Gemeinsamer Bundesausschuss

Justification

of the Resolution of the Federal Joint Committee (G-BA) on the Amendment of the Pharmaceuticals Directive (AM-RL): 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

Contents

1. Legal basis

According to Section 35a, paragraph 3b, sentence 1 SGB V, the Federal Joint Committee (G-BA) can demand the pharmaceutical company to submit routine practice data collections and evaluations for the purpose of the benefit assessment within a reasonable period of time for the following medicinal products:

1. in the case of medicinal products authorised to be placed on the market in accordance with the procedure laid down in Article 14, paragraph 8 of Regulation (EC) No. 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (OJ L 136 from 30.04.2004, p. 1), as last amended by Regulation 162 Rules of Procedure last revised: 16 December 2020 (EU) 2019/5 (OJ L 4 from 07.01.2019, p. 24), or for which a marketing authorisation has been granted in accordance with Article 14-a of Regulation (EC) No. 726/2004; and
2. for medicinal products approved for the treatment of rare diseases under Regulation No. 141/2000.

2. Key points of the resolution

The active ingredient pirtobrutinib received a conditional marketing authorisation for placing on the market (Article 14-a of Regulation (EC) No. 726/2004, as last amended by Regulation (EU) 2019/5) for the treatment of relapsed or refractory mantle cell lymphoma from the European Commission (EC) on 30 October 2023.

The first listing in the directory services in accordance with Section 131, paragraph 4 SGB V, took place on 15 September 2024.

On the basis of the ongoing or completed studies on pirtobrutinib considered for the marketing authorisation, the G-BA identified gaps in the evidence, particularly for the following aspects relevant to the early benefit assessment, which justify the necessity of routine practice data collection and evaluations according to Section 35a, paragraph 3b, sentence 1 SGB V for the active ingredient pirtobrutinib:

- Data to assess the long-term (additional) benefit and harm of treatment with pirtobrutinib for the approved patient population;
- Comparator data of treatment with pirtobrutinib versus existing therapeutic alternatives for the approved patient population

The marketing authorisation of pirtobrutinib is based on data from the pivotal, open-label, single-arm phase 1/2 BRUIN study (NCT03740529).[1] The BRUIN study investigated pretreated patients with B-cell neoplasms, including mantle cell lymphoma. The BRUIN study did not provide any comparator data on pirtobrutinib versus the current therapy standard.

As part of the post-approval implementation obligations, the pharmaceutical company shall submit the data of the phase-III BRUIN-MCL-321 study (NCT04662255) for confirmation of the efficacy and safety of pirtobrutinib in the treatment of patients with mantle cell lymphoma by 31 December 2026.[2] The BRUIN-MCL-321 study is a randomised, open-label phase III study comparing pirtobrutinib with ibrutinib, acalabrutinib and zanubrutinib, at the principal investigator's discretion, in patients with mantle cell lymphoma who have already received

[1] https://www.clinicaltrials.gov/study/NCT03740529
[2] https://www.clinicaltrials.gov/study/NCT04662255

one or more lines of therapy and have not yet been treated with a BTK inhibitor. The currently approved therapeutic indication for pirtobrutinib covers patients with relapsed or refractory mantle cell lymphoma who have been pretreated with a BTK inhibitor. The BRUIN-MCL-321 study is therefore unlikely to provide any further evidence on patients with mantle cell lymphoma after receiving BTK inhibitor therapy.

In the dossier, the pharmaceutical company presented - as part of the benefit assessment according to Section 35a SGB V - an indirect comparison using Matching-Adjusted Indirect Comparison (MAIC) analysis without a bridge comparator, based on the BRUIN study and the retrospective SCHOLAR-2 observational study. These analyses of aggregated study arms were deemed inappropriate in the benefit assessment.

Furthermore, the literature search conducted as part of the assessment of necessity in publicly accessible study registries for the active ingredient pirtobrutinib did not identify any further comparator studies for the field of indication "treatment of adult patients with relapsed or refractory mantle cell lymphoma who have been pretreated with a BTK inhibitor".

By resolution of 6 November 2025, the G-BA initiated a procedure for the requirement of a routine practice data collection according to Section 35a, paragraph 3b, sentence 1 SGB V for the active ingredient pirtobrutinib.

A concept was drawn up in preparation for the resolution on the requirement of routine practice data collection and evaluations. The concept contains in particular requirements for:

1. the type, duration and scope of data collection,
2. the research question (PICO framework: patient/population, intervention, comparison, outcomes) that is to be the subject of the data collection and evaluations, including the patient-relevant endpoints to be collected,
3. the data collection methods,
4. the evaluations by the pharmaceutical company according to Section 50, paragraph 2 of the VerfO.

The G-BA decides whether to prepare the concept themselves or to commission the Institute for Quality and Efficiency in Health Care (IQWiG) to do so. In the present case, the G-BA commissioned IQWiG to prepare the concept. The expert bodies according to Section 35a, paragraph 3b, sentences 7 and 8 SGB V made a written submission in drawing up the concept. The submission took place in such a way that the expert bodies were given the opportunity in writing to comment on the requirements of routine practice data collection and evaluations in accordance with the concept that had been drawn up. In addition, expert consultation was held.

In preparing the concept, ongoing and planned data collections were taken into account, especially those resulting from conditions or other ancillary provisions imposed by the marketing authorisation or licensing authorities.

Due to the aforementioned limitations, the G-BA classifies the studies commissioned by the regulatory authority as being unsuitable for improving the existing body of evidence sufficiently for the purpose of the benefit assessment.

Based on the above-mentioned research question, the G-BA, on the basis of IQWiG's concept and the involvement of the expert bodies in drawing up the concept, decided by the present resolution on the requirements of routine practice data collection and evaluations, as well as on the specifications for the review of the obligation to perform and on the deadline for the submission of evaluations.

2.1 Requirements for routine practice data collection and evaluations

2.1.1 Research question according to PICO scheme

Patient population

According to the marketing authorisation, the target population for the active ingredient pirtobrutinib comprises adult patients with relapsed or refractory mantle cell lymphoma (MCL) who have been pretreated with a Bruton's tyrosine kinase (BTK) inhibitor.

For the present requirement of routine practice data collection and evaluations according to Section 35a, paragraph 3b, sentence 1 SGB V, the pharmaceutical company shall collect and evaluate comparator data for the patient population of adults with relapsed or refractory mantle cell lymphoma who have been pretreated with a Bruton's tyrosine kinase inhibitor.

In a comparator study without randomisation, the comparability of the study populations or the fulfilment of positivity for the therapy options to be compared must be given. The eligibility criteria for treatment with pirtobrutinib should therefore be applied when defining the inclusion and exclusion criteria for the routine practice data collection and evaluations.

Intervention

The intervention includes the active ingredient pirtobrutinib in line with the present requirement of routine practice data collection and evaluations according to Section 35a, paragraph 3b, sentence 1 SGB V. The marketing authorisation and the dosage information in the product information for pirtobrutinib (Jaypirca) must be taken into account.

Comparator therapy

The following criteria were applied:

1. To be considered as a comparator therapy, the medicinal product must, principally, have a marketing authorisation for the therapeutic indication.
2. If a non-medicinal treatment is considered as a comparator therapy, this must be available within the framework of the SHI system.
3. As comparator therapy, medicinal products or non-medicinal treatments for which the patient-relevant benefit has already been determined by the G-BA shall be preferred.
4. According to the generally recognised state of medical knowledge, the comparator therapy should be part of the appropriate therapy in the therapeutic indication.

On 1. In addition to pirtobrutinib, the following active ingredients are approved for the treatment of relapsed or refractory mantle cell lymphoma: Brexucabtagene autoleucel, lisocabtagene maraleucel, ibrutinib, lenalidomide and temsirolimus. Bendamustine, bleomycin, carmustine, chlorambucil, cyclophosphamide, cytarabine, dexamethasone, doxorubicin, etoposide, ifosfamide, methotrexate, mitoxantrone, prednisone, prednisolone, trofosfamide, vinblastine and vincristine have been granted the marketing authorisation for the treatment of non-Hodgkin lymphoma.

On 2. Allogeneic stem cell transplant, autologous stem cell transplant as well as radiotherapy are considered as non-medicinal therapy options in the present therapeutic indication.

On 3. The following resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V are available:

- Pirtobrutinib (resolution of 7 August 2025)
- Autologous anti-CD19-transduced CD3+ cells (resolution of 5 August 2021)
- Ibrutinib (resolution of 21 July 2016)

- Pixantrone (resolution of 16 May 2013)

Annex VI to Section K of the Pharmaceuticals Directive - Prescribability of approved medicinal products in non-approved therapeutic indications (so-called off-label use):

- Use of fludarabine in low or intermediate malignant B-non-Hodgkin lymphoma (B-NHL) other than chronic lymphocytic leukaemia (CLL) as specified in the marketing authorisation
- Rituximab in mantle cell lymphoma

On 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as systematic reviews of clinical studies in the present therapeutic indication.

The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were also involved in writing on questions relating to the comparator therapy in the present indication according to Section 35a, paragraph 7 SGB V (see "Information on Comparator Therapy"). Written statements from the German Society for Haematology and Medical Oncology (DGHO) as well as the AkdÄ were available.

The evidence on the therapy standard for the treatment of relapsed or refractory mantle cell lymphoma after at least one prior therapy including a BTK inhibitor is extremely limited. Various therapy options are mentioned in the present guidelines, whereby reference is made to an individualised treatment decision depending, among others, on the response and duration of remission of the previous treatments as well as the general condition. It is not possible to derive a treatment option that can be considered as the therapy standard for all patients in the present therapeutic indication.[3,4,5]

In the present therapeutic indication, the active ingredients ibrutinib, pirtobrutinib, temsirolimus, lenalidomide as monotherapy, brexucabtagene autoleucel and lisocabtagene maraleucel are explicitly approved as well as rituximab in combination with fludarabine, cyclophosphamide and mitoxantrone (R-FCM), rituximab in combination with cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP) and rituximab in combination with bendamustine (R-bendamustine) can be prescribed in off-label use in accordance with Annex VI of the Pharmaceuticals Directive.

Pirtobrutinib represents the intervention of the routine practice data collection and can therefore be ruled out as a comparator.

Since the patient population in the present therapeutic indication includes patients who have already received a BTK inhibitor, ibrutinib can only be considered as a therapy option for those patients who have not received prior ibrutinib therapy or in whom a relapse occurs after a longer treatment-free interval following prior ibrutinib therapy.

3 Eyre TA et al. Diagnosis and management of mantle cell lymphoma: a British Society for Haematology guideline. Br J Haematol 2024;204(1):108-126.

4 Alberta Health Services (AHS). Lymphoma [online]. Edmonton (CAN): AHS; 2019. (Clinical practice guideline; volume LYHE-002 V20).

5 National Comprehensive Cancer Network (NCCN). B-cell lymphoma: NCCN evidence blocks; version 3.2022 [online]. Plymouth Meeting (USA): NCCN; 2022.

Brexucabtagene autoleucel and lisocabtagene maraleucel are only approved after two prior therapies and are only considered for patients with a sufficiently good general condition.

The G-BA determines lisocabtagene maraleucel as component of the comparator for the routine practice study, taking into account the required duration of the routine practice data collection, during which a new situation may arise in the present therapeutic indication according to the generally recognised state of medical knowledge. In principle, this is to be considered separately from the determination of the appropriate comparator therapy, which only becomes legally binding with the resolution on the benefit assessment according to Section 35a, paragraph 3 SGB V.

No clear therapy recommendation on lenalidomide as monotherapy and temsirolimus can be derived from the available guidelines and further literature. By G-BA's resolution of 21 July 2016, an indication of a considerable additional benefit of ibrutinib compared to temsirolimus in adults with relapsed or refractory mantle cell lymphoma was found. Lenalidomide monotherapy is considered a therapy option in the German healthcare context.[6]

According to the available evidence, a repeat immunochemotherapy in the form of R-FCM, R-CHOP or R-bendamustine is only indicated for adults with a late relapse. R-FCM is also an intensive therapy which, among others, due to myelotoxicity, can only be considered as a therapy option for patients with a sufficiently good general condition. R-bendamustine is a treatment option for adults with a reduced general condition.

The above-mentioned limitations on the use of approved therapy options or those that can be prescribed in off-label use in accordance with Annex VI to the Pharmaceuticals Directive mean that these therapy options cannot be used to provide individualised therapy for all patients covered by this therapeutic indication after at least one prior therapy including a BTK inhibitor, or that these therapy options cannot be considered for relevant patient groups. In addition, the above-mentioned treatment options are no longer considered for adults with more than one prior therapy if they have already been used in an earlier line of therapy.

The present guidelines, the written statements of the AkdÄ and the DGHO and further literature recommend the following further individualised treatment options, which are put to off-label use and for which there is significant evidence from single-arm studies:

- Lenalidomide + rituximab[7]
- VRCAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, prednisone)[8,9]
- R-BAC (rituximab + bendamustine + cytarabine)[10]

6 Onkopedia guideline of the DGHO, Mantle cell lymphoma, last revised June 2023 [online].

7 Wang M et al. Lenalidomide in combination with rituximab for patients with relapsed or refractory mantle-cell lymphoma: a phase 1/2 clinical trial. Lancet Oncol. 2012 Jul;13(7):716-23. doi: 10.1016/S1470-2045(12)70200-0. Epub 2012 Jun 6. PMID: 22677155.

8 Robak T et al; LYM-3002 investigators. Frontline bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone (VR-CAP) versus rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) in transplantation-ineligible patients with newly diagnosed mantle cell lymphoma: final overall survival results of a randomised, open-label, phase 3 study. Lancet Oncol. 2018 Nov;19(11):1449-1458.

9 Fisher RI et al. Multicentre phase II study of bortezomib in patients with relapsed or refractory mantle cell lymphoma. J Clin Oncol. 2006 Oct 20;24(30):4867-74. doi: 10.1200/JCO.2006.07.9665. Epub 2006 Sep 25. PMID: 17001068.

10 McCulloch R et al. Efficacy of R-BAC in relapsed, refractory mantle cell lymphoma post BTK inhibitor therapy; Br J Haematol. 2020 May;189(4):684-688. doi: 10.1111/bjh.16416. Epub 2020 Feb 3.

– Venetoclax.[11]

The available evidence shows that lenalidomide is also a relevant treatment option in combination with rituximab on a patient-individual basis due to higher response rates.

According to the German healthcare context, venetoclax monotherapy is generally suitable for patients who have already received a BTK inhibitor.[5]

According to the generally recognised state of medical knowledge, it can be determined in the overall assessment that the off-label use of the above-mentioned therapy options for relevant patient groups of the present therapeutic indication as part of individualised therapy shall generally be preferred to the medicinal products, which were previously approved in the therapeutic indication; Section 6, paragraph 2, sentence 3, number 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV).

Autologous or allogeneic stem cell transplant is primarily performed in the first or second line of therapy. However, this can also be considered in the present treatment setting for patients who have not yet received a stem cell transplant, if they show a good response and an appropriate general condition. If autologous stem cell transplant was previously performed, allogeneic stem cell transplant should be considered in the case of relapse with corresponding suitability. High-dose therapy with autologous or allogeneic stem cell transplant is therefore considered a relevant therapy option in the context of patient-individual therapy.

Outcome

For the patient population required here, comparator data shall be collected on the following endpoint categories for routine practice data collection in accordance with Section 35a, paragraph 3b, sentence 1 SGB V: mortality, morbidity, health-related quality of life and side effects.

The main therapeutic goal in the present therapeutic indication is the prolongation of overall survival. The assessment of overall survival in the registry study is therefore of great importance for the comparison of pirtobrutinib with individualised therapy in the comparator arm.

In addition, patient-reported endpoints on morbidity as well as health-related quality of life are to be collected with specifically validated tools at uniform data collection time points. The questionnaire of the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core-30 (EORTC-QLQ-C30) in conjunction with the EORTC QLQ-NHL-High Grade 29 module can preferably be used for this purpose.

The EMCL registry has not yet provided for the collection of PRO data (symptomatology and health-related quality of life) by default; however, according to the registry operators, this can be carried out on a project-by-project basis in line with the approach taken in the RPDC for brexucabtagene autoleucel. In the long term, PRO data should be collected by default at the start of a line of therapy and once a year, for example, through the establishment of a patient portal with direct contact of the patients.

For the RPDC, it is essential that the PRO assessment begins at the start of the observation, with fixed data collection time points established several times a year over the entire duration of the RPDC. In this context, an assessment frequency that is adjusted over the course of the study should be chosen (with shorter assessment intervals at the start and longer intervals

11 Eyre, T.A. et al. Efficacy of venetoclax monotherapy in patients with relapsed, refractory mantle cell lymphoma after Bruton tyrosine kinase inhibitor therapy. Haematologica 2018, 104, 68–71.

later on) in order to reduce the burden caused by frequent assessments. An assessment in line with the approach taken in the RPDC for brexucabtagene autoleucel would therefore be appropriate.

The selection of appropriate tools to collect patient-reported endpoints on symptomatology and health-related quality of life in the routine practice data collection for pirtobrutinib should be outlined when preparing the study protocol and statistical analysis plan.

With regard to side effects, the overall rates of serious adverse events (SAEs), severe adverse events and discontinuation due to adverse events should be shown.

In doing so, SAEs should be operationalised as adverse events (AEs) which lead to hospitalisation or prolong an existing hospitalisation, or lead to death.

In addition, defined specific adverse events should be collected (with indication of the respective severity grade).

The specific AEs should address both pirtobrutinib and the comparator therapies and ideally be coded using the MedDRA system.

According to the product information available for the intervention and comparators, relevant specific adverse events in the present therapeutic indication may be, for example, the following:

- Haemorrhages
- Cardiac disorders
- Infections

Specific aspects that may need to be considered in the implementation of routine practice data collection and evaluations due to a different side effect profile between the intervention and comparator groups can be addressed by the pharmaceutical company when preparing the study protocol and statistical analysis plan. Overall, the G-BA considers it feasible to collect the endpoints of side effects at the observation time points resulting from healthcare for the intervention and comparator groups without relevant effects of risk of bias that significantly limit the interpretability of the data.

2.1.2 Type and methods of data collection

According to Section 35a, paragraph 3b SGB V, the Federal Joint Committee can demand indication-related data collection without randomisation for routine practice data collection.

For the present requirement of routine practice data collection, indication registries that meet the requirements for routine practice data collection and at least fulfil the quality criteria specified in the resolution shall be used as the data source. The minimum data quality requirements mentioned are based on the national and international quality criteria for registries mentioned in the IQWiG concept, whereby the focus was on the quality criteria for standardisation and validity of data collection, which were considered particularly relevant for the present requirement, as well as for sample collection.

In order to ensure the suitability of the collected data, the use of an indication registry is also required in which treatment of relapsed or refractory mantle cell lymphoma is carried out according to German daily care or is sufficiently similar to healthcare in Germany. The guarantee of sufficiently similar healthcare in Germany, which is required when using (indication) registries, should make it possible to integrate data from other European countries without compromising data quality. If there are relevant differences in the standard of care in another country, registry data from this country should not be used for the present routine practice data collection and evaluations.

Based on the available information, the EMCL registry is suitable as the primary data source for a routine practice data collection, provided that the still existing limitations are eliminated. The adaptations required for the routine practice data collection relate in particular to the following aspects in accordance with the IQWiG concept[4]:

- Adoption of the methodological approaches already used in the RPDC for brexucabtagene autoleucel and deemed appropriate
- A sufficiently representative sample of patients registered in the EMCL registry for the patient population of interest
- Selection of uniform data collection and reporting time points for both treatment groups
- Implementation of the collection of patient-reported endpoints on symptomatology and health-related quality of life
- Establishment of fixed data collection time points several times a year over the entire duration of the RPDC
- Extension of data collection to include a standardised and mandatory assessment of AEs at fixed data collection time points
- Carrying out a source data verification

For the enrolment in the study and the start of observation of the patients, the time of the treatment decision should be chosen based on an intention-to-treat principle.

It can be assumed that the necessary data are collected as part of the ongoing RPDC for brexucabtagene autoleucel to a sufficient extent and at adequate quality. Consequently, the use of retrospective data for the control group of the RPDC for pirtobrutinib is basically possible. However, it should be noted that the RPDC for brexucabtagene autoleucel only comprises patients with relapsed or refractory mantle cell lymphoma, who have already received 2 or more systemic therapies (including BTK inhibitor therapy) and are eligible for CAR-T cell therapy. The data available to date do not depict patients in the second-line setting and/or those who are ineligible for CAR-T cell infusion.

In summary, the study design for pirtobrutinib requires a non-randomised comparator deemed appropriate for the study design. The routine practice data collection should preferably be carried out as a platform registry study in the EMCL registry.

If a comparator registry study is therefore infeasible for the present requirement of routine practice data collection and evaluations due to the required adaptations to the EMCL registry, a comparator study using a data platform to be set up specifically for the present routine practice data collection (study-specific data collection) is required as an alternative. All requirements described in the resolution for the routine practice data collection and evaluations must be taken into account in the same way when using a data platform to be set up specifically for the present routine practice data collection (study-specific data collection), unless specified otherwise.

2.1.3 Duration and scope of data collection

The duration and scope of routine practice data collection result from the estimated suitable patient-related duration of observation and the estimated required patient number (sample size).

The aim of the routine practice data collection is to determine the long-term benefits and harms of treatment with pirtobrutinib compared to the comparator therapy. A key therapeutic goal in mantle cell lymphoma is to increase overall survival.

A duration of observation of 36 months was assumed in the IQWiG concept. In the studies in the therapeutic indication, the median survival time was between 9.7 and 46.4 months with median durations of observation between 23.5 and 47.5 months. In order to observe sustained effects in the endpoint of overall survival, patients should be followed up for at least 36 months as part of the routine practice data collection.

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.

The effects of an endpoint, in this case overall survival, which was evaluated by means of time-to-event analyses, were calculated; these effects can be detected with a power of 80% for the patient numbers estimated in the present therapeutic indication. Three sample sizes were used: N = 200, N = 300 and N = 400. Based on the available data, percentages of deceased patients - 50%, 60% and 70% - at month 36 were assumed for the control group. For the intervention group, the resulting event percentages were assumed to be between 5% and 50%, up to 60% and up to 70% respectively.

In addition, the significance level $\alpha = 2.5\%$ (1-sided test) and a shifted null hypothesis (H0: HR ≥ 0.5) were assumed. The indicative consideration of the sample size for routine practice data collection of pirtobrutinib is based on the assumptions of Cox regression, in particular the assumption of proportional hazards. Recruitment ratios of 3:1, 1:1 and 1:3 between intervention and comparator therapy were considered.

Approximately 130 to 172 patients were expected in the present therapeutic indication. This results in detectable effects for the endpoint of overall survival with a hazard ratio of 0.16 to 0.36 to the advantage of pirtobrutinib over the comparator therapy.

2.1.4 Evaluations of the data collection for the purpose of the benefit assessment

The general requirements for the evaluation of comparator studies without randomisation must correspond to the planning of the evaluation of comparator studies with randomisation. The information given in the resolution must be taken into account when drawing up the study protocol and statistical analysis plan prior to carrying out the routine practice data collection (see also Section 2.1.5).

The evaluation of data from different data sources, i.e. different registries, should be done separately for each data source.

The G-BA assumes that, under the above-mentioned conditions, in addition to data on pirtobrutinib collected in parallel and the comparator therapy, data on pirtobrutinib that have not been collected in parallel and the comparator therapy, i.e. registry data that have already been collected since the marketing authorisation of the active ingredients pirtobrutinib and in particular brexucabtagene autoleucel, can also be used for the present requirement of routine practice data collection. The evaluation of data collected in parallel and data not collected in parallel should be done separately. The same applies to the use of data from different data sources, i.e. different registries. Here, too, an evaluation should be carried out separately for each registry.

Additional pooled analysis is possible after checking the suitability of data from different data sources. Information on the verification of suitability for pooled analysis should be presented accordingly in advance in the statistical analysis plan.

The pharmaceutical company shall perform the evaluations mentioned in the resolution (interim analyses and final evaluation) according to the specifications in the study protocol and the statistical analysis plan. The interim analyses shall be prepared on the basis of Module 4 of the dossier template with provision of the full texts and study documents, the final evaluations shall be prepared in a dossier in accordance with the provisions in Section 9, paragraphs 1 to 7 of the Rules of Procedure of the G-BA. The relevant times for conducting the interim analyses are the times specified in the resolution under number 2.3 and for submitting the final evaluations to the G-BA the time specified in the resolution under number 3.

In order to assess the duration and scope of the routine practice data collection, an indicative consideration of sample size scenarios, which show the feasibility of the RPDC with a high degree of probability, was carried out in the present procedure. The assessment takes into account the approved therapeutic indication for pirtobrutinib, which also covers later lines of therapy for mantle cell lymphoma, in which patients have already been pretreated with CAR-T cell therapies, and the comments made by the clinical experts in the expert consultation regarding the achievable effects in this treatment setting. The G-BA considers it expedient for the pharmaceutical company to carry out sample size planning in the course of the study. If applicable, this can also be carried out at this time on the basis of endpoints other than those mentioned in the present resolution and taking into account a shifted hypothesis boundary.

2.1.5 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. In this respect, the requirements for the information to be presented as described in the resolution shall be taken into account.

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

Taking into account the time frame required for drafting, the pharmaceutical company shall submit the final drafts of a study protocol and a statistical analysis plan 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.

In order to be able to clarify queries during the preparation of the final drafts for a study protocol as well as for a statistical analysis plan, the pharmaceutical company have the possibility - before submitting the requested documents to the G-BA - 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). 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 02.07.2026 at the latest.

According to Section 35a, paragraph 3b, sentence 10 SGB V, the data obtained and the obligation to collect data must be reviewed by the G-BA at regular intervals, but at least every 18 months.

With regard to the information on the course of data collection (in particular information on the status of recruitment), the pharmaceutical company shall provide the G-BA with information on the number and the respective medicinal treatment of the patients included to date, on patient-related observation periods and on possible deviations with regard to the expected number of recruits at intervals of 18 months.

The subject of the continuous review of the data obtained is in particular the question of whether the data collection is carried out or not, or can no longer be carried out. The pharmaceutical company shall submit two interim analyses to the G-BA 18 and 36 months after the date of commencement of the routine practice data collection to be defined by means of a declaratory resolution.

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.

If applicable, 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.

2.3 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 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.

3. Bureaucratic costs calculation

The proposed resolution does not create any new or amended information obligations for care providers within the meaning of Annex II to Chapter 1 VerfO and, accordingly, no bureaucratic costs.

4. Process sequence

In order to prepare a recommendation for a resolution on the initiation of a procedure for the requirement of a routine practice data collection (amendment of Annex XII of AM-RL) according to Section 35a, paragraph 3b SGB V, the Subcommittee on Medicinal Products commissioned a working group (WG routine practice data collection (RPDC)) consisting of the members nominated by the leading organisations of the care providers, the members nominated by the National Association of Statutory Health Insurance Funds, and the representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions. In addition, the competent higher federal authority, the Paul Ehrlich Institute, was involved in the consultation to assess the requirement of a routine practice data collection according to Section 35a, paragraph 3b, sentence 1 SGB V.

The recommended resolution on the initiation of a procedure for the requirement of a routine practice data collection was discussed at the Subcommittee's session on 28 October 2025 and the draft resolution was approved.

At their session on 6 November 2025, the plenum resolved to initiate a procedure for the requirement of a routine practice data collection.

In conjunction with the resolution of 6 November 2025 regarding the initiation of a procedure for the requirement of a routine practice data collection, the G-BA commissioned IQWiG to scientifically develop a concept for routine practice data collection and evaluations for the purpose of drafting a resolution.

IQWiG's concept was submitted to the G-BA on 6 February 2026. On 27 January 2026, the written submission of the expert bodies according to Section 35a, paragraph 3b, sentences 7 and 8 SGB V was initiated. The deadline for making the written submission was 9 March 2026.

The expert consultation within the framework of the submission by the expert bodies took place on 23 March 2026.

The evaluation of the written submissions received and of the expert consultation was discussed at the Subcommittee's session on 27 May 2026, and the draft resolution was approved.

At their session on 4 June 2026, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
WG RPDC	12 September 2022 7 August 2025 4 September 2025 20 October 2025	Consultation on the initiation of a procedure for the requirement of a routine practice data collection (amendment of Annex XII of the AM-RL)
Subcommittee on Medicinal Products	28 October 2025	Concluding discussion of the draft resolution
Plenum	6 November 2025	Resolution on the initiation of a procedure for the requirement of a routine practice data collection (amendment of Annex XII of the AM-RL)
WG RPDC	16 March 2026	Information on written submissions received, preparation of the expert consultation
Subcommittee on Medicinal Products	23 March 2026	Implementation of the expert consultation
WG RPDC	2 April 2026 13 April 2026 7 May 2026	Consultation on IQWiG's concept and on the specifications for the review of the obligation to conduct and submit evaluations, evaluation of the submission procedure
Subcommittee on Medicinal Products	27 May 2026	Concluding discussion of the draft resolution
Plenum	4 June 2026	Resolution on the requirement of a routine practice data collection (amendment of Annex XII of the AM-RL)

Berlin, 4 June 2026

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

Prof. Hecken