Gemeinsamer Bundesausschuss

Justification

of the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Difelikefalin (Pruritus associated with chronic kidney disease in patients on haemodialysis)

of 6 April 2023

Contents

1. Legal basis

According to Section 35a paragraph 1 German Social Code, Book Five (SGB V), the Federal Joint Committee (G-BA) assesses the benefit of reimbursable medicinal products with new active ingredients. This includes in particular the assessment of the additional benefit and its therapeutic significance. The benefit assessment is carried out on the basis of evidence provided by the pharmaceutical company, which must be submitted to the G-BA electronically, including all clinical trials the pharmaceutical company has conducted or commissioned, at the latest at the time of the first placing on the market as well as the marketing authorisation of new therapeutic indications of the medicinal product, and which must contain the following information in particular:

1. approved therapeutic indications,
2. medical benefit,
3. additional medical benefit in relation to the appropriate comparator therapy,
4. number of patients and patient groups for whom there is a therapeutically significant additional benefit,
5. treatment costs for the statutory health insurance funds,
6. requirements for a quality-assured application.

The G-BA may commission the Institute for Quality and Efficiency in Health Care (IQWiG) to carry out the benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment must be completed within three months of the relevant date for submission of the evidence and published on the internet.

According to Section 35a paragraph 3 SGB V, the G-BA decides on the benefit assessment within three months of its publication. The resolution is to be published online and is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The relevant date for the start of the benefit assessment procedure was the first placing on the (German) market of the active ingredient difelikefalin on 1 October 2022 in accordance with Chapter 5, Section 8, paragraph 1, number 1, sentence 2 of the Rules of Procedure (VerfO) of the G-BA. The pharmaceutical company submitted the final dossier to the G-BA in accordance with Section 4, paragraph 3, number 1 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5, Section 8, paragraph 1, number 1 VerfO on 29 September 2022.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 02 January 2023 on the G-BA website (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA came to a resolution on whether an additional benefit of difelikefalin compared with the appropriate comparator therapy could be determined on the basis of the dossier of the

pharmaceutical company, the dossier assessment prepared by the IQWiG, and the statements submitted in the written statement and oral hearing procedure. In order to determine the extent of the additional benefit, the G-BA has evaluated the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5, Section 5, paragraph 7 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of difelikefalin.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA has come to the following assessment:

2.1 Additional benefit of the medicinal product in relation to the appropriate comparator therapy

2.1.1 Approved therapeutic indication of difelikefalin (Kapruvia) in accordance with the product information

Kapruvia is indicated for the treatment of moderate-to-severe pruritus associated with chronic kidney disease in adult patients on haemodialysis.

Therapeutic indication of the resolution (resolution of 06.04.2023):

See the approved therapeutic indication.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adult patients on haemodialysis with moderate-to-severe pruritus associated with chronic kidney disease (CKD-aP)

Appropriate comparator therapy for difelikefalin:

- Best supportive care

Best supportive care (BSC) is defined as the therapy that provides the best possible, patient-individual, optimised supportive treatment to alleviate symptoms and improve quality of life.

Criteria according to Chapter 5, Section 6 of the Rules of Procedure of the G-BA:

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication in accordance with the generally recognised state of medical knowledge (Section 12 SGB V), preferably a therapy for which endpoint studies are available and which has proven its worth in practical application unless contradicted by the guidelines under Section 92, paragraph 1 SGB V or the principle of economic efficiency.

[1] General Methods, version 6.1 from 24.01.2022. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

In determining the appropriate comparator therapy, the following criteria, in particular, must be taken into account as specified in Chapter 5, Section 6, paragraph 3 VerfO:

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.

Justification based on the criteria set out in Chapter 5, Section 6, paragraph 3 VerfO:

on 1. Besides difelikefalin, no other medicinal products are currently approved for the treatment of pruritus associated with chronic kidney disease (CKD-aP). In principle, the use of a topical basic therapy for skincare is an option for all patients.

on 2. In the present indication, UVB therapy is a non-medicinal treatment that can be provided within the framework of SHI and is eligible as an appropriate comparator therapy.

on 3. In the therapeutic indication to be considered here, there are no resolutions from the G-BA on the benefit assessment of medicinal products with new active ingredients according to Section 35a SGB V:

on 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as systematic reviews of clinical studies in the present indication and is presented in the "Research and synopsis of the evidence to determine the appropriate comparator therapy according to Section 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 indication according to Section 35a, paragraph 7 SGB V (see "Information on Appropriate Comparator Therapy").

The present indication covers the treatment of adult patients on haemodialysis. Due to chronic kidney disease, those affected suffer from moderate-to-severe nephrogenic pruritus. An adequate therapy of the underlying disease - in particular, the implementation and optimisation of haemodialysis - is a prerequisite.

No medicinal treatments are explicitly approved for the treatment of pruritus associated with chronic kidney disease (CKD-aP). The active ingredients mentioned in the therapy recommendations are also not explicitly approved for the treatment of the present indication. Overall, the evidence for the treatment of CKD-aP is limited. In addition, some of the recommendations are inconsistent .

However, there is agreement that a patient-individual therapeutic approach is recommended, which should be based on the severity of the disease and previous

therapies. In principle, the use of a topical basic therapy, especially with emollients to improve the skin barrier function, is recommended for all patients.

In the case of persistent pruritus, there are no approved medicinal therapy options available. Overall, the evidence for medicinal therapy options mentioned in the guidelines for the treatment of pruritus associated with renal disease is limited. Best Supportive Care (BSC) is presently determined as the appropriate comparator therapy. Best supportive care (BSC) is defined as the therapy that provides the best possible, patient-individual, optimised supportive treatment to alleviate symptoms and improve quality of life. According to guideline recommendations, the best possible, patient-individually optimised, supportive treatment to alleviate symptoms and improve the quality of life primarily includes skincare with moisturising and hydrating topicals.

As a non-medicinal therapy, the guidelines recommend the use of UVB therapy, which is a treatment that can be provided under SHI and is considered to be covered by BSC. The application of UVB therapy is presented in the Uniform Value Scale. Thus, UVB therapy can also be used as a non-medicinal therapeutic alternative in the therapeutic indication to be assessed within the framework of BSC.

According to the guidelines, other medicinal treatments such as gabapentin, pregabalin and non-sedating systemic H1-antihistamines can be used as part of systemic therapy, but the guidelines point out that the level of evidence for these medicinal options, and therefore the recommendations as a whole, are limited and inconsistent. Although treatment with gabapentin, pregabalin and non-sedating systemic H1-antihistamines are used in medical treatment practice in certain patients with CKD-aP, they are not considered in the determination of the appropriate comparator therapy because of the limited evidence and the potential side effects.

The findings in Annex XII do not restrict the scope of treatment required to fulfil the medical treatment order.

Change of the appropriate comparator therapy

For adult patients on haemodialysis with moderate-to-severe pruritus associated with chronic kidney disease (CKD-aP), a patient-individual therapy was originally determined as the appropriate comparator therapy, taking into account the respective prior therapies and the severity of the symptomatology. Patient-individual therapy included moisturising and hydrating topicals, UVB therapy, gabapentin, pregabalin and non-sedating systemic H1 antihistamines, after careful risk-benefit assessment.

Taking into account the generally recognised state of medical knowledge and on the basis of the statements of the clinical experts within the framework of the commenting procedure, who questioned the use of gabapentin, pregabalin and non-sedating systemic H1 antihistamines in the present therapeutic indication, in particular due to the limited efficacy or inconsistent evidence as well as the possible side effects, the G-BA considers it necessary to change the appropriate comparator therapy. In the present indication, Best Supportive Care (BSC) is named as the appropriate comparator therapy. Best supportive care (BSC) 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 present therapeutic indication, BSC mainly includes skincare with moisturising and hydrating topicals and, as a non-medicinal therapy, the application of UVB therapy.

2.1.3 Extent and probability of the additional benefit

In summary, the additional benefit of difelikefalin is assessed as follows:

Adult patients on haemodialysis with moderate-to-severe pruritus associated with chronic kidney disease (CKD-aP)

An additional benefit is not proven.

Justification:

Presented KALM 1 and KALM 2 studies

For the assessment of the additional benefit of difelikefalin for the treatment of adult patients on haemodialysis with moderate-to-severe pruritus associated with chronic kidney disease (CKD-aP), the KALM-1 and KALM-2 studies were presented. The KALM-1 and KALM-2 studies have a similar study design. In both studies, the double-blind, randomised, direct comparator treatment phase lasted a total of 12 weeks. This was followed by an open-label, single-arm extension phase that lasted 52 weeks. Adults who received haemodialysis three to a maximum of four times a week for end-stage renal disease (ESRD) and had moderate-to-severe pruritus prior to the start of the study were enrolled.

The KALM-1 and KALM-2 studies investigated endpoints in the categories of mortality, morbidity, health-related quality of life and side effects. The primary endpoint of both studies was the percentage of study participants who achieved an improvement of ≥ 3 points in the weekly mean score of the *Worst Itching Intensity Numeric Rating Scale* (WI-NRS*)* questionnaire.

On the double-blind, randomised controlled treatment phase of the studies presented

At the start of the study, the study medication, either difelikefalin or placebo, was administered randomly in a 1:1 ratio for a duration of 12 weeks as an intravenous bolus injection at the end of each dialysis. Stratification was based, among other things, on the criterion *"use of medication to treat itching within the week before randomisation (yes/no)"*. A prerequisite for study participation was the presence of moderate-to-severe pruritus (CKD-aP), defined as a weekly WI-NRS mean score of > 4 (KALM-1) or ≥ 5 (KALM 2). In addition, concomitant therapies for pruritus - antihistamines, gabapentin, pregabalin, corticosteroids, opioids - were only allowed if they had been administered in stable doses for at least 14 days before screening. During the study, concomitant therapies should not be changed and no new therapies for pruritus should be started. UVB light therapy was not allowed during the studies.

About 50% of the participants in the KALM-1 study and about 39% thereof in the KALM-2 study each received anti-pruritus therapy in the comparator arm. At least one prior therapy against pruritus was given to 51% in the comparator arm of the KALM-1 study and 39% in the KALM-2 study. Prior therapies for pruritus were defined as all therapies that were administered to the patients in the last 3 months before the first dose of the study medication *(multiple answers for the use of different active ingredients are possible*. *If different therapies are used with the same active ingredient, the patient is only considered once for the respective active ingredient)*. No information is available on which prior therapies were administered in a period earlier than 3 months prior to the start of the study.

On the duration of the studies presented

The treatment duration in the randomised direct comparator study phases of the KALM-1 and KALM-2 studies was 12 weeks. A study duration of only 12 weeks is not sufficient for the assessment of additional benefit in the therapeutic indication of moderate-to-severe pruritus associated with chronic kidney disease in patients on haemodialysis who are dependent on long-term therapy due to the chronic course of their disease. A minimum duration of 24 weeks is generally considered necessary for the early benefit assessment for chronic diseases. Consequently, the duration of the studies presented is clearly too short to derive an additional benefit.

Overall assessment

In summary, the studies presented by the pharmaceutical company are not suitable to derive an additional benefit of difelikefalin compared to the appropriate comparator therapy (BSC) . The study duration of only 12 weeks is considered too short in the randomised comparative phase of the study for the early benefit assessment for a chronic disease. An additional benefit is not proven.

2.1.4 Limitation of the period of validity of the resolution

The limitation of the period of validity of the resolution on the early benefit assessment of difelikefalin finds its legal basis in Section 35a, paragraph 3, sentence 4 SGB V. Thereafter, the G-BA may limit the validity of the resolution on the early benefit assessment of a medicinal product. In the present case, the limitation is justified by objective reasons consistent with the purpose of the benefit assessment according to Section 35a, paragraph 1 SGB V.

Since the appropriate comparator therapy was adapted during the ongoing process, the pharmaceutical company is given the opportunity to submit a new benefit assessment dossier to the G-BA, taking into account the current appropriate comparator therapy. The aim of this assessment is to be able to make statements about the additional benefit of difelikefalin compared to best supportive care (BSC) as an appropriate comparator therapy. Best supportive care (BSC) 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 present therapeutic indication, BSC mainly includes skincare with moisturising and hydrating topicals and, as a non-medicinal therapy, the application of UVB therapy.

For the renewed benefit assessment after the expiry of the deadline, the results of a comparison of difelikefalin with the appropriate comparator therapy BSC must be presented in the dossier. For this purpose, the G-BA considers a limitation for the resolution until 15 October 2023 to be appropriate.

A change in the limitation can generally be granted if it is justified and clearly demonstrated that the limitation is insufficient or too long.

In accordance with Section 3, paragraph 7 AM-NutzenV in conjunction with Chapter 5 Section 1, paragraph 2, number 6 VerfO, the procedure for the benefit assessment of the medicinal product with the active ingredient difelikefalin recommences when the deadline has expired. For this purpose, the pharmaceutical company must submit a dossier to the G-BA at the latest on the date of expiry to prove the extent of the additional benefit of difelikefalin (Section 4, paragraph 3, number 5 AM-NutzenV in conjunction with Chapter 5 Section 8, number 5 VerfO). If the dossier is not submitted or is incomplete, the G-BA may determine that an additional benefit is considered as being not proven. The possibility that a benefit assessment

for the medicinal product with the active ingredient difelikefalin can be carried out at an earlier point in time due to other reasons (cf. Chapter 5 Section 1, paragraph 2, nos. 2 – 4 VerfO) remains unaffected hereof.

2.1.5 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Kapruvia with the active ingredient difelikefalin.

Kapruvia is indicated for the treatment of moderate-to-severe pruritus associated with chronic kidney disease in adult patients on haemodialysis.

In the therapeutic indication to be considered, the following patient groups were defined:

Adult patients on haemodialysis with moderate-to-severe pruritus associated with chronic kidney disease (CKD-aP).

The G-BA determined Best Supportive Care (BSC) as the appropriate comparator therapy for the above patient group. Best supportive care (BSC) 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 present therapeutic indication, BSC mainly includes skincare with moisturising and hydrating topicals and, as a non-medicinal therapy, the application of UVB therapy.

The presented KALM-1 and KALM-2 studies are unsuitable for the assessment of the additional benefit. The study duration of only 12 weeks is considered too short in the randomised comparative phase of the study for the early benefit assessment for a chronic disease.

The validity of the resolution is limited to 15 October 2023.

2.2 Number of patients or demarcation of patient groups eligible for treatment

The information on the number of patients is based on the target population in statutory health insurance (SHI).

The G-BA takes into account the patient numbers stated in the pharmaceutical company's dossier.

2.3 Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Kapruvia (active ingredient: difelikefalin) at the following publicly accessible link (last access: 03 February 2023):

https://www.ema.europa.eu/en/documents/product-information/kapruvia-epar-product-information_en.pdf

Treatment with difelikefalin should only be initiated and monitored in a haemodialysis centre by healthcare professionals experienced in the diagnosis and treatment of conditions for which difelikefalin is indicated. Causes of pruritus other than chronic kidney disease should be excluded before initiating treatment with difelikefalin.

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 15 March 2023).

For the presentation of the costs, one year is assumed for all medicinal products.

Costs of the medicinal products:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Section 130 and Section 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis of consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates.

Medicinal product to be assessed: Difelikefalin

According to the product information, difelikefalin is administered 3 times a week at the end of haemodialysis treatment. If a 4th haemodialysis treatment is carried out in a week, difelikefalin should be administered as an additional treatment at the end of haemodialysis according to the recommended dose. No more than 4 doses should be given per week, even if more than 4 haemodialysis treatments are given in a week. For the calculation of the costs of difelikefalin, application of 3 to 4-times per week is therefore taken into account with the formation of a range.

The recommended dose of difelikefalin is 0.5 microgram/kg dry weight (i.e. the target weight after dialysis). For the calculation of the consumption of medicinal products to be dosed according to weight, the G-BA generally uses non-indication-specific average weights as a basis. Therefore, an average bodyweight of 77.0 kg is assumed for the bodyweight according to the official representative statistics "Microcensus 2017"[2]. A dry weight of 77 kg after dialysis is assumed.

Costs of the appropriate comparator therapy Best Supportive Care

The G-BA named Best Supportive Care (BSC) as the appropriate comparator therapy here. Best supportive care (BSC) is defined as the therapy that provides the best possible, patient-individual, optimised supportive treatment to alleviate symptoms and improve quality of life. BSC mainly involves skincare with moisturising and hydrating topicals. The use of UVB therapy, which is recommended by the guidelines and is a non-medicinal treatment that can be provided within the framework of SHI, is also a possible therapeutic alternative within the framework of BSC.

According to the EBM catalogue, the fee structure item 30430 for selective phototherapy (€ 6.09) can be determined for UVB therapy. The frequency of UVB therapy is determined in a patient-individual manner, depending on the symptomatology.

[2] Statistisches Bundesamt (Federal Statistical Office), Wiesbaden 02.08.2018. Microcensus 2017: questions on health - body measurements of the population 2017 [online]. [Accessed: 13.09.2018]. https://www.destatis.de/DE/Publikationen/Thematisch/Gesundheit/Gesundheitszustand/Koerpermasse5239003179004.pdf?__blob=publicationFile

Treatment period:

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Difelikefalin	3 – 4 x within 7 days	52.1	3 – 4	156.3 – 208.4
Appropriate comparator therapy				
Best supportive care	Different from patient to patient			

Consumption:

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Difelikefalin	38.5 µg *[0.5 µg/kg dry weight]*	115.5 µg – 154 µg	1 x 38.5 µg	156.3 – 208.4	156.3 x 38.5 µg – 208.4 x 38.5 µg
Appropriate comparator therapy					
Best supportive care	Different from patient to patient				

Costs:

Costs of the medicinal products:

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
Difelikefalin 50 µg/ml	12 SFI	€ 575.97	€ 2.00	€ 53.60	€ 520.37
Appropriate comparator therapy					
Best supportive care	Different from patient to patient				
SFI = solution for injection					

Costs for additionally required SHI services:

Only costs directly related to the use of the medicinal product are taken into account. If there are regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, the costs incurred for this must be taken into account as costs for additionally required SHI services.

Medical treatment costs, medical fee services, and costs incurred for routine examinations (e.g. regular laboratory services such as blood count tests) that do not exceed the standard expenditure in the course of the treatment are not shown.

Because there are no regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, no costs for additionally required SHI services had to be taken into account.

2.5 Medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with Difelikefalin

According to Section 35a, paragraph 3, sentence 4, the G-BA designates all medicinal products with new active ingredients that can be used in a combination therapy with the assessed medicinal product for the therapeutic indication to be assessed on the basis of the marketing authorisation under Medicinal Products Act.

In accordance with Section 2, paragraph 1, sentence 1 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), only medicinal products containing active ingredients whose effects are not generally known in medical science at the time of initial marketing authorisation are to be considered within the framework of the designation of medicinal products with new active ingredients that can be used in a combination therapy. According to Section 2, paragraph 1, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), a medicinal product with a new active ingredient is considered to be a medicinal product with a new active ingredient for as long as there is dossier protection for the medicinal product with the active ingredient that was authorised for the first time.

The designation of the combination therapies is based solely on the specifications according to Section 35a, paragraph 3, sentence 4. The G-BA does not conduct a substantive review based on the generally recognised state of medical knowledge. Thus, the designation is not associated with a statement as to the extent to which a therapy with the designated medicinal product with new active ingredient in combination with the medicinal product to be assessed corresponds to the generally recognised state of medical knowledge.

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

At its session on 12 April 2022, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 29 September 2022, the pharmaceutical company submitted a dossier for the benefit assessment of difelikefalin to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 1, sentence 2 VerfO.

By letter dated 4 October 2022 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefit of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient difelikefalin.

The dossier assessment by the IQWiG was submitted to the G-BA on 20 December 2022, and the written statement procedure was initiated with publication on the G-BA website on 02 January 2023. The deadline for submitting written statements was 23 January 2023.

The oral hearing was held on 6 February 2023.

In order to prepare a recommendation for a resolution, 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 representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions.

The evaluation of the written statements received and the oral hearing was discussed at the session of the subcommittee on 28 March 2023, and the proposed resolution was approved.

At its session on 6 April 2023, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	12 April 2022	Determination of the appropriate comparator therapy
Working group Section 35a	1 February 2023	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	6 February 2023	Conduct of the oral hearing
Working group Section 35a	15.02.2023; 01.03.2023 21 March 2023	Consultation on the dossier assessment by the IQWiG, assessment of the written statement procedure
Subcommittee on Medicinal Products	7 March 2023 28 March 2023	Concluding discussion of the draft resolution
Plenum	6 April 2023	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 6 April 2023

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

Prof. Hecken