resolution on the requirement of routine practice data collection of 6 November 2025, the following requirements arise:

### 1.1 Research question according to PICO scheme

| | |
|---|---|
| **P**opulation | Adults with relapsed or refractory mantle cell lymphoma who have been previously treated with a Bruton's tyrosine kinase inhibitor. |
| **I**ntervention | ▪ Pirtobrutinib<br>The marketing authorisation and the dosage information in the product information for pirtobrutinib must be taken into account. |
| **C**omparator | Individualised therapy with selection of:<br>▪ bendamustine + rituximab,<br>▪ lenalidomide ± rituximab,<br>▪ R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone),<br>▪ VRCAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, prednisone),<br>▪ R-BAC (rituximab + bendamustine + cytarabine),<br>▪ R-FCM (fludarabine + cyclophosphamide + mitoxantrone + rituximab), |

| | |
|---|---|
| | ▪ ibrutinib,<br>▪ brexucabtagene autoleucel (only for patients with at least 2 prior therapies),<br>▪ lisocabtagene maraleucel (only for patients with at least 2 prior therapies),<br>▪ venetoclax,<br>▪ high-dose therapy with allogeneic stem cell transplant and<br>▪ high-dose therapy with autologous stem cell transplant |
| **O**utcome | Mortality<br>• Overall survival<br><br>Morbidity<br>• Symptomatology<br><br>Health-related quality of life, measured with a validated instrument<br><br>Side effects<br>• Serious adverse events (operationalised as events which lead to hospitalisation or prolong an existing hospitalisation, and lead to death; overall rate)<br>• Discontinuation due to adverse events (overall rate)<br>• Specific adverse events (with indication of the respective severity grade) |

### 1.2 Type and methods of data collection

Taking into account the research question of the routine practice data collection and the methodological limitations of non-randomised comparisons, the following requirements are placed on the study design and the data source for the present routine practice data collection.

#### 1.2.1 Requirements for the study design

- Non-randomised, prospective comparison of pirtobrutinib with the listed comparator preferably as a comparator registry study or, if a comparative registry study is not feasible, as a comparator study using a data platform to be set up specifically for the present routine practice data collection (study-specific data collection).

- If applicable, integration of retrospective data, provided that the data also meet the data quality requirements in Section 1.2.2.

#### 1.2.2 Data source requirement

- Use of registries as a data source that meet the requirements of routine practice data collection and fulfil at least the following quality criteria[1]:

[1]IQWiG A25-140: RPDC concept – pirtobrutinib.

- Detailed registry description (protocol)
- Exact definition or operationalisation of exposures (type and duration of medicinal therapy and other concomitant therapies), clinical events, endpoints and confounders
- Use of standard classifications and terminologies
- Use of validated standard data collection tools (questionnaire, scales, tests)
- Training courses on data collection and recording
- Implementation of a consensus disease-specific core data set
- Use of exact dates for the patient, the disease, important examinations and treatments/ interventions
- Clearly defined inclusion and exclusion criteria for patients
- Strategies to avoid selection bias in patient inclusion to achieve representativeness
- Specifications to ensure completeness of data per data collection time point and completeness of data collection time points
- Source data verification for 100% of patients per data collection site for the primary endpoint and for at least 10% of randomly selected patients per data collection site for all other endpoints over the period since the start of data collection
- When using a registry: ensuring scientific independence and transparency

- Use of a registry in which treatment for relapsed or refractory mantle cell lymphoma is provided in accordance with German daily care or is sufficiently similar to healthcare in Germany

### 1.2.3 Primary data source and integration of further data sources

- Use of the European indication-specific EMCL registry as primary registry; provided that the quality criteria mentioned in Section 1.2.2 are fulfilled
- It is also possible to integrate other registries, taking into account all data source requirements mentioned in Section 1.2.2

### 1.3 Duration and scope of data collection

Taking into account the fact that the patients in the present therapeutic indication show an advanced clinical picture, in which the main therapeutic goal is an extension of overall survival, the following duration of observation should be implemented during routine practice data collection:

- Follow-up of patients for at least 36 months

The available data on pirtobrutinib and the comparator therapies do not provide adequate information for an indicative sample size estimate. Therefore, an indicative consideration of sample size scenarios is carried out, in which effect sizes are shown for a routine practice data collection for the active ingredient pirtobrutinib, which can be detected on the basis of the available patient numbers and taking into account the shifted null hypothesis.

- Assumptions for the indicative consideration of the sample size scenarios:
  - Power of 80%
  - Sample sizes: N = 200, N = 300 and N = 400
  - Event percentages of the intervention group: 5% to 50%, up to 60% or up to 70%, event percentages of the control group: 50%, 60% and 70% at month 36
  - Significance level $\alpha$ = 2.5% (1-sided test)
  - Shifted null hypothesis (H0: HR ≥ 0.5)
  - Recruitment ratios: 3:1, 1:1 and 1:3 (intervention to comparators)
- Approx. 130 to 172 patients to be expected in the therapeutic indication
- Detectable effects for the endpoint of overall survival: hazard ratio = 0.16 to 0.36 to the advantage of pirtobrutinib over the comparator therapy

On the basis of this indicative consideration of sample size scenarios, it can be assumed that a routine practice data collection for the present research question can be realised with a high degree of probability, taking into account the patients who can be recruited in the therapeutic indication. The final sample size planning is part of the study documents to be prepared (statistical analysis plan, study protocol; see section 1.5).

### 1.4 Evaluations of the data for the purpose of the benefit assessment

The pharmaceutical company shall submit the following evaluations to the G-BA:

- Interim analyses

  Evaluations of 2 interim analyses shall be presented. The relevant times for the performance of the interim analyses shall be the times specified in number 2.3.
  The interim analyses shall be performed according to the specifications in the study protocol and statistical analysis plan. In the process, a check for discontinuation due to futility must also be carried out for each interim analysis.

Implementation of the final sample size estimate in interim analyses:

Based on the first interim analysis, a final sample size estimate will be made on the basis of the more precise effect assumptions that are then possible, insofar as this is already possible on the basis of the recruited subjects. If a final sample size estimate cannot be made at the time of the first interim analysis, this must be explained and justified in a comprehensible manner. In these cases, the final sample size estimate can be presented with the interim analysis in which sufficient recruitment has been achieved for a final sample size estimate. For each further interim analysis in which a final sample size estimate cannot yet be made, the reasons for this must be clearly explained. At the latest at the time of the last interim analysis, a final sample size estimate must be presented on the basis of the more precise effect assumptions that are then possible.

The final sample size estimate can also be carried out at the time of its submission on the basis of endpoints other than those mentioned in the present resolution and taking into account a shifted hypothesis boundary in accordance with the procedure in IQWiG's concept.

The interim analyses shall be prepared on the basis of Module 4 of the dossier template, providing the full texts and study documents.

- Final evaluations for the purpose of the renewed benefit assessment

  The final evaluations shall be carried out according to the specifications in the study protocol and statistical analysis plan. For the transmission of the final evaluations to the G-BA, the time specified in number 3 applies.

The final evaluations shall be prepared in a dossier in accordance with the provisions of Section 9, paragraphs 1 to 7 of the Rules of Procedure (VerfO) of the G-BA.

### 1.5 Requirements for the preparation of the study protocol and statistical analysis plan

The pharmaceutical company shall prepare a study protocol and a statistical analysis plan before carrying out routine practice data collection and evaluations.

With regard to the evaluation of the data, the following information in particular must be presented in advance in the study protocol and statistical analysis plan:

- Information on the statistical methods and models used, as well as naming the procedures and the criteria used in model selection and adaptation
- Information on the expected scope and reasons for missing data, as well as measures to avoid missing data and evaluation strategies to deal with missing data
- Information on dealing with implausible data and outliers
- Information on planned sensitivity analyses
- Information on the start of observation of the patients
- Information on the identification, as well as the adequate, pre-specified adjustment for confounders
- Information on the investigation of potential effect modifiers
- Information on subgroup analyses based on the suitability of CAR-T cell therapy, as well as on subgroup analyses based on the line of therapy

- Information on the use of bridging therapies prior to CAR-T cell therapy and on the management of patients receiving pirtobrutinib as a bridging therapy prior to CAR-T cell therapy
- Information on interim analyses, taking into account the requirements set out in number 1.4 and the specifications in number 2.3
- Information on discontinuation criteria due to futility

## 2. Specifications for reviewing whether the pharmaceutical company have fulfilled their obligation to carry out routine practice data collection and evaluations

### 2.1 Submission of a study protocol as well as the statistical analysis plan to the G-BA for approval

The final drafts for a study protocol and for a statistical analysis plan prepared by the pharmaceutical company shall be submitted to the G-BA for approval by 4 November 2026 at the latest.

The G-BA, with the involvement of IQWiG, carries out a review of the study protocol and the statistical analysis plan and usually communicates the result to the pharmaceutical company in writing within 12 weeks.

Before submitting the requested documents to the G-BA, the pharmaceutical company have the option to request consultation with the G-BA according to Section 35a, paragraph 7 SGB V in conjunction with Section 8 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV). The subject of such consultation is, in particular, the drafts for a study protocol as well as for a statistical analysis plan. In order to enable the pharmaceutical company to adequately consider the aspects addressed in the consultation when preparing the study protocol and statistical analysis plan, the request for consultation must be submitted to the G-BA by 2 July 2026 at the latest.

If the G-BA determine during the first submission of the study protocol and statistical analysis plan that the requirements of routine practice data collection and evaluations have been inadequately implemented, the pharmaceutical company is given the opportunity to revise the study documents once. The G-BA shall adopt a declaratory resolution in this regard in the procedure for routine practice data collection and evaluations, which shall set out the necessary need for adaptation of the study documents. The deadline for submission of the revised statistical analysis plan and study protocol is 4 weeks, unless otherwise specified in the declaratory resolution.

The G-BA may come to the conclusion that the routine practice data collection can be carried out on the basis of the submitted study protocol and statistical analysis plan under the condition that further adaptations to the study documents deemed mandatory for the implementation of the requirements from this resolution must be made.

### 2.2 Submission of information on the course of data collection (in particular information on the recruitment status)

6 months, 18 months and 36 months after the date of commencement of the routine practice data collection to be defined by means of a declaratory resolution, the pharmaceutical company shall provide the G-BA in particular with the information on

- the number and the respective medicinal treatment of the patients enrolled so far,
- patient-related observation periods, and

- any deviations regarding the expected number of

recruitments.

### 2.3 Submission of interim analyses

At the following time points after the date of commencement of the routine practice data collection to be defined by means of a declaratory resolution, interim analyses shall be carried out and corresponding evaluations shall be submitted to the G-BA, taking into account the requirements specified in number 1.4:

- 18 months after the start of routine practice data collection
- 36 months after the start of routine practice data collection

The G-BA carry out a review of the interim analyses with the involvement of the IQWiG.

## 3. Deadline for the submission of evaluations of the data collected as part of the routine practice data collection

For the performance of a renewed benefit assessment, the evaluations of data collected as part of the routine practice data collection must be submitted by 1 May 2031 at the latest.

The submission of these evaluations must be made in the form of a dossier in accordance with the provisions of Chapter 5, Section 9, paragraphs 1 to 7 of the Rules of Procedure (VerfO) of the G-BA, taking into account the requirements of this resolution in accordance with Chapter 5, Section 58 VerfO of the G-BA.

**II. The resolution will enter into force on the day of its publication on the internet on the G-BA website on 4 June 2026.**

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

Berlin, 4 June 2026

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Prof. Hecken