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 Epcoritamab (relapsed or refractory diffuse large B-cell lymphoma); requirement of routine practice data collection and evaluations

of 17 July 2025

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, 30.4.2004, p. 1), as last amended by Regulation 162 Rules of Procedure last revised: 16 December 2020 (EU) 2019/5 (OJ L 4, 7.1.2019, 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 epcoritamab (Tepkinly) received a conditional marketing authorisation from the European Commission (EC) on 22 September 2023 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 adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy. The first listing in the directory services in accordance with Section 131, paragraph 4 SGB V, took place on 15 October 2023.

In addition, the active ingredient epcoritamab was approved as a medicinal product for the treatment of rare diseases (orphan drug) under Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999. On 19 July 2024, upon application by the pharmaceutical company, the orphan designation for the medicinal product Tepkinly with the active ingredient epcoritamab was deleted from the Community Register of Orphan Drugs.

On the basis of additional ongoing or completed studies on epcoritamab underlying the marketing authorisation application, 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 epcoritamab:

- Data to assess the long-term (additional) benefits and harms of treatment with epcoritamab for the approved sub-population of adults with relapsed or refractory DLBCL after at least 2 lines of systemic therapy who are not eligible for CAR-T cell therapy and stem cell transplantation;
- comparator data of treatment with epcoritamab versus existing therapeutic alternatives for the approved sub-population of adults with relapsed or refractory DLBCL after at least 2 lines of systemic therapy who are not eligible for CAR-T cell therapy and stem cell transplantation;

By resolution of 16 January 2025, the G-BA initiate 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 epcoritamab.

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 decide whether to prepare the concept itself 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. A review of the ongoing or planned interventional studies on epcoritamab commissioned by the regulatory authority has shown that no comparator data versus the current comparator therapy are likely to be collected as part of the obligation to carry out post-authorisation measures.

The final data from the EPCORE DLBCL-1 study must be submitted as part of the conditional marketing authorisation.[1,2] The randomised, open-label phase III EPCORE DLBCL-1 study (NCT04628494) investigates adults with relapsed or refractory DLBCL who have received at least one prior systemic antineoplastic therapy and who have not tolerated or are not eligible for autologous stem cell transplantation. Patients are treated either with epcoritamab or with a chemotherapy of the principal investigator's choice (rituximab + gemcitabine + oxaliplatin (R-GemOx) or bendamustine + rituximab (BR)). The EPCORE DLBCL-1 study is therefore not expected to provide any direct comparator data versus the current therapy standard.

The final data from the pivotal EPCORE™ NHL-1 study (NCT03625037) are an additional requirement of the conditional marketing authorisation.[3] The single-arm EPCORE™ NHL-1 study investigated adults with different disease entities of relapsed/ refractory B-cell lymphoma. As this is a non-comparator study design, no data on epcoritamab versus the current therapy standard will be available.

Due to the aforementioned limitations, the G-BA classify 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

[1] https://clinicaltrials.gov/study/NCT04628494?intr=epcoritamab&cond=Diffuse%20Large%20B-Cell%20Lymphoma&rank=4
[2] https://www.ema.europa.eu/en/documents/assessment-report/tepkinly-epar-public-assessment-report_en.pdf
[3] https://www.clinicaltrials.gov/study/NCT03625037

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 epcoritamab comprises adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) after two or more lines of systemic therapy. For the present requirement of routine practice data collection and evaluations in accordance with Section 35a, paragraph 3b, sentence 1 SGB V, the pharmaceutical company should collect and analyse comparator data for the patient population of adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), after two or more lines of systemic therapy, who are not eligible for CAR-T cell therapy and stem cell transplantation.

In order to be able to clearly delimit the required patient population, criteria for the demarcation of patients who are not eligible for CAR-T cell therapy and stem cell transplantation must be identified and collected as part of the routine practice data collection.

Intervention

In accordance with the present requirement of routine data collection and evaluations according to Section 35a, paragraph 3b, sentence 1 SGB V, the intervention includes the active ingredient epcoritamab. The marketing authorisation and the dosage information in the product information for epcoritamab (Tepkinly) 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 epcoritamab, the following active ingredients are approved for the present therapeutic indication:

Bleomycin, cyclophosphamide, cytarabine, dexamethasone, doxorubicin, etoposide, glofitamab, ifosfamide, melphalan, methotrexate, methylprednisolone, mitoxantrone, odronextamab, polatuzumab vedotin, prednisolone, prednisone, tafasitamab, trofosfamide, vinblastine, vincristine, vindesine, rituximab, loncastuximab tesirine, axicabtagene ciloleucel, lisocabtagene maraleucel and tisagenlecleucel.

Some of the medicinal products listed have a marketing authorisation for the superordinate therapeutic indication "non-Hodgkin lymphoma". The marketing

authorisations are partly linked to (specified) concomitant active ingredients or do not fully cover the present therapeutic indication.

On 2. In principle, autologous or allogeneic stem cell transplantation can be considered as a non-medicinal treatment for relapsed or refractory DLBCL. In addition, radiotherapy can be administered, for example, to treat localised residual manifestations of the lymphoma after completion of chemotherapy.

On 3. Resolutions on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V:

- Epcoritamab (resolution of 4 April 2024 and 17 April 2025)
- Tisagenlecleucel (resolution of 15 February 2024)
- Glofitamab (resolution of 1 February 2024)
- Axicabtagene ciloleucel (resolution of 21 December 2023)
- Loncastuximab tesirine (resolution of 2 November 2023)
- Lisocabtagene maraleucel (resolution of 6 April 2023)
- Tafasitamab (resolution of 3 March 2022)
- Polatuzumab vedotin (resolution of 20 June 2024)
- Pixantrone (resolution of 16 May 2013)

Directive on Inpatient Treatment Methods (last revised 7 December 2022: allogeneic stem cell transplantation for aggressive B-non-Hodgkin lymphomas):

- Section 4 Excluded methods: Allogeneic stem cell transplantation in adult patients with aggressive B-non-Hodgkin lymphoma who have not yet been treated with autologous stem cell transplantation (exceptions: a) patients who have a very high risk of recurrence and who achieve a response at least in the sense of stable disease after salvage therapy; b) patients in whom sufficient stem cell harvesting for autologous stem cell transplantation was not possible and who achieve a response at least in the sense of stable disease after salvage therapy).
- Annex I - Methods required for hospital care: Allogeneic stem cell transplantation in adult patients with aggressive B-cell non-Hodgkin lymphomas who relapse after autologous stem cell transplantation and achieve a response at least in the sense of stable disease after salvage therapy.

On 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as 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"). A written statement from the German Society for Haematology and Medical Oncology (DGHO) is available.

Among the approved active ingredients listed under 1), only certain active ingredients named below will be included in the comparator therapy, taking into account the evidence on therapeutic benefit, the guideline recommendations and the reality of care.

Overall, the evidence on treatment options for the present advanced treatment setting of relapsed or refractory DLBCL after at least two lines of therapy is limited.

The present research question of routine practice data collection relates to patients who are not eligible for CAR-T cell therapy and stem cell transplantation due to the course of their disease or their general condition. A therapy with curative intent is not

indicated for these patients. According to the guidelines and statement of the German Society for Haematology and Medical Oncology (DGHO) and the German Lymphoma Alliance (GLA) in the benefit assessment procedure for epcoritamab (resolution of 17 April 2025), various chemo- and chemoimmunotherapies as well as newer substances represent therapy options for these patients.

The antibody-drug conjugate polatuzumab vedotin is approved in combination with bendamustine and rituximab (Pola-BR) for the treatment of adults with relapsed or refractory DLBCL if they are ineligible for haematopoietic stem cell transplantation. By resolution of 20 August 2020, a hint for a non-quantifiable additional benefit of polatuzumab vedotin over bendamustine in combination with rituximab was identified within the scope of a first orphan drug assessment since the scientific data did not allow quantification. As part of a new benefit assessment because of exceeding the EUR 30 million turnover limit, the additional benefit of polatuzumab vedotin was determined as not proven by resolution of 20 June 2024.

The CD19-specific antibody tafasitamab is approved in combination with lenalidomide for the treatment of patients with relapsed or refractory DLBCL for who are ineligible for autologous stem cell transplantation. By resolution of 3 March 2022, a hint for a non-quantifiable additional benefit of tafasitamab was identified within the scope of an orphan drug assessment since the scientific data did not allow quantification.

According to the statements of the clinical experts in the written statement procedure for epcoritamab (resolution of 17 April 2025), radiotherapy is not an adequate comparator therapy in the present therapeutic indication and is only used palliatively for local disease control in exceptional cases.

The combination chemotherapies CEOP (cyclophosphamide, etoposide, vincristine, prednisone) and EPOCH (etoposide, vincristine, doxorubicin, cyclophosphamide, prednisone) are also approved for this indication. From the statements of the clinical experts in the benefit assessment procedure for loncastuximab tesirine, it emerged that the combination chemotherapies mentioned have no relevant significance in the present treatment setting - especially as the combination therapies mentioned or the active ingredients contained in these combination therapies have already been used previously within the therapeutic sequence. The combination therapies mentioned are not determined as a comparator therapy.

The active ingredients loncastuximab tesirine and glofitamab are further treatment options in the present therapeutic indication. For loncastuximab tesirine, it was determined by the G-BA's resolution of 2 November 2023 that an additional benefit is not proven, as no suitable data were available to enable an assessment of the additional benefit. By resolution of 1 February 2024, a hint for a non-quantifiable additional benefit of glofitamab was identified within the scope of an orphan drug benefit assessment since the scientific data did not allow quantification.

The active ingredient odronextamab is a new treatment option in the present therapeutic indication. The active ingredient was only recently approved (marketing authorisation on 22 August 2024). The medicinal product with the active ingredient odronextamab has not yet been placed on the market in Germany.

According to the statements of the clinical experts in the submission procedure, the bispecific antibodies and the antibody-drug conjugate loncastuximab tesirine represent relevant therapy options in the present therapeutic indication.

The G-BA determine loncastuximab tesirine, glofitamab and odronextamab as components 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 with regard to the generally accepted state of medical knowledge in the present therapeutic indication. 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.

In the overall assessment of the treatment options used in medical treatment practice, an individualised therapy with the selection of polatuzumab vedotin in combination with bendamustine and rituximab, tafasitamab in combination with lenalidomide, odronextamab, loncastuximab tesirine and glofitamab is determined as the comparator therapy for the present routine practice data collection for adults with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), after two or more lines of systemic therapy, who are not eligible for CAR-T cell therapy and stem cell transplantation.

Individualised therapy is based on the assumption that several treatment options, which allow an individualised medical treatment decision, are available.

Outcome

Comparator data on the following endpoint categories shall be collected for the patient population required here 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 survey of overall survival in the registry study is therefore of great importance for the comparison of epcoritamab 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 instruments 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 selection of appropriate instruments to collect patient-reported endpoints on symptomatology and health-related quality of life in the epcoritamab routine practice data collection should be outlined during the development of the study protocol and statistical analysis plan.

The overall rates of serious adverse events (SAEs) should be mapped. In doing so, SAEs should be operationalised as adverse events (AEs) which lead to hospitalisation or prolong an existing hospitalisation, or lead to death. Furthermore, the overall rate of therapy discontinuation due to adverse events should be collected. In addition, defined specific adverse events should be collected (with indication of the respective severity grade). According to the product information for the intervention and comparators, relevant specific adverse events in the present therapeutic indication may be, for example, the following:

- Cytokine Release Syndrome (CRS)
- Neurological toxicities including immune effector cell-associated neurotoxicity syndrome (ICANS)
- Serious/ severe infections
- Serious/ severe cytopenias (anaemia, leukopenia, thrombocytopenia)
- Serious/ severe neutropenia
- Tumour Lysis Syndrome (TLS)

- Serious/ severe tumour flare
- Serious/ severe effusion or serious/ severe oedema
- Serious/ severe phototoxicity
- Serious/ severe cardiac disorders.

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 placed on the quality criteria for standardisation and validity of data collection, as well as for sample collection, which were considered particularly relevant for the present requirement.

In order to ensure the suitability of the data collected, the use of an indication registry is also required in which treatment of DLBCL is carried out in accordance with German daily care or is sufficiently similar to care in Germany.

The guarantee of sufficiently similar care 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 German Lymphoma Alliance (GLA) as well as the RUBIN registry may be suitable as primary data sources for routine practice data collection, provided that the still existing limitations are eliminated. The adaptations required for the routine practice data collection refer in particular to the following aspects in accordance with the IQWiG[4] concept:

- GLA registry
    - Collection of adverse events
    - Assessment of patient-reported endpoints on symptomatology and health-related quality of life
    - Uniform assessment and reporting dates
    - Definition of further inclusion and exclusion criteria for the clear demarcation of the patient population relevant to the research question
    - Supplementing the measures to ensure the accuracy of the data (introduction of source data verification based on a sample of, e.g. 10% of the data records)
- RUBIN registry
    - Collection of adverse events
    - Assessment of patient-reported endpoints on symptomatology and health-related quality of life

[4] IQWiG A25-07: RPDC concept – Epcoritamab (DLBCL)

- Definition of further survey time points for the patient-reported endpoints
- Definition of further inclusion and exclusion criteria for the clear demarcation of the patient population relevant to the research question
- Supplementing the measures to ensure the accuracy of the data (introduction of source data verification based on a sample of, e.g. 10% of the data records)

The G-BA recommends conducting the routine practice data collection as an adaptive platform registry study as routine practice data collection is also required for the active ingredients odronextamab and loncastuximab tesirine (resolutions of 18 July 2025) in the present therapeutic indication. It is recommended preparing a master protocol for this purpose, which can be used for all three data collections and can be supplemented with active ingredient-specific appendices for the respective interventions to be evaluated in accordance with the requirements of routine practice data collection.

It is recommended carrying out the routine practice data collection in both GLA and RUBIN registries in order to achieve a higher coverage of the relevant study sites and care levels and to increase representativeness. In the expert consultation, the registry operators confirmed that cooperation among the registries and implementation within a platform are possible.

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.

In summary, the study design required for epcoritamab is a non-randomised, prospective comparison versus a comparator determined to be appropriate. The routine practice data collection should preferably be carried out as an adaptive platform registry study in the GLA and RUBIN registries; otherwise, as a comparative registry study.

If a comparative registry study is infeasible for the present requirement of routine practice data collection and evaluations due to the required adjustments to the GLA registry and RUBIN 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 orientating consideration of sample size scenarios.

The aim of the routine practice data collection is to determine the long-term benefits and harms of treatment with epcoritamab compared to the comparator therapy. A key therapeutic goal in DLBCL 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 7.9 and 19.4 months with median observation periods between 7.8 and 65.6 months. Taking into account the effects on the endpoint of overall survival in the present therapeutic indication, the G-BA therefore assumes that a clear effect on overall survival can already be recognised after 24 months. In order to observe possible effects on overall survival, patients should therefore be followed up for at least 24 months during the routine practice data collection.

The available data on epcoritamab 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 epcoritamab, 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 = 500, N = 600 and N = 700. Based on the available data, percentages of deceased patients of 70%, 82.5% and 95% at month 36 were assumed for the control group. For the intervention group, the resulting event percentages were assumed to be between 5% and 70%, up to 80% and up to 90% respectively. In addition, the significance level $\alpha = 2.5\%$ (1-sided test) and a shifted null hypothesis (H0: $HR \geq 0.5$) were assumed. The indicative consideration of the sample size for routine practice data collection of epcoritamab is based on the assumptions of Cox regression, in particular the assumption of proportional hazards. Recruitment ratios of 1:1, 1:3 and 1:5 between intervention and comparator therapy were considered.

Approximately 525 to 700 patients are expected in the present therapeutic indication. This results in detectable effects for the endpoint of overall survival with a hazard ratio of 0.32 to 0.40 to the advantage of epcoritamab 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).

Two registries represent a potentially suitable primary data source for the present routine practice data collection. Although the evaluation of data from different data sources, i.e. different registries can be carried out separately for each data source, it should preferably be carried out as a pooled analysis. Information on the verification of eligibility for pooled analysis should be set out 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, and 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 section 2.3 and for submitting the final evaluations to the G-BA the time specified in the resolution under section 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 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 17 December 2025.

The G-BA, with the involvement of IQWiG, carry out a review of the study protocol and the statistical analysis plan and usually communicate 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 14 August 2025 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 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 new benefit assessment, the evaluations must be submitted by 17 January 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 of the G-BA, taking into account the requirements of this resolution in accordance with Chapter 5 Section 58 of the Rules of Procedure 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 on 7 January 2025 at the subcommittee session and the draft resolution was approved.

At their session on 16 January 2025, the plenum resolved to initiate a procedure for the requirement of a routine practice data collection.

In conjunction with the resolution of 16 January 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 preparing a resolution.

IQWiG's concept was submitted to the G-BA on 16 April 2025. On 17 April 2025, 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 15 May 2025.

The expert consultation within the framework of the submission by the expert bodies took place on 11 June 2025.

The evaluation of the written submissions received and of the expert consultation was discussed at the session of the Subcommittee on 8 July 2025, and the proposed resolution was approved.

At their session on 17 July 2025, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
WG RPDC	13 February 2023 5 December 2024	Consultation on the initiation of a procedure for the requirement of a routine practice data collection (amendment of Annex XII of the AM-RL), involvement of the higher federal authority
Subcommittee on Medicinal Products	7 January 2025	Concluding discussion of the draft resolution
Plenum	16 January 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	19 May 2025	Information on written submissions received, preparation of the expert consultation
Subcommittee on Medicinal Products	11 June 2025	Implementation of the expert consultation
WG RPDC	16 June 2025 3 July 2025	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	8 July 2025	Concluding discussion of the draft resolution
Plenum	17 July 2025	Resolution on the requirement of routine practice data collection (amendment of Annex XII of the AM-RL)

Berlin, 17 July 2025

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

Prof. Hecken