Justification

Gemeinsamer Bundesausschuss

to the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive (AM-RL): Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients According to Section 35a SGB V Cannabidiol (Dravet Syndrome, ≥ 2 years)

of 2 April 2020

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 a rare disease (orphan drugs) that are approved according to Regulation (EC) No. 141/2000 of the European Parliament and of the Council of 16 December 1999, the additional medical benefit is deemed to be proven by the marketing authorisation according to Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V. Evidence of the medical benefit and the additional medical benefit in relation to the appropriate comparator therapy need not 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, Nos. 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 € 50 million during 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). On the basis of the statutory requirement in Section 35a, paragraph 1, sentence 11 SGB V that the additional benefit of an orphan drug is deemed to have been proven through the grant of 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, in the case of 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 provided 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 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 in such a way 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 legal limit of € 50 million and is therefore subject to an unrestricted benefit assessment (*cf* Section 35a, paragraph, 1 sentence 12 SGB V). According to Section 35a, paragraph 2 SGB V, the assessment of 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 forms part of the Pharmaceuticals Directive.

2. Key points of the resolution

The relevant date for the first placing on the market of the active ingredient cannabidiol in accordance with Chapter 5, Section 8, number 1, sentence 2 of the Rules of Procedure of the G-BA (VerfO) is 15 October 2019. 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, number 1 VerfO on 14 October 2019.

Cannabidiol as adjunctive therapy to treat seizures in patients 2 years of age and older with Dravet syndrome is approved as a medicinal product for the treatment of a rare disease under Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999.

According to 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 of the additional benefit and the significance of the evidence are assessed by the G-BA on the basis of the approval studies.

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 15 January 2020 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 G19-17) 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 studies relevant for 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 through 4 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of cannabidiol.

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

2.1 Additional benefit of the medicinal product

2.1.1 Approved therapeutic indication of cannabidiol (Epidyolex®) in accordance with the product information

Epidyolex® is indicated for use as adjunctive therapy of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS), in conjunction with clobazam, for patients 2 years of age and older.

The present resolution relates exclusively to the indication Dravet syndrome.

1 General Methods, Version 5.0 dated 10 July 2017. Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen [Institute for Quality and Efficiency in Health Care], Cologne.

2.1.2 Extent of the additional benefit indicating the significance of the evidence

In summary, the additional benefit of cannabidiol is assessed as follows.

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

Justification:

To assess the additional benefit, the pharmaceutical company presented the results of the pivotal studies GWEP1332 and GWEP1424.

Only those study populations in which, in conformity with the product information, cannabidiol was administered in conjunction with clobazam are relevant for the benefit assessment, i.e., patients in part B of GWEP1332 and in GWEP1424 (each about 65% of the safety population). These sub-populations were not planned *a priori* and were also not randomised in a stratified manner, meaning a potential bias must be taken into account when considering the results.

The double-blind, placebo-controlled study GWEP1332 (Part B) investigated the efficacy of cannabidiol (20mg/kg/d) as an adjuvant antiepileptic treatment compared to placebo in children and adolescents (2 to 18 years) with Dravet syndrome. The patients were randomised at a ratio of 1:1 to the 20mg/kg/d cannabidiol study arm and the placebo study arm. The duration of treatment was 14 weeks, including a 14-day titration period.

GWEP1424 is a randomized, double-blind, placebo-controlled, multi-site phase III study. It investigated the efficacy and safety of cannabidiol as an adjuvant antiepileptic treatment compared to placebo in children and adolescents (2 to 18 years) with Dravet syndrome. The patients were randomized at a ratio of 2:2:1:1 to the study arms 10mg/kg/d cannabidiol, 20mg/kg/d cannabidiol and placebo (with respective dosages of 10 or 20 mg/kg/d), in which individual titration was not planned. Instead, the patients were gradually titrated upwards to the intended dosage over 14 days. Treatment lasted 14 weeks, including a 14-day titration period.

Only the findings for the sub-population of GWEP1424 conforming with the product information (in conjunction with clobazam) and receiving a dosage of 10 mg/kg/d were evaluated and presented by the pharmaceutical company. Thus, a total of N=45 (cannabidiol + clobazam) and N=41 (placebo, each ITT population) patients from this study were presented for the benefit assessment. No findings were presented for the sub-population conforming with the product information in the 20 mg/kg/d study arm of GWEP1332 nor for the GWEP1332 study (likewise receiving 20 mg/kg/d).

The EMA benefit-risk assessment is based on the 10 mg/kg/d and the 20 mg/kg/d findings in conjunction with clobazam. Dosages up to 20 mg/kg/d are also encompassed by the authorisation. The benefit assessment categorically requires that data on all authorised doses be submitted and processed.

As stated in the product information, the 10 mg/kg/d dosage represents the maintenance dosage and thus the standard dosage.

However, gradually increasing the dose beyond 10 mg/kg/d up to a maximum recommended dose of 20 mg/kg/d is permissible, taking into account individual benefits and risks and in compliance with a monitoring plan as per the product information. Dravet syndrome is an epileptic syndrome that is difficult to treat and that always requires individualised therapy within the authorised dosage limits, balancing effects against side effects. Data on dosages of up to 20 mg/kg/d are, therefore, relevant for the benefit assessment.

The following remarks on the patient-relevant outcome findings refer only to the data from patients in GWEP1424 conforming with the product information and treated with a dosage of 10 mg/kg/d.

Mortality

No fatalities occurred during the study.

Morbidity

Frequency of convulsive and non-convulsive attacks

Patients or their caregivers recorded seizures and classified them each day using a telephone diary, with appropriate training offered to caregivers. To improve consistency, it was specified that data always be entered by the same caregiver. Seizures were classified into the following types: tonic-clonic, tonic, clonic, atonic, myoclonic, countable partial, other partial, and absences.

At the end of treatment, a statistically-significant percentage reduction in the frequency of convulsive seizures (all seizures classified as tonic-clonic, tonic-clonic, clonic or atonic) of 37 % compared to baseline was observed in patients taking cannabidiol 10 mg/kg/day versus placebo. A sensitivity analysis revealed a comparable, but not statistically-significant effect. In addition to the differences between the groups, responder analyses were also drawn on in the study. A statistically-significant advantage to the benefit of cannabidiol was found in responders, defined as subjects experiencing a ≥ 75% reduction in the frequency of convulsive seizures. An advantageous effect was likewise evident in all other responder analyses (reductions of ≥25%, ≥50% and 100%), whereby such effects were not statistically significant.

Only those patients who had already reported non-convulsive seizures at baseline were included in the analysis of the endpoint recording changes in non-convulsive seizures (all myoclonic, countable partial and other partial seizures or absences). This population is therefore not identical to the entire sub-population conforming with the product information, and the results are therefore of limited significance. No statistically-significant difference was found.

Status epilepticus

Status epilepticus is defined as any continuous seizure lasting more than 30 min., and this was also recorded in the telephone diary, occurring in both study arms in both convulsive and non-convulsive forms in a number of patients. No statistically-significant differences were observed.

Hospitalisations

Hospitalisations that the investigator considered to be epilepsy related were recorded as epilepsy-related hospitalisations. Six study participants receiving cannabidiol treatment and two receiving placebo were hospitalised due to epileptic seizures. The difference between the treatment arms is not statistically significant.

Caregiver Global Impression of Change (CaGIC)

The study assessed health status by means of the Caregiver Global Impression of Change (CaGIC) scale.

Despite its subjective nature, CaGIC is an important instrument in the therapeutic indication under consideration. Although self-assessment by patients of the effects of the disease is generally preferred in benefit assessments, it can be assumed that the majority of patients with Dravet syndrome are not able to do so due to cognitive impairments. The present benefit assessment can therefore employ CaGIC as an endpoint.

At the conclusion of treatment and at the end of the study, there was found to be a statistically-significant increase in the number of patients with an improved health status in the group receiving cannabidiol compared to the placebo arm.

Quality of life

Quality of Life in Childhood Epilepsy Questionnaire (QOLCE)

The health-related quality of life of subjects was surveyed using the Quality of Life in Childhood Epilepsy (QOLCE) questionnaire. The QOLCE questionnaire records the quality of life of children and adolescents between 4 and 18 years of age with epilepsy. It consists of 77 items in 5 domains and 16 subscales and is completed by the caregiver. It is considered to be validated, but there is no information on the clinical relevance/minimal important difference (MID) of its findings.

In the study, data from the questionnaire were recorded at baseline and at completion of treatment. Between the treatment groups, no statistically-significant difference in the change from baseline to end of treatment was found in the 16 subscales or overall for all scales. The response rates of the cognition and well-being domains were below 70%, so these domains cannot be used for the assessment.

Side effects

Analysis of serious adverse events in the evaluated population revealed no statistically-significant difference between the treatment arms in the study. No relevant data were available for the endpoint serious AEs, as the study did not establish a uniform definition on what severity constituted an SAE. No subjects discontinued treatment due to adverse events. Of the AEs with an incidence of ≥ 10%, only for pneumonia (PT) was a statistically-significant difference found between the two arms, to the detriment of cannabidiol.

Overall assessment

The benefit assessment for cannabidiol for the treatment of Dravet syndrome in patients 2 years of age and older is based on a sub-population of patients in the cannabidiol arm of the GWEP1424 study who received a dosage of 10 mg/kg/d and who conformed with the product information, i.e., those receiving the drug in conjunction with clobazam. Results on mortality, morbidity, quality of life, and side effects are obtained.

In the relevant sub-population no fatalities occurred.

In the morbidity category, reduction in the frequency of seizures is an important therapeutic goal in the therapeutic indication at hand and is of considerable clinical relevance. A statistically-significant advantage to the benefit of cannabidiol over placebo was demonstrated for the clinically-relevant endpoints *frequency of convulsive seizures* and *reduction of convulsive seizures by 75%*. An advantageous effect was likewise evident in other responder analyses, but this was not statistically significant. The health status findings, assessed by caregivers by means of CaGIC scoring, further supports this finding. In the cannabidiol arm, the frequency with which caregivers recorded an improvement in health was significantly higher. No significant effects were seen in the other morbidity endpoints

relevant for assessment (non-convulsive seizures, status epilepticus, hospitalisation). Overall, the benefits in the morbidity endpoint category are assessed as considerable.

In the quality of life category, no statistically-significant or relevant advantages or disadvantages of cannabidiol were discovered based on evaluation of the QOLCE questionnaire.

In the side effects category, no statistically-significant differences were shown in the total rate of patients experiencing serious adverse events, and no discontinuation of treatment due to adverse events occurred.

Considerable benefits were found to be associated with the cannabidiol dosage of 10 mg/kg/d. Nevertheless, the findings in totality provide no way of quantifying the extent of the additional benefit of cannabidiol, as the data on dosages of up to 20 mg/kg/d, which are also relevant for the benefit assessment, were not presented.

Significance of the evidence

The sub-population conforming with the product information (those receiving the drug in conjunction with clobazam) was not planned *a priori* and was not randomised in a stratified manner. Furthermore, no data on adult patients were submitted.

In the overall view, these uncertainties regarding the significance of the data result in a hint for an additional benefit.

2.1.3 Limitation of the period of validity of the resolution

The limitation of the period of validity of the resolution on the benefit assessment of cannabidiol for the therapeutic indication Dravet syndrome has 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 benefit assessment of a medicinal product. The decision to limit the period of validity is justified on the grounds that the data analysed and presented to support the benefit assessment provide no means of quantifying the extent of the additional benefit.

The limit to the period of validity provides the pharmaceutical company time to adequately prepare and resubmit the required data on the 20 mg/kg/d dosage from the two pivotal studies GWEP1424 and GWEP1332 alongside the data already submitted on the 10 mg/kg/d dosage for an assessment of the medicinal product cannabidiol in a new dossier. The G-BA considers six months to be sufficient in this respect.

The possibility that a benefit assessment for the medicinal product cannabidiol can be carried out for other reasons (*cf* Chapter 5, Section 1, paragraph 2 of the Rules of Procedure of the G-BA (VerfO)) remains unaffected by this.

2.1.4 Summary of the assessment

The present assessment concerns the benefit assessment of the new medicinal product Epidyolex® with the active ingredient cannabidiol. Epidyolex® has been granted authorisation as an orphan drug.

Cannabidiol is indicated for use as adjunctive therapy of seizures associated with Lennox-Gastaut syndrome (LGS) or Dravet syndrome (DS), in conjunction with clobazam, for patients 2 years of age and older. The present resolution relates exclusively to patients 2 years of age and older with Dravet syndrome.

The pharmaceutical company has presented the results for this patient group from the pivotal studies GWEP1332 and GWEP1424, in which cannabidiol was compared with placebo.

Only those study populations in which, as per the product information, cannabidiol was administered in conjunction with clobazam are relevant for the benefit assessment (the sub-population in conformity with the product information).

Only the findings for the sub-population conforming with the product information (subjects receiving the drug in conjunction with clobazam) and receiving a dosage of 10 mg/kg/d were evaluated and presented by the pharmaceutical company. No findings were prepared and presented for patients receiving a dosage of 20 mg/kg/d in the sub-populations conforming with the product information in the named studies.

The results for the dosage of 10 mg/kg/d are as follows:

No fatalities occurred during the study.

In this group a statistically-significant advantage to the benefit of cannabidiol over placebo was demonstrated for the clinically-relevant endpoints *frequency of convulsive seizures* and *reduction of convulsive seizures by 75%*. In addition, in the cannabidiol arm, the frequency with which caregivers recorded an improvement in health was significantly higher.

In the quality of life category, no statistically-significant or relevant advantages or disadvantages of cannabidiol were discovered.

In the side effects category, no advantages or disadvantages were demonstrated in the overall rates of adverse events, serious adverse events, and therapy discontinuation due to adverse events.

Considerable benefits were found to be associated with the cannabidiol dosage of 10 mg/kg/d. Nevertheless, the findings in totality provide no way of quantifying the extent of the additional benefit of cannabidiol, as the data on dosages of up to 20 mg/kg/d, which are also relevant for the benefit assessment, were not presented. The evidence is limited in its significance, as the sub-population conforming with the product information assessed in the present benefit assessment was not planned *a priori* and was also not randomised in a stratified manner, and no data on adult patients were presented. Overall, the G-BA considers there is a hint for a non-quantifiable additional benefit as the scientific data does not permit quantification.

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

The information on the number of patients (approx. 1,100–3,100) is based on the target population in statutory health insurance (SHI).

The figures are in line with those presented by the pharmaceutical company and calculated by the Institute for Quality and Efficiency in Health Care (IQWiG). Uncertainties remain as to how transferable the data obtained is to healthcare in Germany and whether the data for Dravet syndrome patients were correctly recorded in the identified studies. In the supplementary routine data analysis, uncertainty exists regarding how representative the dataset is and the applicability criteria for patient selection. Moreover, the fact that only patients aged 2 years and older are considered in the therapeutic indication is not taken into account; all in all, the upper limit can be assumed to represent an overestimation.

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 Epidyolex® (active ingredient: cannabidiol) at the following publicly accessible link (last access: 23 March 2020):

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

Treatment with cannabidiol should only be initiated and monitored by specialists who are experienced in the treatment of patients with epilepsy.

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 2020).

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 is patient-individual and/or is shorter on average. The time unit "days" is used to calculate the "number of treatments/patient/year", time between individual treatments and for maximum treatment duration, if specified in the product information.

Treatment duration:

Designation of the therapy	Treatment mode	Number of treatments/patient/year	Treatment duration/treatment (days)	Treatment days/patient/year
Cannabidiol	continuously, 2 × daily	365	1	365
Clobazam	continuously, 1 to several times daily	365	1	365

Usage and consumption:

In general, initial induction schemes are not taken into account for the cost representation because 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.

In principle, the G-BA does not base the calculation of the consumption of weight-dependent medicinal products to be dispensed on indication-specific average weights. Body weight (BW) is therefore based on the average weight of the German population from the official representative statistics *Mikrozensus 2017 - Körpermaße der Bevölkerung* [Microcensus

2017 – Body measurements of the population][2]. The average bodyweight of children from 2 years of age is 14.1 kg, that of adults (≥ 18 years) is 77.0 kg.

Due to the fact that it is not always possible to achieve the exact calculated dose per day with the commercially available potencies, in these cases, the dose is rounded up or down to the next higher or lower available dose that can be achieved with the commercially available dosage strengths and the scalability of the pharmaceutical form concerned.

In the calculation, the shelf life of the medicinal products was taken into account, and, if relevant, any discard after expiry of the shelf life was likewise factored in.

Designation of the therapy	Dosage/use	Dose/patient/ treatment days	Consumption by potency/treatment day	Treatment days/ patient/ year	Annual average consumption by potency[3]
Minimal dosage for a 2-year-old child					
Cannabidiol (100mg/ml)	70 mg (=5mg/kg)	140 mg	2 × 70 mg	365	6.5 × 100 ml
Clobazam (1mg/ml)	4.2 mg (=0.3 mg/kg)	4.2 mg	4.2 mg	365	13.0 × 150 ml
Maximal dosage for adults					
Cannabidiol (100mg/ml)	770 mg	1,540 mg (20 mg/kg)	2 × 770 mg	365	56.2 × 100 ml
Clobazam	80 mg	80 mg	4 × 20 mg	365	1460 × 20 mg

Costs:

Costs of the medicinal product:

Designation of the therapy	Package 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					
Cannabidiol	100 ml	€ 1,431.70	€ 1.77	€ 78.66	€ 1,351.27
Clobazam suspension	150 ml	€ 159.00	€ 1.77	€ 64.20	€ 93.03
Clobazam tablets[4]	50	€ 23.65	€ 1.77	€ 0	€ 21.88

2 Statistisches Bundesamt [German Federal Office for statistics]. *Microzensus: Fragen zur Gesundheit; Körpermaße der Bevölkerung 2017* [Microcensus: Questions about health; body measurements of the 2017 population].
[on-line]. 2 August 2018 [Accessed: 28 Aug. 2019]. URL: www.gbe-bund.de

3 Rounded interim result

4 Fixed reimbursement rate

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 medical treatment or the prescription of other services when using the medicinal product to be assessed 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 standard expenditure in the course of the treatment are not shown.

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

3. Bureaucratic costs

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 14 October 2019, the pharmaceutical company submitted a dossier for the benefit assessment of cannabidiol to the G-BA in due time in accordance with Chapter 5, Section 8, number 1, sentence 2 VerfO.

The benefit assessment of the G-BA was published on 15 January 2020 together with the IQWiG assessment of treatment costs and patient numbers on the G-BA website (www.g-ba.de), thus initiating the written statement procedure. The deadline for submitting written statements was 5 February 2020.

The oral hearing was held on 24 February 2020.

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 were discussed at the session of the subcommittee on 24 March 2020, and the proposed resolution was approved.

On 2 April 2020, the G-BA resolved by written statement to amend the Pharmaceuticals Directive.

The patient representatives support the resolution.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal Products	28 January 2020	Information of the benefit assessment of the G-BA
Working group Section 35a	18 February 2020	Information on written statements received; preparation of the oral hearing
Subcommittee Medicinal Products	24 February 2020	Conduct of the oral hearing
Working group Section 35a	3 March 2020 17 March 2020	Consultation on the dossier evaluation 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	24 March 2020	Concluding discussion of the draft resolution
Plenum	2 April 2020	Written resolution on the amendment of Annex XII of the AM-RL

Berlin, 2 April 2020

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Prof. Hecken