Justification

Gemeinsamer Bundesausschuss

of 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 - Reassessment after expiry of the deadline (Dravet-Syndrome, ≥ 2 years, combination with Clobazam)

of 15 April 2021

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 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), the additional medical benefit is considered to be proven through the grant of the marketing authorisation 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 evaluation 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 Ordinance on the Benefit Assessment of Pharmaceuticals (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 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, subsection 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 authorisation 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 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 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 pharmaceutical company submitted a dossier for the early benefit assessment for the active ingredient combination cannabidiol (Epidyolex) to be assessed for the first time on 15 October 2019. For the resolution of 2 April, 2020 made by the G-BA in this procedure, a time limit of 15 October 2020 was pronounced.

In accordance with Section 4, paragraph 3 paragraph 5 of the Ordinance on the Benefit Assessment of Pharmaceuticals (AM- NutzenV) in conjunction with Chapter 5 Section 8, paragraph 1, number 5 VerfO, the procedure for the benefit assessment of the medicinal product epidyolex recommences when the deadline has expired.

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 15 October 2020.

Cannabidiol for the adjuvant treatment of seizures is approved as a medicinal product for the treatment of Dravet Syndrome under Regulation (EC) No 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 German Social Code, Book Five (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 on the basis of the authorisation studies by the G-BA.

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 2021 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 made its decision on the basis of the pharmaceutical company's dossier, the dossier assessment carried out by the G-BA, the IQWiG assessment of treatment costs and patient numbers (IQWiG G20-24) and the statements made in the written statements and oral hearing process, as well of the addendum 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 Cannabidiol.

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:

1 General Methods, version 6.0 from 5.11.2020. 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 Cannabidiol (Epidyolex) in accordance with the product information

Epidyolex is a medicine used in addition to clobazam, to treat patients from two years of age with Lennox-Gastaut-Syndrome (LGS) or Dravet Syndrome (DS).

Therapeutic indication of the resolution (resolution from the 15/04/2021):

Epidyolex is used in addition with clobazam, in patients two years of age and older for the adjuvant treatment of seizures associated with Dravet syndrome (DS).

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

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

Hint of a considerable additional benefit

Justification:

For the assessment of the additional benefit, the pharmaceutical company submits the results of the studies GWEP1332 and GWEP1424 that justified the marketing authorisation. For the benefit assessment, only those study populations are relevant in which cannabidiol was administered in addition to a therapy with clobazam according to the product information. This was the case in part B of the GWEP1332 study and in the GWEP1424 study (approx. 65% of the safety population in each case). These sub-populations were not planned a priori and were also not stratified randomised, which means that a potential bias must be taken into account when considering the results. The double-blind, placebo-controlled study GWEP1332 (part B) evaluated the efficacy of cannabidiol (20 mg/kg/d) as an adjunctive antiepileptic treatment compared with placebo in children and adolescents (2 to 18 years) with Dravet syndrome. Patients were randomised in a 1:1 ratio to the study arms cannabidiol 20 mg/kg/d and placebo. The treatment duration was 14 weeks, including a 14-day titration period. Study GWEP1424 is a randomised, double-blind, placebo-controlled, multicentre phase III study. It investigated the efficacy and safety of cannabidiol as an adjunctive antiepileptic treatment versus placebo in children and adolescents (2 to 18 years) with Dravet syndrome. In this study, patients were randomised in a 2:2:1:1 ratio to the study arms cannabidiol 10 mg/kg/d, cannabidiol 20 mg/kg/d and placebo (corresponding to a dosage of 10 or 20 mg/kg/d). The treatment duration, including the titration period, was 14 weeks.

The pharmaceutical company prepares the results of the sub-population (combination with clobazam) of the study GWEP1424 for the patients with a dosage of 10 mg/kg/d that conforms to the product information. For this purpose, data on N = 41 (cannabidiol + clobazam) and N = 41 (placebo, ITT population in each case) patients of this study were submitted for the benefit assessment.

For patients with a dosage of 20 mg/kg/d, the pharmaceutical company prepares the corresponding study arm of the study GWEP1424 and the study GWEP1332 Part B also for the sub-population conforming to the product information. A total of N = 41 (GWEP1424) and N = 40 (GWEP1332 Part B) patients with the treatment cannabidiol + clobazam or N = 41 (GWEP1424) and N = 38 (GWEP1332 Part B) patients with placebo treatment (ITT population) were submitted for the benefit assessment. The placebo group of the GWEP1424 study is pooled data from the two placebo groups for the 10 mg and 20 mg doses.

Subsequently, the two studies on the 20 mg dose were combined post-hoc meta-analytically. For the benefit assessment, the use of the fixed effects model is appropriate due to the

similarity of the two studies and the small number of studies. Further calculations with random effects submitted by the pharmaceutical company are not considered. Where meta-analysis results are available for the 20 mg dosage, these are used. A meta-analysis was not performed for non-parametric analyses (treatment effect based on median differences).

In principle, the submission and processing of data on all approved dosages is required within the framework of the benefit assessment. The dosage of 10 mg/kg/d according to the product information is the maintenance dose and, therefore, the regular dosage. However, the dose may be gradually increased beyond 10 mg/kg/d, taking into account individual benefit and risk, and following a monitoring plan according to the product information, up to a maximum recommended dose of 20 mg/kg/d. Dravet syndrome is a difficult-to-treat epilepsy syndrome that generally requires individualised therapy design within the possibilities of the approved dosages, taking into account the effect and side effects. Data on doses of up to 20 mg/kg/d are therefore relevant for the benefit assessment. However, it must be taken into account in the assessment that the dosage in the studies was not titrated individually for each patient. Instead, patients were gradually titrated to the intended dosage (10 or 20 mg/kg/d) over 14 days.

Mortality

There were no deaths in the study

Morbidity

Frequency of convulsive and non-convulsive seizures

Seizures were recorded and classified daily by the patient or their carer via telephone diary, with appropriate training provided for caregiver. For consistency, the recording should always be done by the same caregiver. Seizures were classified into the following types: tonic-clonic, tonic, clonic, atonic, myoclonic, countable partial, other partial, absences.

At the end of treatment, cannabidiol 10 mg/kg/day showed a statistically significant percentage reduction in the frequency of convulsive seizures (all seizures classified as tonic-clonic, tonic, clonic or atonic) compared to placebo, with an overall reduction of 37% compared to baseline. A sensitivity analysis using the median change from baseline showed a similar but not statistically significant effect. For the 20 mg/kg/d dose, statistically significant effects were found in the sensitivity analysis only.

In addition to the group differences, responder analyses were used. Here, for responders with a reduction of ≥ 75% in the frequency of convulsive seizures, there was a statistically significant advantage for 10 mg/kg/d cannabidiol. Below 20 mg/kg/d, there were statistically significant advantages for cannabidiol in the reduction of 25%, 50% and 75%, as well as in the evaluation as an increase in the frequency of convulsive seizures (evaluation in each case in the meta-analysis). In the analysis of the endpoint of change in non-convulsive seizures (all myoclonic, countable partial and other partial seizures or absences), only those patients who already reported non-convulsive seizures at baseline were considered. Thus, this is not the entire subject-compliant sub-population, which limits the significance of the results. No statistically significant difference was found.

Status epilepticus

Status epilepticus, defined as any seizure lasting 30 minutes or longer, was also recorded via the telephone diary and occurred in both convulsive and non-convulsive forms in some patients in the studies. Statistically significant differences were not observed.

Hospitalisations

Hospitalisations that were considered by the investigator to be epilepsy-related were recorded as epilepsy-related hospitalisations. Treatment with 10 mg/kg/d cannabidiol resulted in epilepsy-related hospitalisations in 6 study participants and placebo in 2 study participants. The difference between the treatment arms was not statistically significant. With 20 mg/kg/d cannabidiol, 5 (GWEP1424) and 2 (GWEP1332 B) patients were hospitalised due to epilepsy compared to 0 and 2 patients with placebo. The difference was not statistically significant in the meta-analysis.

The data collected were adjusted post-hoc if the hospitalisation was considered to be non-epilepsy related. The unadjusted data initially showed 5 hospitalised patients in the GWEP1332 Part B study, which resulted in a statistically significant effect compared to placebo (0 patients). Uncertainties remain as the criteria for adjustment were not described and whether adjustment was the same in both studies.

Global caregiver impression (CGI-C)

The overall impression of health status was assessed in the studies using the Caregiver Global Impression scale for change (CGI-C).

Despite the subjective assessment by the caregiver, the instrument should be considered in the present therapeutic indication. In principle, the patients' self-assessment of their disease state is to be preferred for the benefit assessment, but in the present disease Dravet syndrome it can be assumed that a majority of the patients is not able to do this due to cognitive impairments. The endpoint can therefore be used for this benefit assessment.

At the end of the study, there were statistically significantly more patients with an improvement in health status under cannabidiol (for both doses) compared to the placebo arm. The results for the responder criterion "deterioration" at the end of the study show no statistically significant differences.

Quality of life

Health-related quality of life was assessed using the Quality of Life in Childhood Epilepsy (QOLCE) questionnaire. The QOLCE is an instrument for measuring quality of life in children and adolescents between 4 and 18 years of age with epilepsy. The questionnaire consists of 77 items in 5 domains and 16 subscales and is completed by the caregiver. It is considered validated, but no information is available regarding the clinical relevance of change (MID). In the studies, data were collected at baseline as well as at the end of treatment. There is no statistically significant difference in the change from baseline to end of treatment between the treatment groups, neither in the 16 subscales nor in the total scale. Only 20 mg/kg/d cannabidiol showed a statistically significant difference in the item "physical limitations" in the study GWEP1424, although irrelevance cannot be excluded when considering the standardised mean differences (per hedge's g). The return rates of the domains cognition and well-being were below 70%, so that these domains cannot be used for the assessment.

Side effects

For the evaluated population, only study GWEP1332 Part B showed a statistically significant difference between the treatment arms to the disadvantage of cannabidiol in the evaluation of serious adverse events. No suitable data were available for the endpoint severe AEs, as no uniform definition was made in the studies depending on the severity. Under 20 mg/kg/d cannabidiol, statistically significantly more therapy discontinuations due to adverse events occurred than under placebo. In the analysis of AEs with an incidence of ≥ 10%, a statistically significant difference to the disadvantage of cannabidiol was only found for the event pneumonia (PT) under 10 mg/kg/d cannabidiol, under 20 mg/kg/d for AEs from the system organ classes gastrointestinal disorders, general disorders and administration site conditions, examinations, metabolic and nutritional disorders, nervous system disorders and psychiatric

disorders in the individual studies. Below 20 mg/kg/d, there is also a statistically significant disadvantage for the serious AE "Infections and infestations".

Overall assessment

For the benefit assessment of cannabidiol for the treatment of Dravet syndrome in patients 2 years of age and older, the sub-population conforming to the product information, i.e. those patients with additional clobazam treatment, is considered. Results on mortality, morbidity, quality of life and side effects were obtained. No deaths occurred in the sub-population considered. In the morbidity category, a reduction in the frequency of seizures is an important therapeutic goal in the present therapeutic indication and of high clinical relevance. A statistically significant advantage of cannabidiol over placebo was shown for the clinically relevant endpoints of frequency of convulsive seizures and reduction of convulsive seizures by 75% in this therapeutic indication, for the dosage of 20 mg/kg/d furthermore for the reduction by 25% and by 50% and for the increase > 0%. The results on health status, assessed by the caregiver using CGI-C, support the result: In the cannabidiol arms, an improvement in health status was noted significantly more often. There were no relevant effects for the other morbidity endpoints relevant for evaluation (non-convulsive seizures, status epilepticus, hospitalisations). The benefits in the endpoint category morbidity are assessed as considerable overall.

In the quality of life category, no statistically significant and relevant advantages or disadvantages of cannabidiol result in the evaluations of the QOLCE questionnaire. In the category of side effects, there are statistically significant disadvantages, in particular in the overall rate of therapy discontinuations due to UE below 20 mg/kg/d cannabidiol.

These disadvantages, which were exclusively shown under the dosage of 20 mg/kg/d, are not considered sufficient for a downgrading of the advantages assessed as considerable in the category morbidity. In particular, it can be assumed that the risk for the occurrence of such negative effects in everyday care can be reduced by an individual dose titration provided for in the marketing authorisation, which was not depicted in the studies.

Significance of the evidence

The sub-population in accordance with the product information (combination with clobazam) was not planned a priori and also not stratified randomised. Uncertainties also arise from the fixed dosing scheme in the studies, which does not reflect the intended patient-specific titration, and the study duration, which can be assessed as short for the present therapeutic indication. In addition, no data on adult patients were presented.

Cannabidiol inhibits the degradation of the active metabolite of the benzodiazepine clobazam via the inhibition of cytochrome P 450 2C19, which has a half-life of approx. 79 hours (Frisium product information, as of November 2020); in addition, there is a pharmacogenetically determined variability in the activity of CYP2C19 with up to 25% slow ('poor') and intermediate or 20 % fast ('ultra-rapid') metabolisers among Caucasians (see https://www.arzneimitteltherapie.de/heftarchiv/2012/07/portrat-eines-enzyms-cyp2c19.html). Also, against this background, the overall study duration of 14 weeks is considered to be short, and the size of the study population relevant for evaluation is considered to be relatively small, which means that the significance of the data presented on the efficacy and toxicity of cannabidiol in combination with clobazam must be assessed as limited.

Overall, the uncertainties mentioned with regard to the significance of the evidence result in a hint of an additional benefit.

2.1.3 Summary of the assessment

The present assessment is a new benefit assessment of the medicinal product "Epidyolex" with the active ingredient cannabidiol due to the expiry of the time limit of the resolution of 2.04.2020.

Epidyolex was authorised as an orphan drug for the adjuvant treatment of seizures associated with Lennox-Gastaut-Syndrome or Dravet Syndrome.

The therapeutic indication assessed here is as follows: Epidyolex is used in addition with clobazam, in patients two years of age and older for the adjuvant treatment of seizures associated with Dravet syndrome (DS).

For this patient group, the pharmaceutical company presents results from RCT GWEP1424 (for a cannabidiol dose of 10 mg/kg/d) and RCTs GWEP1424 and GWEP1332 B (20 mg/kg/d) comparing cannabidiol with placebo. The data on the 20 mg dose were summarised meta-analytically.

There were no deaths in the study

There were statistically significant and relevant advantage of cannabidiol for the frequency of convulsive seizures and the reduction of convulsive seizures by 50%, at 20 mg/kg/d also for the reduction by 25% and 75%, and at 20 mg/kg/d for the increase in the frequency of convulsive seizures. The results on health status (CGI-C) support the result.

There were no relevant differences in quality of life (QOLCE questionnaire).

With regard to side effects, there were disadvantages in therapy discontinuations due to AE below 20 mg/kg/d cannabidiol. In particular, it can be assumed that the risk for the occurrence of such negative effects in everyday care can be reduced by an individual dose titration provided for in the marketing authorisation, which was not depicted in the studies.

Uncertainties remain due to the duration of the study, which is to be regarded as short in the present therapeutic indication and against the background of the possible pharmacokinetic interactions of cannabidiol with clobazam, the small study population, and the fact that a patient-specific titration was not depicted in the studies. The sub-population in accordance with the product information (combination with clobazam) was not planned a priori and also not stratified randomised. In addition, no data on adult patients were presented.

In the overall view, a hint of considerable additional benefit is identified.

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 data follow the representations of the pharmaceutical company and the assessment of IQWiG. Uncertainties exist in the transferability of the data determined to the situation in Germany, the up-to-dateness of and the correct recording of patients with Lennox-Gastaut syndrome in the identified studies. In the additionally conducted routine data analysis, there are uncertainties with regard to the representativeness of the data basis and the selection criteria with regard to patient selection. In addition, it is not taken into account that only patients aged 2 years and older are included in the therapeutic indication. Overall, an overestimation can be assumed for the upper limit.

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 acid at the following publicly accessible link (last access: 11 December 2020):

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

Treatment with cannabidiol should only be initiated and monitored by doctors experienced in treating patients with epilepsy.

The combination of cannabidiol with clobazam causes pharmacokinetic interactions that can lead to an increase in adverse drug reactions. If somnolence or sedation occurs, a reduction in the dose of clobazam should be considered.

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 2021).

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 intervals between individual treatments and for the 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)	Days of treatment/ patient/ year
Cannabidiol	continuously, 2 times a day	365	1	365
Clobazam	continuously, 1 - several times a day	365	1	365

Consumption:

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.

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. For the bodyweight (KG), the average weight of the German population from the official representative

statistics "Mikrozensus 2017 - Körpermaße der Bevölkerung" [2]is therefore used as a basis. The average body weight of children from 2 years of age is 14.1 kg, that of adults (≥ 18 years) is 77.0 kg.

As it is not always possible to achieve the exact calculated dose per day with the commercially available dose strengths, in these cases rounding up or down to the next higher or lower available dose that can be achieved with the commercially available dose strengths as well as the scalability of the respective dosage form.

In the calculation, the shelf life of the medicinal products was taken into account, and, if applicable, the discard due to expiry of the shelf life was included.

Designation of the therapy	Dosage/Indication	Dosage/ patient/ days of treatment	Usage by potency / day of treatment	Days of treatment/ patient/ year	Annual average consumption by potency[3]
Minimum dosage 2-year-old child					
Cannabidiol (100mg/ml)	70 mg (=5mg/kg)	140 mg	2 x 70 mg	365	6.5 x 100 ml
Clobazam (1mg/ml)	4.2 mg (=0.3 mg/kg)	4.2 mg	4.2 mg	365	13 x 150 ml
Maximum dosage adult					
Cannabidiol (100mg/ml)	770 mg	1,540 mg 20 mg/kg	2 x 770 mg	365	56.2 x 100 ml
Clobazam	80 mg	80 mg	4 x 20 mg	365	1,460 x 20 mg

Costs:

Costs of the medicinal product:

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					
Cannabidiol	100 ml	€ 1,256.39	€ 1.77	€ 0.00	€ 1,254.62
Clobazam Suspension	150 ml	€ 86.69	€ 1.77	€ 3.59	€ 81.33
Clobazam tablets[4]	50	€ 23.65	€ 1.77	€ 0	€ 21.88

LAUER-TAXE® last revised: 15 March 2021

2 Statistisches Bundesamt (Federal Statistic Office) Microcensus: Microcensus questions on health - body measurements of the population 2017
[online]. 2.08.2018 [access: 23/02/2021): 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 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 or patient information leaflet, the differences 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.

For the cost representation no additionally required SHI services are considered.

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 15 October 2020, 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, paragraph 1, number 5 VerfO.

The benefit assessment of the G-BA was published on 15 January 2021 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 the written statements was 5 February 2021.

The oral hearing was held on 22 February 2021.

An amendment to the benefit assessment with a supplementary assessment of data submitted in the comments procedure was submitted on 11 March 2021.

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 7 April 2021, and the draft resolution was approved.

At its session on 15 April 2021, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee Medicinal products	26 January 2021	Information of the benefit assessment of the G-BA

Working group Section 35a	16 February 2021	Information on written statement procedures received; preparation of the oral hearing
Subcommittee Medicinal products	22 February 2021	Conduct of the oral hearing
Working group Section 35a	3 March 2021 16 March 2021 30 March 2021	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	7 April 2021	Concluding consultation of the draft resolution
Plenum	15 April 2021	Adoption of the resolution on the amendment of Annex XII AM-RL

Berlin, 15 April 2021

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

Prof. Hecken