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 Pitolisant (new therapeutic indication: narcolepsy, with or without cataplexy, (children and adolescents, 6 - 17 years))

of 21 September 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.

For medicinal products for the treatment of rare diseases (orphan drugs) that are approved according to Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999, the additional medical benefit is considered to be proven through the grant of the marketing authorisation according to Section 35a, paragraph 1, sentence 11, 1st half of the sentence German Social Code, Book Five (SGB V). Evidence of the medical benefit and the additional medical benefit in relation to the appropriate comparator therapy do not have to be submitted (Section 35a, paragraph 1, sentence 11, 2nd half of the sentence SGB V). Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V thus guarantees an additional benefit for an approved orphan drug, although an assessment of the orphan drug in accordance with the principles laid down in Section 35a, paragraph 1, sentence 3, No. 2 and 3 SGB V in conjunction with Chapter 5 Sections 5 et seq. of the Rules of Procedure (VerfO) of the G-BA has not been carried out. In accordance with Section 5, paragraph 8 AM-NutzenV, only the extent of the additional benefit is to be quantified indicating the significance of the evidence.

However, the restrictions on the benefit assessment of orphan drugs resulting from the statutory obligation to the marketing authorisation do not apply if the turnover of the medicinal product with the SHI at pharmacy sales prices and outside the scope of SHI-accredited medical care, including VAT exceeds € 30 million in the last 12 calendar months. According to Section 35a, paragraph 1, sentence 12 SGB V, the pharmaceutical company must then, within three months of being requested to do so by the G-BA, submit evidence according to Chapter 5, Section 5, paragraphs 1–6 VerfO, in particular regarding the additional medical benefit in relation to the appropriate comparator therapy as defined by the G-BA according to Chapter 5, Section 6 VerfO and prove the additional benefit in comparison with the appropriate comparator therapy.

In accordance with Section 35a, paragraph 2 SGB V, the G-BA decides whether to carry out the benefit assessment itself or to commission the Institute for Quality and Efficiency in Health Care (IQWiG). Based on the legal requirement in Section 35a, paragraph 1, sentence 11 SGB V that the additional benefit of an orphan drug is considered to be proven through the grant of the marketing authorisation the G-BA modified the procedure for the benefit assessment of orphan drugs at its session on 15 March 2012 to the effect that, for orphan drugs, the G-BA initially no longer independently determines an appropriate comparator therapy as the basis for the solely legally permissible assessment of the extent of an additional benefit to be assumed by law. Rather, the extent of the additional benefit is assessed exclusively on the basis of the approval studies by the G-BA indicating the significance of the evidence.

Accordingly, at its session on 15 March 2012, the G-BA amended the mandate issued to the IQWiG by the resolution of 1 August 2011 for the benefit assessment of medicinal products with new active ingredients in accordance with Section 35a, paragraph 2 SGB V to that effect that, in the case of orphan drugs, the IQWiG is only commissioned to carry out a benefit assessment in the case of a previously defined comparator therapy when the sales volume of the medicinal product concerned has exceeded the turnover threshold according to Section 35a, paragraph 1, sentence 12 SGB V and is therefore subject to an unrestricted benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment by the G-BA 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 on the internet and is part of the Pharmaceuticals Directive.

2. Key points of the resolution

The active ingredient pitolisant was listed for the first time on 1 August 2016 in the "LAUER-TAXE®", the extensive German registry of available drugs and their prices.

On 24 February 2023, the medicinal product Wakix with the active ingredient pitolisant received marketing authorisation for a new therapeutic indication to be classified as a major type 2 variation as defined according to Annex 2, number 2, letter a to Regulation (EC) No. 1234/2008 of the Commission of 24 November 2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products (OJ L 334, 12.12.2008, sentence 7).

The medicinal product Wakix with the active ingredient pitolisant for the treatment of narcolepsy with or without cataplexy is approved as a medicinal product for the treatment of rare diseases under Regulation (EC) number 141/2000 of the European Parliament and the Council of 16 December 1999.

In accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V, the additional benefit is considered to be proven through the grant of the marketing authorisation. The extent and probability of the additional benefit are assessed on the basis of the approval studies by the G-BA.

On 4 April 2023, the pharmaceutical company has submitted a dossier in accordance with Section 4, paragraph 3, number 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) in conjunction with Chapter 5, Section 8, paragraph 1, number 2 of the Rules of Procedure (VerfO) of the G-BA on the active ingredient pitolisant with the new therapeutic indication (narcolepsy, with or without cataplexy, (children and adolescents, 6 - 17 years)).

The G-BA carried out the benefit assessment and commissioned the IQWiG to evaluate the information provided by the pharmaceutical company in Module 3 of the dossier on treatment costs and patient numbers. The benefit assessment was published on 3 July 2023 together with the IQWiG assessment on the website of the G-BA (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA has adopted its resolution on the basis of the dossier of the pharmaceutical company, the dossier evaluation carried out by the G-BA, the assessment of treatment costs and patient numbers (IQWiG G23-06) and the statements made in the written statement and oral hearing procedure, as well of the amendment drawn up by the G-BA on the benefit assessment.

In order to determine the extent of the additional benefit, the G-BA has evaluated the studies relevant for the marketing authorisation with regard to their therapeutic relevance (qualitative) in accordance with the criteria laid down in Chapter 5 Section 5, paragraph 7, sentence 1, numbers 1 – 4 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of pitolisant.

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

2.1 Additional benefit of the medicinal product

2.1.1 Approved therapeutic indication of Pitolisant (Wakix) according to product information

Wakix is indicated in adults, adolescents and children from the age of 6 years for the treatment of narcolepsy with or without cataplexy.

Therapeutic indication of the resolution (resolution of 21.09.2023):

Wakix is indicated in children and adolescents (6 – 17 years) for the treatment of narcolepsy with or without cataplexy.

2.1.2 Extent of the additional benefit and significance of the evidence

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

Children and adolescents (6 – 17 years) with narcolepsy with or without cataplexy

Hint for a non-quantifiable additional benefit since the scientific data does not allow quantification.

Justification:

For the assessment of the additional benefit, the pharmaceutical company submits the results of the label-enabling study P11-06.

The study P11-06 is a double-blind, multicentre, randomised, placebo-controlled study over a period of 8 weeks, followed by a single-blind 1-week washout period and an open-label treatment phase to investigate the efficacy and safety of pitolisant. Children and adolescents aged 6 to 17 years with narcolepsy with or without cataplexy were enrolled.

A total of 110 study participants were randomised in a 2:1 ratio to the intervention (N = 72) and control (N = 38) arm. Patients in the intervention arm received pitolisant in daily doses of 4.5 mg, 9 mg, 18 mg or 36 mg; patients in the control arm received placebo.

The double-blind 8-week treatment phase was divided into a 4-week titration phase and a 4-week stable treatment phase. This was followed by a 1-week, single-blind washout period in which patients in both treatment groups received placebo. The total study duration of the blinded study phase from receipt of study medication was 9 weeks.

A priori, the PDSS total score was planned as the primary endpoint. In the course of the study, this was changed to the UNS total score, which the pharmaceutical company justifies with a better reliability and change sensitivity of the UNS compared to the PDSS (based on investigations on reliability and validity as part of the study P11-06).

Other endpoints included changes in cataplexy and excessive daytime sleepiness, depressive symptoms, suicidality and side effects.

Mortality

Deaths were recorded in the study as part of the safety assessment. No deaths occurred during the blinded 9-week study phase.

Morbidity

Cataplexy and excessive daytime sleepiness (EDS) using CGI-C

The endpoint CGI-C is the clinical assessment of cataplexy and EDS using a 7-point scale by the medical investigators. A higher value indicates deterioration of the symptomatology.

In principle, the patients' self-assessment of their disease state is to be preferred for the benefit assessment, but for the present benefit assessment, an external medical assessment of disease-specific symptoms can also be used since it is unclear whether a self-assessment is possible for all patients (children and adolescents) included in the therapeutic indication or the study population.

The pharmaceutical company submits results of responder analyses on CGI-C cataplexy and EDS with the pre-specified response criterion of CGI-C ≤ 3 at the end of the double-blind 8-week treatment phase.

For the endpoint of CGI-C EDS, there is a statistically significant advantage of pitolisant over placebo.

For the endpoint of CGI-C cataplexy, there is no statistically significant difference between the treatment arms of the study.

Depressive symptomatology using CDI-2 SF

The Children's Depression Inventory (CDI-2 SF) is a tool for assessing depressive symptomatology in children and adolescents. The total score ranges from 0 to 24 points, with higher scores indicating deterioration of symptomatology.

The endpoint was recorded as part of the safety assessment. For the present benefit assessment, the endpoint is assigned to the morbidity category, as depressive symptoms are assessed as a disease consequence of narcolepsy in children and adolescents.

No statements on the extent of an additional benefit can be derived for this endpoint as only descriptive results are available for the evaluations of the CDI-2 SF.

Suicidality using C-SSRS

The Columbia Suicide Severity Rating Scale (C-SSRS) is a standardised clinical interview designed to systematically assess and strictly monitor the occurrence, intensity and frequency of suicide-related thoughts and behaviours. The evaluation in the present study was dichotomised (suicide risk yes/no).

The endpoint was recorded as part of the safety assessment. For the benefit assessment, the endpoint is assigned to the morbidity category, as depressive symptoms and a resulting increased suicidal behaviour are estimated to be a disease consequence of narcolepsy in children and adolescents.

The operationalisation is partly comprehensible and the assessment is only partly classified as valid. No information could be identified on the extent to which trained staff conducted the

interview and on the reference period to which the baseline assessments should refer. In addition, there is no information on the extent to which the manual was followed in the assessment of suicide risk.

The endpoint is presented despite the limitations mentioned above. No statements can be derived on the extent of an additional benefit for this endpoint as only descriptive results are available for the evaluations of the C-SSRS.

Narcolepsy symptoms using UNS (presented additionally)

The Ullanlinna Narcolepsy Scale (UNS) is a patient-reported questionnaire to investigate the intensity and frequency of symptoms of narcolepsy. The UNS is divided into a cataplexy score and an excessive daytime sleepiness (EDS) score. A total score of 0 - 44 points can be achieved, with higher scores indicating higher disease activity.

In the study, the cataplexy subscale was only evaluated in subjects with type 1 narcolepsy, which does not include the total study population: If cataplexies only occur at a later point in time in patients with type 2 narcolepsy, they are not recorded by not including them from the beginning of the study.

Overall, the available evidence does not allow for a reliable assessment of the validity of both the UNS total score as well as the cataplexy and EDS subscales.

Due to the limitations described, the endpoint is not used for the benefit assessment.

Daytime sleepiness using PDSS

The Paediatric Daytime Sleepiness Scale (PDSS) is a measurement tool for examining daytime sleepiness in children and adolescents with a focus on school performance and symptoms of daytime sleepiness in the morning.

The validity of the questionnaire was investigated using healthy children and adolescents. However, no information could be identified on test-retest reliability and other aspects of validity (convergent validity) as well as on change sensitivity.

The symptoms addressed by the questionnaire are not directly specific to narcolepsy-related excessive daytime sleepiness. Excessive daytime sleepiness as a symptom of narcolepsy, which is associated, for instance, with sudden falling asleep or concentration problems, is not mapped via the PDSS.

The results on the PDSS are not taken into account for the assessment of the additional benefit since the direct patient relevance for the present therapeutic indication cannot be conclusively assessed and important data on validity are also missing.

Weekly cataplexy rate via sleep diary

The pharmaceutical company presents results on the responder analysis Weekly Cataplexy Rate (WKR) < 1 for patients with type 1 narcolepsy, which was collected using a sleep diary.

The endpoint is not considered in the context of the benefit assessment due to uncertainties in the operationalisation (e.g. no differentiation of partial vs total cataplexy; ambiguities regarding assistance by caregivers/ external assessment when filling out the diary) as well as in the validation.

Quality of life

No endpoints on quality of life were assessed.

Side effects

When recording side effects, symptoms of the underlying disease should not be considered an adverse event and should only be reported as an adverse event in case of their deterioration or occurrence in an unusual form. Hallucinations, sleep attacks and sudden falling asleep are mentioned as examples, but a complete definition of these symptoms to be distinguished from adverse events is not listed. In addition, there is no complete listing of all disease-related signs and symptoms that were considered in the evaluation of the overall rates.

There was no statistically significant difference in the overall rate of serious adverse events. Neither serious adverse events nor discontinuations due to adverse events occurred in either treatment arm of the study.

In detail, the analysis of specific adverse events with an incidence of ≥ 10% for SOC "Infections and infestations" shows a statistically significant advantage of pitolisant over placebo.

Overall assessment

For the benefit assessment of pitolisant for the treatment of children and adolescents (6 - 17 years) with narcolepsy with or without cataplexy, results of the 9-week randomised, double-blind and placebo-controlled study P11-06 are available.

There were no deaths in either treatment arm of the study. No statements on the extent of additional benefit can be derived for the mortality category.

In the morbidity category, pitolisant showed an advantage over placebo in the CGI-C endpoint of excessive daytime sleepiness. In contrast, there were no statistically significant differences in the evaluations of cataplexy symptomatology (using CGI-C cataplexy). For the endpoints of depressive symptomatology (assessed by CDI-2 SF) and suicidality (assessed by C-SSRS), no statements on the extent of an additional benefit can be derived as only descriptive results are available.

No data are available on quality of life.

In the category of side effects, there was no statistically significant difference for the serious adverse events. Serious adverse events and discontinuations due to adverse events did not occur in either treatment arm of the study. In detail, the specific adverse events for SOC "Infections and infestations" show a statistically significant advantage of pitolisant over placebo.

In summary, only the endpoint of excessive daytime sleepiness using CGI-C shows an advantage of pitolisant over placebo. However, this advantage is not reflected in any other endpoints of morbidity and side effects. In addition, only descriptive results are available for some endpoints. Data on quality of life were not collected.

Against this background - even taking into account the short duration of the study - a quantification of the extent of the additional benefit is not possible.

In the overall assessment of the available results on the patient-relevant endpoints, the G-BA therefore classifies the extent of the additional benefit of pitolisant for the treatment of children and adolescents (6 - 17 years) with narcolepsy with or without cataplexy on the basis of the criteria in Section 5, paragraph 8 in conjunction with Section 5, paragraph 7, sentence 1, numbers 1 to 4 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV) as non-quantifiable because the scientific data basis does not allow quantification.

Significance of the evidence

This assessment is based on the results of the 9-week randomised and placebo-controlled study P11-06. The study duration is divided into a double-blind 8-week treatment phase (including a 4-week titration phase and a 4-week stable treatment phase) and a 1-week, single-blind washout period, during which patients in both treatment groups received placebo.

The risk of bias at the study level is estimated to be low.

Uncertainties arise due to the study duration, which can be assessed as short for the present therapeutic indication. This is insufficient for a final assessment of the sustainability of the effects and the safety of pitolisant.

In the overall assessment, the significance of the evidence is rated as a hint due to the short directly comparative treatment period of 8 weeks (thereof a 4-week titration phase and a 4-week stable treatment phase).

2.1.3 Summary of the assessment

The present assessment is the benefit assessment of a new therapeutic indication for the active ingredient pitolisant.

The medicinal product Wakix was approved as an orphan drug. The therapeutic indication assessed here is as follows: Wakix is indicated in children and adolescents (6 – 17 years) for the treatment of narcolepsy with or without cataplexy.

For this patient group, the pharmaceutical company presents results of the study P11-06, in which pitolisant was compared to placebo over a period of 9 weeks (including a 1-week washout period).

There were no deaths in either treatment arm of the study.

In the morbidity category, there is an advantage of pitolisant over placebo for the endpoint of excessive daytime sleepiness. No statements on the extent of additional benefit can be derived for the endpoints of depressive symptomatology and suicidality.

No data are available on the quality of life category.

For the endpoint category of side effects, there is no statistically significant difference in the comparison of pitolisant versus placebo. Serious adverse events and discontinuations due to adverse events did not occur in either treatment arm of the study.

In summary, only the endpoint of excessive daytime sleepiness using CGI-C shows an advantage of pitolisant over placebo. However, this advantage is not reflected in any other endpoint. Data on quality of life were not collected.

Against this background – also considering the short treatment duration - a quantification of the extent of the additional benefit is not possible.

In the overall assessment, a hint for a non-quantifiable additional benefit of pitolisant over placebo is identified since the scientific data does not allow quantification.

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 provided by the pharmaceutical company in the dossier and in the written statement procedure.

The assessment of the pharmaceutical company is based on data on the incidence based on two retrospective observational studies[2] [3]as well as the mathematical determination of the SHI target population by using the cumulative incidence, taking into account the SHI proportion among those affected.

Overall, the estimate is subject to uncertainties due to the small size of the database and the limitations regarding the transferability of the incidence data based on the above-mentioned publications to the target population (children and adolescents aged 6 to 17 years). Moreover, the present estimate refers exclusively to diagnosed patients. In view of the presumed percentage of misdiagnosed or undiagnosed patients with narcolepsy, the available figures could be an underestimate of those actually affected in the SHI target population.

In summary, the data on the SHI target population are thus subject to significant uncertainties. It cannot be ruled out that the actual number of patients in the SHI target population is higher than the upper limit specified.

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 Wakix (active ingredient: pitolisant) at the following publicly accessible link (last access: 1 September 2023):

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

Treatment with pitolisant should only be initiated and monitored by doctors experienced in treating sleep disorders.

[2] Oberle D, Drechsel-Bäuerle U, Schmidtmann I, Mayer G, Keller-Stanislawski B. Incidence of Narcolepsy in Germany. Sleep. 2015 Oct 1;38(10):1619-28. https://doi.org/10.5665/sleep.5060

[3] Kallweit U, Nilius G, Trümper D, Vogelmann T, Schubert T. Prevalence, incidence, and health care utilisation of patients with narcolepsy: a population-representative study. J Clin Sleep Med. 2022 Jun 1;18(6):1531-1537. https://doi.org/10.5664/jcsm.9910

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: 1 September 2023).

If no maximum treatment duration is specified in the product information, the treatment duration is assumed to be one year (365 days), even if the actual treatment duration varies from patient to patient and/or is shorter on average. The time unit "days" is used to calculate the "number of treatments/ patient/ year", time intervals between individual treatments and for the maximum treatment duration, if specified in the product information.

For the cost representation, only the dosages of the general case are considered. Patient-individual dose adjustments (e.g. because of side effects or co-morbidities) are not taken into account when calculating the annual treatment costs.

In general, initial induction regimens are not taken into account for the cost representation, since the present indication is a chronic disease with a continuous need for therapy and, as a rule, no new titration or dose adjustment is required after initial titration.

The recommended dose of pitolisant is between 4.5 mg and 36 mg once a day. The lowest annual treatment costs occur for the daily dose of 18 mg. The highest annual treatment costs are reached for a daily dose of 9 mg per day.

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				
Pitolisant	Continuously, 1 x daily	365	1	365

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					
Pitolisant	4.5 mg	4.5 mg	1 x 4.5 mg	365	365 x 4.5 mg
	9 mg	9 mg	2 x 4.5 mg		730 x 4.5 mg
	18 mg	18 mg	1 x 18 mg		365 x 18 mg

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
	36 mg	36 mg	2 x 18 mg		730 x 18 mg

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					
Pitolisant 4.5 mg	30 FCT	€ 270.51	€ 2.00	€ 24.60	€ 243.91
Pitolisant 18 mg	90 FCT	€ 788.86	€ 2.00	73.80	€ 713.06
Abbreviations: FCT = film-coated tablets					

LAUER-TAXE® last revised: 1 September 2023

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.

No additionally required SHI services are taken into account for the cost representation.

2.5 Designation of 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 the assessed medicinal product

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

On 4 April 2023, the pharmaceutical company submitted a dossier for the benefit assessment of pitolisant to the G-BA in due time in accordance with Chapter 5 Section 8, paragraph 1, number 2 VerfO.

The benefit assessment of the G-BA was published on 3 July 2023 together with the IQWiG assessment of treatment costs and patient numbers on the website of the G-BA (www.g-ba.de), thus initiating the written statement procedure. The deadline for submitting statements was 24 July 2023.

The oral hearing was held on 8 August 2023.

An amendment to the benefit assessment with a supplementary assessment was submitted on 25 August 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 12 September 2023, and the proposed resolution was approved.

At its session on 21 September 2023, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	27 June 2023	Information of the benefit assessment of the G-BA
Working group Section 35a	1 August 2023	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal products	8 August 2023	Conduct of the oral hearing
Working group Section 35a	15 August 2023 5 September 2023	Consultation on the dossier assessment by the G-BA, the assessment of treatment costs and patient numbers by the IQWiG, and the evaluation of the written statement procedure
Subcommittee Medicinal products	12 September 2023	Concluding discussion of the draft resolution
Plenum	21 September 2023	Adoption of the resolution on the amendment of the AM-RL

Berlin, 21 September 2023

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

Prof. Hecken