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 Fedratinib (myelofibrosis); requirement of routine data collection and evaluations

of 3 November 2022

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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 authorised for the treatment of rare diseases under Regulation No. 141/2000.

2. Key points of the resolution

The active ingredient fedratinib was approved by the European Commission (EC) on 8 February 2021 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 for the treatment of disease-related splenomegaly or symptoms in adults with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis.

The first listing in the directory services in accordance with Section 131, paragraph 4 SGB V, took place on 15 March 2021.

On the basis of the ongoing or completed studies on fedratinib 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 requirement of routine practice data collection and evaluations according to Section 35a, paragraph 3b, sentence 1 SGBV for the active ingredient fedratinib:

- Data to assess the long-term (additional) benefit and harm of treatment with fedratinib in subjects for whom ruxolitinib is a patient-individual appropriate comparator therapy.
- Comparator data of treatment with fedratinib versus ruxolitinib for subjects for whom ruxolitinib is a patient-individual appropriate comparator therapy.

The marketing authorisation of fedratinib for the relevant sub-population of patients not pretreated with a Janus Associated Kinase (JAK) inhibitor is based on data from the randomised, double-blind phase III EFC12153 (JAKARTA) study comparing fedratinib versus

placebo. In the benefit assessment according to Section 35a SGB V, it was determined that the JAKARTA study is subject to significant uncertainties and limitations. A relevant uncertainty existed in particular with regard to the fact that the study had to be discontinued prematurely due to cases of suspicion of Wernicke's encephalopathies. This leads to a shortened observation period overall. Significant data for the endpoint of overall survival are not available due to premature study discontinuation. Another uncertainty regarding the study conducted from 2012 to 2014 was due to the fact that, according to clinical experts, the comparator used in the study does not reflect the current German standard of care. The extent of the described limitations and uncertainties of the present study results was assessed to be so significant in the overall assessment that it did not permit a quantification of the overall additional benefit despite the significant advantage in morbidity.

On the basis of the pivotal data and the data submitted for the benefit assessment according to Section 35a SGB V, it was therefore not possible to quantify the extent of the additional benefit. Further comparator data on patient-relevant endpoints for treatment with fedratinib versus existing therapeutic alternatives are not available or expected for the patient population that is not pretreated with a Janus Associated Kinase (JAK) inhibitor.

Since ruxolitinib is approved as another JAK inhibitor in the present therapeutic indication and represents an appropriate patient-individual comparator therapy, the question of routine practice data collection, taking into account the gaps in the evidence described, includes the assessment of the (long-term) benefit and harm profile of fedratinib versus ruxolitinib.

By resolution of 21 October 2021, the G-BA initiates 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 fedratinib.

A concept was drawn up in preparation for the resolution on the requirement of routine 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 recorded,
3. the data collection methods,
4. the evaluations by the pharmaceutical company according to Section 50, paragraphs 2 and 3 of the VerfO.

The G-BA decides 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 the 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. However, there are no suitable ongoing or planned studies for the question of routine practice data collection.

Based on the above-mentioned question, the G-BA, on the basis of IQWiG's concept and the submission 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 Question according to PICO scheme

Patient population

The marketing authorisation of fedratinib relates to the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis who are not pretreated with a Janus Associated Kinase (JAK) inhibitor or have been treated with ruxolitinib. The tyrosine kinase inhibitor ruxolitinib is also approved for the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis. For the present requirement of routine data collection and evaluations according to Section 35a, paragraph 3b, sentence 1 SGB V, the pharmaceutical company is to collect and evaluate comparator data for the patient population which is not pretreated with a Janus Associated Kinase (JAK) inhibitor and for which ruxolitinib is the appropriate patient-individual comparator therapy. The suitability for ruxolitinib should be evaluated in particular with regard to the symptomatology, the platelet count and the risk profile.

For non-pretreated patients for whom ruxolitinib is not the appropriate patient-individual comparator therapy, data from the JAKARTA study versus placebo were available in the benefit assessment of fedratinib. With regard to patients who have been pretreated with ruxolitinib, data from the still ongoing FREEDOM2 clinical study are expected. Against the background of these expected data, the resolution on the benefit assessment of fedratinib for the group of pretreated patients (patient group b)) was limited in time.

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 fedratinib. The marketing authorisation and the dosage information in the product information of fedratinib (Inrebic®) 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 fedratinib, ruxolitinib is approved for the treatment of disease-related splenomegaly or symptoms in adults with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis.

On 2. In the present therapeutic indication, allogeneic stem cell transplantation, splenic irradiation and splenectomy can be considered as non-medicinal treatments.

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

- Fedratinib: Resolution of 2 September 2021
- Ruxolitinib: Resolution of 6 November 2014

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 Appropriate Comparator Therapy”). A written statement from the German Society for Haematology and Medical Oncology (DGHO) was available.

According to the available evidence, allogeneic stem cell transplantation is currently the only curative therapy available for the treatment of patients with primary myelofibrosis (PMF), post polycythemia vera myelofibrosis (PPV-MF) or post essential thrombocythaemia myelofibrosis (PET-MF). However, this is only an option for select subjects, partly because of the risks associated with the therapy. For the present treatment setting, it is assumed that an allogeneic stem cell transplantation is not indicated at the time of therapy.

For symptomatic patients with primary or secondary myelofibrosis, the tyrosine kinase inhibitor ruxolitinib is available in addition to fedratinib as the first active ingredient approved for the present indication. In these guidelines, ruxolitinib or fedratinib

therapy is indicated for previously untreated symptomatic patients with both lower-risk and higher-risk conditions. The written statement of the DGHO (German Society for Haematology and Medical Oncology) also refers to therapy with ruxolitinib or fedratinib for patients with disease-related splenomegaly or symptoms.

As the present requirement of routine data collection and evaluations refers to fedratinib as an intervention, fedratinib cannot be an appropriate comparator therapy.

By resolution of the G-BA of 6 November 2014, a hint for a considerable additional benefit was identified in the benefit assessment for ruxolitinib compared to best supportive care. Ruxolitinib and fedratinib are not primarily indicated in the presence of thrombocytopenia. In this respect, ruxolitinib and fedratinib should only be used from a platelet count of ≥ 50 000/µl according to the product information and the therapy recommendations in guidelines.

In addition to ruxolitinib, various treatment options for improving the symptomatology are listed in guidelines, which are assigned to the therapy concept of best-supportive care. In principle, differentiation in the guidelines is done especially by the respective symptomatology and the risk profile. Depending on this, best supportive care is also a treatment option for some patients in addition to ruxolitinib.

Best Supportive Care is defined as the therapy that provides the best possible, patient-individual, optimised supportive treatment to alleviate symptoms and improve quality of life. In the context of best supportive care in the present therapeutic indication, the following active ingredients can be considered on the basis of the treatment options listed in guidelines for the improvement of symptomatology: Corticosteroids, erythropoietin, hydroxycarbamide, interferons (interferon alfa-2b, peg-interferon alfa-2a, peg-interferon alfa-2b), thalidomide, lenalidomide, pomalidomide. These active ingredients are not approved in the present therapeutic indication. Thus, there is a discrepancy between medicinal therapies approved in the indication and those recommended by guidelines or used in care.

In addition to medicinal treatments, splenic irradiation (as a non-medicinal treatment) can be another treatment option in best supportive care. In contrast, splenectomy is not considered a treatment option as part of best supportive care, particularly because of therapy-related mortality and morbidity.

In the present question, only those patients are considered for whom ruxolitinib is the appropriate patient-individual comparator therapy, which is why best supportive care is not relevant as a comparator.

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.

In the present therapeutic indication, the improvement of symptomatology and quality of life is of particular relevance for patients. Against this background, the survey of symptomatology and quality of life in the registry study is of high importance for the comparison of fedratinib versus ruxolitinib.

In the GSG-MPN registry, symptomatology has so far been assessed using the MPN-SAF questionnaire. With regard to the MPN-SAF questionnaire, there are uncertainties about the validity of the version used in the registry. There are other measurement instruments, such as the MFSAF, which are suitable for assessing the symptomatology in the present therapeutic indication and could be used as part of routine practice data collection. Fatigue is often a particularly distressing symptom in the present indication. If, as in the MPN-SAF, fatigue is only assessed with one item, consideration should be given to assessing fatigue with another specific instrument (e.g., FACIT fatigue). Furthermore, the health-related quality of life, which has so far been determined in the registry on the basis of a single question, should be assessed with a validated questionnaire (e.g., FACT-G, EORTC QLQ-C30).

In the participation procedure, it was pointed out that the spleen response is also to be collected as a relevant endpoint in the registry study. The G-BA considers the spleen response to be patient-relevant in terms of an improvement in symptomatology. However, this is an endpoint that is primarily collected in interventional clinical studies and requires the measurement of spleen volume via imaging techniques such as MRI or CT for valid data interpretation. In everyday clinical care, spleen volume is predominantly determined by palpation or, if necessary, by ultrasound examination. Therefore, in the view of the G-BA, the spleen response cannot be validly recorded within the framework of non-interventional routine practice data collection.

In addition to the recording of symptomatology and health-related quality of life, the recording of overall survival is also considered essential, as the individual symptomatology of the subjects can have an influence on life expectancy.

With regard to side effects, the overall rates of serious adverse events (SAEs), severe adverse events (AEs) and discontinuations due to AEs should be collected. In addition, specific adverse events are to be recorded as part of the routine practice data collection. Relevant specific AEs in the present therapeutic indication may be, for example, the occurrence of infections as well as thrombocytopenia or anaemia. It was pointed out by the registry operators in the expert consultation that a valid recording of side effects in the registry can be implemented.

2.1.2 Type and methods of data collection

According to Section 35a, para. 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 collected data, the use of an indication registry is also required in which treatment of primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis is carried out according to 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, none of the identified registries is suitable as a primary data source for routine practice data collection without extensive adaptations. In principle, the German indication-specific GSG-MPN (German Study Group MPN) registry can be a suitable primary data source. The adaptations required for the routine practice data collection refer in particular to the following aspects in accordance with the IQWiG concept[1]:

- Demarcation between patients treated with fedratinib and ruxolitinib
- Significant increase in the inclusion rate with approach to completeness
- Collection of patient-reported endpoints on symptomatology and health-related quality of life using validated questionnaires at shorter, standardised intervals
- Implementation of the assessment of adverse events
- Systematic identification of relevant confounders and expansion of the data set to include previously unrecorded, relevant confounders
- Supplementing the measures to ensure the accuracy of the data (introduction of source data verification based on a sample of, e.g., 5% or 10% of the data records)

Provided that the quality criteria and requirements of routine practice data collection specified in this resolution can be implemented in the GSG-MPN registry, the GSG-MPN registry is to be used as the primary registry. Regarding the implementation of the assessment of adverse events as well as patient-reported endpoints on symptomatology and health-related quality of life, please refer to the explanations in section 2.1.1.

A comparison of two active ingredients without randomisation poses in principle a potentially high risk of bias. Therefore, additional factors with a potentially high risk of bias such as the use of different data sources for the comparator group or data of different quality within one data source should be avoided.

According to the IQWIG concept[1], an endpoint-specific integration of retrospective data originating from the GSG-MPN registry should be examined. However, an essential

[1] IQWiG Rapid Report A21-142 - Concept for routine practice data collection - Fedratinib

prerequisite for the integration of this data is that the specific JAK inhibitor used (fedratinib or ruxolitinib) can be post-documented. In addition, any necessary expansion of this data to include relevant confounders identified by the systematic literature search must be checked and source data verification must be ensured to an appropriate extent.

In summary, the study design required for fedratinib is a non-randomised, prospective comparison versus ruxolitinib. This should preferably be conducted as a comparator registry study in the GSG-MPN registry. In addition, an endpoint-specific integration of retrospective data should be examined.

As described above, adaptations of the GSG-MPN registry are necessary in the present case for the implementation of routine practice data collection. If a comparative registry study is therefore not feasible for the present requirement of routine data collection and evaluations, a comparative 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 number of patients (sample size).

Taking into account the available evidence, it can be assumed that the efficacy of ruxolitinib decreases with regard to reduction of symptoms after about three years in a relevant percentage of patients.

For the routine practice data collection, the duration of observation should be a further 24 months from the end of recruitment. In doing so, the G-BA takes into account that the subjects included early in the RPDC had already been observed for a longer period of time by the end of recruitment and that the additional 24-month duration of observation for the entire study population results in a median observation period of 36 months, which enables an appropriate assessment of the comparator data.

As an approximation of the suitable sample size for the routine practice data collection, an orienting sample size estimate based on the endpoints of severe AEs with CTCAE grade ≥ 3 in the system organ class (SOC) infections and infestations as well as serious AEs in the SOC of infections and infestations results in case numbers of 1,200 and 2,400 patients, respectively, based on different assumptions. These are sample calculations based on estimated or theoretically established effect assumptions, which are intended to show that the routine practice data collection can in principle generate significant evidence. The exemplary sample sizes presented are of a magnitude where it can be assumed that routine practice data collection is feasible in principle for the question at hand. The final sample size planning is part

of the preparation of the statistical analysis plan and the study protocol by the pharmaceutical company.

The endpoints of severe and serious AEs in the SOC of infections and infestations are patient-relevant endpoints, which are, however, not considered individually in the context of the benefit assessment. In accordance with the PICO scheme listed in the resolution under section 1.1, further patient-relevant endpoints including the overall rates of serious and severe AEs are also to be collected and included in the consideration within the scope of the routine practice data collection.

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. Additional pooled analysis is possible after checking the suitability of data from different data sources. 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, 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.

The orienting sample size estimate is subject to uncertainties due to the small information base available and therefore represents a first hint of the required size of the study population. Against this background, the G-BA considers it expedient that a review is carried out by the pharmaceutical company during the course of the study, which may lead to an adjustment of the sample size. If necessary, this can also be carried out at this time on the basis of benefit 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[1].

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 has fulfilled its 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 3 April 2023.

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 has 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 01.12.2022 at the latest.

According to Section 35a para. 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 (status report), 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 6 months, 18 months, 36 months and 54 months after the date of commencement of the routine practice data collection to be defined by means of a declaratory resolution.

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 three interim analyses to the G-BA 18 months, 36 months and 54 months after the date of commencement of the routine practice data collection to be defined by means of a declaratory resolution. Within the framework of the first interim analysis, a review of the sample size estimate on the part of the pharmaceutical company is also to be carried out.

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 5 October 2028 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 SHI umbrella organisation, 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 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 12 October 2021 at the subcommittee session and the draft resolution was approved.

At its session on 21 October 2021, the plenum resolved to initiate a procedure for the requirement of a routine practice data collection.

In conjunction with the resolution of 21 October 2021 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 30 June 2022. On 1 July 2022, 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 29 July 2022.

The expert consultation within the framework of the submission by the expert bodies took place on 22 August 2022.

The evaluation of the written submissions received and of the expert consultation was discussed at the session of the Subcommittee on 25 October 2022, and the proposed resolution was approved.

At its session on 3 November 2022, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
WG RPDC	12 August 2021 9 September 2021	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 Medicinal products	12 October 2021	Concluding discussion of the draft resolution
Plenum	21 October 2021	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	15 August 2022	Information on written submissions received, preparation of the expert consultation
Subcommittee on Medicinal Products	22 August 2022	Implementation of the expert consultation
WG RPDC	1 September 2022 12 September 2022 6 October 2022 17 October 2022	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	25 October 2022	Concluding discussion of the draft resolution
Plenum	3 November 2022	Resolution on the requirement of routine practice data collection (amendment of Annex XII of the AM-RL)

Berlin, 3 November 2022

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

Prof. Hecken