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 Risdiplam (spinal muscular atrophy); Requirement of Routine Practice Data Collection and Evaluations

of 21 July 2022

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

2. Key points of the resolution

The active ingredient risdiplam was approved by the European Commission (EC) on 26 March 2021 as a medicinal product for the treatment of rare diseases (orphan drugs) under Regulation (EC) No. 141/2000 of the European Parliament and of the Council of 16 December 1999 for the treatment of spinal muscular atrophy. The first listing in the directory services in accordance with Section 131, paragraph 4 SGB V, took place on 1 May 2021.

On the basis of the ongoing or completed studies on risdiplam 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 risdiplam:

- Comparator data of treatment with risdiplam versus existing appropriate therapeutic alternatives for patients according to the planned extension of the therapeutic indication, including data for pre-symptomatic patients

At present, only data from symptomatic SMA patients are available for the active ingredient risdiplam without a direct comparison with existing therapeutic alternatives. Taking into account the aforementioned gaps in the evidence, the question of routine practice data collection comprises the assessment of the benefit and harm profile of risdiplam in comparison with existing appropriate therapeutic alternatives and in comparable healthcare contexts in order to improve the evidence base for patients with 5q spinal muscular atrophy for whom treatment with risdiplam is indicated.

By resolution of 7 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 risdiplam.

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 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. A review of the ongoing or planned data collection for the active ingredient risdiplam commissioned by the marketing authorisation authority has shown that none of the three non-interventional observational studies commissioned will conduct a comparison. The extension studies of the intervention studies, the assessment of which was the subject of the early benefit assessment of risdiplam, do not enrol any further patients and cannot remedy the deficit of the unstudied patient populations and the lack of comparison with existing appropriate therapeutic alternatives.

Due to the aforementioned limitations, the G-BA classifies the studies commissioned by the marketing authorisation authority as not suitable for improving the existing evidence base sufficiently and for the purpose of the benefit assessment.

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 populations

According to the marketing authorisation, the target population for the active ingredient risdiplam so far includes patients with 5q spinal muscular atrophy (SMA) 2 months of age and older, with a clinically diagnosed SMA Type 1, Type 2 or Type 3 or with one to four SMN2 gene

copies. The pharmaceutical company submitted an application to the EMA in January 2022 for an extension of the therapeutic indication for the treatment of patients under 2 months of age based on the interim results of the BN40703 study (RAINBOWFISH).[1] At the time of the resolution, the marketing authorisation for the extension of the therapeutic indication was not yet available. Against the background of the expected extension of the therapeutic indication of risdiplam, the G-BA is extending the scope of the resolution on the requirement of routine practice data collection and evaluations to include patients aged 0 to 2 months.
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 following patient population, taking into account the planned extension of the therapeutic indication:
Pre-symptomatic patients with 5q-associated SMA and up to three SMN2 gene copies, symptomatic patients with clinically diagnosed SMA Type 1, symptomatic patients with clinically diagnosed SMA Type 2 and up to three SMN2 gene copies, and symptomatic patients with clinically diagnosed SMA Type 3 and up to three SMN2 gene copies.

Pre-symptomatic patients with 5q-associated SMA and four SMN2 gene copies, as well as symptomatic patients with clinically diagnosed SMA Type 2 and SMA Type 3 and ≥ four copies each of the SMN2 gene are also included in the approved therapeutic indication for risdiplam.

On the basis of the limited evidence available and taking into account the current German healthcare context, the G-BA determined a therapy according to doctor's instructions under consideration of nusinersen and BSC as the appropriate comparator therapy for risdiplam for pre-symptomatic patients with 5q-associated SMA and four SMN2 gene copies. In its written submission, the AkdÄ also points out that in patients with SMA and four SMN2 gene copies, a milder course of SMA can be assumed with a high degree of probability and that it is possible to wait until the first symptoms or neurophysiological abnormalities appear with disease-specific medicinal treatment under close monitoring.

The percentage of patients with 5q-associated SMA and four SMN2 gene copies in the total number of patients with SMA is low (approx. 15%) according to the literature**Fehler! Textmarke nicht definiert.**. Similarly, the SMArtCARE registry currently includes only very few patients who are treated exclusively with BSC. Since, on the basis of the above points, it cannot be assumed that sufficiently reliable data can be obtained for pre-symptomatic patients with 5q-associated SMA and four SMN2 gene copies who only receive BSC for a comparator benefit assessment versus a therapy according to doctor's instructions under consideration of nusinersen and BSC, the G-BA considers the requirement of routine practice data collection for pre-symptomatic patients with 5q-associated SMA and four SMN2 gene copies to be disproportionate.

Based on the limited evidence available and taking into account the lack of comparator study data of the approved active ingredients, as well as the current German healthcare context, the G-BA has determined a therapy according to doctor's instructions for symptomatic patients with clinically diagnosed SMA Type 2 and SMA Type 3, taking into account nusinersen and onasemnogene abeparvovec, as an appropriate comparator therapy for risdiplam. However, onasemnogene abeparvovec is only approved for symptomatic patients with clinically diagnosed SMA Type 2 and SMA Type 3 and up to three copies each of the SMN2

1 https://www.ema.europa.eu/en/documents/minutes/minutes-chmp-meeting-24-27-january-2022_en.pdf

gene. Against the background of a necessary comparison with the specific appropriate therapeutic alternatives according to the doctor's instructions, the G-BA considers the requirement of routine practice data collection for symptomatic patients with a clinically diagnosed SMA Type 2 and SMA Type 3 and ≥ four SMN2 gene copies each to be disproportionate.

Symptomatic patients with a clinically diagnosed SMA Type 2 and SMA Type 3 and ≥ four SMN2 gene copies each, as well as pre-symptomatic patients with a 5q-associated SMA and four SMN2 gene copies, are accordingly not part of the requirement of routine practice data collection and evaluations according to Section 35a, paragraph 3b, sentence 1 SGB V for the active ingredient risdiplam.

Intervention

In accordance with the present requirement of routine practice data collection and evaluations according to Section 35a, paragraph 3b, sentence 1 SGB V, the intervention includes the active ingredient risdiplam.

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. The active ingredient nusinersen is approved for the treatment of 5q spinal muscular atrophy. The active ingredient onasemnogene abeparvovec is approved for the treatment of patients with 5q spinal muscular atrophy (SMA) with a biallelic mutation in the SMN1 gene and a clinical diagnosis of SMA Type 1, or patients with 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene.

On 2. Supportive measures and symptom treatment include, for example, physiotherapy, occupational therapy as well as voice, speech and language therapy in accordance with the remedies catalogue, surgical measures (e.g. tracheostomy), ventilation, respiratory hygiene, nutrition management, aids.

On 3. In the mentioned therapeutic indication, there is a resolution of the G-BA on the benefit assessment of nusinersen and onasemnogene abeparvovec in accordance with Section 35a SGB V.

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 indication and is presented in the "Research and synopsis of the evidence to determine the appropriate comparator therapy according to § 35a SGB V". 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 therapeutic indication according to Section 35a paragraph 7 SGB V.

Overall, the evidence in the therapeutic indication of SMA is limited.

In its resolution of 20 May 2021, the G-BA conducted a new benefit assessment for the active ingredient nusinersen after the €50 million turnover limit was exceeded. For patients with 5q SMA Type 1, the G-BA found an indication of a considerable additional benefit for nusinersen compared with the appropriate comparator therapy best supportive care (BSC), and a hint of considerable additional benefit for patients with 5q SMA type 2, and for pre-symptomatic patients with 5q SMA and 2 SMN2 gene copies a hint for a considerable additional benefit, and for pre-symptomatic patients with 5q SMA and 3 SMN2 gene copies a hint for a non-quantifiable additional benefit. An additional benefit for nusinersen compared to BSC is not proven for patients with 5q SMA Type 3 / 4, as well as for pre-symptomatic patients with 5q SMA and more than 3 SMN2 gene copies. However, the G-BA indicated that nusinersen may be a relevant treatment option for patients with 5q SMA Type 3 / 4 and for pre-symptomatic patients with 5q SMA and more than 3 SMN2 gene copies, taking into account the evidence presented on the medical benefit, the severity of the disease and the opinions of the scientific-medical societies on the current reality of care.

In its resolution of 4 November 2021 on the benefit assessment after exceeding the €50 million turnover limit for onasemnogene abeparvovec, the G-BA determined for all patient groups that an additional benefit compared to the appropriate comparator therapy is not proven.

Likewise, the G-BA indicated that onasemnogene abeparvovec may be a relevant treatment option for patients with 5q SMA Type 1, Type 2 or Type 3 and up to 3 SMN2 gene copies and for pre-symptomatic patients with 5q SMA and up to 3 SMN2 gene copies, taking into account the evidence presented on the medical benefit, the severity of the disease and the opinions of the scientific-medical societies on the current reality of care.

The evidence synopsis included Cochrane reviews on medicinal treatment for patients with spinal muscular atrophy type 1, type 2 and type 3, as well as systematic reviews on the treatment of SMA with nusinersen. Accordingly, treatment with nusinersen to improve motor function is recommended for patients with early and late onset SMA based on a high level of evidence. It should be noted that there is currently insufficient evidence to support efficacy in SMA Types 3 and 4 or to initiate treatment in adults. The evidence synopsis also includes a guideline with recommendations for the non-medicinal treatment of SMA.

Owing to the limited higher-quality evidence and for the purpose of reflecting the German healthcare context, an S1 guideline of the Society for Neuropaediatrics was also included in the evidence synopsis for the diagnosis and treatment of spinal muscular atrophy. The guideline states that treatment with nusinersen and onasemnogene abeparvovec showed an improvement in motor function in clinical studies in infants and children, but that the success of the treatment depends mainly on the timing of the treatment and thus, on the stage of the disease. No treatment recommendations are made.

In its written submission, the AkdÄ points out that the prescription of the active ingredients approved for SMA in everyday care is also based on the authorisation status of the medicinal

products due to a lack of comparator study data. Clinical experience also shows that a relevant percentage of patients with SMA and up to three SMN2 gene copies receive gene therapy with onasemnogene abeparvovec in early treatment. The Society for Neuropaediatrics also states in its written submission that it considers therapy with nusinersen or onasemnogene abeparvovec to be an appropriate comparison for patients with SMA Type 1 or patients with SMA and up to 3 SMN2 copies.

On the basis of the limited evidence available and taking into account the lack of comparator study data on the approved active ingredients, as well as the current German healthcare context, the G-BA has approved a therapy according to medical criteria for pre-symptomatic patients with 5q-associated SMA and up to three SMN2 gene copies, for symptomatic patients with clinically diagnosed SMA Type 1, and for symptomatic patients with clinically diagnosed SMA Type 2 and SMA Type 3, each with up to three SMN2 gene copies, a physician-directed therapy including nusinersen and onasemnogene abeparvovec has been determined as the appropriate comparator therapy for risdiplam.

Outcome

Comparator data on the following endpoint categories shall be collected for the patient populations required here for routine practice data collection in accordance with Section 35a, paragraph 3b, sentence 1 SGB V: Mortality, morbidity and side effects.
In particular, deaths (mortality category) and at least one endpoint from each of the following patient-relevant morbidity categories should be collected: Motor function (assessed with age-appropriate tools), achievement of motor milestones ("motor development milestones" of the WHO), respiratory function (need for [permanent] ventilation) and bulbar function (e.g. ability to swallow and speak, need for oral nutritional support) and further complications of the disease (e.g. pain, orthopaedic complications). The endpoint of necessity for [permanent] ventilation is not limited to the necessity for permanent ventilation, but includes a survey and evaluation of the necessity for ventilation.

With regard to side effects, serious adverse side effects and serious specific adverse side effects identified on the basis of the information in the Risk Management Plan and the EPAR of the intervention risdiplam and the comparators nusinersen and onasemnogene abeparvovec shall be collected.

Due to the lack of sufficiently suitable and valid measurement instruments for the required patient population, data on health-related quality of life are not part of the requirement of routine practice data collection and evaluations according to Section 35a, paragraph 3b, sentence 1 SGB V for the active ingredient risdiplam.

In the SMArtCARE registry, no data on quality of life are currently collected due to the lack of a suitable and valid measurement instrument. When using the SMArtCARE registry as the primary registry, the waiver of a requirement for data on health-related quality of life consequently also allows the use of already collected (not collected in parallel) data on nusinersen and onasemnogene abeparvovec, if these are suitable.

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, non-randomised comparisons within a study (parallel control) or the comparison of individual arms of different (single or multi-arm) studies (parallel or historical control) can be considered accordingly.

The comparison of individual arms from different studies is fundamentally associated with a risk of bias caused by the use of different data sources (among other things, due to different data collection time points or different definitions of data points or any changes in the examination and treatment methods).

To avoid these factors with an additional risk of bias in a non-randomised comparison of two medicinal products with an already high risk of bias, a non-randomised comparison of risdiplam and a therapy according to doctor's instructions under consideration of nusinersen and onasemnogene abeparvovec using parallel controls within one data source is required for the routine practice data collection for risdiplam.

Taking into account an uncertain future distribution of patients with spinal muscular atrophy in Germany who are treated with the intervention therapy risdiplam or with the comparator therapies nusinersen and onasemnogene abeparvovec, the G-BA considers it necessary to additionally carry out a comparison of risdiplam and data on nusinersen and onasemnogene abeparvovec that were not collected in parallel within one data source, provided that the data that were not collected in parallel also meet the stated requirements for data quality under section 1.2.2 in the resolution.

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 spinal muscular atrophy is carried out in accordance with German daily care or is sufficiently similar to care in Germany.

According to an international analysis, there are relevant differences in the standard of care between different countries[2], this concerns, for example, standards for and availability of non-medicinal interventions including the provision of remedies and aids, different standards for ventilation (invasive vs non-invasive) and the availability of nusinersen, onasemnogene abeparvovec and risdiplam, as well as their quality-assured application.

When examining the suitability of the registry with regard to transferability to the German healthcare context, the aforementioned aspects in particular should be taken into account. If there are relevant differences in the standard of care in another country, registry data from

[2] Bladen CL, Thompson R, Jackson JM, Garland C, Wegel C, Ambrosini A et al. Mapping the differences in care for 5,000 spinal muscular atrophy patients, a survey of 24 national registries in North America, Australasia and Europe. J Neurol 2014; 261(1): 152-163.

this country should not be used for the present routine practice data collection and evaluations.

Based on the available information, the SMArtCARE registry appears to be the most suitable primary data source at present. Provided that the quality criteria specified in this resolution are met, the SMArtCARE registry is to be used accordingly as the primary registry.

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).

In the present clinical picture, the assessment of motor development is of particular importance. The WHO describes the motor development of infants with 6 milestones, which are passed by healthy children at about 18 months of age (sitting without support to walking without support[3]). In the benefit assessment of risdiplam versus nusinersen in patients with SMA type I for endpoints on motor functioning and achievement of motor milestones, there were no statistically significant group differences or sufficiently large effects that could not be based on systematic risk of bias alone. For patients with SMA Type 2 and 3, no suitable data were available to assess motor development.

Considering that risdiplam is a permanent therapy and taking into account the child's developmental process based on the motor milestones according to WHO, 36 months of observation of motor development or maintenance of motor function during therapy is considered sufficient.

As an approximation of the appropriate sample size for routine practice data collection, a sample size of approx. 125 patients is assumed as a result of an orienting sample size estimate based on the combined endpoint of mortality or permanent ventilation.

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 pharmaceutical company must therefore prepare a study protocol and a statistical analysis plan before carrying out routine practice data collection and evaluations, in which in particular the information specified in the resolution must be taken into account.

The G-BA assumes that under the above-mentioned conditions, in addition to data on nusinersen and onasemnogene abeparvovec collected in parallel, data on nusinersen and onasemnogene abeparvovec that have not been collected in parallel, i.e. registry data that have already been collected since the marketing authorisation of the active ingredients nusinersen and onasemnogene abeparvovec, can 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

[3] WHO Multicentre Growth Reference Study Group. WHO Motor Development Study: windows of achievement for six gross motor development milestones. Acta Paediatr Suppl 2006; 95(S450): 86-95.

different data sources, i.e. different registries. Here, too, an evaluation should be carried out separately for each registry.

An additional pooled analysis is possible after checking the suitability both for data collected in parallel and not in parallel, as well as for data from different data sources. Information on the verification of eligibility for pooled analysis should be set out accordingly in advance in the SAP.

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 other benefit endpoints (such as motor development or a different operationalisation of mandatory ventilation) and taking into account a shifted hypothesis boundary in accordance with the procedure in IQWiG's concept[4]. Alternatively, if the pharmaceutical company does not seek an advantage in benefit endpoints (such as the aforementioned achievement of motor milestones), a sample size estimate based on another endpoint can be made. The G-BA points out that when deriving the additional benefit on the basis of harm endpoints, the non-inferiority on the benefit side is also considered in the new benefit assessment.

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 Requirements for checking 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 the drafting, before the routine practice data collection, the pharmaceutical company shall submit the final drafts for the study protocol and the statistical analysis plan to the G-BA for approval no later than 4 weeks after the

4 IQWiG Rapid Report A20-61: Concept for a routine practice data collection – onasemnogene abeparvovec

positive opinion for the extension of the therapeutic indication of risdiplam for patients aged 0 to 2 months, but no earlier than 5 months after the entry into force of the present resolution.

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 19 August 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 (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 6 months, 18 months and 30 months after the time of the start of routine practice data collection, which is 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.

In order to review the orienting sample size estimate and to review the suitability of the data obtained for the purpose of the new benefit assessment, in particular with regard to the question of whether the data collection will provide sufficient evidence for a new benefit assessment or whether there is a need for an adjustment of the specifications in the resolution according to Chapter 5, Section 58 VerfO, interim analyses shall be submitted to the G-BA 18 months (interim analysis for the sample size estimate), as well as 30 months after the time of the start of routine practice data collection, which is to be defined by means of a declaratory resolution.

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 1 August 2026 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 (Section 35a) 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 28 September 2021 at the subcommittee session and the draft resolution was approved.

At its session on 7 October 2021, the plenum resolved to initiate a procedure for the requirement of a routine practice data collection.

In conjunction with the resolution of 7 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 for the purpose of preparing a resolution.

IQWiG's concept was submitted to the G-BA on 15 February 2022. On 16 February 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 16 March 2022.

The expert consultation within the framework of the submission by the expert bodies took place on 26 April 2022.

The evaluation of the written submissions received and of the expert consultation was discussed at the session of the Subcommittee on 12 July 2022, and the proposed resolution was approved.

At its session on 21 July 2022, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Working group Section 35a	2 June 2021 17 August 2021 31 August 2021 14 September 2021 21 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	28 September 2021	Concluding discussion of the draft resolution
Plenum	7 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)
Working group Section 35a	6 April 2022	Information on written submissions received, preparation of the expert consultation
Subcommittee on Medicinal Products	26 April 2022	Implementation of the expert consultation
Working group Section 35a	4 May 2022 18 May 2022 1 June 2022 15 June 2022 6 July 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	12 July 2022	Concluding discussion of the draft resolution
Plenum	21 July 2022	Resolution on the requirement of routine practice data collection (amendment of Annex XII of the AM-RL)

Berlin, 21 July 2022

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

Prof. Hecken